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ORAL DISEASES EPIDEMIOLOGY IN ITALIAN AND NON-ITALIAN POPULATION. A MULTICENTER CROSS-SECTIONAL STUDY

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ORAL DISEASES EPIDEMIOLOGY IN ITALIAN AND NON-ITALIAN POPULATION. A MULTICENTER CROSS-SECTIONAL STUDY

Doctoral Thesis

PhD in Preventive Dentistry

Department of Biomedical Sciences – University of Sassari

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"*Tu naturaleza no ha cambiado*
sigues siendo un ser alado
y hasta el último de mis días
pongo mi mano e tu mano"

Dedicated to the life of Dr. Mídore Lara Capi

Comenzamos este capítulo de mi vida juntas y hoy que lo concluyo recuerdo cuando hace cuatro años cumpliste tu sueño de ser doctora. Nunca olvidaré cuando te graduaste, ese instante en el que me miraste a los ojos y sonreíste con la más pura alegría, como si no existiera ningún obstáculo cuando se va en busca de la felicidad: entonces supe que eras la persona mas valiente que he conocido.

Daría todo porque estuvieras sentada junto a mí en este día tan importante, eres mi primer y mi último pensamiento del día y te extraño con toda el alma… pero se que estás presente y que te sientes orgullosa de mí. Te dedico este y cada uno de mis logros, a ti, a tu amor por la vida, a tu fuerza y a tu determinación, a tu bondad y generosidad, eres y serás siempre mi más grande inspiración, mi mas precioso sentimiento y mi mayor orgullo.

Gracias por todo lo que me enseñaste y por todo lo que me amaste.

Bubu

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PROLOGUE

The doctoral work I am presenting: “Oral diseases epidemiology in Italian and non-Italian population. A multicenter cross-sectional study” has been achieved during a three-year period in the international scenery to promote the cooperation between institutions from different parts of the world.

The thesis is divided into two chapters that contain the main topics of the research: Dental Caries and Dental Erosion (Erosive wear). Under the dental caries chapter, the subjects covered are: Diagnosis, Risk, Early detection technologies, Minimally Invasive Therapy, Behavioral and socio-cultural factors, Taste preference and Prevention.

The chapter on erosive wear focuses on the condition and starts from the Tooth wear definition and classification, Differential diagnosis, Measurement of wear and the BEWE model.

A third part of the volume contains a detailed account of the Multicenter study achievements in three different countries: Italy, Mexico and Saudi Arabia.

Each chapter contains the relative scientific evidence published and presented in international journals and congresses.

This dissertation conceives the current oral health status of three different populations, the advanced approaches on its diagnosis and treatment.

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ABSTRACT

Oral diseases epidemiology in Italian and non-Italian population. A multicenter cross-sectional study

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Aims: To assess the prevalence of the major oral diseases and the impact of the risk factors in adolescents from three different countries representative of Europe, Latin America and Middle East: Italy, Mexico and Saudi Arabia.

Methods: Caries (ICDAS and DMFS), erosion (BEWE), gingival status (Silness-Löe Index) were recorded. Body Mass Index (BMI) was calculated (WHO guidelines). A questionnaire investigated dietary patterns, oral habits and socio-economic status. Sweet taste evaluation was performed to determine threshold (TT) and preference (TP).

Results: 909 subjects (Italy n= 220; Saudi n=225; Mexico Urban n=224; Mexico rural n=240). Mean DMFS was 2.96 SD 4.01. The prevalence of erosion was higher in Mexico (18.7%), followed by Italy (12,7%) and Saudi (6.7%) while caries experience was higher in Saudi (3.0±4.0), followed by Italy (1.4±2.3) and Mexico (1.2±1.5)($p<0.001$). The frequency of soft drinks intake was a constant variable for erosion ($p<0.01$). Overweight (BMI) was positively related to caries severity. TP and caries had a significant correlation ($p<0.01$). Subjects in the rural area presented less caries ($p<0.01$).

Conclusions: The distribution of oral diseases is related to behavioral, socio-cultural and geographic situations. Both caries and dental erosion are associated to diet and diet being determinant to BMI is decisive in oral and general health where prevention can make a decisive change in the quality of life.

INTRODUCTION

Great improvements have been accomplished in oral health all over the globe, yet in under-privileged populations, both in the developed world as in developing countries, this remains to be addressed. The distribution and severity of oral diseases diverge between different parts of the world and within the same country or region. Socio-behavioral and environmental factors play a fundamental role in oral disease making necessary the surveillance of the patterns and the evaluation of the risk factors in order to develop and implement community preventive measures.[1]

Oral diseases are a main public health problematic with an outcome on the quality of life. The diversity between their prevalence, incidence and development requires operative health programs. The most common oral diseases reported worldwide are:

1. Dental caries
2. Periodontal disease
3. Tooth loss
4. Oral mucosal lesions
5. Oropharyngeal cancers
6. Human immunodeficiency virus/Acquired immunodeficiency syndrome (HIV/AIDS) -related oral disease
7. Dental trauma* (although is not a disease, is a highly prevalent linked condition and influences the quality of life).

Risk factors:

1. Poverty
2. Oral hygiene
3. Tobacco
4. Alcohol

Another conditions that affect oral health:

1. NOMA (a form of orofacial gangrene).
2. Developmental disorders.
3. Down syndrome, cerebral palsy and genetic defects.
4. Fluorosis of teeth.

Table 1. *Comparison among the characteristics of prevalent oral diseases.*

CARIES	PERIO DISEASE	TOOTH LOSS	ORAL LESIONS AND CANCER	Oral health and HIV/AIDS	DENTAL TRAUMA
Children: High in the Americas and Europe. (60-90%) Lower in most African countries. Adults: almost 100% worldwide (1-3)	Higher prevalence of periodontal health in the African and the European region. Lowest in the South-East Asia. (1-3)	Increasing in developing countries while reducing in developed ones. Italy has one of the lowest prevalence (13%), while countries like Albania (69%) and Canada have the highest (58%). (2) Highly related with periodontal health. (4)	Leukoplakia is the most frequent form of oral precancer. Erythroplakias are less common but more dangerous. (1%). (5-6) Oropharyngeal cancer is more common in developing countries, more prevalent in men and South-center Asia, and is the 8° cancer in the world. (7)	40-50% who are HIV positive have oral diseases. Most prevalent: pseudo-membranous oral candidiasis, oral hairy leokyplakia, HIV gingivitis and periodontitis, Kaposi sarcoma and Non Hodgkin lymphoma. (8-9)	15% in Latin-American children. 5-12% in Middle East. 16-40% in 6 years old children from industrial countries. (12) High presence of dental erosion. (13)

Table 2. *Comparison of the most frequently related conditions that affect oral heath.*

NOMA (camcrum oris)	DEVELOPMENTAL DISORDERS	FLUOROSIS OF TEETH
Starts as a gingival ulceration and is characterized by a black necrotic center. 70-90% mortality (10) Prevalent in 1-4 years old population. Mostly reported in Africa and Asia (1) Major risk: poverty Related to: malnutrition, poor sanity, infectious diseases like malaria and tuberculosis. (11)	Frequency: 1° Congenital diseases of enamel or dentine. 2° Number, size and shape of teeth. 3° Craniofacial birth defects as cleft lip/palate. Highest incidence: Native Americans and Asians. Lowest incidence: Africans and Caucasians. Risk factors: 1° Folic acid deficiency, 2° Maternal smoking and 3° Maternal age. (14)	Main cause: drinking water with more than 1.5ppm of fluoride. Highly prevalent in: East Africa, India and North Thailand. (15-16)

To acknowledge the way that oral diseases compromise the health status of different populations is a public health matter that concerns us all. Its identification and description are important for the education and prevention worldwide. The impacts of oral disease in the general health condition as well as in the economy are high. Is the fourth most expensive in the majority of the industrialized countries, and there difference between developed and developing countries is quite large.[16] Its relation with living conditions, lifestyle and prevention is a valuable information to determinate the populations at risk and implement effective health programs. [17]

CHAPTER A

DENTAL CARIES

Dental caries is a demineralization process, a disease caused by the action of bacteria that can result in a lesion (initial caries) that can affect the enamel and dentinal surface (manifest caries).

The World Health Organisation (WHO) has recorded dental caries globally through its oral disease surveillance systems. Although preventive programmes have had a positive effect on the caries figures in developed countries, several factors may act on the disease. In developing countries on the other hand, the adoption of a western lifestyle in absence of public prevention programmes have caused a rapid increase in the develop of the dental disease. [18]

Caries is a growing oralh health problem that needs to be appraised in:

I. Diagnosis – ICDAS criteria

II. Risk - Caries Risk Assessment and Risk Factors

III. Early detection - DIFOTI technology

IV. Minimally Invasive Therapy - Chemical removal of caries using Carisolv

V. Behavioral and Socio-cultural Risk factors – Diet, BMI and poverty

VI. Taste Preference

VII. Prevention - Polyols

I. DIAGNOSIS

Caries diagnosis is mainly evaluated with the World Health Organization criteria, this is, the DMFT/DMFS (Decay, Missing or Filled Tooth/Surface) that registers only obvious caries lesions along with the missing and restored teeth.

A new model, called ICDAS, has been developed to assess both enamel (non-cavitated) and dentin (cavitated) lesions, and is capable to record appropriate the pertinent information of the presence of caries and the relationship between the primary and the permanent dentition.[19,20]

Characteristics of ICDAS

- Reliable
- Reproducible
- Practical

Evaluates

1. Lesions according to the type of teeth (anterior, posterior)
2. According to the surfaces (occlusal, proximal and free smooth)

Criteria

- Visual examination
- plaque-free surfaces
- wet and dried teeth [21]

Training

The ICDAS Committee provides an e-learning program. As well, calibration programs can improve the reliability of the method for the use of both epidemiologist and clinicians.

Scoring system

ICDAS evaluates the overall caries experience: tooth status (previous treatment: Range 0 to 8) and the caries status (current status: Range 0 to 6) and using one code for each giving as a final result a two-digit code. [22]

ICDAS CHART

	17	16	15	14	13	12	11	21	22	23	24	25	26	27
O														
B														
P														
D														
M														
TOOTH	**47**	**46**	**45**	**44**	**43**	**42**	**41**	**31**	**32**	**33**	**34**	**35**	**36**	**37**
O														
B														
L														
D														
M														

Tooth status (1st number):

0= Sound
1= Sealant, partial
2=Sealant full
3=Tooth coloured restoration
4=Amalgam restoration
5=Stainless steel crown
6=Porcalain or gold PFM crown or veneer
7=Lost or broken restoration
8=Temporary restoration
9=Used for the following conditions:
97=Tooth extraxted because of caries (all tooth surfaces will be coded 97)
98=Tooth extracted for reasons othe rthan caries
99= Unerupted (all tooth surfaces coded)

Caries status (2nd number):

0=Sound
1=First visual change in enamel
2=Distinct visual changes in enamel
3=Localized enamel breakdown due to caries with no visible dentin
4=Non-cavitated surfaces with underlying dark shadow from dentin
5=Distinct cavity with visible dentin
6=Extensive distinct cavity with visible dentin and extensive cavity involves at least half of the tooth surface and possibly reaching the pulp
7=Tooth extraxted bacause of caries (all tooth surfaces will be coded 97)
8=Tooth extracted for reasons othe rthan caries (all tooth surfaces coded 98)
9= Unerupted (all tooth surfaces coded 99)

II. CARIES RISK ASSESSMENT AND RISK FACTORS

Caries risk assessment is the identification of individuals at risk for future caries and it is a science that lies within the field of health risk assessment.

Etiology of caries

- The host, mainly represented by tooth resistance, saliva factors and remineralization capacity.
- The microflora, amount of plaque and type of oral microorganisms
- The substrate, diet, its content and frequency of intakes
- Time needed before a cavity becomes visible.

Table 3. *Caries risk factors (Beck 1998).* [23]

Caries risk factors	HIGH RISK	LOW RISK
Clinical evidence	New lesions Premature extractions Anterior caries or restorations Multiple restorations No fissure sealants Fixed appliance orthodontics Partial dentures	No new lesions Nil extractions for caries Sound anterior teeth No or few restorations Restorations inserted years ago Fissure sealed No appliance
Dietary habits	Frequent sugar intake	Infrequent sugar intake
Social history	Social depreciation High caries in siblings Low knowledge of dental disease Irregular attendance Ready availability of snacks	Social advantage Low caries siblings Dentally aware Regular attendance limited availability o f snacks High dental aspirations

	Low dental aspirations	
Use of fluoride	Drinking water not fluoridated No fluoride supplements No fluoride tooth paste	Drinking water fluoridated Fluoride supplements used Fluoride toothpaste used
Plaque control	Infrequent ineffective cleaning Poor manual control	Frequent, ineffective cleaning Good manual control
Saliva	Low flow rate Low buffering capacity High *S. mutans* and lactobacillus counts	Normal flow rate High buffering capacity Low *S. mutans* and lactobacillus counts
Medical history	Medically compromised Physical disability Xerostomia Long-term cariogenic medicine	No medical problems No physical problems Normal salivary flow No long term medication

Moderate Risk

Individuals who do not clearly fit into high or low risk categories are considered to be at moderate risk.

CARIOGRAM. A tool for the assessment of caries.

A model developed at the Dental University in Goteborg that illustrates the multifactorial background of dental caries in a simple way. It was computer-based by the Dental University in Malmo.

Main purpose

To improve the understanding of the multifactorial aspects of dental caries and to estimate the caries risk where the patient is seen as a “whole”.

Evaluation

1. Collecting relevant information.

2. Scoring according to a standardized protocol.

3. Entering the scores into the computer program.

Description

Cariogram is a pie-circle diagram divided into colored sectors. There are five sectors:

1. Green (actual chance to avoid new cavity).

2. Dark blue (diet contents and diet frequency).

3. Red (bacteria). A combination of amount of plaque and *mutans streptococci*

4. Light blue (susceptibility). Based on a combination of fluoride program, saliva secretion and saliva buffer capacity.

5. Yellow (circumstances). Comprises the combination of caries experience and related diseases.

Scoring

For all patients the factor “0” is the best while “3” (or “2” where that is maximum) the most unfavorable scores.

The assessment of the risk of dental caries has been showed to benefit from the use of computer-based programs. The caries risk profile in a group of Sardinian schoolchildren evaluated the caries prevalence, gingival conditions, diet, oral hygiene and saliva with success, determining that more than a quarter had less than 40% possibility to avoid dental caries. [24]

Table 4. Caries related factors and the date needed to create a Cariogram

Factor *	Comment	Info/data needed
Caries experience	Past caries experience, including cavities, fillings and missing teeth due to caries. Several new cavities definitely appearing during preceding year should give a high score even if number of fillings i slow.	DMFT, DMFS, new caries experience in the past year.
Related diseases	General disease or conditions associated with dental caries.	Medical history, medications.
Diet, contents	Estimation of the cariogenicity of the food, in particular sugar contents.	Diet history, lactobacillus test count.
Diet, frequency	Estimation of number of meals and snacks per day, mean for “normal days”.	Questionnaire results, 24 h recall or dietary recall (3 days).
Plaque amount	Estimation of hygiene, for example according to Silness-Loe Plaque Index (PI). Crowded teeth leading to difficulties in removing plaque interproximally should be taken into account.	Plaque index.
Mutans streptococci	Estimation of levels of Mutans streptococci (*Streptococcus mutans, Streptococcus sobrinus*) in saliva, for example using Strip mutans test.	Strip mutans test or other laboratory tests giving comparable results
Fluoride program	Estimation of to what extent fluoride is available in the oral cavity over the coming period of time.	Fluoride exposure, interview patient.
Saliva secretion	Estimation of amount of saliva, for example using paraffing-stimulated secretion and expressing results as ml saliva per minute.	Stimulated saliva test- secretion rate.
Saliva buffer capacity	Estimation of capacity of saliva to buffer acids, for examples using the Dentobuff test.	Dentobuff test or other laboratory tests giving comparable results

III. EARLY CARIES DETECTION

Early diagnosis and treatment of caries is necessary to implement strategies. [25] The clinical diagnosis of caries lesions is fundamental, and the use of radiopgraphs has enhance practitioners. However, although radiographs are highly sensitive specially for detection of interproximal caries, it has been showed to be limited to a comprehensive diagnosis. [26]

DIFOTI

A Digital Imaging Fiber-optic Transillumination Device, also known as DIFOTI, was designed to support the identification of cavitated and non-cavitated lesions aloft the gingiva that differs the optical properties of the lesion with the ones from the sound dental tissue (DIAGNOcam 2170 KaVo). DIFOTI uses digital image processing in real time that permits quantitative information to monitore lesions in present and in time. [27,28]

Transillumination

Transillumination of the teeth with intense fiber-optic light amplifies the change in scattering and absorption of light photons in the carious tissue and thereby makes the caries lesion appear as a dark shadow.

Advantages

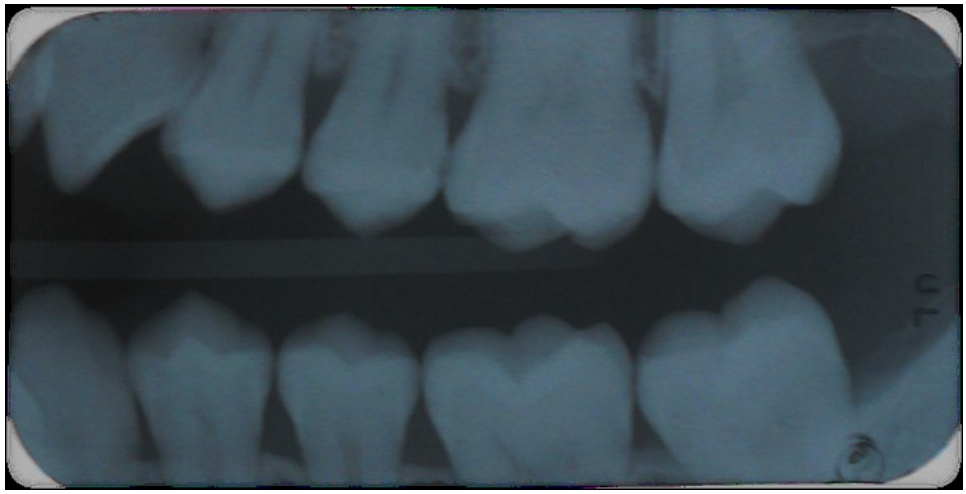
The main asset of this technology is that, unlike x-rays, is noninvasive. This give the opportunity to use it as many times necessary and to follow the arrest or progression of the lesions by capturing an digital image on the computer that can be stored and take again if needed. [29] It has also the potential to detect missing homogeneity in the tooth structure by accentuating the features of the lesions. This is very important given the recent reports about the risk related to dental radiographic exposure and the suggestion of radiographic selection criteria. [30]

DIFOTI in the literature

Clinical studies to measure the lesions and correlate the obainted results with the ones given by radiographs is limited. [31] Although DIFOTI has demonstrated to be more effecive than radiographs to detect enamel lesions under in vitro conditions, further analysis is needed to validate the scale of diagnosis and the intra-examiner and inter-examiner reproducibility of the method. [29]

This is the reason we developed a study design to evaluate the effectiveness of the DIFOTI technology in the clinic of the University of Sassari as well as to assess the reproducibility of the instrument in dental professionals with different backgrounds belonging to different parts of the country.

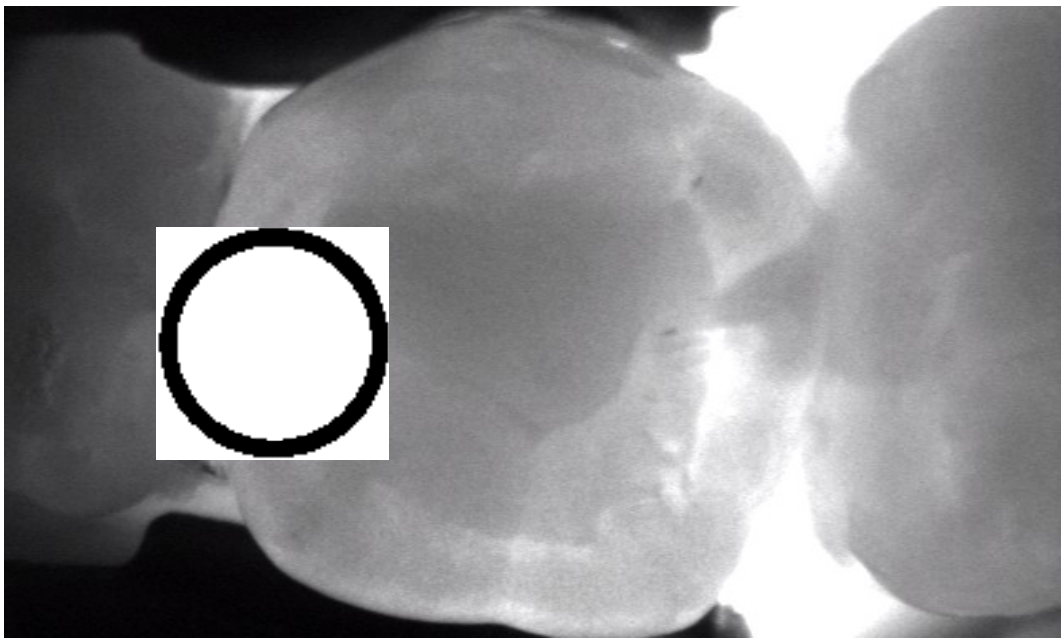
CASE 1. Clinical and radiographical evaluation of an lower left second premolar.

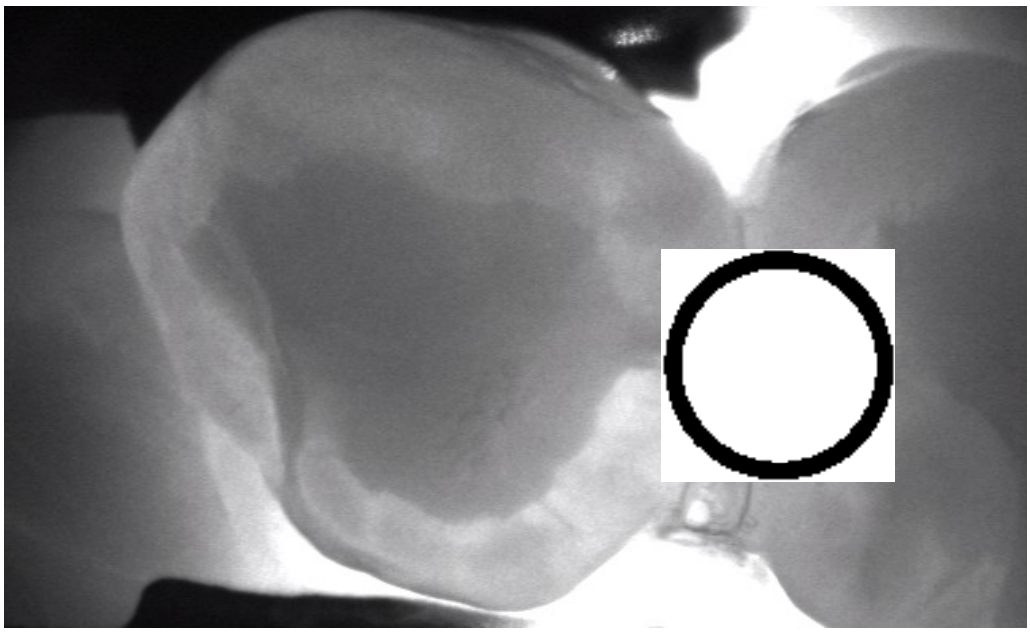


Dx: Premolar No. 35 was classified as caries free, as no color change or demineralization was observed during the clinical analysis and bitewing radiographic examination.

DIFOTI Evaluation

A defined dark area is detected with the DIFOTI device in the mesial and distal surfaces of the second mandibular premolar. It was corroborated that is not a shadow produced by the inclination of the instrument. In different shoots, this was confirmed.





ANNEX I

Digital Imaging Fiber-optic Transillumination Device versus Radiographic and Clinical Examination in the Detection of Dental Caries

Caries Research

Digital Imaging Fiber-optic Transillumination Device versus Radiographic and Clinical Examination in the Detection of Dental Caries

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Digital Imaging Fiber-optic Transillumination Device versus Radiographic and Clinical Examination in the Detection of Dental Caries

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Caries detection using DIAGNOcam

Key Words

Caries detection - DIFOTI - ICDAS - Radiographs

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Abstract

Aim: To evaluate the reliability of a Digital Imaging Fiber-Optic Transillumination device (DIFOTI) for the detection of caries lesions and compare it with the results of clinical or radiographic examinations. In addition, the reliability of DIFOTI method was evaluated in a group of dental professionals. *Methods:* 52 selected subjects were included into the study. Two calibrated dentists evaluated premolars and molars using DIFOTI (DIAGNOcam) and a clinical examination (CE) for assessing caries lesions on occlusal surfaces (CAMo), and DIAGNOcam and a radiographic examination (BW) for caries in approximal surfaces (CAMa). Forty-eight trained dental professionals evaluated thirty randomly selected surfaces (EVA1) derived from CAMo/a images analysis. One month later, the same dentists re-evaluated the same images (EVA2). Cohen's Kappa was used to evaluate the grade of accordance while Intra-Class Correlation coefficients (ICC) for the reproducibility for each surface. *Results:* The number of detected occlusal caries lesions was similar for CAMo and CE (Kappa=0.99). DIAGNOcam identified a higher number of approximal lesions compared to BW (Kappa=0.91). The same number of lesion in dentine (Kappa=1) was identified by the two detection methods, while in enamel a low agreement was found with more lesions detected by CAMa (Kappa=0.24). For EVA1, 87.5% of the participants had high concordance of Cohen's Kappa compared to DIAGNOcam images and an higher concordance in EVA2. The intra-examiner reliability was substantial/almost perfect in 59.4% of the participants. *Conclusion:* DIAGNOcam images may be useful for early caries detection on approximal surfaces. The device seems easy to decode for professionals without experience.

INTRODUCTION

Caries clinical management is linked to the number of teeth and surfaces affected, as well as the severity (depth) and the activity (progression or new development) of the lesions. Caries detection, including assessment of non-cavitated and cavitated carious lesions, is an important issue in operative dental practice [Pitts, 2004; Piovesan et al., 2013]. Radiographic examination is a highly sensitive method to detect carious lesions on surfaces that can not be inspected visually, such as approximal surfaces. However, limitations in its sensitivity to diagnose early lesions have been reported [Bader et al., 2002]. In addition, the risk related to radiographic exposure needs to be taken into consideration [Ludlow et al., 2008].

There is a need for improvement of the current methods for caries detection. As a complementing aid to visual examination, a Digital Imaging Fiber-Optic Transillumination Device (DIFOTI) was designed with the task to support clinicians in the identification of caries lesions in different stages [Keem and Elbaum, 1997, Schneiderman et al., 1997; Astvaldsdóttir et al., 2012]. Using the specific optical properties of a carious tissue, transillumination of the teeth with DIFOTI amplifies the change in scattering and absorption of light photons and thereby, makes the lesion appear as a dark shadow [Astvaldsdóttir et al., 2012]. DIFOTI was developed to facilitate in real time the detection, localization and quantitative characterization of lesions [Schneiderman et al., 1997]. The major advantage of the method is that it is non-invasive and therefore can be used as frequently as needed, providing an immediate digital image capture that can be stored and compared with previously acquired images [Astvaldsdóttir et al., 2012]. Caries lesion activity may be monitored by quantification of the changes in mineral content of the lesion over time using the comparison of DIFOTI images acquired at different time points. The detection of early lesions is extremely relevant from clinical point of view as implies an uplift caries activity and the need for additional non-invasive intervention [Keem & Elbaum, 1997; Astvaldsdóttir et al., 2012].

Although it is subjective, the interpretation of the DIFOTI images seems to be relatively easy to learn. In literature, clinical studies that compare the in situ depth of carious lesions with DIFOTI versus radiographs are quite limited [Bin-Shuwaish et al., 2008]. A recent in vitro study used the transillumination device to identify approximal

carious lesions and compared the diagnostic accuracy/efficacy of the device with both traditional and digital x-ray examination, finding that DIFOTI identified a higher number of enamel caries by detecting lesions at an earlier stage than radiographs, providing more accurate results. In contrast, radiographs showed a better sensitivity in deeper lesions, this is, DIFOTI identified a higher number of incorrect dentin lesions. Radiography is able to identify great change in lesion depth although small changes in the mineral content are not detectable. Moreover, DIFOTI and film radiography showed a high intra-examiner concordance [Astvaldsdóttir et al., 2012]. The International Caries Detection and Assessment System (ICDAS) is a more a visual scoring systems than tactile, developed to assess the caries lesions at both initial and manifest thresholds [International Caries Detection and Assessment System Coordinating Committee, 2005; Honkala et al., 2011].

Meticulous and reliable data collection is vital for success in all fields of research [Lesaffre et al, 2004]. The training of the examiners is fundamental, and it can be defined, according to the Guidance on the Statistical Aspects of Training and Calibration of Examiners for Surveys of Child Dental Health by British Association for the Study of Community Dentistry (BASCD) [Pine et al, 1997; Assaf et al., 2006; Agustsdottir et al., 2010], as teaching the agreed interpretation of the diagnostic criteria.

The main aim of this study was to evaluate the effectiveness and reliability of the DIAGNOcam. The null-hypothesis was that the reliability of a DIFOTI device (KaVo DIAGNOcam 2170) for the detection of caries lesions did not differ from that obtained through the clinical or radiographic examinations. To validate this hypothesis, an observational study was designed and evaluated as well in a group of dental professionals. In the first part of the study, the DIAGNOcam was compared with a clinical examination appraising the occlusal surfaces and with x-ray bitewings assessing the approximal surfaces. In the second part, the reproducibility of image evaluation using DIAGNOcam was determined in a group of dental professionals.

Materials and Methods

The study was approved by the Ethical Committee at the University of Sassari (authorization number 389/2013) and it was conducted over 6 weeks from June 9th

to July 15th 2014.

Study design

The study was designed in two parts: the first was a comparison among three detection methods (DIFOTI, bitewing radiographs and clinical examination), the second was a reliability study among dental professionals using the DIFOTI imagines derived from the first part.

Comparison among three detection methods

The new KaVo DIAGNOcam 2170 is a camera system that reads the tooth's structure to verify occlusal, approximal and secondary caries lesions when the tooth is transilluminated. A digital video camera records the image and displays it on a computer screen.

For the radiographic examination, Planmeca intraoral radiographic equipment (Planmeca, Helsinki, Finland) and Kodak UltraSpeed DF42 films, with settings of 70 kV and 7 mA and an exposure time of 0.25 s, were used for bitewing radiographs. The radiographs were manually developed via conventional standard conditions and standard processing times, and examined according to O'Mullane criteria [O'Mullane et al., 1997].

The clinical examinations were performed under standard conditions. The subjects were seated in a dental unit and the teeth were examined using a plan mirror (Hahnenkratt, Königsbach, Germany) and the WHO CPITN ballpoint probe (Asa-Dental, Milan, Italy) under optimal light.

Calibration of the examiners

Calibration exercises for all the three methods (DIAGNOcam unit visual, clinical caries diagnostic system (ICDAS) and radiographic examination) were carried out by two dentists before the start of the study. One of the authors (GCampus) acted as benchmark, training and calibrating the two examiners. The calibration process was divided for each diagnostic method in four steps:

• lectures regarding the disease and the method (i.e. DIAGNOcam, ICDAS, x-ray) for eight hours;

• first examination, no discussion was allowed between the examiners and the dental advisors as to the interpretation of the criteria during the calibration sessions;

• re-evaluation by the examiners after 72 hours (clinical examination) and one week (DIAGNOcam and x-ray)

• evaluation of the agreement or disagreement and statistical analysis.

Fifty volunteers were clinically examined for presence of caries lesions in a dental chair using the ICDAS criteria and re-examined after 72 hours. Intra- and inter-examiner reliability was calculated through percent agreement and Cohen's Kappa statistics. Good inter-examiner reliability was found with no significant difference from benchmark values (p=0.15) and a low mean square of error (0.47). The Pearson's correlation coefficient between the two examiners was high ($r = 0.83$, $p < 0.01$, $R2 = 0.71$). Intra-examiner reliability was also high, Cohen's K=0.88.

Forty extracted human teeth (10 premolars and 30 molars), in total 80 approximal and 40 occlusal surfaces, were selected for the calibration of the DIFOTI device and the radiographic examination. The teeth were selected from a pool of extracted teeth from the Department of Oral Surgery at the University of Sassari. The teeth were cleaned, any remaining soft tissues and calculus were removed, and they were subsequently frozen at -20° until used. Selection criteria match the line of the first evaluation. Evaluations were carried out at one-week interval; Kappa values for inter- and intra-examiner agreement were high for both methods (0.79 for DIFOTI and 0.83 for x-ray). The Pearson's correlation coefficient for the two examiners was high ($r = 0.84$, $p < 0.01$, $R2 = 0.74$). The clinical examiner did not have the opportunity to look at DIAGNOcam (CAMo/a) or BW images for the entire period.

Study population

The study population consisted of students of the School of Medicine of the University of Sassari, Italy. To be suitable for enrolment, subjects had to meet these inclusion criteria: no missing teeth, no secondary caries and no fillings in premolars or molars. The exclusion criteria were subjects wearing fixed orthodontic appliances and subjects unable to be exposed to x-rays for medical/specific reasons. All students (n=1145) attending the School of Medicine were invited to participate via email/leaflet where the aim of the study was described in detail. A total of 678

students accepted and were examined (59.2% acceptance rate) and 52 subjects (19-23 years, mean age 21.2±1.2) fulfilled the inclusion/exclusion criteria.

Power analysis (G*Power 3 software) was performed to establish the number of subjects needed to evaluate the estimated difference in caries diagnosis using DIFOTI and/or clinical evaluation and x-ray. Data [Virajsilp et al., 2005] related to the reliability of two diagnostic methods were used to calculate the sample size, even if data used were on primary teeth. The standardized effect was set at 0.39 with a sample size of 48 subjects and an upper 95% one- sided confidence limit of 0.52. All subjects (n=52) that fulfilled the inclusion/exclusion criteria were enrolled. Each subject was codified with a number in order to protect his/her identity. The flow chart of the study is displayed in Figure 1.

The DIFOTI device was used to assess caries lesions on occlusal surfaces (CAMo) and on approximal surfaces (CAMa). In addition, a clinical examination of the occlusal surfaces (CE) and a radiographic examination (BW) for approximal surfaces were performed.

Each tooth were cleaned for 30 seconds with a prophylaxis paste (Clinpro™ Prophy Paste: 3M ESPE Dental Products, USA) and then rinsed by a water spray for 10 seconds. The clinical examination was performed under standardized conditions describe above after drying teeth for 5 seconds. The students were examined and analysed during the same day by both examiners, first attending the clinical and radiographic examination and afterwards they were asked to go to another room where the DIFOTI device was installed with a computer in a dental chair. The International Caries Detection and Assessment System (ICDAS) was recorded for both enamel and dentinal lesions [International Caries Detection and Assessment System Coordinating Committee, 2005; Ismail et al., 2007; Honkala et al., 2011]. The radiographs were taken using an 8-inchround cone that was placed in contact with the ring of the film-holding system (RINN XCP, Dentsply, York), which in turn was placed in contact with the patient's cheek during exposure. Not perfectly clear or overlapping images were taken a second time. Then the DIFOTI device was used according to the manufacturer's instructions, placing the mouthpiece over the occlusal surfaces. The image appeared in real time on the computer monitor, and the examiner saved it in the electronic patient record.

The DIAGNOcam was used for the detection of occlusal and approximal caries at enamel or dentine. When a defined approximal shadow in the enamel was present, it was scored as 1 and when reaching into the dentine it was scored as 2. Due to the impossibility to measure the lesion vertically all dark occlusal areas were scored as 1. The ICDAS scores were performed on the occlusal surface. Radiographs were examined according to O'Mullane criteria [O'Mullane et al., 1997] and mesial and distal surfaces were assessed.

Reliability among dental professionals using DIFOTI

Forty-eight Italian dental professionals with no experience of the DIFOTI device were asked to participate in the second part of the study. Their professional experience was at least 7 years. On the day of the study they underwent at 60-minute training session describing the DIFOTI technology and the DIAGNOcam by one of the authors (CLC). Immediately after the training session, each participant had to diagnose ten teeth images randomly obtained from the first part of the study, analysing 10 occlusal, 10 mesial and 10 distal surfaces. Participants were asked to fill in a form containing two possible answers (1 - presence of caries, 2 - absence of caries) (EVA1). One month later, participants were contacted via email and were asked to revaluate the same images with the same criteria (EVA2). These results were compared with their previous answers.

Statistical Analysis

All data were analysed using STATA 13. For all analysis a p-value <0.05 was considered statistically significant. The general grade of accordance between the different detection methods was evaluated using the Cohen's Kappa [Cohen, 1960], while the reproducibility for the two methods for each surface (occlusal or approximal) was assessed using Intra-Class Correlation coefficients (ICC). ICC values equal to 0 represent agreement equivalent to that expected by chance, while 1 represents full agreement.

The inter-examiner DIFOTI reliability among dental professionals compared to the results derived from DIAGNOcam analysis was evaluated categorizing the kappa value of each professional respect to DIAGNOcam following the criteria described by Landis and Koch [1977], who characterized values <0 as indicating no concordance and 0-0.20 as slight, 0.21-0.40 as fair, 0.41-0.60 as moderate, 0.61-0.80 as

substantial, and 0.81-1 as almost perfect concordance. The method by Bland and Altman [1986] was used to display the variability of the two examinations (EVA1 and EVA2) by each examiner and the plot of EVA1 respect to the DIAGNOcam results, the plot of EVA2 respect to DIAGNOcam and the comparison between EVA1 and EVA2. This method allows to investigate the existence of any systematic difference between the measurements and to identify possible outliers.

Results

Comparison among the three detection methods

A total of 2496 surfaces (832 mesial, occlusal and distal, respectively) were analysed. The occlusal surfaces were analysed using DIAGNOcam (CAMo) and Clinical Examination (CE), while the approximal surfaces were analysed with DIAGNOcam (CAMa) and Bite-Wing radiographs (BW). The total number of occlusal caries lesions detected was similar, 149 using CAMo and 152 with CE with a Cohen's Kappa of 0.99. The ICC for the occlusal, mesial and distal surfaces of each tooth is reported in Figure 2. The mean ICC for the occlusal surface was 0.93 with a lowest value for maxillary right second molar (ICC=0.78), while a perfect agreement (ICC=1) was observed for several premolars. Approximal caries identified using CAMa were 83 and 70 using BW (Cohen's Kappa of 0.91). CAMa and BW identified the same number (31) of caries in dentine. The Cohen's Kappa was 0.24 for enamel lesions with a low agreement, while a complete concordance (Kappa=1) was observed for dentinal lesions (Table 1). The mean ICC for approximal surfaces was 0.97 for the distal and 0.95 for the mesial surfaces (Figure 2). Regarding enamel lesions, 17 lesions in molars were detected with CAMa, while 16 with the BW method (Cohen's kappa=0.97); 35 lesions were detected in premolars with CAMa respect to 23 with BW (Cohen's kappa=0.21). Twenty-nine decayed mesial surfaces were registered with CAMa respect to 23 with BW (Cohen's kappa=0.39). For the distal surfaces, 23 lesions were recorded with CAMa and 16 with BW (Cohen's kappa=0.34). A complete concordance was observed for dentinal lesions between the two methods.

Reliability among dental professionals using DIFOTI

Forty-eight dental professionals participated in the first evaluation (EVA1) and thirty-two (drop out rate 33.3%) in the second evaluation (EVA2). The Cohen's Kappa of each subject regarding the reliability between the two evaluations was categorized following the scale proposed by Landis and Koch [1977] (Table 3). Regarding inter-examiner reliability, in EVA1 the majority of the examiners (87.5%) had either a substantial (46.9%) or an almost perfect concordance (40.6%) compared to DIAGNOcam results, while in EVA2 a higher percentage had a substantial concordance (75.00%) and a lower percentage an almost perfect (18.8%), with a shift towards substantial concordance grade. Nineteen examiners (59.4%) showed a substantial/almost perfect agreement, while 13 examiners (40.6%) a fair/moderate agreement (Figure 3). The Bland-Altman plot showed a good intra-examiner (Figure 3a) and a higher over-rating of the number of the lesions in EVA2 (Figure 3c).

Discussion

The main findings of this study are that the DIFOTI device (DIAGNOcam) proved to be consistent to clinical examination for the detection of lesions on the occlusal surface and to bite-wing x-ray for dentinal lesions on approximal surfaces; a higher number of enamel lesions was detected by DIAGNOcam compared with x-rays, especially in premolars. In the calibration process, no statistically significant differences were observed between benchmark and examiners and no systematic bias between examiners' scores was noted. The level of concordance among dental professionals, with respect to the DIAGNOcam analysis result derived from the first part of the study, was really high in both examinations (EVA1/EVA2). The intra-examiner reliability of the dental professionals was quite good even if in 40% of the examiners the level of agreement was moderate or less.

The DIFOTI device used in this study, KaVo DIAGNOcam 2170, is a non-invasive real-time recording tool that was developed for regular practice use with no exposure of ionizing radiations to the patient. The device was designed to be useful to identify lesions at the initial caries stage and the technique allows for more frequent re-evaluations of these diagnoses than what is feasible using radiographs [American Dental Association, 2012]. The DIFOTI method has been shown to be more sensitive

than radiography to detect early changes in enamel [Young and Featherstone, 2005; Bin-Shuwaish et al., 2008; Astvaldsdottir et al., 2012]. Overall, the use of DIFOTI along with radiographic analysis is able to improve the diagnostic accuracy and to identify early approximal lesions with respect to presence and size [Bin-Shuwaish et al., 2008]. The outcome of this paper confirms these findings. The DIAGNOcam identified a higher number of approximal lesions in enamel than the radiographic technique, allowing an earlier detection of incipient lesions than traditional detection methods. Proper and early caries detection is crucial for optimal treatment decisions, helping the clinician to choose between a restorative treatment or chemically remineralisation, as that occurring in the early stages of caries development [Young and Featherstone, 2005].

Intraoral radiographs are, in addition to clinical evaluation, considered the first choice for caries detection. Nevertheless, radiographs are unable to detect initial demineralization of the tooth resulting in low sensitivity, since 40 to 60% of tooth decalcification is needed to produce a radiographic imaging of caries resulting in false-negative test [Machlulskiene et al., 1999; Chong et al., 2003; Yang et al., 2005]. Conversely, the use of the DIFOTI method might lead to an over-detection as the device has a lower specificity compared with radiographs [Young, 2002].In this in vivo trial the DIAGNOcam findings were compared to radiographs, used as golden standard. The “true” status of the lesion was not evaluated since the teeth were not extracted after the in vivo evaluation. Regarding occlusal surfaces the DIAGNOcam was able to detect the presence of carious lesions but not to determinate the extension of the lesion since the device is able to capture the light emerging from the tooth surface that is closest to the digital camera as specified by the manufacturer instructions.

Over-diagnosis can occur owing to lower specificity of DIFOTI compared with bite-wing radiographs. Dark areas in the images can be attributed to scatter and absorption of light as it passes through demineralized enamel, consequently white spots can be falsely identified as cavitations [Schneiderman et al., 1997].

Some strengths of the present study should to be considered. The DIFOTI device was compared to clinical examination for the occlusal surface and to bitewing for the approximal, and this is the first study comparing in vivo the DIAGNOcam to traditional

caries detection methods. The study outline may be seen as a limit since the findings may not compete with the “surface/teeth true status”, as only in vitro study can assess.

As X-rays are an important part of the record in clinical practice, so DIAGNOcam images could become an important tool in the coming future. Is therefore important to estimate whether the oral health professionals are capable to correctly interpret these images as a complementary diagnostic aid. The reliability of the DIFOTI among professionals showed a quite good intra-examiner concordance, even if an important shift to an over detection (EVA1 vs EVA2) was noted. Since only images in doubt are tested in the clinic practice, the probability of a detection of a lesion will be increased [Chu et al., 2010] with a high specificity and a low sensitivity. Moreover, a bias is probably ascribed to the study design, as the first evaluation was performed with a strict time limit while the second evaluation was more “free”. Examiners received an email with the images and no time limit was provided. A stochastic drift might be also postulated as the misclassification performed by examiners in EVA2 happened unconsciously leading to a higher inter-examiner concordance. A further weak point might be ascribed to study design: EVA2 was designed to be carried out one month later than EVA1, and this might have affected the results; otherwise the results of EVA2 still showed a good concordance with EVA1 and the DIAGNOcam results derived from the first part of the study.

The results of this paper suggest that the DIAGNOcam can be helpful in everyday clinical practice. However, the cost effectiveness of the DIFOTI method in community dentistry may be seen as a concern as at least 15 minutes is required to examine the whole dentition. Therefore, the DIFOTI technique may be particularly useful for early detection and monitoring of the progression of dental caries at individual sites.

Conclusion

DIAGNOcam might be a useful device for early caries detection, especially for early non-cavitated lesions on approximal surfaces. The DIFOTI images are quite easy to decode even for professionals without any experience of the use of the method. More information is needed to standardize the scoring of the lesions to help the clinicians to give an accurate interpretation of the images.

Authors' contributions:

Cynthia Lara-Capi: participated in the study design, performed the clinical examination and data collection;

Peter Lingström: design of the study, final revision of the paper;

Gianfranco Lai: participated in the study design and data collection;

Maria Grazia Cagetti: participated in the study design and drafting of the manuscript;

Fabio Cocco: participated in the study design, data and statistical analysis;

Charlotte Simark: participated in the study design and revision of the manuscript;

Guglielmo Campus: participated in the study design and drafting of the manuscript.

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Figure legends

Figure 1. Flow chart of the study design.

Figure 2. Comparison among the three detection methods. Intraclass Coefficient Correlation between the DIAGNOcam and Clinical Evaluation for the occlusal surfaces (o) and between DIAGNOcam and Bite-wing for the approximal surfaces; mesial (m) and distal (d) are reported.

Figure 3. Reliability among dental professionals using DIAGNOcam. Intra-examiner reliability using Bland-Altman plot of difference. Each small dot is the average value of one single examiner observation, larger dots are the sum of two or more examiners. Shaded region indicates 95% limits of agreement around the dashed line representing the mean.

Table 1. Comparison among the three detection methods. Caries lesions (enamel and dentinal lesions) according to the radiographic evaluation (BW) and the DIAGNOcam on approximal surfaces (CAMa). Percentage were calculated based on the total of the surfaces examined (n=1664)

	Bitewing (BW) *n (%)*	DIAGNOcam (CAMa) *n (%)*	Cohen's kappa *value (SE) 95% CI*
Enamel	39 (2.3)	52 (3.1)	0.24 (0.06) 0.12-0.36
Dentine	31 (1.9)	31 (1.9)	1

Table 2. Comparison among the two detection methods, the DIAGNOcam readings and the Bitewing examination. Distribution of carious lesions in enamel and in dentine by type of tooth and surfaces is shown; Coehn's Kappa was calculated

Lesions for	**Enamel**			**Dentine**		
teeth/surfaces	**DIAGNOcam (CAMa)** n=52 *n (%)*	**Bitewing (BW)** n=39 *n (%)*	Cohen's kappa *value (SE) 95% CI*	**DIAGNOcam (CAMa)** n=31 *n (%)*	**Bitewing (BW)** n=31 *n (%)*	Cohen's kappa *value (SE) 95% CI*
Molars	17 (32.7)	16 (41.03)	0.97 (0.03) 0.91-1.00	13 (41.94)	13 (41.94)	1
Premolars	35 (67.3) etc	23 (58.97)	0.21 (0.08) 0.05-0.36	18 (58.06)	18 (58.06)	1
Mesial	29 (55.77)	23 (58.97)	0.39 (0.08) 0.23-0.56	11 (35.48)	11 (35.48)	1
Distal	23 (44.23)	16 (41.03)	0.34 (0.10) 0.15-0.54	20 (64.52)	20 (64.52)	1

Table 3. Reliability among dental professionals using the DIFOTI technique. Inter and Intra-examiner reliability categorized following the scale of the concordance degree proposed by Landis and Koch [1977] after two examinations (EVA1 and EVA2). n = 33

	Fair concordance *n (%)*	**Moderate concordance** *n (%)*	**Substantial concordance** *n (%)*	**Almost perfect concordance** *n (%)*
EVA 1	--	4 (12.50)	15 (46.87)	13 (40.63)
EVA 2	- -	2 (6.25)	24 (75.00)	6 (18.75)
				$\chi^2=10.96\ p<0.01$
Drop-out after EVA1 *n=16*	--	4 (25.00)	6 (37.50)	6 (37.50)
Intra-examiners reliability EVA1/EVA 2	4 (12.50)	9 (28.12)	10 (31.25)	□□□□□□□□□□

IV. MINIMALLY INVASIVE THERAPY

Carious lesions treatment has been linked to the available materials during the history of operative therapy. The preparation of the cavities was required to be extensive to retain the materials or to remove anatomical features that could retain dental plaque with the use of drilling instruments (high-speed and slow handpieces). [32,33]

The conventional therapy regards the drilling instruments and the complications are: over-preparation (removing larger amount of tissue) and under-preparation (leaving carious tissue to avoid the overextention) of the structure. [34]

Thanks to the evolution in biomaterials as well as in the knowledge of the caries process, dental treatment has arrive to the present focus on minimally invasive therapy. [35]

Chemo-mechanical caries removal

A new approach is the chemo mechanical removal of caries, with a product that selects the infected carious dentine for its remotion, avoiding pain and the unnecessary remotion of sound dentine and requires composites or glass ionomers that don't require a mechanical retention of the restoration. [36]

It comprises hand excavation method that removes only infected dentine and maintains the demineralized tissue for its remineralization with the goal to preserve the most tissue possible. [37]

Carisolv system

Carisolv system is a gel-based containing three amino acids (lysine, leucine and glutamic acid) and is designed to not affect healthy tissue. First introduced in Sweden, has been used during the last 15 years.

The reported advantages of the system are: equal caries removal efficacy, pain reduction during caries removal and the reduction of the need of local anesthesia, and the preservation of healthy dental tissue. The disadvantage is that it takes longer than the drilling instruments technique.

Carisolv has been projected specially in pediatric dentistry with great success, but little information is found about the in vivo efficacy against the rotatory instrumentation ("traditional therapy"). [38]

This findings drove us to search the current information in the literature and we developed a systematically review and a meta-analysis.

ANNEX II

Comparison of Carisolv system vs traditional rotating instruments for caries removal in the primary dentition: A systematic review and meta-analysis

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REVIEW ARTICLE

Comparison of Carisolv system vs traditional rotating instruments for caries removal in the primary dentition: A systematic review and meta-analysis

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Abstract

Objective. The purpose of this systematic review and meta-analysis was to evaluate the reliability of the Carisolv system with respect to drilling regarding the full removal of decayed hard tissues in primary dentition. A systematic review of the literature was conducted to identify controlled trails, randomized controlled trials and clinical trials that compared the Carisolv system to the traditional mechanical caries removal in the primary dentition. **Materials and methods.** The main relevant databases were searched: MEDLINE via PUBMED, Web of Science and SCOPUS. Complete caries removal, length of working time and need of local anesthesia were the outcomes evaluated. **Results.** A total of 195 studies were identified and complete analysis of 28 studies was performed; finally, 10 papers were included. The trials included involved a total of 348 patients for 532 treated teeth. There was no significant difference in terms of clinical efficacy between the Carisolv and the rotary instrument ($z = 0.68$, $p = 0.50$), whereas the treatment with Carisolv was significantly longer in terms of time with respect to the rotary instruments ($z = 10.49$, $p < 0.01$). The chemo mechanical technique reduces the need for local anesthesia, with a difference between two types of treatment near to statistical significance ($z = 1.91$ $p = 0.06$). **Conclusions.** This systematic review indicates that the clinical efficacy of chemo-mechanical removal with Carisolv seems as reliable as the rotary instruments. However, the results should be interpreted cautiously due to the heterogeneity among study designs and to the shortage of available data. Further large-scale, well-designed randomized controlled trials are needed.

Key Words: carisolv, chemo mechanical caries removal, dental caries, primary dentition, rotating instruments

Introduction

According to the World Health Organization [1], dental caries is defined as a localized, post-eruptive, pathological process of external origin, involving softening of the hard dental tissues and proceeding to the formation of a cavitation. Dental caries is one of the most commonly occurring diseases worldwide and its treatment has considerable implications in term of economic resources and biological costs [2].

In the past, carious lesions operative treatment was related to the knowledge of the disease pattern and the restorative materials that were available at that time [3]. In the late nineteenth century, the principle of 'extension for prevention' was proposed: cavity preparation required the loss of sound tissue, extending to anatomical sites that might otherwise encourage plaque accumulation [4]. Due to a deeper knowledge of the caries evolving processes and the coming of adhesive restorative materials, the approach to the disease switched from the 'broaden to prevent' era to 'minimally invasive dentistry' [5]. Modern restorative dentistry offers alternatives to the traditional tissue removal using drilling instruments: a possible alternative is the chemo mechanical removal.

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In 1976, the possibility of removing decayed material chemically, using N-monochloroglycine, was reported [6]. A few years later, the Caridex system was introduced as the first chemo mechanical method for caries removal [7]. The chemo mechanical method allows for saving of healthy tissue, providing, at the same time, the patient's comfort [8].

In 1998, a gel-based system used with specially designed non-cutting hand instruments was developed, its name is Carisolv©. This product selectively removes infected carious dentine. When the gel of three amino acids (lysine, leucine and glutamic acid); 53mM and the gel containing 0.27M hypochlorite are mixed, amino acids bind chlorine and form chloramines at a pH of 11. This chlorination affects the secondary and/or quaternary structure of the collagen, by disrupting hydrogen bonding and, thus, brings about proteolytic reaction. It does not affect healthy dentine because amino acids act as homing devices for active chlorine. The chlorine atom of hypochlorite is transferred to the amino group of each amino acid and in this way it is made less reactive and less aggressive to healthy tissue [9]. The chemo mechanical method of caries removal is considered useful, especially in pediatric dental practice, reducing the noise, vibration and pain produced by the use of high- and low-speed rotary instrument [10]. Other products for the chemo mechanical caries removal based on papaya plant extract (Papacarie and Carie-care) were launched on the dental market, but scarce scientific data are present on these products [11–13].

Few in vivo studies evaluate Carisolv© efficacy: the results seem to support the reliability of the chemo mechanical caries removal [9,10,14–18].

Therefore, this study aimed at systematically evaluating the current literature by means of a meta-analysis. The primary outcome variable of interest was the clinical efficacy in primary caries removal and secondary parameters were the clinical efficiency (treatment time) and patient's comfort (need of local anesthesia).

Materials and methods

This systematic review was performed following the guidelines of the Transparent Reporting of Systematic Reviews and Meta-Analyses (PRISMA) [19].

Focused PICO question

In primary dentition, what is the efficacy of Carisolv in caries removal rate (clinically appreciated) compared to the traditional drill technique, the clinical efficiency (treatment time) and patient's comfort (need of anesthesia)?

Eligibility criteria

The studies included in the present review are Clinical Trials, Randomized Clinical Trials and Controlled Trials assessing the efficacy on the primary dentition of Carisolv compared to traditional mechanical caries removal (control) with drilling instruments. Only studies where total caries removal in each group was completed using Carisolv systems or rotary instruments used without any time limit were considered eligible. The studies including other experimental groups in addition to Carisolv and drilling were also included in this review. Studies assessing the complete caries removal different from clinical criteria (i.e. using a sharp probe) were excluded.

Search strategy

For the identification of studies to evaluate for this review, a unique search strategy to be applied for each database research was developed (Figure 1). The following key words were used: Carisolv and Chemo mechanical Caries Removal. No Mesh term match was found. The terms were searched following the Boolean term 'OR' for a total of three inquiries.

Database research:

- MEDLINE via PUBMED (from 1948 to December 2014);
- Web of Science (from 1948 to December 2014); and
- SCOPUS (from 1969 to December 2014).

A comparison of the different searches was carried out to delete the repeated studies. Then, two authors (GL and CLC), on charge to evaluate the eligibility of the studies, examined independently all abstracts of the selected papers. If an abstract didn't supply enough information to determine if the paper met the inclusion criteria, the full report was obtained. All studies which appeared to meet the inclusion criteria were obtained in the full text format. The two authors assessed the papers independently, to establish whether or not the studies met the inclusion criteria. Disagreements were resolved by discussion. If not possible, other authors were consulted.

Data analysis

The outcomes considered in the studies were: the caries removal rate clinically appreciated (binary yes/no), the time required to complete the tissue removal (continuous) and the pain threshold during the procedure, assessed through the need for local anesthesia by patients (binary yes/no). When raw data was not available in the text, tables or graphs, single authors were contacted to obtain such information. To compare dichotomous data, a calculation of the Odd Ratio

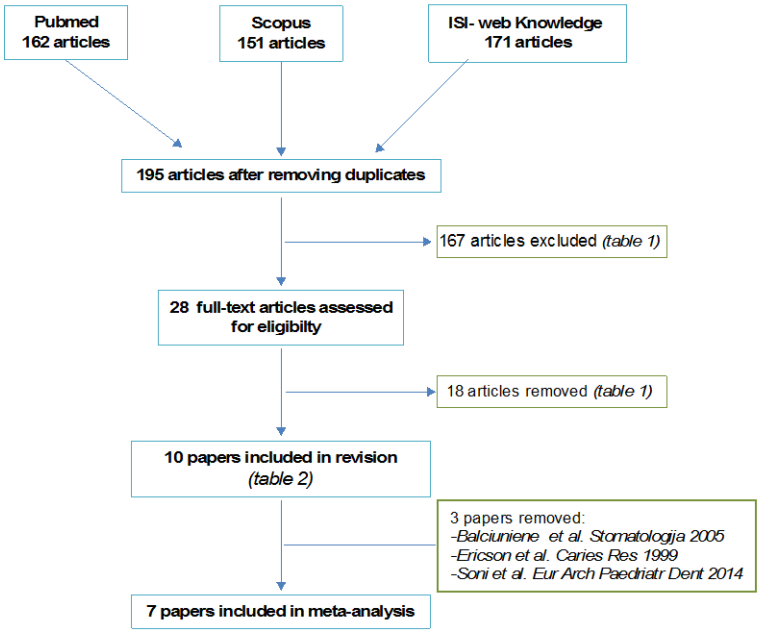

Figure 1. Flowchart of search strategy.

(OR) along with 95% Confidence Intervals (CIs) was used, whereas, for continuous data, the Mean Difference (MD) with 99% Confidence Intervals (CIs) was calculated. Also, for each comparison the Z-test was used. A random-effect model was applied to reassess all data extracted from the included studies.

Analysis was performed using Review Manager 5.3 software provided by the Cochrane Collaboration [20].

Results

A total of 195 studies published from 1999–2014 were identified and assessed (Table I). Twenty-eight papers were analyzed and 10 studies met the eligibility criteria (Table II).

The trials included in the review involved a total of 348 patients and 532 treated teeth. In three studies [14,16,21] it was not possible to extract the number of patients treated and so these studies were excluded.

From the selected studies, two were conducted in India [9,21], one in Venezuela [18], two in Greece [10,22], one in Lithuania [16], one in Serbia [15], one in Sweden [14], one in the US [23] and one in both Denmark and Portugal [17]. Two of the papers reported data from multi-center (Sweden; Denmark and Portugal) studies.

One of the studies had a crossover design [18], three were split mouth [16,17,22] and six had a parallel group design [9,10,14,15,21,23].

Most studies compared the Carisolv system [7] with the conventional rotary drill excavation for caries removal, but in three papers four different methods were reported [9,14,21].

In two studies no details about the operator and co-investigator were reported [9,21], in another two studies there was Testo one operator and one co-investigator [15,16], while in another one there was one operator and two co-investigators [18], in another one [10] two operators but no co-investigator and, finally, in two studies there was only one operator [21,23]. In one of the two multi-center studies there was one operator and one co-investigator for each center [14,17].

Six of the trials included only primary teeth [9,10,17,18,22,23] with participants' ages ranging from 28 months to 11 years. Four trials were carried out on permanent teeth also [14–16,21] and the ages of the subjects ranged from 30 months to 85 years.

In five trials [10,14–17] the teeth involved in the studies were molars and anterior primary teeth; in four studies [9,18,22,23] only primary molars with occlusal caries were treated; while in one study [21] primary molars were treated, but it was not mentioned which surfaces were treated.

Table I. List of excluded studies.

Authors	Year	Journal	Reason for exclusion	Authors	Year	Journal	Reason for exclusion
Ammari et al.	2014	Braz Oral Res	Microbiological study	Amaral et al	2011	Am J Dent	In vitro study
Boob et al.	2014	Int J Clin Pediatr Dent	In vitro study	Chang et al.	2011	Journal of Southern Medical University	Chinese language
Bussadori et al.	2014	Oral Health Prev Dent	In vitro study	Gugnani et al.	2011	J Conserv Dent	No group with Carisolv
Bussadori et al.	2014	J Contemp Dent Pract	No group with Carisolv	Imbronito et al.	2011	Int J Periodontics Restorative Dent	In vitro study
Garcia-Contreras et al.	2014	In vivo	In vitro study	Kochhar et al.	2011	J Clin Pediatr Dent	Evaluation with caries detector
Geetha Priya et al.	2014	J Indian Soc Pedod Prev Dent	No clinical evaluation	Li et al.	2011	J Dent	In vitro study
Gil-Montoya et al.	2014	Clin Oral Investig	Only permanent teeth	Neves Ade et al.	2011	J Dent	In vitro study
Hamama et al.	2014	Aust Dent J	Review	Neves Ade et al.	2011	Dent Mater	In vitro study
Hamama et al.	2014	J Endod	In vitro study	Neves Ade et al.	2011	J Dent	In vitro study
Jingarwar et al.	2014	J Clin Diagn Res	Review	Shabzendedar et al.	2011	J Contemp Dent Pract	In vitro study
Li et al.	2014	J Oral Rehabil	Review	Zawaideh et al.	2011	Pediatr Dent	In vitro study
Motta et al.	2014	J Appl Oral Sci	No group with Carisolv	Banerjee et al.	2010	J Dent	In vitro study
Pradeep Kumar	2014	Int J Pharma Bio Sci	No group with Carisolv	Gianini et al.	2010	Am J Dent	In vitro study
Schwendicke et al.	2014	J Dent	Review	Tsanova et al.	2010	Folia Med	In vitro study
Aggarwal et al.	2013	Aust Dent J	In vitro study	Yamada et al.	2010	J Clin Pediatr Dent	In vitro study
Banerjee	2013	Br Dent J	Review	Alleker et al.	2009	Int J Antimicrob Agents	Review
Bijle et al.	2013	J Contemp Dent Pract	Statistical survey	Bertassoni et al.	2009	Scanning	In vitro study
Cecchin et al.	2013	Braz J Oral Sci	In vitro study	Fure et al.	2009	Oral Health Prev Dent	No control group
Goomer et al.	2013	J Int Oral Health	Clinical eval caries detector	Kotb et al.	2009	J Clin Pediatr Dent	No group with Carisolv
Gupta et al.	2013	J Clin Pediatr Dent	No group with Carisolv	Martins et al.	2009	J Dent Child (Chic)	In vitro study
Hamama et al.	2013	Aust Dent J	In vitro study	Pai et al.	2009	J Conserv Dent	In vitro study
Juntavee et al.	2013	Int J Clin Pediatr Dent	In vitro study	Prabhakar et al.	2009	Pesqui Bras Odontopediatria Clin Integr	In vitro study
Kathuria et al.	2013	J Clin Diagn Res	In vitro study	Topaloglu-Ak et al.	2009	Clin Oral Investig	No control, no clin eval
Moldovanu et al.	2013	Rev Chim	In vitro study	Abdelnur et al.	2008	J Dent Child	Case report
Zenen et al	2013	Cumhuriyet Dent J	In vitro study	Barata et al.	2008	J Appl Oral Sci	Study in permanent teeth

Table I. (Continued).

Authors	Year	Journal	Reason for exclusion	Authors	Year	Journal	Reason for exclusion
Rajakumar et al.	2013	J Clin Pediatr Dent	No group with Carisolv	Bussadori et al.	2008	J Clin Pediatr Dent	Case report
Ramamoorthi et al.	2013	J Conserv Dent	In vitro study	Corra et al.	2008	J Clin Pediatr Dent	In vitro study
Venkataraghavan et al.	2013	J Int Oral Health	Review	Corra et al.	2008	Eur Arch Paediatr Dent	In vitro study
Viral et al.	2013	J Clin Pediatr Dent	In vitro study	Guar et al.	2008	Spec Care Dentist	No clinical evaluation
Yildiz et al.	2013	Eur J Paediatr Dent	In vitro study	Gurbuz et al	2008	Eur J Dent	In vitro study
Zhang et al.	2013	Aust Dent J	In vitro study	Hosein et al.	2008	J Coll Physicians Surg Pak	Only permanent teeth
Ahmed et al.	2012	Caries Res	In vitro study	Piva et al.	2008	Braz Oral Res	In vitro study
Anegundi et al.	2012	Contemp Clin Dent	No group with Carisolv	Perić et al.	2008	Srpski Arhiv za Celokupno Lekarstvo	No data
Arora et al.	2012	Eur Arch Paediatr Dent	In vitro study	Rupf et al.	2008	J Dent Res	In vitro study
Avinash et al.	2012	J Indian Soc Pedod Prev Dent	In vitro study	Subramaniam et al.	2008	J Clin Pediatr Dent	Microbiological study
Azzouz et al.	2012	SJKFU	Only permanent teeth	Tachibana et al.	2008	Lasers Med Sci	In vitro study
Banerjee	2012	Ann R Australas Coll Dent Surg	Review	Yamada et al.	2008	J Dent	In vitro study
Bhardwaj et al.	2012	RJPBCS	No clinical study	Corra et al.	2007	J Clin Pediatr Dent	In vitro study
El-Tekeya et al.	2012	Pediatr Dent	In vitro study	De Oliveira et al.	2007	Journal of Adhesion	In vitro study
Galuscan et al.	2012	Rev Chim	Clin evalu with caries detector	Giza	2007	Ann Acad Med Stetin	Polish language
Kumar et al.	2012	Indian J Dent Res	No control group	Inglehart et al.	2007	J Am Dent Assoc	No clinical evaluation
Schlafer et al.	2012	J Nat Prod	In vitro study	Kirzioglu et al.	2007	Clin Oral Investig	No control group
Singhal et al.	2012	Indian J Dent Res	In vitro study	Okida et al.	2007	Braz Oral Res	In vitro study
Sirin Karaarslan et al.	2012	J Dent	In vitro study	Pandit et al.	2007	J Indian Soc Pedod Prev Dent	No control group
Verma et al.	2012	J Indian Soc Periodontol	In vitro study	Peric T et al.	2007	Eur J Paediatr Dent	In vitro study
Yamada et al.	2012	J Clin Pediatr Dent	In vitro study	Topaloglu-Ak	2007	J Appl Oral Sci	Endodontic study
Zhao et al.	2012	Chinese Journal of New Drugs	No clinical evaluation	Topaloglu-Ak et al.	2007	J Appl Oral Sci	No control group
Yamada et al.	2007	J Clin Pediatr Dent	In vitro study	Kakaboura et al.	2003	Quintessence Int	Only permanent teeth
Antonio et al.	2006	J Oral Sci	Study on the bovine	Kinoshita et al.	2003	J Clin Laser Med Surg	In vitro study
Bonsor and Pearson	2006	Dent Update	Microbiological study	Lager et al.	2003	Caries Res	In vitro study

Table I. (Continued).

Authors	Year	Journal	Reason for exclusion	Authors	Year	Journal	Reason for exclusion
Clementino-Luedemann et al.	2006	Dent Mater J	In vitro study	Lumbau et al.	2003	Minerva stomatol	No clinical evaluation
Dammaschke et al.	2006	Aust Dent J	Study on the rats	Rafique et al.	2003	Caries Res	Only permanent teeth
De Magalhaes et al.	2006	Braz Dent J	In vitro study	Sakoolnamarka et al.	2003	Am J Dent	In vitro study
Grisi et al.	2006	Braz Dent J	In vitro study	Tonami et al.	2003	J Med Dent Sci	In vitro study
Lennon et al.	2006	Oper Dent	In vitro study	Yazici et al.	2003	J Oral Rehabil	In vitro study
Lenters M et al.	2006	Eur Arch Paediatr Dent	Full text not available	Arvidsson et al.	2002	J Dent	In vitro study
Marquezan et al.	2006	Braz Oral Res	Review	Arvidsson et al.	2002	Biomaterials	In vitro study
Meller et al.	2006	Eur J Paediatr Dent	In vitro study	Dammaschke et al.	2002	J Dent	Study on the rats
Mhaville et al.	2006	Eur Arch Paediatr Dent	Clinical evaluation with RX	Kubo et al.	2002	Oper Dent	In vitro study
Roeleveld et al.	2006	Eur Arch Paediatr Dent	No clinical evaluation	Nemes et al.	2002	Fogorvosi szemle	Review
Sabola et al.	2006	Oper Dent	No clinical evaluation	Sakoolnamarka et al.	2002	Aust Dent J	In vitro study
Bussadori et al.	2005	J Clin Pediatr Dent	No group with Carisolv	Yazici et al.	2002	Oper Dent	In vitro study
Dammaschke et al.	2005	Acta Odontol Scand	In vitro study	Arvidsson et al.	2001	Gerodontology	In vitro study
El-Kholany et al.	2005	J Adhes Dent	In vitro study	Beeley et al.	2001	Ned Tijdschr Tandheelkd	Review
Fickiger et al.	2005	J Dent	In vitro study	Dammaschk et al.	2001	J Dent	Study on the rats
Hosoya Y et al.	2005	J Dent	In vitro study	Hosoya et al.	2001	J Dent	In vitro study
Hu et al.	2005	Med J Wuhan Uni	In vitro study	Ilewicz et al.	2001	Acta Pol Toxicol	In vitro study
Lima et al.	2005	J Appl Oral Sci	Microbiological study	Maragakis et al.	2001	Int Dent J	Review
Morrow et al.	2005	Am J Dent	In vitro study	Munshi et al.	2001	J Clin Pediatr Dent	No control group
Rahman et al.	2005	Int Endod J	Study on the ovine	Nadanovsky et al.	2001	Caries Res	Only permanent teeth
Sakoolnamarka et al.	2005	Aust Dent J	In vitro study	Splieth et al.	2001	Clin Oral Investig	In vitro study
Sonoda et al.	2005	J Dent	In vitro study	Yamada et al.	2001	J Clin Laser Med Surg	In vitro study
Yamada et al.	2005	J Clin Pediatr Dent	In vitro study	Young et al.	2001	J Dent	Study on the rats
Yazici et al.	2005	Quintessence Int	In vitro study	Banerjee et al.	2000	J Dent	In vitro study
Zeeswitz et al.	2005	Schweizer Monatt fr Zahnmedizin	German language	Beeley et al.	2000	Br Dent J	Review
Ziskind et al.	2005	Quintessence Int	Review	Fure et al.	2000	Caries Res	Only permanent teeth
Arvidsson	2004	Acta Odontol Scand	In vitro study	Haak et al.	2000	Eur J Oral Sci	In vitro study

Table I. (Continued).

Authors	Year	Journal	Reason for exclusion	Authors	Year	Journal	Reason for exclusion
Azrak et al.	2004	Int J Paediatr Dent	Microbiological study	Morrow et al.	2000	Dent Update	Full text not available
Berto et al.	2004	Gen Dent	Study on the rats	Yamada et al.	2000	J Clin Laser Med Surg	In vitro study
Bulut et al.	2004	J Dent	In vitro study	Cederlund et al.	1999	Acta Odontol Scand	In vitro study
Erhardt et al.	2004	Quintessence Int	In vitro study	Cederlund et al.	1999	Int J Periodontics Restorative Dent	In vitro study
Fure et al.	2004	Clin Oral Investig	Only permanent teeth	Hannig	1999	Clin Oral Investig	In vitro study
Grbz T	2004	Pain Clinic	No clinical evaluation	Banerjee et al.	2000	Caries res	In vitro study
Hahn et al.	2004	Caries Res	In vitro study	Banerjee et al.	2000	Br Dent J	In vitro study
Sepet et al.	2004	J Dent	In vitro study	Wennerberg et al.	1999	Eur J Oral Sci	In vitro study
Al-Kilani et al.	2003	Int Endod J	In vitro study	Lai	1990	Rivista italiana di odontoiatria infantile	
Ansari et al.	2003	J Oral Rehab	No clinical evaluation	Bianchi et al.	1989	Dental Cadmos	In vitro study
Beyth et al.	2003	Refuat Hapeh Vehashinayim	Review	Bianchi et al.	1989	Dental Cadmos	Only permanent teeth
Burrow et al.	2003	Aust Dent J	In vitro study	Scheutzel	1989	Deutsche zahnarztliche Zeitschrift	German language
Cehreli et al.	2003	J Dent	In vitro study	Goldman et al.	1988	J Pedod	In vitro study
Chaussain-Miller et al.	2003	Clin Oral Investig	Only permanent teeth	Anusavice et al.	1987	J Dent Res	No clinical evaluation
Fritz	2003	J Orofac Orthop	Review	Moriot	1986	Le Chirurgien-dentiste de France	Full text not available
Hossain et al.	2003	Oper Dent	In vitro study				

Table II. Summary of the characteristics of the included study.

Author (year)	Patients characteristics	Carisolv/drill	Interventions: Study design	Interventions: Carisolv	Interventions: Drill	Outcomes (Carisolv/drill): Clinical efficacy	Outcomes (Carisolv/drill): Time taken	Outcomes (Carisolv/drill): Need for anesthesia
Soni et al. (2014)	120 patients (4–14 years); 120 primary and permanent teeth.	30/30	RCT parallel group	30 Carisolv/special hand instrument until cavity was hard on probing	Rotary instruments until the cavity clinically caries free			
Bohari et al. (2012)	120 patients (5–9 years); 120 primary teeth. Lesion dentine/ occlusal surfaces	30/30	RCT parallel group	30 Carisolv/special hand instrument until cavity was hard on probing	Rotary instruments until the cavity clinically caries free		474.7–43.0 s (30)/ 206.7–22.1 s (30)	
Peric (2009)	120 patients (3–17 years); 74 primary teeth. At least one primary carious lesion	40/34	RCT parallel group	30 Carisolv/special hand instrument until cavity was hard on probing	Rotary instruments until the cavity clinically caries free. The cavity checked by an operator		648–162 s (40)/ 432–84 s (34)	
Peters et al. (2006)	50 patients (6–11 years); 50 primary molars. One primary occlusal carious lesion for each tooth.	26/24	RCT parallel group	30 Carisolv/special hand instrument until cavity was hard on probing. Time limit was 15 min	Rotary instruments until the cavity clinically caries free. Time limit was 15 min		604.2–227.5 s (26)/60.7–84 s (24)	
Lozano-Chourio (2006)	40 patients (7–9 years); 80 primary teeth. At least two caries in primary molars	40/40	RCT cross-over design	30 Carisolv/special hand instrument until cavity was hard on probing. The cavity checked by an operator	Rotary instruments until the cavity clinically caries free. The cavity checked by an operator	100% (40 of 40)/ 100% (40 of 40) caries free	450.6–109.8 s (40)/ 148.2–126 s (40)	0% (0 of 40)/ 5% (2 of 40)
Balciuniene (2005)	30 patients. (2.5–13 years); 60 primary and permanent teeth. At least two lesions	30/30	Controlled clinical trial split mouth design	30 Carisolv/special hand instrument until cavity was hard on probing. The cavity checked by an independent examiner	Rotary instruments until the cavity clinically caries free. The cavity checked by an independent examiner			

Table II. (Continued).

			Interventions		Outcomes (Carisolv/drill)			
Author (year)	Patients characteristics	Carisolv/drill	Study design	Carisolv	Drill	Clinical efficacy	Time taken	Need for anesthesia
Kavvadia et al. (2004)	31 patients (28 months–9 years); 92 primary teeth. At least one primary carious lesion	65/27	Controlled clinical trial parallel group	30 Carisolv/special hand instrument until cavity was hard on probing. The cavity checked by two operators	Rotary instruments until the cavity clinically caries free. The cavity checked by two operators	100% (65 of 65)/ 100% (27 of 27) were caries free	486–318 ss (65)/ 166–114 s (27)	2.3% (1 of 43)/ 23.5% (4 of 17) requested anesthesia
Bergmann et al. (2005)	46 patients (4–11 years); At least two active dentinal caries lesions in primary teeth	46/46	RCT split mouth design. A multi-center study	30 Carisolv/special hand instrument until cavity was hard on probing. The cavity checked by an operator one for each center	Rotary instruments until the cavity clinically caries free. The cavity checked by an operator one for each center	100% (46 of 46)/ 97.8% (45 of 46) were caries free	402–174 s (46)/ 198–138 s (46)	
Maragakis et al. 2001	16 patients (67–109 months); two contralateral primary molar with occlusal primary decay	16/16	Controlled clinical trial split mouth design	Application of Carisolv/special hand instrument until cavity was hard on probing. The cavity checked by an operator. Time limit was 15 min	Rotary instruments until the cavity clinically caries free. Time limit was 15 min			
Ericson et al. (1999)	137 patients. (3–85 years). At least one active dentinal primary caries	16/1	RCT parallel group multi-center study	20 Carisolv/special hand instrument until cavity was hard on probing. The cavity checked by an operator	Rotary instruments until the cavity clinically caries free. The cavity checked by an operator		618–336 s (16)/no data	

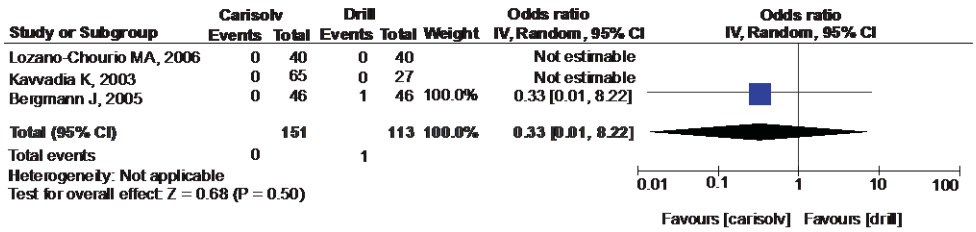

Figure 2. Forest plot of comparison: Individual and overall Odds Ratio in the comparison of clinical efficacy between the Carisolv group and the rotary instrument group.

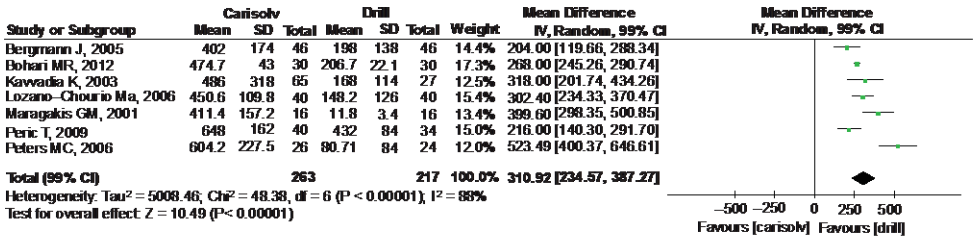

Figure 3. Forest plot of comparison: Individual and overall Mean Difference in the comparison of time taken between the Carisolv group and the rotary instrument group.

Data regarding the clinical efficacy in decayed tissue removal of the Carisolv system vs a control group were obtained from three papers [10,17,18], with a total of 264 analyzed teeth. Complete caries removal was obtained in 100% (151 of 151) of the teeth using Carisolv and 99.2% (112 of 113) using the drill. When data were combined in meta-analysis, the summary OR was 0.33 (99% CI = 0.00–22.65). On the basis of the available evidence, there was no statistically significant difference in caries removal between the chemomechanical system (Carisolv) and the rotary instruments (z = 0.68 p = 0.50) (Figure 2).

Data on the time required (seconds) to complete the procedure (mean ± SD) was obtained from seven studies [9,10,15,17,18,22,23] with a total of 480 teeth involved. The maximum time required for caries removal was 648 s for Carisolv and 206.7 s for the rotary instrument, whereas the minimum time of treatment was 402 s for the chemo mechanical removal and 80.7 s with the use of drills. The chi-square value was 48.38, with six degrees of freedom (df) and $p < 0.01$. The treatment with Carisolv required a statistically significant greater time amount than that required with the use of rotary instruments. The z-test for overall effect for the Carisolv group vs rotary instruments was $z = 10.49$, $p < 0.01$ (Figure 3).

Finally, data regarding the pain threshold were obtained from four studies only [10,18,22,23] with a total of 222 teeth involved. With the Carisolv system, 4% of the children requested local anesthesia, while 26.8% used the conventional method. When data were combined in meta-analysis, the summary OR was 0.09 (95% CI = 0.01–1.07) with a difference between two types of treatment near to statistical significance (z = 1.91, p = 0.06), with fewer patients who needed local anesthesia in the Carisolv group (Figure 4).

Discussion

A multitude of technique and materials are proposed in the dental market to use in restorative dentistry and so the need of a strong scientific evidence for the 'new' methods is essential before their use in everyday practice.

Carisolv was introduced in the dental market (Sweden) in 1998 [9] and during the last 15 years it has been used almost exclusively in pediatric dentistry; as the use of Carisolv in clinical practice might be limited because of the material cost [24]. In the literature, there is no availability of systematic review on the efficacy of Carisolv system in caries removal in primary dentition. Hence, this meta-analysis review was performed in an attempt to gain further insight into the reliability of the Carisolv system. Seven studies were included, with a total of 450 primary teeth involved. The heterogeneity of the results generated by different studies on the use of Carisolv limits an overall correlation among outcome variables.

The parameter to evaluate the effectiveness of the Carisolv against rotary instruments was the caries removal rate, clinically appreciated. This evaluation

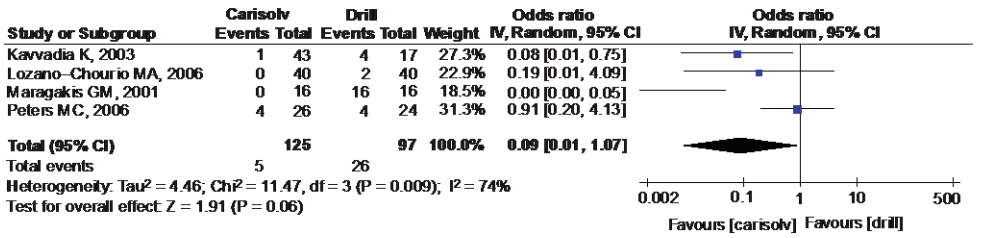

Figure 4. Forest plot of comparison: Individual and overall Odds Ratio in the comparison of need for anesthesia between the Carisolv group and the rotary instrument group.

method seems empirical and inaccurate, however it is the main and simple approach to check the caries removal [25]. This method only required a visual estimation and a tactile evaluation using a sharp probe. Other methods to evaluate the complete caries removal, like caries detectors, are a matter of controversy in the literature [26].

The comparison of the clinical evaluations data indicated that no statistically significant difference exists between the Carisolv group and the control group with rotary instruments in terms of caries removal efficacy.

Outcomes regarding the time required to complete the procedure were reported in five of seven studies selected. There was a significant difference regarding time required by the Carisolv procedure and the conventional drilling: treatment time was statistically significantly longer using Carisolv than drilling. This difference was related to the need of multiple applications of Carisolv gel, especially when big carious lesions were treated. Only one paper reported that the lesions in both groups were similar in terms of size, but the time taken for caries removal using Carisolv was 3-times longer [18]. A previous clinical investigation [27] found the depth of carious lesions was an important parameter for the excavation time with Carisolv.

Pain is a commonly reported phenomenon when removing dental caries and the use of local anesthesia is often required. Data on pain threshold or need of local anesthesia were reported in four papers. Carisolv seems to reduce the use of local anesthesia and this difference may be related to the use, together with Carisolv gel, of sharp hand instruments. However, it is necessary to consider that the four studies were heterogeneous in design and the Carisolv group was more numerous than the control group.

Conclusion

Within the limitations of the available data, the clinical efficacy of chemo mechanical instruments in caries removal with Carisolv seems as reliable as that obtained using rotary instruments. Data analysis suggests that the difference in terms of time taken was statistically significant: the Carisolv system takes more time than the traditional method to remove dental caries. Regarding patient's comfort, this systematic review indicates that the Carisolv system can reduce the use of local anesthesia. However, these results should be interpreted cautiously due to the heterogeneity among study designs and to the shortage of data usable. To confirm these conclusions there is the need of further large-scale, well-designed RCTs.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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V. BEHAVIORAL AND SOCIO-CULTURAL RISK FACTORS

The significant role of socio-behavioral and environmental factors in oral disease has been studied as it's surveillance and the analysis of the patterns of risk is elemental to plan and evaluate preventive programs in the community to promote oral health.

Every culture has its own identity and traditions and the socio-economic status determine the access to health services and the early treatment and surveillance of the disease benefits a small part of the population especially in developing countries. To understand the relationships among behavioral and socio-cultural factors is essential to improve the oral health status, especially when it comes to unprivileged populations. [39]

Diet

The main cause of tooth loss is dental caries in which diet plays an important role as the ingestion of sugars and carbohydrates results in the fall of the dental plaque pH that causes demineralization of the tooth making it susceptible to the acid attack and therefore to caries. [40] As well, the consumption of sugars is a risk for obesity and the correlation with dental diseases are currently been evaluated.

BMI

Body Mass Index (BMI) is an index used to classify underweight, overweight and obesity and is defined as the weight in kilograms divided by the square of the height in meters (kg/m^2). The health risks associated with increasing BMI are continuous and the interpretation of BMI grading in relation to risk may differ for different populations so its important to report information about the associations. [41]

The relationship between the Body Mass Index (BMI) and oral conditions such as caries and periodontal disease has been studied. The relationship between BMI and socioeconomic status is a question that has been of interest for the researchers. A diet rich in fat and sugar and overweight are considerable aspects but it is also malnutrition.

Indeed, malnutrition could also predispose to dental caries as deficiencies in protein or energy foods may lead to protein-energy malnutrition, decreased salivary flow, calculus formation and high levels of caries. [42] Many studies haven't found any significant association between the body mass index and dental caries in adolescents belonging to different backgrounds and different countries like the US, France or India. [43-46] Actually, some studies have reported that obese children were less likely to present caries. [46-47] To contrast, some studies describe a significant relationship exists between overweight and caries experience especially in children from developed countries. [48]

There is evidence that dental caries is associated with both high and low BMI yet significant disagreement still exist regarding the real relationship between dental caries and BMI.

Poverty as a risk factor

It is indisputable that the vast majority of clinical research findings published in the medical literature are the product of studies conducted in industrial nations rather than in the developing world, but it may be time to cross borders as the developing area constitutes 80% of the world's population. [49]

Communities in less developed regions share common characteristics such as being relatively young and exhibiting a traditional age pyramid, large families, live in close proximity and, in rural communities, population influx is extremely low. To focus more on these rural and isolated communities there is considerably socio-economic and thus environmental homogeneity that minimizes the potential impact of confounding factors for data interpretation.

In less developed countries, access to dental care in rural communities, when available, is invariably limited to extractions for tooth pain, so that treatment experience is universally restricted and in epidemiological research, a beneficial consequence is that valuable information is conserved so we can expand knowledge about the progression of the disease itself. [49]

Caries status in Latin America

Latin-American countries have a common socio-cultural background and present disparities in the distribution of wealth. The important factor of these differences in the maintenance of health and understanding the health status of unprivileged populations is fundamental.

Trends of dental caries in Latin American and Caribbean children and adolescents are diverse. There is a clear downward trend in caries severity between 1970 and 2000. The mean DMFT in Mexico was reported to be as high as 4.6 (SD 3.2) and as low as 2.8 (SD 2.9) in 1987 and 2.5 (SD 2.4) in 1997. In Brazil, the trend changed from 9.2 in the 70's to 6.3 in 1997. Mean DMFT in Argentina, Uruguay, Dominican Republic and Panama was of 3.2, 4.2, 5.5 and 4.1 respectively. [50]

These analysis was the rationale to evaluate the oral health status of children in two contrasting populations in Mexico, an urban and a rural, to understand the status of the disease and the corresponding risk factors associated with the disease.

ANNEX III

Differences on the impact of BMI and behavioural factors on dental caries in Mexican urban and rural populations: a comparative study

International Journal of Paediatric Dentistry - manuscript proof

INTERNATIONAL JOURNAL OF
PAEDIATRIC DENTISTRY

Differences on the impact of BMI and behavioural factors on dental caries in Mexican urban and rural populations: a comparative study.

Journal:	*International Journal of Paediatric Dentistry*
Manuscript ID	Draft
Manuscript Type:	Original Article
Keywords:	caries, BMI, children, Latin America, ICDAS

Summary

Background: Caries and overweight are related to common risk factors and behaviours.

Aim: To elucidate the impact of BMI on caries in two different Mexican populations (urban/rural) and analyse the relationship between behavioural factors/disease.

Design: Children from Veracruz city (UA) and town Tepancan (RA). Caries was recorded (ICDAS) and Body Mass Index (BMI) was calculated (kg/m^2) and classified (normal weight/overweight). Oral habits (toothbrushing/flossing/check-ups) and dietary patterns (sweet intake) were assessed. A dummy variable (BMI/Area) was generated. Data were analyzed (STATA) and a multinomial logistic regression model (MLRM) was run (dependent variable ICDAS).

Results: Four hundred sixty-four 12-15-year-old participated (UA=224; RA=240). BMI and area of residence were significantly associated (χ^2=12.59 p<0.01). Area was also associated to caries severity (χ^2=24.23 p<0.01) with highest number of dentin caries in RA. BMI/Area was related to caries severity (χ^2=27.47 p<0.01): more overweight with dentin caries (n=14.46%) in RA. UA recorded higher prevalence of enamel caries and lower of dentin (p<0.01), better oral habits but superior sweet intake (p=0.04). BMI/Area was significantly associated to caries (MLRM)(p<0.01).

Conclusions: BMI was not indicative for the overall population respect to caries yet when associated with the area overweight was a significant risk factor for caries severity in RA children.

Introduction

Great improvements have been accomplished in oral health all over the globe, yet in under-privileged populations, both in the developed world as in developing countries, this remains to be addressed.[1] The aetiology of caries is complex[2]. The fundamental etiological factor is diet; the consumption of sugars and fermentable carbohydrates results in dental plaque pH decrease that results in demineralization[3]. In fact, the intake of sugared foods and drinks is a common behavioural risk factor that caries and obesity share[4] and its significant association have been mainly studied in the young population of industrialized countries[5] with the help of an index that classifies and interprets weight and height (Body Mass Index)[6].

Another important factors are oral hygiene habits; self-efficacy to perform a correct toothbrushing practice as well as the access to regular dental check-ups is related with the improvement of oral health conditions[7] .

Even though the prevalence of oral disease has declined, in Latin American countries such as Mexico caries is still a health policy problem connected with economic, educational, and social inequalities, affecting a prevalently young population[8,9]. The caries prevalence in this age group oscillates from 38.0% to 98.0%[10,11] influenced by multiple variables as the area of residence. In the rural areas of Mexico, the presence of caries has been reported to be higher than in the urban areas[12]. Indeed, rural populations present worse oral health conditions due to the higher percentage of poverty and lower health and dental care access than urban populations; in Mexico, this represents over 15 million people[13,14]. It is crucial to understand the risk factors and their relationship with the oral health status in order to plan and perform preventive strategies[15].

Populations in less developed regions have some similar common characteristics and behaviours like a traditional age pyramid, families live in proximity and, especially in rural communities, population influx is usually low. In rural areas an environmental and socio-economic homogeneity is present respect urban areas or industrial countries[16].

Starting from these premises, a cross-sectional study was designed with the aim to elucidate the

impact of overweight (BMI) on caries disease in two different Mexican adolescent populations: urban and rural. Ancillary aim was to analyse the relationship between caries related background patterns (behavioural factors) and disease.

Materials and methods

Study population

Urban Area (UA): Subjects living in the industrial city of Veracruz, Veracruz, Mexico attending middle school. The population consisted of 224 children.

Rural Area (RA): Subjects sharing a common background and socio-economic status living within the area of Tepancan, a township of the State of Veracruz, enrolled in a rural middle school system. The population consisted of 240 children.

The reported fluoride concentration in drinking water in the two areas was well under the recommended level of <0.7 mg/L (0.15 mg/L in UA and 0.24 mg/L in RA)[17].

The study was approved by the Secretary of Education of Veracruz. For both groups, the parents signed an informed consent.

Clinical Examination

Height (cm) and weight (kg) were measured by one operator (CLC) using a mechanical physician scale with integrated measuring rod (Rice Lake RL-MPS, WI, USA) and scored in meters and kilograms, respectively. BMI then was calculated dividing the weight by the square of the height (kg/m^2), according to WHO criteria[6]. Caries was recorded according to the ICDAS criteria[18]. Each subject was examined inside the school under natural lighting using a mouth mirror No. 5 and a WHO explorer.

Questionnaire

A pre-tested questionnaire was administered to each subject. The questionnaire was divided into three domains: (1) vital statistics; (2) dietary patterns *i.e.* description of meals, consumption of

sugared drinks and sweets as snacks; (3) oral hygiene habits *i.e.* toothbrushing habits, the frequency of dental floss and the frequency of dental check-ups.

Data analysis

Evidence from the clinical examination and questionnaire was entered in the FileMaker Pro 9.0 Runtime database and then exported to Excel Microsoft spread sheet. The children were classified into two age groups: 12-13 years olds and 14-15 years olds. Body Mass Index was classified for the respective age group as: Normal weight (>15 – 21 and >16 – 23 respectively for the two age groups) and overweight (>21 and >23) according to the WHO guidelines[19]. Dental examination data were treated as numerical ordinal data for ICDAS (ICDAS=0 healthy; ICDAS=1-3 enamel caries; ICDAS=4-6 dentin caries). Subjects affected by systemic diseases like diabetes, asthma, cardio-vascular diseases, etc. were classified as not in good general health.

Questionnaire data were categorized as follows: the toothbrushing frequency was split in “once a day”, “twice a day” and “more than twice a day”; the use of dental floss into “irregular” if less than once a day and “regular” if at least once a day; the frequency of dental check-up as “irregular” if only when in pain and “regular” if attended scheduled check-ups. The consumption of sugared drinks was divided into “never”, “less than twice a day” and “more than twice a day” and sweets was divided into “never”, “less than 3 times a day” and “over 3 times a day”.

Descriptive statistics cross tabulations and linear trends were calculated for normal weight and overweight, caries severity (ICDAS) and area of residence, gender, age, toothbrushing frequency, use of dental floss, dental check-ups, consumption of sugared drinks and sweets as snacks. The process of handling the data allows discovering that overweight and area were statistically associated, therefore a dummy variable as the sum of overweight data and area was generated (“BMI/Area”).

Next, multinomial logistic regression models were performed using ICDAS scores as the dependent variable. The Akaike information criterion (AIC) was used to measure the goodness of fit of the

statistical model[20]. The possible modifying effects of covariates on the outcomes were tested by an interaction model (likelihood ratio test statistic). Multicollinearity might sometimes cause problems with regression results. This problem was solved using the DFBETA command in STATA, dropping the information that have too much influence on the regression line. However, after the data elaboration, no statistically significant multicollinearity was observed and so it was decided to report findings without outliers. All data were analyzed using the software STATA (Mac version 10.1). For all analyses, the statistical significance level was set at α=0.05.

Results

A total of 464 children (251 males and 213 females, mean age 13.5±0.9) participated in the study (224 urban; 240 rural). The ICDAS and BMI scores are displayed in figure 1. Caries figures were higher in the RA groups regarding ICDAS 4-6 respect to UA (6.68% vs 1.94%). The sample distribution across BMI and caries disease by area is displayed in Table 1. BMI and Area were statistically significant associated (χ^2=12.59 p<0.01), while in UA the sample was perfectly split in two (normal and overweight), in RA the number of overweight subjects was double (n=159) respect to those with normal weight (n=81). The area of residence was statistically associated (χ^2=24.23 p<0.01) to caries severity with the highest number of subjects with dentin caries in the RA group; in the overall population BMI was not statistically related to caries severity.

The variable BMI/Area was associated to caries severity (χ^2=27.47 p<0.01) *i.e.* the percentage of overweight subjects with dentin caries (14.46%) living in RA was higher than the percentage of normal weight subjects with dentin caries (6.25%) living in UA.

ICDAS scored 0 for 129 children from UA and 159 from RA. Urban subjects had a higher prevalence of enamel caries compared to the rural population (38.39% and 20.76%) and a lower prevalence of dentin caries lesions (4.02% and 12.86%, respectively) (p<0.01). The relationship between dental check-ups and caries was relevant only in the urban population (p<0.01). The distribution of behavioural habits was more homogeneous in RA than in UA (*data not in tables*).

Consumption of sweets was higher in UA (p=0.04). The consumption of sweets was null for 19.61% of the population, moderate for 65.96% (1 to 3 times a day) and high for 14.43% (>3 times a day). On the other hand, 9.27% of the children did not consume any sugared drinks, while 46.12% had a high intake. The relationship between both irregular flossing and higher number of enamel caries and poor general health and dentine caries was statistically significant (Table 2).

Using the multinomial logistic regression model with ICDAS as dependent variable (0 = no caries; 1= enamel caries and 2= dentin caries) including BMI/Area, Good General Health and Flossing ($p<0.01$), the BMI/Area variable was always reported to be significant respect to enamel and dentinal caries ($p<0.01$). Flossing was statistically significant in the presence of enamel caries (p=0.02), while health status was related to dentin caries (p=0.02) (Table 3).

Discussion

The main goal of this paper was to elucidate the impact of BMI on caries disease in children living in urban and rural area of Mexico. The results failed to establish a statistical impact of BMI on caries disease for the overall population; however the area of residence was statistically significant associated to BMI and to caries severity (ICDAS score) and the association was even higher when BMI and living area were put together in a single variable. In literature there are described dissent results on the relationship between caries disease and overweight[21-25]. The lack of association between overweight and dental caries was reported mainly in Latin American countries respect to Europe[26]. Population's access to oral health services, the availability of fluoridated substances, socioeconomic status and dietary habits may lead to a negative or positive association between obesity and caries presence.

Diet plays an important role in overweight and obesity development due to the higher consumption of foods rich in fat and carbohydrates[27]. Diet plays an important role in caries too, since foods and drinks rich in fermentable carbohydrates are metabolized by cariogenic bacteria in acids[28]. Dietary habits of children are strongly related to the socio-economic status of the family and to the

geographical location (northern/southern side of the High Atlas range) and area of residence (urban/rural)[29]. In this survey BMI and area of residence were statistically significant associated with caries severity (ICDAS). Overweight subjects in the rural area had more caries in dentin than the rest of the sample, while normal weight subjects that lived in urban area presented more enamel caries. In the rural area, overweight subjects were twice more respect to normal weight. A possible reason may be that although this agriculture society has maintain the traditional dietary habits (based mainly in corn, rice and beans), subjects have also access to refined sugar; moreover they have adopted a more sedentary lifestyle similar to modern cultures so the intake and burning of food is not balanced.

Behavioural factors differed in urban and rural area. Urban subjects reported better oral hygiene habits and frequent check-ups, but a higher consumption of sugars as snacks and soft drinks; in this group a higher number of caries lesions was also recorded. In the rural area on the other hand, a lack of health service facilities and inadequate oral hygiene habits were reported, and this explains why even if the number of lesions was lower, when present, the severity was higher: in fact, the number of dentin caries was more than the triple respect to those recorded in children living in urban area. These results suggest also that in the balance between risk and protective factors for caries development, diet has a higher weight than oral hygiene habits.

It is possible to speculate about the existence of an environmental homogeneity in the rural area, compared to what is found in the urban area, that reduces the impact of confounding factors on data analysis and interpretation[17]. These results suggest that different actions are needed to be taken to address the presence of oral disease not only generally but within the same country and region[30].

Conclusions

BMI was not indicative for the overall population respect to caries disease; yet when associating it with the area, overweight was a statistically significant risk factor associated to the severity of caries in the rural population.

Higher caries prevalence with lower severity was observed in children from urban area despite adequate oral hygiene habits and frequent dental check-ups were reported; this caries figure was probably linked to the higher consumption of sugared food and drinks recorded in this population. Lower number of caries lesions but at higher severity was recorded in children from rural area probably related to the lack of adequate oral hygiene habits and limited access to oral health services.

Bullet points

Why this paper is important to paediatric dentists?

- Overweight and caries shared diet as a risk factor affecting more children everyday due to the change of lifestyle not only in western countries but globally and it is necessary to report the distribution and involved risk factors from children worldwide.
- Children from urban and rural areas in a developing country as Mexico have different behaviours, so different preventive actions need to be taken to address the presence of oral disease not only within the same country but also within the same region.
- Homogeneity in rural areas may reduce misinterpretation on data analysis and therefore provide answers about the problematic in this child population where oral health status is related to the lack of treatment feasibility and the impact of the environment.

Disclosure Statement

The authors declare they have no affiliations or financial interest in this manuscript, or any source of conflict of interest.

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Legends

Table 1. Sample distribution across weight and caries disease (ICDAS) by area. Caries severity (ICDAS 0=caries-free, ICDAS 1/3= enamel caries, ICDAS 4/6= dentin caries) according to the area (Urban/Rural), BMI (Normal weight/overweight) and BMI/Area as a single variable.

Table 2. Sample distribution across caries severity. Distribution according to gender, age, general health, oral hygiene habits (toothbrushing and flossing), dental check-ups and frequency of the consumption of sweets (drinks and snacks).

Table 3. Relative Risk Ratios after multinomial logistic regression model using ICDAS as dependent variable. ICDAS=0 caries-free, ICDAS=1 enamel caries, ICDAS=2 dentin caries.

Figure 1. Distribution of caries severity (ICDAS 0, ICDAS 1-3, ICDAS 4-6) and Body Mass Index (BMI) in the urban and rural areas.

Table 1. Sample distribution across weight and caries disease (ICDAS) by area.

		Caries-free (ICDAS 0) n (%)	Enamel Caries (ICDAS 1/3) n (%)	Dentin Caries (ICDAS 4/6) n (%)	P>|z|
Area					
	Urban	129 (57.59)	86 (38.39)	9 (4.02)	**< 0.01**
	Rural	159 (65.98)	50 (20.76)	31 (12.86)	
BMI					
	Normal weight	121 (62.70)	57 (29.53)	15 (7.78)	0.86
	Over weight	167 (61.62)	79 (29.15)	25 (9.22)	
BMI/Area					
	Normal weight Urban Area	64 (57.14)	41 (36.61)	7 (6.25)	
	Over weight Urban Area	65 (58.03)	45 (13.15)	2 (2.15)	**< 0.01**
	Normal weight Rural Area	57 (62.64)	16 (17.58)	8 (8.79)	
	Over weight Rural Area	102 (64.15)	34 (21.38)	23 (14.46)	

BMI	**Urban**	**Rural**	
Normal weight	112 (58.03)	81 (42.97)	**< 0.01**
Over weight	112 (41.37)	159 (58.67)	

Table 2. Sample distribution across caries severity. Distribution according to gender, age, general health, oral hygiene habits (toothbrushing and flossing), dental check-ups and frequency of the consumption of sweets (drinks and snacks).

		Caries-free (ICDAS 0) n(%)	Enamel Caries (ICDAS 1/3) n(%)	Dentin Caries (ICDAS 4/6) n(%)	P>|z|
Gender					
	Male	163 (35.13)	74 (15.95)	24 (5.17)	0.81
	Female	125 (26.94)	62 (13.36)	16 (3.45)	
Age					
	12-13 yy	158 (34.05)	70 (15.09)	24 (5.17)	0.61
	14-15 yy	130 (28.02)	66 (14.22)	16 (3.45)	
Good general health					
	Yes	278 (59.91)	131 (28.23)	35 (7.54)	**0.03**
	No	10 (2.16)	5 (1.08)	5 (1.08)	
Toothbrushing frequency					
	1/day	66 (14.22)	38 (8.19)	11 (2.37)	
	2/day	89 (19.18)	41 (8.84)	13 (2.80)	0.79
	>2/day	133 (28.66)	57 (12.29)	16 (3.45)	
Flossing					
	Irregular	147 (31.68)	89 (19.18)	21 (4.53)	**0.02**
	Regular	141 (30.39)	47 (10.13)	19 (4.09)	
Dental check-ups					
	Irregular	164 (35.35)	89 (19.18)	27 (5.82)	0.15
	Regular	124 (26.72)	47 (10.13)	13 (2.80)	
Sugared drinks					
	Never	25 (5.39)	12 (2.59)	6 (1.29)	
	<2/day	132 (28.45)	58 (12.50)	17 (3.66)	0.50
	>2/day	131 (28.23)	66 (14.23)	17 (3.66)	
Sweet snacks					
	Never	60 (12.93)	22 (4.74)	9 (1.94)	
	<3/day	186 (40.09)	95 (20.48)	25 (5.39)	0.78
	>3/day	42 (9.05)	19 (4.09)	6 (1.29)	

Table 3. Relative Risk Ratios after multinomial logistic regression model using ICDAS as dependent variable. ICDAS=0 healthy, ICDAS=1 enamel caries, ICDAS=2 dentinal caries.

		RRR	Std. Err.	P>|z|	[95% Conf. Interval]
0		(base outcome)			
1	**BMI/Area**	0.73	0.10	**0.03**	0.56 – 0.96
	Flossing	0.56	0.12	**< 0.01**	0.36 – 0.85
	Good General Health	1.04	0.59	0.95	0.34 – 3.13
2	**BMI/Area**	1.78	0.45	**0.02**	1.08 – 2.91
	Flossing	0.90	0.31	0.77	0.46 – 1.77
	Good General Health	4.65	2.74	**< 0.01**	1.47 – 14.75
Number of obs = 464		p < 0.01		Log likelihood = **-** 389.27	

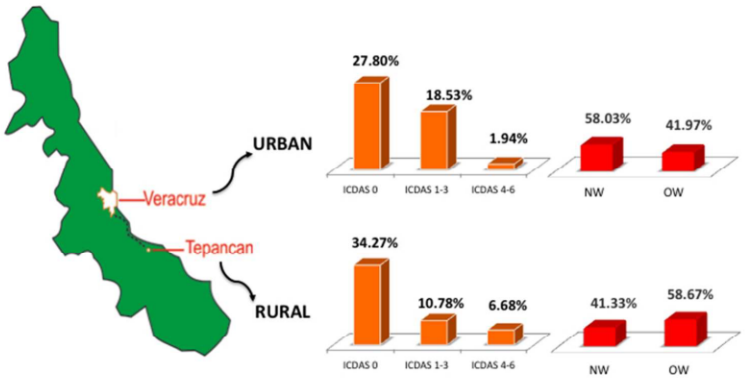

Figure 1. Distribution of caries severity (ICDAS 0, ICDAS 1-3, ICDAS 4-6) and Body Mass Index (BMI) in the urban and rural areas.
254x190mm (72 x 72 DPI)

VI. TASTE PREFERENCE

If the high consumption of sugar is related with high caries experience, then the taste thresholds may be fundamental for the frequency of the sugar intake, and genetic sensitivity to taste is related to the preference for some foods that can determine the selection on the dietary habits. [51]

The preference for the sweet taste is innate, in fact, sweeteners increase the pleasure of eating. Sweeteners contain carbohydrates and give energy, they are naturally in foods or may be added in food that is processed. The higher intake of added with the development many diseases. [52]

As well, it has been reported that the variation in dental caries and the consumption of sweet preference contains a significant genetic contribution proving the heritability of dental caries traits. [53]

The frequency of the consumption of sugar in meals and between them is associated with the caries experience and among the factors that can influence this frequency is the taste preference. Sweet taste receptor genes have been identified and it is reported that sweet taste preference changes with age so the determinance of sweet preference in young children is very important. On the other hand, the estimation of the cultural and social risk factors determine sweet preference too. By associating both, we can conclude that childhood sweet preference is determined by both genetic and non-genetic factors and by interpret these preferences we may understand diet-based diseases and its implications. Sugar often refers to sucrose, a derivated from sugar cane or beets but it is also commonly found in fruits, vegatables and many foods or can be added to an already natural sweet foods and beverages.

This preference of taste as well as the threshold were investigated in three different

populations distinctive from Europe, The Americas and Middle East.

Table 1. *Significance of Taste threshold (TT) and taste preference (TT) in relation with caries experience (DMFS) in Italy, Mexico and Saudi Arabia*.

VARIABLE/ COUNTRY	**ITALY**	**MEXICO**	**SAUDI ARABIA**
TT	65.0213 H	7.5137 L	37.7251 M
TP	231.8761 M	25.4513 L	320.1441 H
DMFS	1.4455 M	1.1563 L	2.9600 H
Initial	.1864 L	.8304 M	6.7422 H

ANNEX IV

Taste Preference in Relation to Dental Caries in Italian Adolescents

Taste Preference in Relation to Dental Caries in Italian Adolescents

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Background: Sweet substances cause a pleasurable sensation and trigger the salivation reflex, the deglutition and the preparation of the digestive tract for digestion and absorption.

Aim: This paper was aimed to clarify the potential relationship between sweet taste preference and caries experience in italian adolescents.

Methods: A cross-sectional evaluation was designed and carried out among 220 adolescents randomly selected (range 13-15 years old, 6.58% of the total youth population living in the Sassari area). Clinical evaluation was performed at schools under standardized conditions with artificial light, an intra-oral mirror and a WHO-CPI probe. Caries was assessed following ICDAS criteria, categorized as: caries free (ICDAS=0), initial caries lesion (ICDAS=1-3) or manifest caries lesion (ICDAS=4-6). A sweet taste test was executed to determine the children's sweet taste threshold (TT) and sweet taste preference (TP) using a modified version of the Nilsson and Holm´s method. Test solutions varied in sugar concentration from 0 to 2,4 M/L. Dietary habits were also investigated using a standardized questionnaire.

Results: Caries was recorded in 67.0% of the examined population. In 29.1% of the sample only initial lesions were recorded, while 27.8% registered at least one manifest lesion. Gender was found to be unrelated to caries and taste preference. While no statistical significant association was detected between ICDAS scores and taste threshold and/or taste preference (p=0.07 and p=0.08, respectively) [Table 1, Table 2], sweet taste preference could be considered as a risk for caries disease (p=0.04 sweet preference, p=0.03 for the sweet threshold). Sweet taste seems to be more perceived in individuals with a diet rich in fermentable carbohydrates.

Conclusions: This paper results suggest that the preference to the taste of sweet may have an impact on oral and dental health.

Table 1. Association between taste threshold and caries experience.

Taste threshold	*Caries presence* *n (%)*	*Caries free* *n (%)*	*Odds ratio* *(95% IC)*
Low sensitivity	*0,63%*	*8,22%*	*0,077 (0,01-0,58)*
Medium sensitivity	*5,06%*	*12,02%*	*0,42 (0,18 -0,96)*
High sensitivity	*32,28%*	*41,78%*	*0,78 (0,55-1,11)*

Score test for trend of odds: chi2(1) = 7.83

Pr>chi2 = 0.0051

Table 2. Association between sweet taste preference and caries experience.

Sweet preference	*Caries presence* *n (%)*	*Caries free* *n (%)*	*Odds ratio* *(95% IC)*
Low	*8,22%*	*26,59%*	*0,31 (0,17-0,58)*
Medium	*1,90%*	*1,26%*	*1,50 (0,25 -8,9)*
High	*27,84%*	*34,17%*	*0,81 (0,55-1,21)*

Score test for trend of odds: chi2(1) = 6.43

Pr>chi2 = 0.0112

ANNEX V

Taste Perception in Relation to Dental Caries in Saudi Schoolchildren

#192256

Taste Perception in Relation to Dental Caries in Saudi Schoolchildren

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Background

Among the main causing factors for dental caries are dietary habits and the frequency of sucrose consumption. The sweet taste perception has an influence on the sucrose intake and therefore affects the subject's predisposition to dental caries.

Purpose

The aim of the study was to investigate the caries experience in Saudi schoolchildren and elucidate potential relations between sweet taste threshold and preference, body mass index (BMI) and caries.

Methods

A cross sectional survey was done for 225 Saudi schoolchildren (114 boys/111 girls) aged 13-15 years randomly cluster selected. Children were examined in the school using dental mouth mirror and a dental probe. Caries was diagnosed using ICDAS and converted into DMFS. Weight and length for calculation of BMI was recorded. Sweet taste test was performed to determine the children's sweet taste threshold (TT) and sweet taste preference (TP) using a modified version of the Nilsson and Holm´s method. Test solutions varied in sugar concentration from 0 to 2,4 M/L. Statistical comparison was done using Independent t-est. $p<0.05$ was considered statistically significant.

Results

The DMFS for all children was 3.0 ± 4.0 (mean ± SD). Thirty-three percent of the children were caries-free (DMFS=0) and 76% had caries (DMFS≥1) with a DMFS of 4.4 ± 4.2. A statistically significant difference for TT was found between the two groups with 4.3 ± 1.5 and 5.0 ± 1.6 for the caries-free respectively children with caries ($p<0.05$). The corresponding values for TP were 7.0 ± 1.8 respective 8.0 ± 1.8 ($p<0.01$). Higher BMI was found in the children with caries (24.0) compared to the caries-free (23.5) (ns). Boys showed a higher mean value for all variables (DMFS, TT, TP and BMI) compared to girls ($p<0.05$ or 0.01). A significant correlation was found between DMFS and TT ($p<0.05$, $r=0.139$) respectively TP ($p<0.01$, $r=0.185$). No correlation was found in relation to BMI.

Conclusions

The findings suggest a relationship between the taste perception and the caries experience in a group of Saudi schoolchildren.

Table 1. Different caries variables for boys, girls and all children.

	Boys (n=114)	Girls (n=111)	All (n=225)
DMFS	3.1 ± 4.5	2.9 ± 3.5	3.0 ± 4.0
$D_{manifest}$	1.7 ± 3.6	0.9-±1.6	1.3±2.8
$D_{initial}$	4.9±4.5	8.6±9.8	6.7±7.8
DMFS=0	39 (34.2%)	35(31.5%)	74 (33%)

Table 2. Taste treshold (TT), taste preference (TP) and body mass index (BMI) data for boys, girls and all children..

	Boys (n=114)	Girls (n=111)	All (n=225)
$TT_{Caries\ free}$	4.5±1.7	4.1±1.2	4.3±1.5
TT_{Caries}	5.6±1.6	4.4±1.3	5.0±1.6
$TP_{Caries\ free}$	7.3±2.1	6.7±1.3	7.0±1.8
TP_{Caries}	8.9±1.4	7.2±1.8	8.0±1.8
$BMI_{Caries\ free}$	25.2±7.2	21.8±4.4	23.5±6.3
BMI_{Caries}	25.0±6.7	22.98±4.9	24.0±6.0

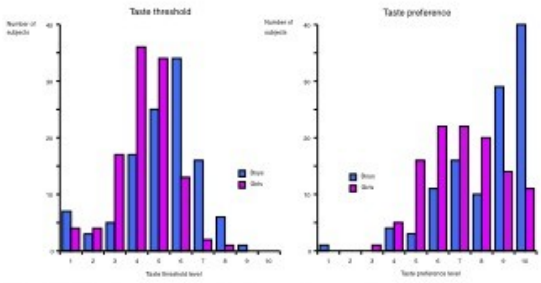

Fig 1. Taste threshold and taste preference showed for boys and girls. n = 225

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The Sahlgrenska Academy

UNIVERSITY OF GOTHENBURG

ANNEX VI

Taste Perception and Dental Caries – A Multicenter Study

#2526

Taste Perception and Dental Caries – A Multicenter Study

H. ASHI[1], G. CAMPUS[2], C. CAPI[2], and P. LINGSTRÖM[1]
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Background

Dietary habits and particularly the intake frequency of fermentable carbohydrates (*i.e.* sucrose) are of major importance for development of dental caries. The sweet taste perception is believed to have an influence on the sucrose intake and therefore affects the subject's predisposition to dental caries.

Purpose

The aim of the study was to investigate the different caries experience and taste perception in children from three different geographical areas (Italy, Mexico and Saudi Arabia) and to elucidate the potential relation between sweet taste preception and caries in schoolchildren.

Methods

A cross sectional survey was done including 669 school child ren (, 220 Italian, 224 Mexican and 225 Saudi) aged 13–15 years randomly cluster selected. The children were examined in their school setting using dental probe and mirror under natural light. Sweet taste perception test was determined by the sweet taste threshold (TT) and sweet taste preference (TP). The sweet test was preformed using a modified version of the Nilsson and Holm´s method (1983) with sucrose solutions that varied in sugar sucrose concentration from 1.63 to 821.52 g/L. ICDAS index was used to diagnose caries and converted to DMFS using a cut-off point ≥4 for the D component.

Results

The Saudi school children showed the highest mean values for TP and DMFS followed by Italian and Mexican. A statistically significant difference for TP, TT and DMFS was found between the three countries (p<0.001; ANOVA). A correlation between TP and DMFS was found for Saudi (p<0.01; r=0.260; Spearman rank correlation) respectively Mexico (p<0.01; r=0.260), while no correlation was found for Italy (ns). Similar findings apply when correlating the TT and DMFS (Saudi: p=0.01;r=0.166 and Mexico: p<0.01;r=0.247, Italy:ns). A statistically significant difference was found for taste preference when comparing the groups based according to their caries experience (p<0.01; T test).

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Table. *Mean ± SD for DMFS, Taste threshold and Taste preference for the three countries.*

	Italy (n=220)	Mexico (n=224)	Saudi Arabia (n=225)
DMFS	1.4 ± 2.3	1.2 ± 1.5	3.0 ± 4.0
Taste threshold	65.0 ± 8 2.6	7.5 ± 4.4	37.7 ± 47.5
Taste preference	231.9 ± 315.1	25.4 ± 315.1	320.0 ± 301.9

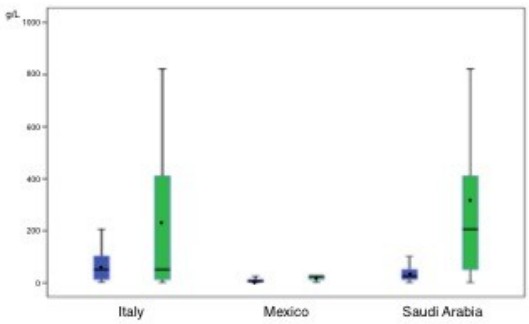

Fig 1*. Taste threshold (■) and taste preference (■) shown as box plots (line indicates the median, circle the mean, box the 25th and 75th percentiles and the whiskers the 10th and 90th percentiles).*

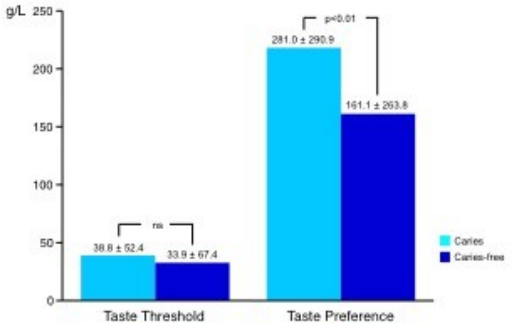

Fig 2*. Taste threshold and Taste preference in relation to caries experience (caries vs caries-free).*

Conclusions

The findings suggest that there is a variation in taste perception between the three countries. This variation seems to influence the caries outcome of the children in respective country.

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VII. PREVENTION

Dental caries is a multifactorial disease with a complex origin that includes also the acidogenicity of the dental plaque that may affect the tooth. [54]

Polyols (also referred to as sugar alcohols) add sweetness with less energy and may reduce risk for dental caries. Foods containing polyols are considered as sugar-free and are recognized as safe food additives. [52]

The use of polyols has been implemented to stop the high consumption of sugar that has increased over the last years due to the westernized lifestyle in both western and non-western world as an adjunctive to food products and drinks. The frequent use of these substitutes has demonstrated a decrease in the oral bacteria in the mouth as well as a reduction in the dental plaque growth; as well, it has been related to contribute to the remineralization of existing caries. [55-56]

The polyols most frequently used in the market are: xylitol, sorbitol, maltitol, mannitol, hexitol, erythritol, ribitol, polyol and inositol. [57-59]

Vast organizations have promoted the use of xylitol chewing gum in caries prevention across the world, especially in Europe and the US, this is due to the fact that its molecule promotes the anti acid attack of the sweeteners into the tooth. [58]

Although many studies have shown a benefit effect on the use of polyols, further analysis needs to be address to understand their valid approach in the prevention of dental caries. [60]

This is the reason of the study that aims to identify the scientific validation of polyols, to evaluate the proper administration of the product and to control the evidence of the beneficial effects on the prevention of dental caries.

ANNEX VII

The use of polyols in caries prevention: a systematic review and meta-analysis

Title: The use of polyols in caries prevention: a systematic review and meta-analysis

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ABSTRACT

Aim: to analyze the reported scientific evidence indicating the beneficial effects of polyols on caries prevention and to evaluate the effects on caries risk factors and clinical outcomes.

Methods: A meta-analysis evaluated compared sorbitol and/or mannitol and/or maltitol or no intervention group, in terms of ΔDMFS/dmfs, salivary count of Mutans S. (MS) and plaque pH. Randomized controlled trials assessing chewing gums, tablets, candies, lozenges, containing or xylitol or erythritol or maltitol or sorbitol or mannitol, were tested versus a control group (sorbitol and/or mannitol and/or maltitol) or versus no intervention group.

Results: We found 518 studies involving 5464 patients (1975 to 2015); fifty-one papers were analysed and twenty-one met eligibility criteria. Three were not included. We clustered groups as A) MS count: 1) Xilitol gum versus sorbitol gum; 2) Sorbitol gum versus no gum; 3) Xylitol tablet versus no tablet; 4) Xylitol tablet versus control tablet; 5) Erythritol tablet versus no tablet; 6) Erythritol tablet versus control tablet; 7) Sorbitol tablet versus no tablet; 8) Xylitol candy versus no candy; 9) Erythritol candy versus no candy. B) DMFS: 1) Xylitol gum versus sorbitol gum; Xylitol gum versus no gum; Sorbitol gum versus no gum; Xylitol lozenges versus no lozenges; Xylitol candy versus no candy. C) DMFS + dmfs: 1) Xylitol candy versus no candy; 2) Erythritol candy versus no candy. D) dmfs: 1) Xylitol tablet versus no tablet. E) plaque pH: 1) Xylitol gum versus sorbitol gum – $AUC_{5.7}$; 2) Xylitol gum versus sorbitol gum – $AUC_{6.2}$ and 3) Xylitol lozenges versus sorbitol lozenges – $AUC_{7.0}$.

Conclusions: This meta-analysis showed that the use of xylitol via gum, tablet candy or lozenge could inhibit the MS growth, especially in short-term period. The data on the effect of erythritol on MS are poor however this polyol seem to inhibit the MS growth.The xylitol and sorbitol gum could reduce the increase of DMFS index.

Sorbitol should be considered a low-cariogenic sweetener. However sorbitol fermented by MS could increase the plaque acidogenicity respect xylitol

Introduction

The prevention of caries is a public health goal. The use of sugar substitutes as "polyols" or "sugar alcohols" has been implemented to halt the high consumption of sugar that has increased over the decades. The frequent use of sugar substitutes like polyols has demonstrated to have a role in the decrease in oral bacteria and dental plaque growth (Deshpande, 2008, Thaibuis, 2013).

Chewing gums, lozenges or candies, are the primary vehicles of administration of polyols. (Fontana, 2012)

The polyols most frequently used are: xylitol, sorbitol, maltitol, mannitol and erythritol (Lingstrom, 2003, Makinen, 2011, Antonio, 2011). Many global INO health promotion institutions and organizations have promoted the use of xylitol produtcs particularly chewing gums in caries prevention across the world, especially in Europe and the US. (Makinen, 2011). The use of chewing gums, candies or/lozenges has been recommended for at least three times/day for a daily quantity that oscillates from 5 to 11 grams (Rethman, 2011; Campus, 2011).

Although many studies have shown a benefit effect on the use of polyols, further analysis needs to be address to verify the scientific evidence and understand the specific role in the prevention of caries (Fontana, 2012).

In this meta-analysis, the scientific evidence indicating the beneficial effects of polyols on caries prevention was investigated, evaluating the efficacy as well as the effects on caries risk factors and on clinical outcomes.

Methods

Focused PICO Question

What is the efficacy in caries prevention, of polyols compared to the sorbitol and/or mannitol and/or maltitol or no intervention group, in terms of ΔDMFS/dmfs, salivary count of Mutans S. and plaque pH?

Search strategy and selection criteria

The papers included in this meta-analysis review were randomized controlled trials (RCT) assessing the efficacy in caries prevention of chewing gums, tablets, candies, lozenges, mouthrinses and toothpastes containing polyols. We selected the studies that involved both children and adults in which gum or tablets or candies or lozenges, contained or xylitol or erythritol or maltitol or sorbitol or mannitol, were tested versus a control group (sorbitol and/or mannitol and/or maltitol) or versus no intervention group. In addition, we have included studies where experimental agents other than polyols were tested.

We considered as primary outcome:

- Dental caries increment.
- Level of S. Mutans in the saliva.
- Plaque pH.

We have excluded the studies where the control group used sucrose in gum, candies, tablets or lozenges,. As well, we excluded studies where subjects had disabilities, wore orthodontics appliances or were pregnant. The studies in which the follow-up was performed under 4 weeks were excluded. For the statistical comparison of incidence of caries the minimum follow-up time was determined 2

years. For the rest of the variables no timing was settled. The length of the experimental period was classified in short-term (between 1 - 5 months), medium-term (between 6 – 11 months) and long-term (more than 12 months). When controls were performed more than one time in the short term, in the medium term or in the long term we have considered the last data performed in the same period. If in the studies the polyols were tested in different way in terms of dose and frequency of administration, we choose the data of group in which the polyols were administer according to the guidelines (Rethman, 2011). If the follow-ups were longer than the administration period of polyols, we extract only the data of the three primary outcomes until the last control.

Considering that the dental caries increment can be reported differently in different trials, we decided to include in the meta-analysis only two types of data: decayed-filled-missing tooth (ΔDMFS – Δdmfs) or the data of decayed surface increment. Furthermore, considering that in the studies the clinical examination to determine the presence of caries could have been made in different modalities and the lesion could have been classified in different ways, we established a priori how to designate the data: data from "combined clinical and radiological examination" were chosen over data from "separated clinical and radiological" and as a second choice we included "only clinical" data when radiological examination was not performed; data for non-cavitated lesions combined with cavitated lesions was choose over only cavitated lesion; when more than one follow-up performed over 2 years was present, we included the data for each follow-up performed.

For the data of S. Mutans count in the saliva we have considered for the meta-analysis only the data expressed in CFU/ml. Finally, the data of the plaque pH contemplated for the meta-analysis was only the data of the areas under the plaque pH curve for each pH value as cut-off presented in paper. The studies that satisfied the inclusion criteria but data was not serviceable, were included only in the systematic review.

The outcomes considered in the studies were: the dental caries increment (continuous and dichotomous), salivary S. Mutans count (continuous) and plaque

pH (continuous). When the raw data was not present in the text or tables, single authors were contacted to obtain such information. If the authors did not answer the petition, we extracted the information from the graphs. The data comparison of the primary outcome was done separately for the gums, lozenges, tablets and candies. The comparison of DMFS and dmfs index was done separately and if this it was not possible we have used to comparison the number of new surface or teeth decayed. Into each device (gum, lozenges, tablets and candies) and for each primary outcome we compared separately data between control group and/or no intervention and experimental polyols group. To compare dichotomous data, a calculation of the Odd Ratio (OR) along with 95% Confidence Intervals (CIs) was used, whereas, for continuous data, the Mean Difference (MD) with the 95% Confidence Intervals (CIs) was calculated. Also, for each comparison the Z-test was used. A Fixed-effect model was applied to reassess all data extracted from the included studies. We have compared the data of salivary count of S. Mutans and plaque pH at baseline, at short-term, at medium-term and at long-term. For the dental caries increment we have compared data only at follow-ups. Data of gums, lozenges, tablets and candies were compared separately. Analysis was performed using Review Manager 5.3 software provided by the Cochrane Collaboration (The Cochrane Collaboration, 2012).

For the identification of studies to be included or considered for this review we developed two search strategies: one was used in two electronic databases (PUBMED and EMBASE) and the other was used in SCOPUS (*tab. 1* and *tab. 2*). We did not place any restriction on language or date of publication when searching the electronic database.

We searched the following electronic databases:

- MEDLINE via PUBMED (to March 2015)
- EMBASE (to March 2015)
- SCOPUS (to March 2015)

A comparison of the different searches was carried out to exclude the repeated studies. Then, two authors, on charge to evaluate the eligibility of the papers, examined independently all abstracts and titles of the studies found. If the information contained in abstract or in the title was no enough to determinate if the studies met inclusion criteria, the full paper was obtained. All studies that appeared to meet inclusion criteria were obtained in the full text format. The two authors assessed the papers independently to establish whether or not the studies met the inclusion criteria. Disagreements were resolved by discussion.

Results

A total of 518 studies published from 1975 to 2015 were found. Fifty-one papers were analysed and twenty-one met the eligibility criteria. Three papers (Makinen, 1996; Seki 2011, Lekkeri, 2011) were not included in the meta-analysis but only in the systematic review because primary outcome data was missing. (*fig.1*). The trials admitted in the review involved a total of 5464 patients. One of the studies included in the meta-analysis (Spieth, 2009) did not specify the randomization method of the sample. All the other studies had a randomization clinical trial with parallel arms design. Five studies (Honkala, 2014; Makinen, 2005; Alanen, 2000; Peng, 2004; Machiulskiene, 2001) used a cluster-randomized design. Eleven studies (Milgrom, 2006; Honkala, 2014; Makinen, 2005; Stecksen-Blicks, 2008; Martinez-Pabon, 2014; Runnel, 2013; Holgerson, 2006; Campus, 2013; Campus, 2011; Campus, 2009, Splieth, 2009) were double blind and one single blind (Oscarson, 2006). Seven studies were performed in adults (Hildebrandt, 2000; Milgrom, 2006; Simons, 2002; Martinez-Pabon, 2014; Ly, 2006; Campus, 2011; Splieth, 2009), eleven in patients with mixed dentition, aged between 6 and 13 years old, (Szoke, 2001; Honkala, 2014; Beiswanger; 1998; Runnel, 2013; Holgerson, 2007; Campus, 2013; Campus, 2009; Stecksen-Blicks, 2007;

Machiulskiene, 2001; Alanen, 2000; Peng, 2004) and one in children with deciduous dentition (Oscarson, 2006).

In fifteen studies (Campus, 2009; Campus, 2011; Campus, 2013; Holgerson, 2007; Ly, 2006; Simons, 2002; Martinez-Pabon, 2014; Machiulskiene, 2001; Peng, 2004; Beiswanger, 1998; Szoke, 2001; Milgrom, 2006; Hildebrandt, 2000) were used gums and in thirteen of these studies were tested xylitol and in eight paper was used as control gum with sorbitol and/or mannitol or maltitol, while in the other 5 the control group did not received gum. In two studies (Szoke, 2001; Beiswanger, 1998) was tested a combination of sorbitol and mannitol versus a control group with no gum. In two study (Hildebrandt, 1998, Mäkinen, 2005) as control group were present both sorbitol and no intervention group. From two studies (Campus, 2009; Campus, 2011), which tested gums, we could extract two types of data: salivary count of S. Mutans and plaque pH. From seven studies (Campus, 2013; Holgerson, Ly, 2006; Simons, 2002; Martinez-Pabon, 2014; Milgrom, 2006, Hildebrandt, 2000) we extracted data of S. Mutans count whereas from four studies (Szoke, 2001; Beiswager, 1998; Machiulskiene, 2001; Peng, 2004) we gained data of dental caries increment. From study of Ly et al. the data of salivary count of S. Mutans at baseline was no present in the text. We contact the authors to obtain this data but we had no answer. The data of follow-up were deduced from graph in the papers. In also we extracted the data of salivary count of S. Mutans from the graph in the paper text from Simons et al., 2006 study.

In two studies included in the meta-analysis were used lozenges (Splieth, 2009; Stecksen-Blicks, 2007) and in both studies were tested xylitol. In the study of Splieth et al., was used as control group lozenges with sorbitol while in Stecksen-Blicks et al. paper in the control group was not administrated any lozenges. From Splieth et al. study we extracted data of plaque pH while from Stecksen-Blicks et al. paper we gained data of ΔDMFS.

In two studies included in the meta-analysis were used tablets (Makinen, 2005; Oscarson, 2006) as device. In the paper of Oscarson et al. was tested xylitol while in the study of Makinen et al. the polyols tested were two: erythritol, xylitol and sorbitol. In both studies in the control group was not administrated any tablets.

From one study (Makinen, 2005) was gained data of salivary count of S. Mutans while from the other study (Oscarson, 2006) we extracted data of Δdmfs.

In two studies included in the meta-analysis were used candies (Runnel, 2013; Honkala, 2014) as device. In both studies were tested erythritol and xylitol while in control group were used candies with sorbitol. From one studies (Honkala, 2014) we extracted data of number of decayed surface while in the other we gained data of salivary count of S. Mutans. From the study of Honkala et al. the data of decayed surface interest both the primary teeth and permanent teeth.

In the study of Alanen et al. were used both candies and gum. In the study was tested xylitol while in the control group the subject did not received gum or candy. From this study were extracted data of ΔDMFS.

Xylitol gum versus control gum - MS count

For this comparison we considered seven studies (Campus, 2009; Campus, 2011, Campus, 2013; Hildebrandt, 200; Holgerson, 2007; Milgrom, 2006; Ly, 2006). At baseline and at short term we have found data in six studies, in medium term we extracted data from two studies and in long term only one study presented data of MS (Mutans S.) salivary count. At baseline we have no found difference in MS salivary count (mean difference (MD) 0.01, 95% confidence interval (CI) -0.04 to 0.06, P value = 0.78). At short term (*tab. 3*) the MS salivary count is significantly lower in the Xylitol group (MD -0.20, 95% CI -0.28 to -0.12, P value = 0.002). At medium term (*tab. 3*) was not found difference between gum with xylitol and gum with sorbitol in terms of reduction of MS salivary count (MD -0.16, 95% CI -0.32 to 0.01, P value = 0.26. At long term (*tab. 3*) from the analysis of Campus et al., 2013 study, we found that the MS salivary count is less high in xylitol gum group than control group with sorbitol gum (MD -0.70, 95% CI -1.31 to -0.09, P =0.02).

Xylitol gum versus no gum – MS count

For this comparison we had included three studies (Hildebrandt, 2000; Martinez-Pabon, 2014; simons, 2002). At baseline and at short term we have found data in all studies whereas for the comparison in medium and long terms the only one study (Simons, 2002) was used to extract MS salivary count. At baseline we have no found difference in MS salivary count (MD -0.17; 95% CI -0.58 to 0.24, P value = 0.42). At short term (*tab. 3*) MS salivary count was significantly lower in Xylitol group (MD -0.70, 95% CI -1.14 to -0.25, P = 0.002). At medium and long term were not found difference in MS salivary count: at medium term P value = 0.08 and at long term P value = 0.85 (*tab. 3*).

Sorbitol gum versus no gum – MS count

For this comparison we had extracted data from one study (Hildebrandt, 2000). In this study was present control at baseline and at short term. At baseline there was not difference in terms of MS salivary count (MD 0.10, 95% CI -0.47 to 0.67, P = 0.73). At control in short term period we have no found difference between sorbitol gum and control group without chewing gums (MD 0.30, 95% CI -0.21 to 0.81, P = 0.25)

Xylitol tablet versus no tablet – MS count

For this comparison we had included only one study (Makinen, 2005) and we have data at baseline and at medium term. At baseline there was not difference in MS salivary count (MD 0.32, 95% CI -0.71 to 0.07, P = 0.10) whereas at medium term salivary presence of MS is significantly lower in xylitol group than control group (MD -0.70, 95% CI -1-12 to -0.28, P = 0.001) (*tab. 3*).

Xylitol tablet versus control tablet– MS count

For this comparison we had included only one study (Makinen, 2005) and we have data at baseline and at medium term. No significant difference was found at baseline in MS salivary count (MD -0.03, 95% CI -0.40 to 0.34, P = 0.87) whereas at medium term the MS salivary count resulted higher in xylitol group than control group (MD -0.61, 95% CI -1.01 to -0.21, P = 0.003) (*tab. 3)*.

Erythritol tablet versus no tablet – MS count

For this comparison we had included only one study (Makinen, 2005) and we have data at baseline and at medium term. At baseline there was not difference in MS salivary count (MD -0.04, 95% CI -0.48 to -0.40, P = 0.86) whereas at medium term salivary presence of MS is significantly lower in xylitol group than control group (MD -0.85, 95% CI -1.26 to -0.44, P < 0.0001) (*tab. 3)*.

Erythritol tablet versus control tablet – MS count

For this comparison we had included only one study (Makinen, 2005) and we have data at baseline and at medium term. No significant difference was found at baseline in MS salivary count (MD 0.25, 95% CI -0.18, 0.68, P = 0.25) whereas at medium term the MS salivary count resulted higher in control group than erythritol group (MD -0.76, 95% CI -1.15 to -0.37, P = 0.0001) (*tab. 3)*.

Sorbitol tablet versus no tablet – MS count

For this comparison we had included only one paper (Makinen, 2005) and we have data at baseline and at medium term. No significant difference in terms of MS salivary count was found at baseline (MD -0.29, 95% CI -0.71 to 0.13, P = 0.17) and at medium term (MD -0.09, 95% CI -0.52 to 0.34, P = 0.68).

Xylitol candy versus control candy – MS count

For this comparison we have found one study (Runnel, 2013) and we in the paper were presented data at baseline and at long term. At baseline the MS salivary count was significantly higher in xylitol group (MD 0.11, 95% CI 0.09 to 0.13, P < 0.00001) whereas at control in long term the situation that we found was the opposite: the MS salivary count was lowest in the xylitol group (MD -0.18, 95% CI -0.20, -0.16, P < 0.0001).

Erythritol candy versus control candy – MS count

For this comparison we had included only one study (Runnel, 2013) and we have data at baseline and at long term. At baseline there was not difference in MS salivary count (MD 0.02, 95% CI -0.00 to -0.04, P = 0.08) whereas at medium term (tab. 1) salivary presence of MS is significantly lower in xylitol group than control group (MD -0.44, 95% CI -0.46 to -0.42, P < 0.0001) (*tab. 3)*.

Xylitol gum versus control gum – DMFS

For this comparison we had included one study (Machiulskiene, 2001) and we have data at 2 years and at 3 years of follow-ups. The data comparison of ΔDMFS at two years showed, in control group with sorbitol gum, a significantly smallest increase of decayed surface (MD 2.45, 95% CI 2.20 to 2.70, P < 0.00001. At 3 years the increment of DMFS is higher in control group with sorbitol gum (MD -0.90, 95% CI -1.35 to 0.45, P < 0.0001) (*tab. 4)*.

Xylitol gum versus no gum – DMFS

For this comparison we had included three studies (Machiulskiene, 2001; Peng, 2004; Alanen, 2000); from one studies (Machiulskiene, 2001) we had extracted data at 2 and at 3 years follow-ups whereas from studies of Peng et al. and Alanen et al. the follow-up was performed respectively at 2 and 3 years. At 2 years the increase of DMFS was significantly lowest in the xylitol group (MD -0.01, 95% CI -0.17 to -0.02, P = 0.01). This trend was confirmed at 3 years of follow-up: the ΔDMFS was smaller in the xylitol than control group (MD -0.69, 95% CI -1.08 to 0.30, P = 0.0005) (*tab. 4)*.

Sorbitol gum versus no gum – DMFS

For this comparison we had included three studies (Machiulskiene, 2001; Skoze, 2001; Beiswanger, 1998); from two studies (Machiulskiene, 2001, Beiswanger, 1998) we had extracted data at 2 and at 3 years follow-ups whereas from studies of Szoke et al. the follow-up was performed only at 2 years. At 2 years the increase of DMFS was significantly lowest in the xylitol group (MD -0.01, 95% CI -0.17 to -0.02, P = 0.01). This trend was confirmed at 3 years of follow-up: the

ΔDMFS was smaller in the xylitol than control group (MD -0.69, 95% CI -1.08 to 0.30, P = 0.0005) (*tab. 4)*.

Xylitol lozenges versus no lozenges – DMFS

For this comparison we have found data in one study (Stecksen-Blick, 2008) and the follow-up was performed at 2 years. We have no found difference in terms of ΔDMFS between xylitol lozenges and group without lozenges (MD 1.00, 95% CI -0.42 to 2.42, P = 0.17).

Xylitol candy versus no candy – DMFS

For this comparison we have found data in one study (Alanen, 2000) and the follow-up was performed at 3 years. At 2 years the increase of DMFS was significantly lowest in the xylitol group (MD -1.65, 95% CI -2.67 to -0.63, P = 0.002) (*tab. 4)*.

Xylitol candy versus no candy – DMFS + dmfs (number of decayed surface/total surface analysed)

For this comparison we have found data in one study (Honkala, 2014) in which the follow-up was performed at 3 years. We have no found difference between xylitol group and control group (OR 1.05, 95% CI 0.96 to 1.15, P = 0.26).

Erythritol candy versus no candy – DMFS + dmfs (number of decayed surface/total surface analysed)

For this comparison we have found data in one study (Honkala, 2014) in which the follow-up was performed at 3 years. At 3 years the surface decayed in control group were significantly higher than erythritol group (OR 0.83, 95% CI 0.75 to 0.91, P < 0.0001) (*tab. 4)*.

Xylitol tablet versus no tablet – dmfs

For this comparison we have found data in one study (Oscarson, 2006) and the follow-up was performed at 2 years. At 2 years we have no found difference between xylitol group and control group (MD -0.42, 95% CI -1.12 to 0.28, P = 0.24).

Xylitol gum versus sorbitol gum – $AUC_{5.7}$ of plaque pH

For this comparison we had included two studies (Campus, 2009; Campus, 2011). In both studies we have found data at baseline and short term whereas only one study performed (Campus, 2009) the control at medium term. At baseline we had found that the AUC5.7 of plaque was significantly bigger in xylitol group than control group (MD 0.98; 95% CI -0.82 to 1.14, P < 0.00001). At short terms the $AUC_{5.7}$ of plaque was less big in xylitol group than control group (MD -1.28, 95% CI -1.43 to -1.13, P < 0.00001). Also at medium terms we have found the $AUC_{5.7}$ in xylitol group was smaller than control group (MD -2.50, 95% CI -2.64 to -2.36, P<0.00001) (*tab. 5)*.

Xylitol gum versus sorbitol gum – $AUC_{6.2}$ of plaque pH

For this comparison we had included two studies (Campus, 2009; Campus, 2011). In both studies we have found data at baseline and short term whereas only one study performed (Campus, 2009) the control at medium term. At baseline comparing the data of two studies we had found that the $AUC_{6.2}$ of plaque pH was significantly biggest in xylitol group (MD 1.28; 95% CI 1.09 to 1.46, P < 0.00001). At short terms the $AUC_{6.2}$ of plaque pH was less big in xylitol group than control group (MD -6.22, 95% CI -6.37 to -6.07, P < 0.00001). Also at medium terms we have found the $AUC_{6.2}$ of plaque pH in xylitol group was smaller than control group (MD -5.50, 95% CI -5.67 to -5.33, P<0.00001) (*tab. 5)*.

Xylitol lozenges versus sorbitol lozenges – $AUC_{7.0}$ of plaque pH

For this comparison we had included one study (Splieth, 2009) in which the controls were performed at baseline and at short terms. At baseline comparing the data we had found that $AUC_{7.0}$ of plaque pH was bigger in control group than experimental group with xylitol lozenges (MD -25.80, 95% -44.30 to -7.30). At control in short term we have not found difference between two groups (MD -4.60, 95% CI -13.04 to 3.84, P =0.29).

Discussion

Dental caries is one of the most commonly occurring diseases worldwide and its treatment has considerable implications in term of economic resources and biological costs (Ricketts D, 2013). Several preventive programs to control caries

rick factors focusing on dietary modification have been recommended. In order to reduce caries risk, the use of sugar substitutes is common. Today, nonfermentable sweeteners are incorporated into many products, such as chewing gums, candies, tablets and lozenges. The main sugar substitutes used are polyols (Campus, 2011).

In the literature, there is no availability of meta-analysis on the efficacy of polyols in caries prevention. Hence, this study was performed in an attempt to gain further insight into the reliability in caries prevention of the polyols in chewing gums, candies, tablets and lozenges. Twenty-three studies were included, with a total of 5464 patients involved.

Mutans S. is considered to be the main pathogen responsible for dental caries. Numerous studies have shown an association between the number of carious lesions and the levels of Mutans S. in both adults and children. Also, a significant correlation between caries and Mutans S. was found (ElSalhy M, 2012).

Regarding the effects of polyols on Mutans S. we found studies that tested or xylitol, sorbitol and erythritol, vs. or control gum or no intervention group, or sorbitol. The devices used to administer polyols were gum, candies and tablets.

In the comparison between xylitol gum and control gum in short terms we have found, after comparison of data extracted from six studies (Campus, 2009; Campus, 2011; Hildebrandt, 2000; Holgerson, 2007; Ly, 2006; Milgrom, 2006), a higher reduction of salivary S. Mutans count in patients which consumed xylitol gum. This trend was not confirmed in medium term where we have analysed data from two studies (Campus, 2009; Holgerson, 2007) and we have no found difference. At long term we evaluated only one study (Campus, 2013) that showed a significant reduction of salivary S. Mutans count in subject that consumed xylitol gum. One study (Runnel, 2013) included in this meta-analysis showed a significant difference in salivary MS count between control group with sorbitol candies and experimental group with xylitol candies. For the comparison between xylitol tablets and control tablets we included in meta-analysis one (Makinen, 2005) study included that showed a significant reduction of salivary MS count in xylitol group. These results reflected the properties of two polyols;

sorbitol, even if has not effect on the growth of dental plaque could stimulate the growth of some strains of mutans streptococci (Makinen, 2011). While numerous studies have demonstrated that habitual xylitol consumption decrease count of mutans streptococci. Several mechanisms can be proposed to be responsible for the mutans streptococci decrease as follows: growth inhibition, a decrease in the amount of plaque, elevated pH in the mouth, a decrease of adhesive polysaccharides produced by mutans streptococci (Söderling, 2015).

In comparison between xylitol gum vs. no intervention group we founded three studies (Hildebrandt, 2000; Martinez-Pabòn, 2014; Simons, 2002) that showed at short term a higher reduction in salivary S. Mutans count in subject allocated in xylitol group. At medium and long term the only study (Simons, 2002) analysed showed no difference between xylitol gum and no intervention group. These results were confirmed also in the studies that tested xylitol tablets vs. no tablets: at medium term the subjects in the xylitol group showed a significant reduction of salivary S. Mutans count (Makinen, 2005). Xylitol has been used as a substitute for refined white sugar for more than 30 years, and is thought to have an inhibitory action on the major causative bacteria in dental caries, S. Mutans. Xylitol and can also promote an ecological shift, resulting in less cariogenic environment (Holgerson, 2007). These results would seem confirm the antimicrobial effect against S. Mutans of xylitol (Deshpande, 2008) when was administrated via gum, tablets, candies or lozenges.

The erythritol was tested against S. Mutans in two studies: in one paper (Makinen, 2005) were used as device tablets and as control were used no intervention group and sorbitol tablet, while in the other study (Runnel, 2013) candies. In the study that test tablets (Makinen, 2005) at medium term the salivary S. Mutans count was significantly less high in erythritol group compared both whit no intervention group and with control group. The same result has been found at long term in the study that test erythritol candies (Runnel, 2013). Information on oral biological effect of erythritol has been scant. However the few reports on erythritol suggest that this sugar alcohol may be of significant dental benefit (Makinen, 2005).

The two studies included in this review investigated on the efficacy against S. Mutans of sortibol gum vs. no gum and sorbitol tablets vs. no tablets, showed no difference between two groups. These results reflected the few data reported in literature: sorbitol could stimulate the growth of some strains of mutans streptococci (Makinen, 2011).

Regarding the protective effects of polyols on dental caries in terms of DMFS/dmfs increment we found study that tested or xylitol, sorbitol and erythritol, vs. or control gum or no intervention group, or sorbitol. The devices used to administer polyols were gum, lozenges, candies and tablets.

For the comparison between xylitol gums vs. control gums we found one study (Machiulskiene, 2001). This paper showed a significantly less DMFS increment at 2 years follow-up in subject that consumed sorbitol gum while at 3 years follow-up the analysis of data indicated a significantly less DMFS increment in xylitol gums group. In study that compared xylitol candies vs. control candies (Honkala, 2014) were analysed only the number of surface decay and not the DMFS index. The comparison of data showed no difference. Vedere discussion Honkala (cercare letteratura a riguardo)

For the comparison between xylitol gums vs. no intervention group we found three studies (Machiulskiene, 2001; Peng, 2004; Alanen, 2000). The comparison showed an effect protective in terms of DMFS increment at 2 and 3 years follow-up of xylitol gum. For the comparison between xylitol lozenges and no intervention group we have included one study (Stecksen-Blicks, 2008) that no showed no protective effect in terms of DMFS score. In the study (Alanen, 2000) that compared xylitol candies vs. no intervention group, the DMFS increment was significantly less high in experimental group at 3 years follow-up. One paper (Oscarson, 2006) investigated the xylitol tablets vs. no intervention group in term of caries preventive effect on deciduous teeth: no difference was found in dmfs increment. The scientific evidence of the anticariogenic effects of the xylitol has been under debate (Stecksen-Blick, 2008; Oscarson, 2006). This meta-analysis suggested there were protective properties of xylitol when this was dispensed via

gum. The single studies on xylitol candies, tablets and lozenges did not showed clearly protective effects in terms of DMFS and dmfs increment when compared whit no intervention.

In literature we found only one study (Honkala, 2014), included in this meta-analysis that investigated the caries preventive effect of erythritol. This paper compared erythritol candies vs. sorbitol candies (control group) and for the statistical comparison were used the number of surface decayed. The results of this study suggested that the erythritol could have a protective effect against dental.

For the comparison between sorbitol gums vs. no intervention group we have included three studies (Beiswanger, 1998; Machiulskiene, 2001; Szoke, 2001). The analysis of data showed a less increment in DMFS score in experimental group at 2 and 3 years follow-up. This data confirmed the anti-caries benefits of the sorbitol gums vs. no intervention described in literature (Szoke, 2001)

Regarding the AUC of pH we included in the meta-analysis studies that test xylitol in gum and lozenges vs. control group with sorbitol. For the comparison between xylitol gums vs. control gum we have included two studies (Campus, 2009; Campus, 2011). At baseline we found difference among experimental and control group. However the $AUC_{5.7}$ and $AUC_{6.2}$ of pH is greater in xylitol group. At short and medium term there has been a reversal in the $AUC_{5.7}$ and $AUC_{6.2}$ of pH value.

These results could reflect the ability of mutans streptococci to ferment sorbitol while the xylitol cannot be metabolised by mutans streptococci (Oscarson, 2006). Indeed sorbitol should be considered a low-cariogenic sweetener rather than a non-cariogenic one. Sorbitol may be fermented by mutans streptococci could increase the plaque acidogenicity (Campus, 2009).

In the study (Splieth, 2009) that compared xylitol lozenges and sorbitol lozenges we found a difference between two groups at baseline. At control there was no reversal of pH value.

Conclusions

This meta-analysis shown that the use of xylitol via gum, tablet, candy or lozenge could inhibit the growth of MS especially in short-term period. The data on the effect of erythritol on MS are poor, however this polyol seems to inhibit the MS growth.

The use of xylitol or sorbitol when administer via gum could reduce the increase of DMFS index.

Sorbitol should be considered a low-cariogenic sweetener. However sorbitol fermented by MS could increase the plaque acidogenicity respect xylitol.

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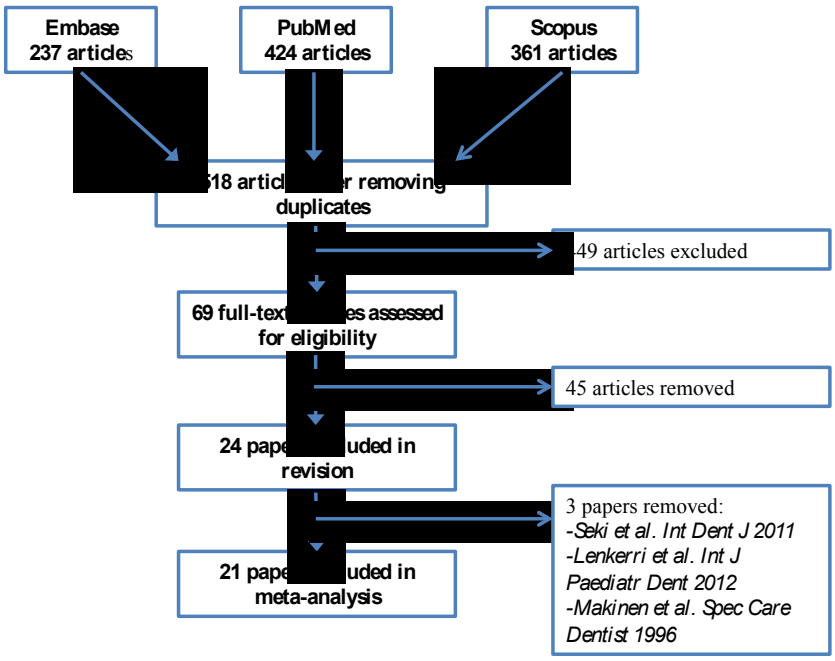


Fig. 1 Flow chart of search strategy

#1 randomized clinical trial [pt] #2 dental caries AND (candies OR chewing gums OR lozenges OR mannitol OR maltitol OR erythritol OR sorbitol OR xylitol OR sugar alcohols OR polyols OR plaque pH OR streptococcus mutans OR lactobacillus) [tiab] #3 dmft AND (candies OR chewing gums OR lozenges OR mannitol OR maltitol OR erythritol OR sorbitol OR xylitol OR sugar alcohols OR polyols) [tiab] #4 lactobacillus AND (candies OR chewing gums OR lozenges OR mannitol OR maltitol OR erythritol OR sorbitol OR xylitol OR sugar alcohols OR polyols OR) [tiab] 5# streptococcus mutans AND (candies OR chewing gums OR lozenges OR mannitol OR maltitol OR erythritol OR sorbitol OR xylitol OR sugar alcohols OR polyols OR) [tiab] 6# plaque pH AND (candies OR chewing gums OR lozenges OR mannitol OR maltitol OR erythritol OR sorbitol OR xylitol OR sugar alcohols OR polyols OR) [tiab] #7 #2 OR #3 OR #4 OR #5 OR #6

Tab. 1 Search strategy used in MEDLINE and EMBASE database

#1 randomized clinical trial [tiab] #2 dental caries AND (candies OR chewing gums OR lozenges OR mannitol OR maltitol OR erythritol OR sorbitol OR xylitol OR sugar alcohols OR polyols OR plaque pH OR streptococcus mutans OR lactobacillus) [tiab] #3 dmft AND (candies OR chewing gums OR lozenges OR mannitol OR maltitol OR erythritol OR sorbitol OR xylitol OR sugar alcohols OR polyols) [tiab] #4 lactobacillus AND (candies OR chewing gums OR lozenges OR mannitol OR maltitol OR erythritol OR sorbitol OR xylitol OR sugar alcohols OR polyols OR) [tiab] 5# streptococcus mutans AND (candies OR chewing gums OR lozenges OR mannitol OR maltitol OR erythritol OR sorbitol OR xylitol OR sugar alcohols OR polyols OR) [tiab] 6# plaque pH AND (candies OR chewing gums OR lozenges OR mannitol OR maltitol OR erythritol OR sorbitol OR xylitol OR sugar alcohols OR polyols OR) [tiab] #7 #1 OR #2 OR #3 OR #4 OR #5 OR #6

Tab. 2 Search strategy used in SCOPUS database

Tab. 3 Significative results in MS salivary count

Type of comparison	Authors	Short term				Medium term				Long term			
Xylitol gum vs. control gum		Xylitol	Control	Intervals	p value	Xylitol	Control	Intervals	P value	Xylitol	Control	Intervals	P value
	Campus 2009	5.28 (0.6) – 80	5.36 (0.2) – 85	-0.08 [-0.22, 0.06]		5.25 (0.6) – 78	5.36 (0.5) – 85	-0.11 [-0.28, 0.06]					
	Campus 2011	5.29 (0.3) – 40	5.4 (0.2) – 39	-0.11 [-0.22, 0.00]									
	Campus 2013									1.9 (0.8) - 74	2.6 (2.4) - 66	-0.70 [-1.31, -0.09]	
	Hildebrandt 2000	3.6 (1.2) – 42	4.7 (1.2) – 47	-1.10 [-1.60, -0.60]									
	Holgerson 2007	4.18 (4.54) – 64	4.92 (4.25) – 64	-0.74 [-2.26, 0.78]		4.3 (1.2) – 27	5.2 (1.3) - 28	-0.90 [-1.56, -0.24]					
	Ly 2006	4.35 (0.4) - 33	4.95 (0.5) – 33	-0.60 [-0.82, -0.38]									
	Milgrom 2006	4.7 (1.1) – 30	5.3 (1.1) – 30	-0.60 [-1.16, -0.04]									
					P<0.01				P=0.06				P=0.02
Xylitol gum vs. no gum		Xylitol	No gum	Intervals	p value	Xylitol	No gum	Intervals	p value	Xylitol	No gum	Intervals	p value
	Hildebrandt 2000	3.6 (1.2) – 42	4.4 (1.3) – 46	-0.80 [-1.32, -0.28]									
	Martinez-Pabòn 2014	6.42 (6.4) – 46	6.97 (6.89) – 36	-0.55 [-3.46, 2.36]									
	Simons 2002	1.8 (2.3) - 57	2.2 (2.5) - 52	-0.40 [-1.30, 0.50]		1.8 (2.1) - 57	2.5 (2.1) - 52	-0.70 [-1.49, 0.09]		3.9 (2.3) - 37	4 (2) - 31	-0.10 [-1.12, 0.92]	

Tab. 4 Significative results in ΔDMFS, Δdmfs increment

Type of comparison	Authors	2 years follow-up				3 years follow-up			
Xylitol gum vs. control gum – DMFS		**Xylitol**	**Control**	**Intervals**	**p value**	**Xylitol**	**Control**	**Intervals**	**p value**
	Machiulskiene 2001	5.45 (0.95) – 105	3 (0.9) – 107	2.45 [2.20, 2.70]		8.1 (1.3) – 99	9 (1.6) – 71	-0.90 [-1.35, -0.45]	
					P<0.01				P<0.01
Xylitol gum vs. no gum –DMFS		**Xylitol**	**No gum**	**Intervals**	**p value**	**Xylitol**	**No gum**	**Intervals**	**p value**
	Alanen 2000					1.87 (2.55) – 115	4.42 (4.36) – 146	-2.55 [-3.40, -1.70]	
	Machiulskiene 2001	5.5 (1.1) – 107	5.4 (1.3) – 102	0.10 [-0.23, 0.43]		8.1 (1.3) – 99	8.3 (1.6) – 80	-0.20 [-0.63, 0.23]	
	Peng 2004	0.15 (0.42) – 363	0.26 (0.67) – 410	-0.11 [-0.19, -0.03]					
					P=0.01				P<0.01
Sorbitol gum vs. no gum – DMFS		**Sorbitol**	**No gum**	**Intervals**	**p value**	**Sorbitol**	**No gum**	**Intervals**	**p value**
	Beiswager 1998	5.71 (4.72) – 874	6.05 (5.15) – 944	-0.34 [-0.79, 0.11]		8.1 (6.07) – 657	8.63 (6.54) – 746	-0.53 [-1.19, 0.13]	
	Machiulskiene 2001	3 (0.9) – 105	6.7 (1.2) – 102	-3.70 [-3.99, -3.41]		9 (1.6) – 80	12.4 (1.35) - 68	-3.40 [-3.88, -2.92]	
	Szoke 2001	0.814 (0.102) - 269	1.327 (0.105) - 278	-0.51 [-0.53, -0.50]					
					P<0.01				P<0.01
Xylitol candy vs. no candy – DMFS		**Xylitol**	**No candy**	**Intervals**	**p value**	**Xylitol**	**No candy**	**Intervals**	**p value**
	Alanen 2000					2.77 (3.05) – 66	4.42 (4.36) – 146	-1.65 [-2.67, -0.63]	
									P<0.01
Erythritol candy vs. no candy – DMFS+ dmfs *		**Erythritol**	**No candy**	**Odds Ratio**	**p value**	**Erythritol**	**No candy**	**Intervals**	**p value**
	Honkala 2014					860 (18763)	1022 (18596)	0.83 [0.75, 0.91]	
									P<0.01

Tab.5 Significative results in $AUC_{5.7}$ and $AUC_{6.2}$ pH

Type of comparison	Authors	Short term				Medium term				Long term			
Xylitol gum vs. control gum pH $AUC_{5.7}$		**Xylitol**	**Control**	**Intervals**	**p value**	**Xylitol**	**Control**	**Intervals**	**p value**	**Xylitol**	**Control**	**Intervals**	**p value**
	Campus 2009	10.2 (0.5) – 80	11.7 (0.6) – 85	-1.50 [-1.67, -1.33]		5.5 (0.5) – 78	8 (0.4) – 85	-2.50 [-2.64, -2.36]					
	Campus 2011	9.8 (0.6) – 40	10.2 (0.9) – 40	-0.40 [-0.74, -0.06]									
					P<0.01				P<0.01				
Xylitol gum vs. control gum pH $AUC_{6.2}$		**Xylitol**	**Control**	**Intervals**	**p value**	**Xylitol**	**Control**	**Intervals**	**p value**	**Xylitol**	**Control**	**Intervals**	**p value**
	Campus 2009	10.2 (0.5) – 80	17.6 (0.6) – 85	-7.40 [-7.57, -7.23]		8 (0.4) – 78	13.5 (0.7) – 85	-5.50 [-5.67, -5.33]					
	Campus 2011	18.6 (0.9) – 40	19 (0.8) – 40	-0.40 [-0.77, -0.03]									
					P<0.01				P<0.01				

CHAPTER B

EROSIVE WEAR

Tooth wear is defined as the loss of dental hard tissue due to various forms of physical and chemical impacts not involving bacteria and excluding trauma. [61]

The chapter on this condition is divided into the topics:

I. Differential diagnosis

II. Measurement of wear (Diagnosis and risk factors)

III. BEWE (Basic Erosive Wear Examination)

I. DIFFERENTIAL DIAGNOSIS

Comprises:

- The effect of exogenous material forced over tooth substances
- The impact of tensile and compressive forces during tooth flexure
- The action of opposing teeth
- The chemical dissolution of tooth mineral

Considering that the lost tissue cannot regenerate, the wear process is of great clinical significance. [62]

Table 5. Classification of tooth wear lesions.

Abrasion	**Attrition**	**Abfraction**	**Erosion**
Physical wear as a result of mechanical processes involving foreign substances or objects (two or three body wear).	Physical wear as a result of the action of antagonistic teeth with no foreign substances intervening (two body wear).	Physical wear as a result of tensile and compressive forces in the cervical region due to flexing of teeth under occlusal loads, provoking microfractures in enamel and dentine (fatigue wear).	Chemical wear as a result of extrinsic or intrinsic acids or chelators acting on plaque-free tooth surfaces.

The morphology and severity of the resulting tooth wear lesions may vary substantially depending on the predominant etiological factor.

Table 6. Subforms and diagnostic criteria (63-64)

Abrasion	**Erosion**	**Attrition**	**Wedge shaped defects**
-Morphological changes can be diffuse or localized. -Due to the lower microhardness of dentine, it mainly occurs on exposed root surfaces and exposed coronal dentine. (on occlusal surfaces its hard to distinguish it from erosion)	- *At early stages:* appears as loss of the physiological surface luster. - *In advanced stages*: changes occur in the original tooth morphology. - *On smooth surfaces:* the convex areas flatten and concavities can develop, the width of which clearly exceeds the depth. - *Lesions* are located coronal to the enamel-cementum junction, with an intact border of enamel along the gingival margin. - *Occlusal erosion* leads to a rounding of the cusps, grooves on the cusps and incisal edges, and restorations rising above the level of the adjacent tooth surfaces, - *In severe cases*: the entire occlusal morphology disappears	- Characterized by antagonistic glossy plane facets with sharp margins that only occur on occluding surfaces. - The occluding surfaces match in excursive jaw movements, usually with similar degrees of wear in both arches.	- Typically located at the enamel-cementum junction. - Usually the coronal part has a sharp margin that cuts at right angles into the enamel surface, whereas the apical part runs out onto the root surface. - In contrast to erosive defects, the depth of these clearly exceeds the width.

II. MEASSUREMENT OF WEAR

Although between 5 and 100% of children and adolescents, and between 76 and 100% or adults have erosive tooth wear. [65-66] Little attention has been paid to the indices to measure and predict the development of the condition over time. [67]

No indicator of dental erosion has been yet included in EU or WHO oral health policies, probably because the lack of a standardized index. There is now interest from the World Health Organization to develop methods to evaluate dental erosion.

Table 7. Diagnosis and risk factors

Dental erosion is a multi-factorial condition.
Diagnosis requires a thorough knowledge of both morphological patterns typical of this type or wear and of the factors that are likely to contribute to the development.
Risk factors can be categorized into chemical, biological and behavioral factors.
The two most often cited chemical parameters, pH and titratable acidity, can only partly explain the erosive potential of acidic food or drinks.
Saliva is considered to be one important biological factor in erosion protection, but also the acquired enamel pellicle, tooth structure and positioning in relation to soft tissues may be of particular relevance.
Behavioral factors can play a role in dental erosion both during and after an acidic challenge, as the manner of dietary acids in the mouth before swallowing, the timing of acidic consumption/exposure and daily work/pleasure/sport activities.
Anorexia and bulimia nervosa, rumination, chronic alcoholism and gastro-oeasophageal reflux are risks for erosive tooth wear due to the intrinsic acid.
Certain occupations such as professional wine tasting and industrial work involving exposure to acidic vapors or dust are considered factors for the development of erosion.

III. BEWE

The Basic Erosive Wear Examination (BEWE) has been designed to provide a simple tool for use in general practice and to allow comparison to other more discriminative indices. [62]

Aim

To increase the awareness of tooth erosion amongst clinicians and general dental practitioners and to provide a guide as to its management.

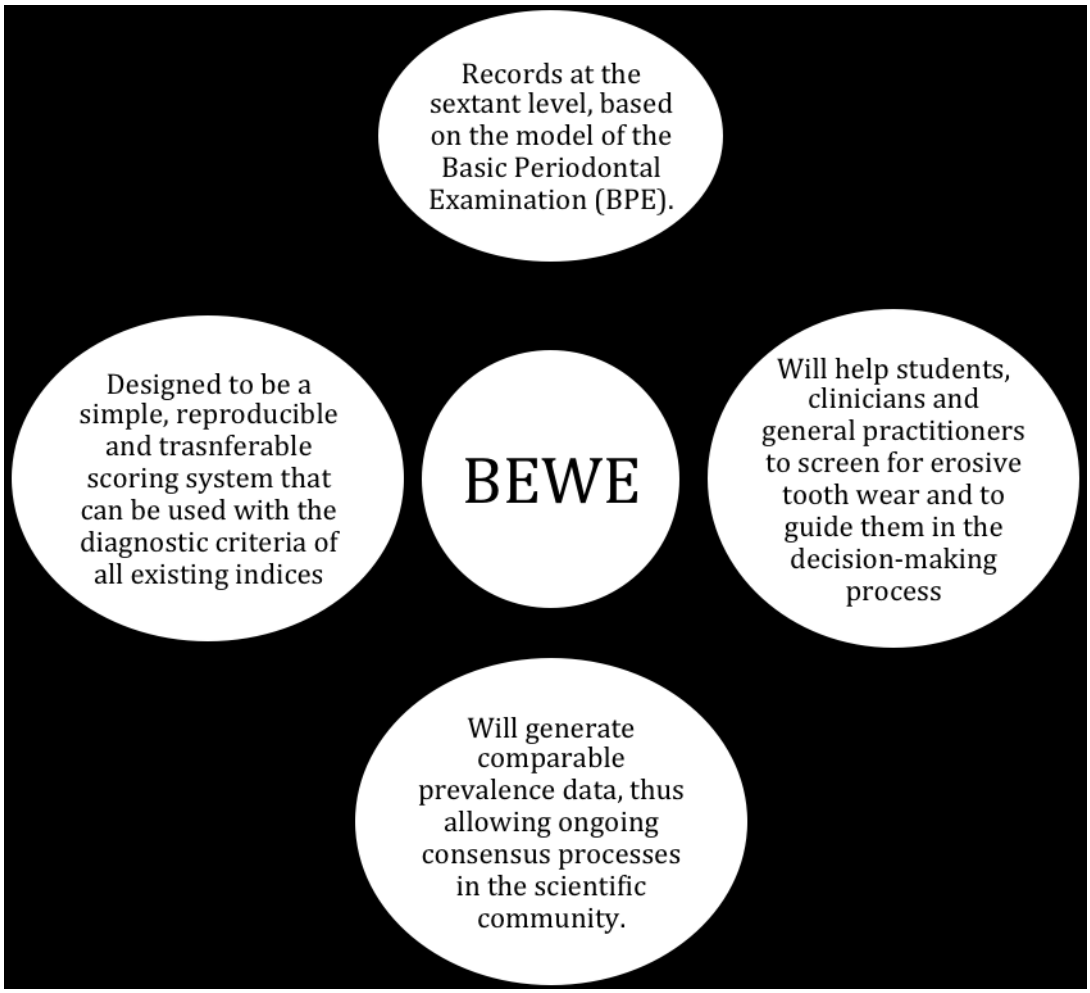
The most several affected surface in each sextant is recorded with the use of a four level score, then the cumulative score is classified and matched to the corresponding risk levels which guide the management of the condition. BEWE allows the re-analysis and integration of results from existing studies to eventually lead to the integration of a standardized and validated index.

Table 8. Criteria for grading erosive wear

0	No erosive tooth wear
1	Initial loss of surface texture
2*	Distinct defect, hard tissue loss <50% of the surface area
3*	Hard tissue loss >50% of the surface area

*in scores 2 and 3 dentine often is involved

Figure 1. Characteristics of the BEWE



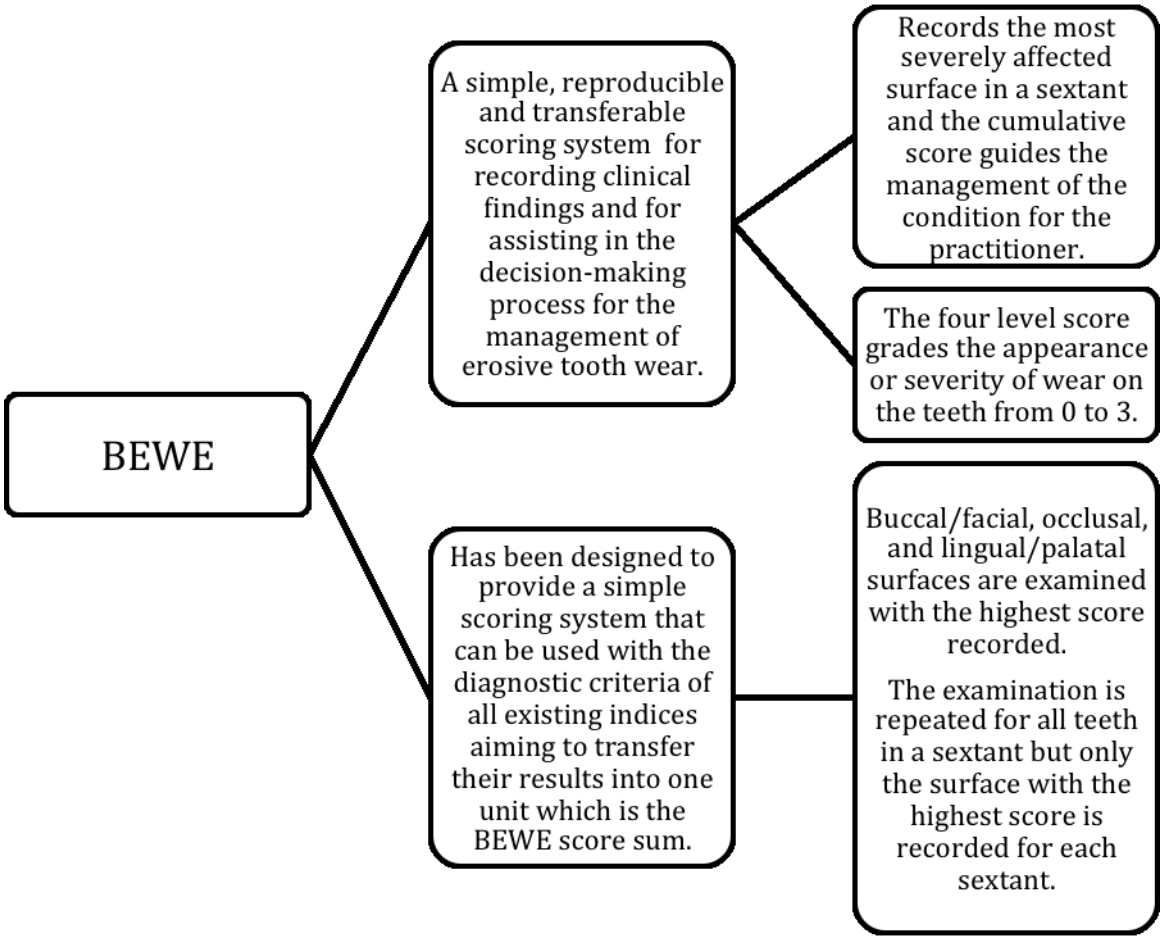


Figure 2. Description of the BEWE methodology.

Once all the sextants have been assessed, the sum of the scores is calculated as indicated on the grid that follows:

Table 9. BEWE Scores

Highest score +	Highest score	Highest score	Highest score	Highest score	=
1. Sextant	2. Sextant	3. Sextant	4. Sextant	5. Sextant	6. Sextant
(17-14)	(13-23)	(24-27)	(37-34)	(33-43)	(44-47)

Table 10. Risk levels as a guide to clinical management

Risk level	Cumulative score of all sextants	Management
None	Less than/ equal 2°	Routine maintenance and observation
		Repeat at 3-year intervals
Low	Between 3 and 8°	Oral hygiene and dietary assessment, and advice, routine maintenance and observation
		Repeat at 2-year intervals
Medium	Between 9 and 13°	Oral hygiene and dietary assessment, and advice, identify the main etiological factor(s) for tissue loss and develop strategies to eliminate respective impacts
		Consider fluoridation measures or other strategies to increase the resistance of tooth surfaces.
		Ideally, avoid the placement of restorations and monitor erosive wear with study casts, photographs, or silicone impressions
		Repeat at 6-12 month intervals
High	14 and over°	Oral hygiene and dietary assessment, and advice, identify the main etiological factor(s) for tissue loss and develop strategies to eliminate respective impacts.
		Consider fluoridation measures or other strategies to increase the resistance of tooth surfaces.
		Ideally, avoid restorations and monitor tooth wear with study casts, photographs, or silicone impressions.
		Especially in cases of severe progression consider special care that may involve restorations.
		Repeat at 6-12 month intervals

Impact of the measurement of Erosive Wear

BEWE will encourage epidemiologist, clinicians, dental students and general dental practitioners to pay more attention to erosive wear and hence will be beneficial for patient care.

Clinical and experimental observations show that individual tooth wear rarely occurs alone, but they interact one with the other [68] and this interaction is the main factor for tooth wear. [61] The study of the factors that contribute to the development of the condition is fundamental for the improvement of oral health status.

ANNEX VIII

Erosive Wear In Adolescents from Italy, Mexico And Saudi Arabia: A Multicenter Study

Erosive Wear In Adolescents From Italy, Mexico And Saudi Arabia: A Multicenter Study

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Running head: evaluation of erosion in adolescents from three different countries

Key Words: Erosion, BEWE, diet, adolescents

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Abstract

Aim: to evaluate the trend of dental erosion in adolescents from three different backgrounds from Europe (Italy), Latin America (Mexico and Middle East (Saudi Arabia) and to identify the different etiological risk factors for each population.

Materials and methods: Subjects between 13 to 15 years old enrolled in a high school system. They were classified according to sex (M or F), age (13-15 years old), and geographical area. Each subject was examined inside the school under natural lighting using a mouth mirror No. 5 and a WHO explorer. Erosion was measured and the risk level was calculated using the Basic Erosive Wear Examination BEWE. A questionnaire was administrated; for each country, a specific set of questions was performed to cover their particular dietary habits.

Results: A total of 675 adolescents from Italy (n=220), Mexico (n=230), and Saudi Arabia (n=225) participated in the study, mean age was 14.09±0.81. The global experience of erosive wear was 12.7%. The prevalence of erosion was higher in Mexico (M) (18.7%), followed by Italy (I) (12,7%) and Saudi Arabia (S) (6.7%) ($p=0.001$). The severity of erosion was 1 (Initial loss of surface texture) in 93.0% of the cases and 2 (Distinct defect, hard tissue loss <50% of the surface area) in 7.0%. The mean BEWE score for the erosive lesions was 3.64 in I, 3.04 in M and 1.2 in S.). The high frequency of soft drinks intake was a constant variable for the presence of erosion, 77.9% of the subjects with erosion reported a high consumption ($p<0.01$).

Conclusions: The trend of dental erosion in adolescents is highly related to the diet in all the three countries. The misguided intake of soft drinks was the determinant factor for the presence of erosive wear.

INTRODUCTION

Tooth wear is defined as the gradual loss of the hard tissue of the tooth as a result of physical and chemical impacts and can be classified into erosion, abrasion, abfraction and attrition and this processes can be present in combination or alone (Addy et al., 2006)

Dental erosion or erosive tooth wear is multifactorial lost of tissue by acid dissolution (intrinsic or extrinsic) and a scrupulous understanding of the morphology and risk factors is fundamental for the diagnosis. The factors that contribute to the erosive wear are chemical, biological and behavioral. The predominance of behavioral factors such as diet, tooth brushing and ingestion of certain medicines can contribute to the condition as dental erosion depends on the frequency and intensity of the acidic exposure (Addy et al., 2006, Barlett et al., 2008, Young et al., 2008).

It has been reported that around 5 to 100% of children and 76 to 100% of adults present erosive tooth wear (Lussi et al., 2006, Van't Spijker et al., 2009) and some evidence points that its presence in the primary teeth is prognosticative for the permanent dentition (Ganss et al., 2001, Harding et al., 2010). When erosion is established, the lesions may increase in quantity and severity compromising the oral health status (Lussi et al., 2000; El Aidi et al., 2008, Bartlett et al., 2008). A recent study demonstrated that subjects that have manifest erosive lesions are in greater risk than subjects with no erosion, as they possess lower pH levels and diminished capacity to recover after acidic exposure (Lussi et al., 2012).

Diet has a fundamental role, nowadays the ingestion of acidic food and beverages such as soft drinks has increased, particularly in western countries, making the practitioner in need to be aware of the erosive potential of the individual diet to be able to determine the risk (Lussi 2006). The frequency and duration of the acidic ingestion, the difference in lifestyle and behavior such as the abuse of acidic

fruits, vegetables, candies or soft drinks, unusual hygiene practices with abrasive toothpaste and the socioeconomic status are part of the etiology of erosion (Zero et al., 2006).

The diagnosis is made by the differentiation of the anatomical tooth morphology as well as the distinction from the other forms of wear. The Basic Erosive Wear Examination (BEWE) is a tool directed to the general clinician to address tooth erosion providing a direction on how to identify and classify the lesions and to manage the risk of the patient (Barlett et al., 2008).

This study aims to evaluate the trend of dental erosion in adolescents from three different countries from Europe, Latin America and Middle East and to identify the different etiological risk factors for each population.

AIM

To evaluate the prevalence of dental erosion and its relationship with the etiological risk factors in adolescents between 13 and 15 years old in three different countries: Italy, Mexico and Saudi Arabia.

MATERIALS AND METHODS

A cross-sectional evaluation was carried out to investigate the trend of dental erosion in each country and to compare its relationship with the reported risk factors.

The research project took place during a 2-year period, from February 2013 to February 2015 in 1) Sassari, Italy; 2) Veracruz, Mexico and 3) Jeddah, Saudi Arabia.

Study population

Subjects between 13 to 15 years old enrolled in a high school system. They were classified according to sex (M or F), age (13-15 years old), and geographical area (Europe, Latin America, Middle East). The total population consisted of 220 adolescents from Italy, 230 from Mexico and 225 from Saudi Arabia. Eligibility for the inclusion consisted on having a common background and/or socio-economic status (SES) and living within the same urban area (according to the country). Subjects wearing fixed orthodontic appliances were excluded.

Clinical examination

Each subject was examined inside the school under natural lighting using a mouth mirror No. 5 and a WHO explorer. Erosion was measured and the risk level was calculated using the Basic Erosive Wear Examination BEWE (Barlett et al., 2008).

Questionnaire

A pretested questionnaire was administered individually to each subject. The questionnaire was divided into four domains: 1) vital statistics: gender height (cm) weight (Kg), general health status, assumption of medication; 2) dietary patterns: description of meals, consumption in quantity and frequency, of acidic drinks and food *i.e.* freshly made natural or bottled fruit juices, sport drinks, diet and regular soft drinks, fruits ; 3) oral hygiene habits *i.e.* toothbrushing habits and frequency, type of toothbrush 4) Socio-economical status i.e. education of the parents, house property.

For each country, a specific set of questions was performed to cover their particular dietary habits. In Mexico the consumption of lemon and salt along with fruits or vegetables as snacks,

acidic candies and vinegar and lemon pepper sauces was recorded. In Italy, the tomato sauce and vinegar intake was registered. In Saudi Arabia, the traditional diet is based on dates and oriental desserts so no indication of erosive food or drinks was signed. Every question was divided for the place of intake, at school or not at school.

Data analysis

Evidence from the examination and questionnaire was entered in the FileMaker Pro 9.0 Runtime database. Individuals were classified into three age groups: 13,14 and 15 years olds. Subjects affected by systemic diseases were classified as not healthy. The assumption of medication was treated as Yes or No.

Questionnaire findings were assort as follows: the toothbrushing frequency was split in “once a week”, “more than once a week”, “once a day”, twice a day” and “more than twice a day”; the use of electric toothbrush was classified as “yes” or “no”. The consumption of freshly made natural and bottled fruit juices, sport drinks and diet and regular soft drinks and acidic snacks and food was divided into “low” (never or less than once a week), “moderate” (1 to 5 times a week) and “high” (at least once a day). The place where the drinks and food were consumed was split into “at school” or “not at school” (home). Education of the parents was split in “none”, “basic education”, “high school diploma” and “university graduates” while the socio-economic status (SES) into “low” (rent property) or “high” (owned property).

Clinical examination data were treated as numerical ordinal data for Erosion (0= no erosive tooth wear,1= initial loss of surface texture, 2=distinct defect, hard tissue loss <50% of the surface area and 3= hard tissue loss >50% of the surface area). BEWE score was calculated

by summing the highest point for each sextant (Range 0 to 18). Risk level was treated as None (<2), Low (3-8), Medium (9-13) and High(>14). All data were analyzed using the software STATA (Mac version 10.1). The statistical significance level was set at α=0.05.

RESULTS

A total of 675 adolescents from Italy (n=220), Mexico (n=230), and Saudi Arabia (n=225) participated in the study, 51.1% were males and 48.9% females. Mean age was 14.09±0.81.

The global experience of erosive wear was 12.7%. The prevalence of erosion was higher in Mexico (18.7%), followed by Italy (12,7%) and Saudi Arabia (6.7%) (p=0.001). The severity of erosion was 1 (Initial loss of surface texture) in 93.0% of the cases and 2 (Distinct defect, hard tissue loss <50% of the surface area) in 7.0%. The mean BEWE score for the erosive lesions was 3.64 in Italy, 3.04 in Mexico and 1.2 in Saudi Arabia.

In the subjects presenting erosion, the overall reported level of acidic drinks intake was not significant for natural juice fruits, while the consumption of bottled fruit juices was statistically significant: 46.5% of the subjects with erosive lesions consumed bottled fruit juices over once a day (p<0.01). The high frequency of soft drinks intake was a constant variable for the presence of erosion, 77.9% of the subjects with erosion reported a high consumption (p<0.01).

Regarding the specific dietary patterns, in Mexico the consumption of both fresh made acidic snacks and packed acidic snacks was significantly related to the presence of erosion (p<0.01). In Italy and Saudi Arabia the observation of specific dietary patterns was not significant.

When comparing the relevance of the place where erosive drinks and snacks are consumed, if at school or not at school, In Italy was statistically significant, 85.7% of the subjects that presented erosion had consumption at school and a 100% at home ($p=0.04$). For the general consumption of acidic drinks and food, In Mexico, 54.8% of the subjects reported a double intake, both at school and not at school ($p<0.01$) and of the subjects presenting erosion, 100% consumed them at home while 83.7% at school. In Saudi Arabia was not significant.

Risk factors as general health status and assumption of medications, the level of education of the parents, Socio-economic status, and toothbrushing habits were not significant for the population.

DISCUSSION

The objective of our study was to identify the trend of dental erosion in three different geographical areas with distinctive traditions and background and to understand the associated risk factors.

The evaluation of erosive wear has not been reported in many nations so important information from cross-sectional and incidence investigations that would help to determine the presence, evolution and allocation of the condition is missing (Jaeggi et al., 2006). We found a significant difference between Italy, Mexico and Saudi Arabia. Mexico presented a higher prevalence of the condition and it can be explained with the dietary habits rich in citric fruits and snacks, while Saudi Arabia presented a very low presence of erosive lesions, having basically a sweet diet.

It has been reported that the socioeconomic status (SES) can compromise erosion due to the fact that higher education and income can influence oral hygiene habits and the diet into a western style (Zero et al., 2006), in our study, Mexico had the highest prevalence of erosive lesions and the highest intake of soft drinks due to the influence of western lifestyle in urban centers of the country, yet in this case

the consumption of soft drinks is more common in low-income families as carbonated soda is cheaper than milk for example.

We found that the daily high intake of soft drinks was the indicative factor for the presence of erosion, more than any other element agreeing with what has been reported that when more than one risk factor is present, patients who have over 4 dietary acid intakes have a higher risk for erosive wear (Lussi et al., 2014).

There is evidence that the condition of erosion is increasing, but is difficult to compare the different reports as they have utilized different scoring systems (Jaeggi et al., 2014). Our study used the BEWE to standardize the data collection and analysis.

Even thought there was a significance difference in the distribution of erosion in the three countries, being highly prevalent in Mexico and very low in Saudi Arabia, a low risk level was reported for all the subjects who presented the condition. The understanding of the erosion behavioral risk factors as the excessive consumption of erosive food and drinks is fundamental for implementing prevention strategies (Carvalho et al., 2014).Although data about erosion is not homogeneous, an emphasized trend of erosion in young people has been observed (Jaeggi et al., 2014).

CONCLUSIONS

The trend of dental erosion in adolescents is highly related to the diet in all the three countries. The misguided intake of soft drinks was the determinant factor for the presence of erosive wear. The behavioral risk factors were not significantly related in any of the populations.

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MULTICENTER STUDY

AIM

The main purpose of this doctoral research was to assess the prevalence of the major oral diseases and to evaluate the etiology and risk factors in the Italian and non-Italian population by age, sex and distribution. The data collection took place in three different countries that are representative of Europe, Latin America and Middle East: Italy, Mexico and Saudi Arabia and included a population of adolescents for each country between 12 and 15 years old.

Objectives

1. To assess the prevalence of the major oral diseases and to evaluate the etiology and risk factors population by age, sex and distribution.

2. To investigate the association between caries experience, gingival status, erosive wear, oral hygiene, BMI and dietary habits among adolescents 13 to 15 years old.

3. To analyze the erosive wear status in relation to behavioral factors.

4. To examine the impact of overweight (BMI) on caries experience.

5. As well, in order to compare the heterogeneous urban fraction with an homogenous population, a rural area of Mexico was included.

This cross-sectional descriptive study aimed to incentive the cooperation between National and International institutions to evaluate the oral health status in the community. It was divided into three stages:

1. Data Collection Phase (Stage I)
2. Analysis Phase (Stage II)
3. Informative Phase (Stage III)

Stage I. Data Collection Phase

Materials and Methods

The aim is to identify the characteristics and risk factors of the most prevalent oral diseases in a selected young population from different parts of the globe.

Study population

The subjects were classified according to sex (M or F), age (13-15 years old), and geographical area (Europe, Arabian Peninsula and the Americas). The population consisted of 909 subjects (Italy n= 220; Saudi Arabia n=225; Mexico Urban n=224; Mexico rural n=240). The visited areas were Sassari (Italy), Jeddah (Saudi Arabia) Veracruz city (Mexico) and the rural town of Tepancan (Mexico).

Eligibility

- Students between 12 to 15 years old
- Having a common background and/or socio-economic status (SES)
- Living within the same urban area (according to the country)

Exclusion criteria

- Subjects with systemic medical problems
- Subjects undergoing orthodontic treatment with fixed orthodontic appliances.

Clinical examination

The parents signed an informed consent. Each subject was examined inside the school facilities under natural lighting using a mouth mirror No.5 and a WHO explorer. Caries was recorded according to the ICDAS criteria. As well, DMFS was scored following WHO guidelines. Dental erosion was scored using the Basic Erosive Wear Examination (BEWE). Gingival Index was assessed using the Silness-Löe Index.

Questionnaire

A pre-tested questionnaire was administered to each subject. The questionnaire was divided into four domains: (1) vital statistics *i.e.* gender, height, weight; (2) dietary patterns *i.e.* description of meals, consumption of sugared drinks and sweets as snacks; (3) oral habits *i.e.* toothbrushing habits, the frequency of dental floss and the frequency of dental check-ups; (4) socio-economic level i.e. educational level of the parents, property of the household. Height (cm) and weight (kg) were measured by one operator (CLC) using a mechanical physician scale with integrated measuring rod (Rice Lake RL-MPS) and scored in meters and kilograms, respectively. BMI then was calculated dividing the weight by the square of the height (kg/m^2) according to WHO criteria [9]. Moreover, a dietary record was collected for 3 days.

For each country, a specific set of questions was performed to cover their

particular dietary habits. In Mexico the consumption of lemon and salt along with fruits or vegetables as snacks, acidic candies and vinegar and lemon pepper sauces was recorded. In Italy, the tomato sauce and vinegar intake was registered. In Saudi Arabia, the traditional diet is based on dates and oriental desserts so no indication of erosive food or drinks was signed. Every question was divided for the place of intake, at school or not at school.

Taste preference test

Sweet taste preference evaluation was performed using sucrose solutions with different concentrations from 1.63 to 821.52 g/L, starting from lowest to the highest. Each subject tasted the solutions with a full mouth technique and responded at which solution they perceived the sweet taste and which one they preferred.

Stage II. Analysis Phase

Aim: The objective of this phase was to examine and describe the frequency and distribution of the oral health diseases. Data was sorted and highlighted, and analysis methods and statistics were carried out.

The results for each country were compared to identify the prevalence and status of the oral diseases in the study population.

Statistical Analysis

Evidence from the dental examination and questionnaire was entered in the FileMaker Pro 9.0 Runtime database and then exported to Excel Microsoft spread sheet. The adolescents were classified into two age groups: 12-13 years olds and 14-15 years olds. Subjects affected by systemic diseases were classified as not healthy. The assumption of medication was treated as Yes or No. Body Mass Index was classified for the respective age group as: Normal weight (>15 – 21 and >16 - 23) overweight (>21 – 24 and >23 - 26) and obese (>24 and >26) according to the WHO guidelines [20] and data was treated as “normal weight” or “overweight” (overweight and obese). Subjects affected by systemic diseases like diabetes, asthma, cardio-vascular diseases, etc. were classified as not in good general health. Education of the parents was split in “none”, “basic education”, “high school diploma” and “university graduates” while the socio-economic status (SES) into “low” (rent property) or “high” (owned property).

Questionnaire data were categorized as follows: the toothbrushing frequency was split in “once a day”, “twice a day” and “more than twice a day”; the use of dental floss into “rarely” less than once a day and “frequently” at least once a day; the frequency of dental check-up as “irregular” if only when in pain and “regular” if attended scheduled check-ups. The consumption of sugared drinks

was divided into “never”, “once a day”, “twice a day” and “more than twice a day” and sweets was divided into “never”, “less than 3 times a day” and “over 3 times a day”. The place where the drinks and food were consumed was split into “at school” or “not at school” (home).

Clinical examination data for caries were treated as numerical ordinal data for ICDAS (ICDAS=0 healthy; ICDAS=1-3 enamel caries; ICDAS=4-6 dentin caries), and continuous variable for DMFS. Gingival Index was scored 0 for normal gingiva, 1 for mild inflammation, 2 for moderate and 3 for severe inflammation. Descriptive statistics, cross tabulations and linear trends were calculated for caries prevalence (DMFS>0), caries severity (ICDAS) and zone, gender, age, BMI, toothbrushing frequency, the use of dental floss, dental check-ups, the consumption of sugared drinks and sweets as snacks, and gingival index.

Clinical examination data for Erosion were treated as numerical ordinal data (0= no erosive tooth wear, 1= initial loss of surface texture, 2=distinct defect, hard tissue loss <50% of the surface area and 3= hard tissue loss >50% of the surface area). BEWE score was calculated by summing the highest point for each sextant (Range 0 to 18). Risk level was treated as None (<2), Low (3-8), Medium (9-13) and High (>14).

Next, multinomial logistic regression models were performed using as the dependent variable: ICDAS scores. The Akaike information criterion (AIC) was used to measure the goodness of fit of the statistical model [21]. The possible modifying effects of covariates on the outcomes were tested by an interaction model (likelihood ratio test statistic). Multicollinearity might sometimes cause problems with regression results. This problem was solved using the DFBETA command in STATA, dropping the information that have too much influence on the regression line. However, after the data elaboration, no statistically significant multicollinearity was observed and so it was decided to report

findings without outliers. The possible correlated variables were analyzed using the principal component analysis (PCA).

All data were analyzed using the software STATA (Mac version 10.1). For all analyses, the statistical significance level was set at $\alpha=0.05$.

Results

The population consisted of 909 subjects (Italy n= 220; Saudi Arabia n=225; Mexico Urban n=224; Mexico rural n=240).

Total mean DMFS was 2.96 ± 4.01, and it was higher in Saudi Arabia (3.0±4.0), followed by Italy (1.4±2.3) and Mexico (1.2±1.5) ($p<0.001$). Subjects in the urban area presented more caries than subjects in the rural area ($p<0.01$).

Mean BMI was 23.87 SD 6.07 with the 46.6% being normal weight, 19.5% overweight, 16.4% underweight and 17% obese.

Mean taste threshold (TT) was 5 out of 10 and taste preference (TP) was 7.72 out of 10. Plaque score was 4.07. TT was higher in Italy, followed by Saudi Arabia and Mexico while TP was higher in Saudi Arabia, followed by Italy and Mexico. A relationship was found between sweet taste preference and caries ($p<0.01$). Saudi Arabia had the highest mean values for both TP and caries followed by Italy and Mexico ($p<0.001$).

The use of dental flossing was statistically significantly associated to enamel caries ($p=0.02$). The relationship between dental check-ups and caries was relevant ($p<0.01$).

Table 1. *Distribution of the population from Italy, Mexico and Saudi Arabia by age and Body Mass Index (BMI).*

Mean	Males	Females	Total
Age	14.61±0.51	14.84±0.37	14.72±0.46
BMI	25.09±6.68	22.60±4.82	23.87±6.07

Table 2. *Distribution of the population from Italy, Mexico and Saudi Arabia by Taste Threshold (TT).*

Mean	Males	Females	Total
TT	5±1.73	4±1.28	5±1.59
TP	8±1.82	7±1.71	7.72 ±1.87

Table 3. *Distribution of caries according to the DMFS Index (Decay, Missing, Filled Surface).*

Surfaces	Males (n)	Females (n)	Total (n)
D1	272	250	522
D2	164	594	758
D3	122	115	237
D4	138	78	216

D5	44	17	61
D6	16	5	21
M	3	4	7
F	152	215	367
DMF	353	319	672

Erosion

The global experience of erosive wear was 12.7%. The prevalence of erosion was higher in Mexico (18.7%), followed by Italy (12,7%) and Saudi Arabia (6.7%) ($p=0.001$). The severity of erosion was 1 (Initial loss of surface texture) in 93.0% of the cases and 2 (Distinct defect, hard tissue loss <50% of the surface area) in 7.0%. The mean BEWE score for the erosive lesions was 3.64 in Italy, 3.04 in Mexico and 1.2 in Saudi Arabia.

In the subjects presenting erosion, the overall reported level of acidic drinks intake was not significant for natural juice fruits, while the consumption of bottled fruit juices was statistically significant: 46.5% of the subjects with erosive lesions consumed bottled fruit juices over once a day ($p<0.01$). The high frequency of soft drinks intake was a constant variable for the presence of erosion, 77.9% of the subjects with erosion reported a high consumption ($p<0.01$).

Regarding the specific dietary patterns, in Mexico the consumption of both fresh made acidic snacks and packed acidic snacks was significantly related to the presence of erosion ($p<0.01$). In Italy and Saudi Arabia the observation of specific dietary patterns was not significant.

When comparing the relevance of the place where erosive drinks and snacks are consumed, if at school or not at school, In Italy was statistically significant, 85.7% of the subjects that presented erosion had consumption at school and a 100% at home (p=0.04). For the general consumption of acidic drinks and food, In Mexico, 54.8% of the subjects reported a double intake, both at school and not at school (p<0.01) and of the subjects presenting erosion, 100% consumed them at home while 83.7% at school. In Saudi Arabia was not significant.

Risk factors as general health status and assumption of medications, the level of education of the parents, Socio-economic status, and toothbrushing habits were not significant for the population.

Erosion and Basic Erosion Wear Examination (BEWE)

Table 1*. Distribution of the population from Italy, Mexico and Saudi Arabia by erosion prevalence and severity (0= none; 1=initial lost of surface; 2=* Distinct defect, hard tissue loss <50% of the surface area*).*

Severity	Freq.	Percent	Cum.
0	589	87.26	87.26
1	80	11.85	99.11
2	6	0.89	100.00
Total	675		

Table 2. *Distribution of the population by BEWE score.*

BEWE score	Freq.	Percent	Cum.
0	589	87.26	87.26
1	12	1.78	89.04
2	23	3.41	92.44
3	5	0.74	93.19
4	26	3.85	97.04
5	4	0.59	94.63
6	16	2.37	100.00
Total	675	100.00	

Table 3. *Distribution of erosion (absent =0; present =1) in Italy (I), Mexico (M) and Saudi Arabia (S).*

Country	EROSION 0	EROSION 1	Total
I	192	28	220
M	187	43	230
S	210	15	225
Total	589	86	675
Pearson chi2(2) = 14.8031 Pr = 0.001			

Erosion and Behavioral factors

Table 4. *Distribution of erosion (absent =0; present =1) according to the education of the parents (1=basic; 2=middle and high school; 3=university)*

Education	EROSION 0	EROSION 1	Total
1	132	29	161
2	137	21	158
3	253	29	282
Total	522	79	601
Pearson chi2(2) = 5.3662 Pr = 0.068			

Table 5. *Distribution of erosion (absent =0; present =1) according to the SES (socio-economic status) (1=low; 2=high)*

Education	EROSION 0	EROSION 1	Total
1	48	12	60
2	541	74	615
Total	589	86	675
Pearson chi2(1) = 3.1215 Pr = 0.077			

Impact of diet on erosion distribution

Table 6. *Distribution of erosion (absent =0; present =1) according to the consumption of fresh fruit juices (1=low; 2=moderate; 3=high)*

Consumption	EROSION 0	EROSION 1	Total
1	299	37	336
2	218	20	238
3	72	29	101
Total	589	86	675
Pearson chi2(2) = 28.1069 Pr = 0.000			

Table 7. *Distribution of erosion (absent =0; present =1) according to the consumption of bottled fruit juices (1=low; 2=moderate; 3=high)*

Consumption	EROSION 0	EROSION 1	Total
1	239	25	264
2	194	21	215
3	156	40	196
Total	589	86	675
Pearson chi2(2) = 14.6150 Pr = 0.001			

Table 8. *Distribution of erosion (absent =0; present =1) according to the consumption of sport drinks (1=low; 2=moderate; 3=high)*

Consumption	EROSION 0	EROSION 1	Total
1	371	51	422
2	158	14	172
3	60	21	81
Total	589	86	675
Pearson chi2(2) = 16.1048 Pr = 0.000			

Table 9. *Distribution of erosion (absent =0; present =1) according to the consumption of softt drinks (1=low; 2=moderate; 3=high)*

Consumption	EROSION 0	EROSION 1	Total
1	159	11	170
2	251	8	259
3	179	67	246
Total	589	86	675
Pearson chi2(2) = 74.2057 Pr = 0.000			

Impact of diet on erosion distribution by Country

Table 10. *Distribution of erosion (absent =0; present =1) in Italy according to the consumption of soft drinks (1=low; 2=moderate; 3=high)*

Consumption	EROSION 0	EROSION 1	Total
1	47	3	50
2	90	0	90
3	55	25	80
Total	192	28	220
Pearson chi2(2) = 39.8730 Pr = 0.000			

Table 11. *Distribution of erosion (absent =0; present =1) in Mexico according to the consumption of soft drinks (1=low; 2=moderate; 3=high)*

Consumption	EROSION 0	EROSION 1	Total
1	45	5	50
2	76	3	79
3	66	35	101
Total	187	43	230
Pearson chi2(2) = 30.9434 Pr = 0.000			

Table 12. *Distribution of erosion (absent =0; present =1) in Saudi Arabia according to the consumption of soft drinks (1=low; 2=moderate; 3=high)*

Consumption	EROSION 0	EROSION 1	Total
1	67	3	70
2	85	5	90
3	58	7	65
Total	210	15	225
Pearson chi2(2) = 2.5746 Pr = 0.276			

Table 13. *Distribution of erosion (absent =0; present =1) in Mexico according to the consumption of fruits and vegetables with the adjunction of lemon (1=low; 2= high)*

Consumption	EROSION 0	EROSION 1	Total
1	90	11	101
2	97	32	129
Total	187	43	230
Pearson chi2(1) = 7.2161 Pr = 0.007			

Table 14. *Distribution of erosion (absent =0; present =1) in Mexico according to the consumption of soft drinks (1=low; 2= high)*

Consumption	EROSION 0	EROSION 1	Total
1	102	15	117
2	85	28	113
Total	187	43	230
Pearson chi2(1) = 5.4078 Pr = 0.020			

Impact of the place on the ingestion of erosive food/drinks

Table 15. *Distribution of erosion (absent =0; present =1) in the overall population according to the consumption of erosive food/drinks at school (1=no; 2= yes)*

School	EROSION 0	EROSION 1	Total
1	275	25	300
2	314	61	375
Total	589	86	675
Pearson chi2(1) = 9.4353 Pr = 0.002			

Table 16. *Distribution of erosion (absent =0; present =1) in the overall population according to the consumption of erosive food/drinks at home (1=no; 2= yes)*

Home	EROSION 0	EROSION 1	Total
1	51	0	51
2	538	86	624
Total	589	86	675
Pearson chi2(1) = 8.0551 Pr = 0.005			

Table 17. *Distribution of erosion (absent =0; present =1) in Italy according to the consumption of erosive food/drinks at school (1=no; 2= yes)*

School	EROSION 0	EROSION 1	Total
1	111	4	115
2	81	24	105
Total	192	28	220
Pearson chi2(1) = 18.5570 Pr = 0.000			

Table 18. *Distribution of erosion (absent =0; present =1) in Mexico according to the consumption of erosive food/drinks at school (1=no; 2= yes)*

School	EROSION 0	EROSION 1	Total
1	42	7	49
2	145	36	181
Total	187	43	230
Pearson chi2(1) = 0.7966 Pr = 0.372			

Table 19. *Distribution of erosion (absent =0; present =1) in Saudi Arabia according to the consumption of erosive food/drinks at school (1=no; 2= yes)*

School	EROSION 0	EROSION 1	Total
1	122	14	136
2	88	1	89
Total	187	43	225
Pearson chi2(1) = 7.2709 Pr = 0.007			

Table 20. *Distribution of erosion (absent =0; present =1) in Italy according to the consumption of erosive food/drinks at home (1=no; 2= yes)*

Home	EROSION 0	EROSION 1	Total
1	24	0	24
2	168	28	196
Total	192	28	220
Pearson chi2(1) = 3.9286 Pr = 0.047			

Table 21. *Distribution of erosion (absent =0; present =1) in Mexico according to the consumption of erosive food/drinks at home (1=no; 2= yes)*

Home	EROSION 0	EROSION 1	Total
1	12	0	12
2	175	43	218
Total	187	43	230
Pearson chi2(1) = 2.9112 Pr = 0.088			

Table 22. *Distribution of erosion (absent =0; present =1) in Saudi Arabia according to the consumption of erosive food/drinks at home (1=no; 2= yes)*

Home	EROSION 0	EROSION 1	Total
1	15	0	15
2	195	15	210
Total	210	15	225
Pearson chi2(1) = 1.1480 Pr = 0.284			

Rural vs Urban

Subjects in the urban area presented more caries than subjects in the rural area ($p<0.01$). Our results show a total DMFS of 1.27±2.15, being 1.16±1.48 for UA, (Range 0-7) and 1.38±2.63 for RA (Range 0-20) with a total caries prevalence of 38.0%.

A total of 129 adolescents from UA and 159 from RA had an ICDAS score of 0. Urban subjects had a higher prevalence of enamel caries respect to the rural population (63.2% and 36.8%) and a lower prevalence of dentin caries lesions (22.5% and 77.5%, respectively) ($p<0.01$).

The percentage of caries severity (ICDAS) and the percentage of BMI (underweight / normal weight / overweight / obese) in the two groups are displayed in Figure 1. For the population between 12–13 years old, BMI of <15 was classified as Underweight, >15-21 was classified as Normal weight, >21-24 as Overweight and >24 as Obese; for 14 to 15 years old, the values were <16, >16-23, >23-26 and >26 respectively. BMI mean was 21.92±2.91 and it was higher in the urban area.

Overweight subjects presented a lower number of enamel caries (n=27) compared to obese (n=52) and normal weight (n=57). For dentin caries, the overweight group presented a lower prevalence (1.9%) compared to the normal weight (3.2%) and obese (3.5%) children.

The use of dental flossing was statistically significantly associated to enamel caries ($p=0.02$). The relationship between dental check-ups and caries was relevant in the urban population ($p<0.01$).

The reported consumption of sugars was absent for 19.6% of the population, moderate for 66.0% (1 to 3 times a day) and high for 14.4% (>3 times a day). Of the subjects, 61.2% consuming sweets belonged to UA (p=0.04). On the other hand, 9.3% of the adolescents did not take sugar drinks (RA 69.8%; UA 30,2%) and 46.1% reported a high consumption (>3 times a day), being 57.5% of the urban area.

The Gingival Index was 1 for 10.8% of the rural population, 2 for 5.4% and 3 for 2.1% while in the urban population was 1 for 19.2%, 2 for 13.4% and 3 for 3.6%.

Table 1. *Sample distribution across caries severity. Distribution according to area, gender, age, Body Mass Index, general health, oral hygiene habits (toothbrushing and flossing), dental check-ups and frequency of the consumption of sweets (drinks and snacks).*

		Caries-free (ICDAS 0) n(%)	Enamel Caries (ICDAS 1/3) n(%)	Dentin Caries (ICDAS 4/6) n(%)	P>|z|
Area					
	Urban	129 (27.80)	86 (18.53)	9 (1.94)	< 0.01
	Rural	159 (34.27)	50 (10.78)	31 (6.68)	
Gender					
	Male	163 (35.13)	74 (15.95)	24 (5.17)	0.81
	Female	125 (26.94)	62 (13.36)	16 (3.45)	
Years					
	12-13	158 (34.05)	70 (15.09)	24 (5.17)	0.61
	14-15	130 (28.02)	66 (14.22)	16 (3.45)	
BMI					
	Normal weight	121 (26.08)	57 (12.28)	15 (3.23)	
	Overweight	59 (12.71)	27 (5.82)	9 (1.94)	0.99
	Obese	108 (23.28)	52 (11.21)	16 (3.45)	
Good General Health					
	Yes	278 (59.91)	131 (28.23)	35 (7.54)	0.03
	No	10 (2.16)	5 (1.08)	5 (1.08)	
Toothbrushing Frequency					
	1/day	66 (14.22)	38 (8.19)	11 (2.37)	
	2/day	89 (19.18)	41 (8.84)	13 (2.80)	0.79
	>2/day	133 (28.66)	57 (12.29)	16 (3.45)	
Flossing					
	Rarely	147 (31.68)	89 (19.18)	21 (4.53)	0.02
	Frequently	141 (30.39)	47 (10.13)	19 (4.09)	
Dental check-ups					
	Irregular	164 (35.35)	89 (19.18)	27 (5.82)	0.15
	Regular	124 (26.72)	47 (10.13)	13 (2.80)	
Sugared Drinks					
	Never	25 (5.39)	12 (2.59)	6 (1.29)	
	1/day	132 (28.45)	58 (12.50)	17 (3.66)	0.50
	2/day	84 (18.10)	34 (7.33)	9 (1.94)	
	>2/day	47 (10.13)	32 (6.90)	8 (1.72)	
Sweet snacks					
	Never	60 (12.93)	22 (4.74)	9 (1.94)	
	<3/day	186 (40.09)	95 (20.48)	25 (5.39)	0.78
	>3/day	42 (9.05)	19 (4.09)	6 (1.29)	

Table 2. *Relative Risk Ratios after multinomial logistic regression model using ICDAS as dependent variable. ICDAS=0 healthy, ICDAS1 enamel caries, ICDAS2 dentinal caries.*

		RRR	Std. Err.	P>|z|	[95% Conf. Interval]
0			(base outcome)		
1	Zone	0.50	0.11	< 0.01	0.32 – 0.76
	BMI	1.03	0.04	0.41	0.96 – 1.10
	Good General Health	1.05	0.60	0.93	0.34 – 3.23
	Flossing	0.59	0.13	0.02	0.39 – 0.91
2	Zone	2.86	1.15	< 0.01	1.30 – 6.27
	BMI	0.95	0.06	0.48	0.84 – 1.09
	Good General Health	4.01	2.37	0.02	1.26 – 12.75
	Flossing	0.83	0.29	0.58	0.42 – 1.63
Number of obs = 464			p < 0.01		Log likelihood = - 383.57

Multinomial logistic regression model

Using the multinomial logistic regression model with ICDAS as dependent variable (0 = no caries; 1= enamel caries and 2= dentin caries) including Zone (UA=1; RA=2), BMI, Good General Health, Flossing and Gingival Index ($p<0.01$), the zone was always reported to be significant both in 1 and 2 ($p<0.01$). Flossing was statistically significant in the presence of enamel caries ($p=0.02$) while health status was related to dentin caries in 2 ($p=0.02$).

Principal Component Analysis

A principal Component Analysis (PCA) was performed on the data set, first on the total sample and in the two groups stratified by zone (urban and rural). The analysis included: gender, BMI, DMFS, GI (gingival index), sweets (daily sweet snacks consumption), sugar drinks, flossing and dental check-ups. In the PCA analyses, the first two characteristic values(eigenvalues) obtained from distance matrix between groups, collectively account for more than 66.0% of the total variance (77.2%; 45.8 and 31.4%, respectively the first two eigenvalues, in the total sample; 71.9% (47.3% and 24.6%) in the urban area and 72.9% in rural area (33.5% and 39.4%). An Orthogonal Rotation (varimax) displays of the first two principal coordinates in the total sample and in the areas.

In the total sample (1) there are three clear clusters, the first contains gender, BMI and DMFS; the second includes flossing and dental check-ups and the third contains sugar drinks and sweets. In the urban area (2) also three clusters were grouped: the first is DMFS and GI, the second includes flossing and dental check-ups and the third includes sugar drinks and sweets. In the rural zone (3) only two clusters were identified: in the first cluster gender and GI tended to group a cluster and in the second one DMFS and BMI.

Figure 1. *PCA Principal Component Analysis. Orthogonal rotation (varimax) (1= total sample, 2=urban, 3=rural). The variables are: Gender, BMI (Body Mass Index), DMFS (Decayed, Missing or Filled surface), GI (gingival index), Sweets (frequency of sweet snacks consumption), Sugar drinks (intake frequency), Flossing and Dental check-ups.*

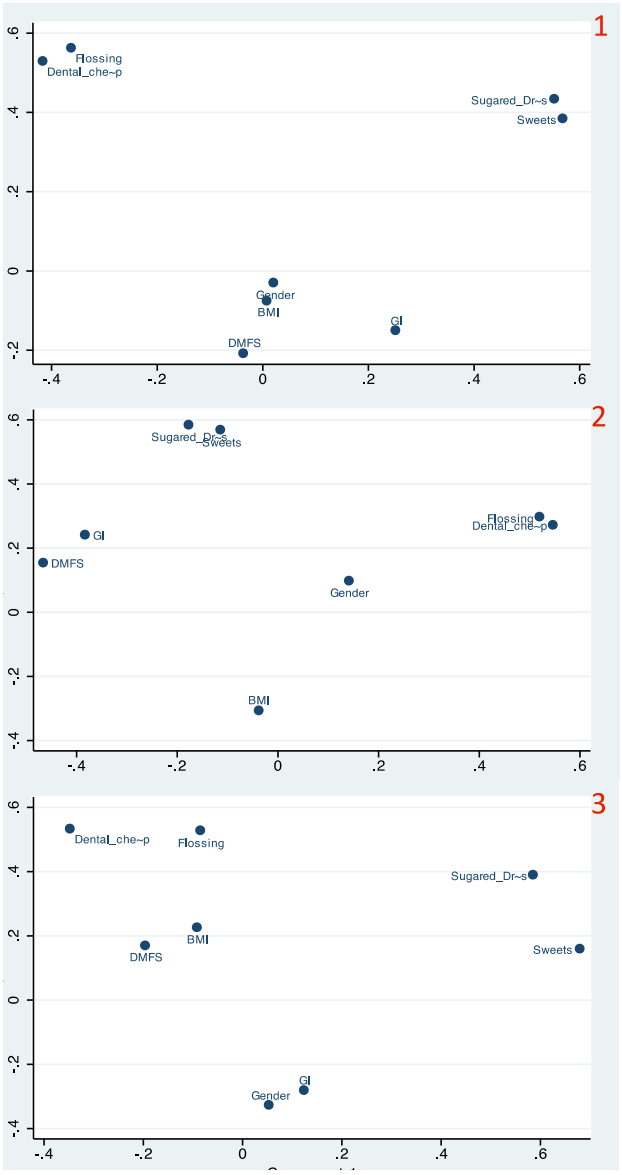
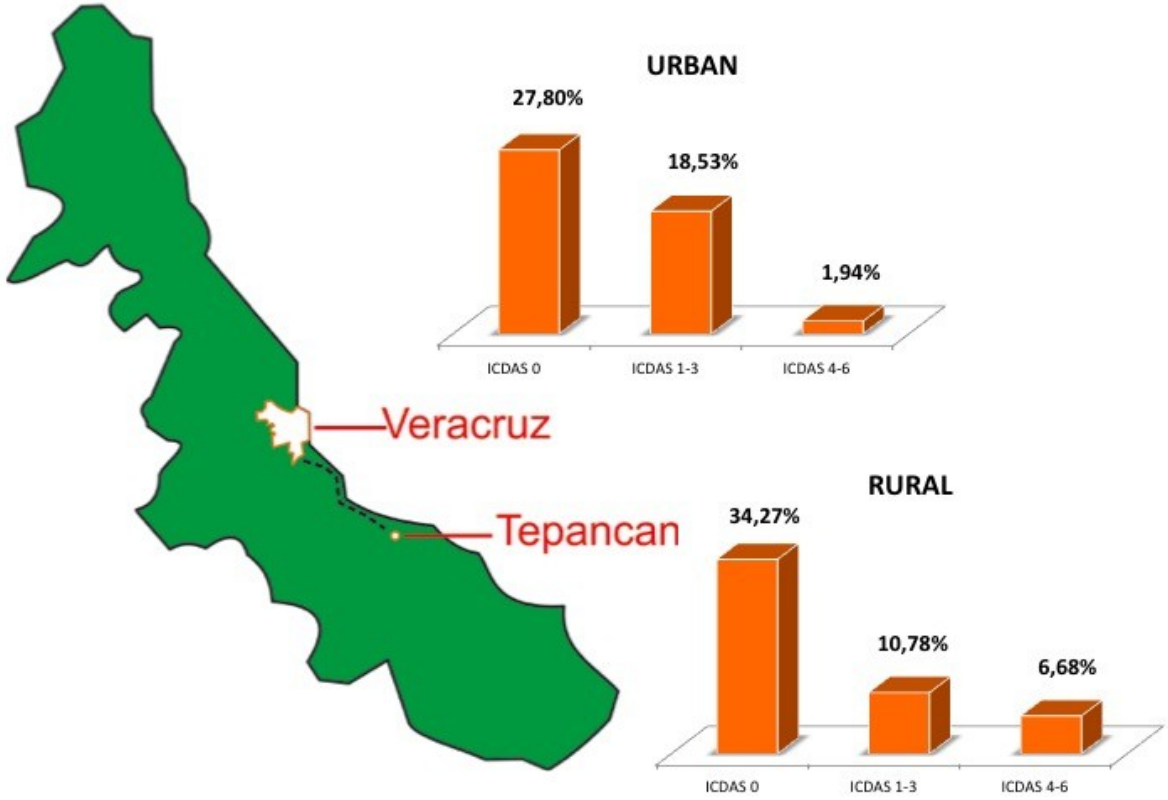


Figure 2. *Distribution of caries presence and severity (ICDAS 0, ICDAS 1-3, ICDAS 4-6) in the Urban and the Rural area.*



Discussion and Conclusions

This paper results suggest that the distribution of oral diseases is related to the behavioral, socio-cultural and geographic situations.

Caries experience was higher in Saudi Arabia, where diet was mainly based on sweets, in the diet questionnaire they responded to have a high consumption of oriental desserts and dishes and they were prevalently ingested at home. They reported as well the lowest taste threshold, this is, they were able to recognize sweet flavor at higher dissolutions and as well, they had the highest taste preference: they preferred more sweet. In contrast, they presented the least erosive wear status and the highest socio-economic background.

In Mexico on the other hand, adolescents had the highest erosive wear status over Italy and Saudi Arabia while they presented the lowest caries prevalence of the three countries, as well as the lowest taste threshold and preference. They reported a high consumption of soft drinks that were significantly related to the presence of erosion. The diet was based of fruits and vegetables and although mean Body Mass Index was similar in the urban and in the rural population, in the last one BMI was significantly related to caries severity: overweight subjects had more dentin caries. As well, adolescents with systemic diseases presented higher severity of caries. Rural populations reported the worst oral hygiene habits, infrequent dental check-ups (mainly when in pain) and limit access to health care facilities; yet, the urban fraction had more caries lesions. This was correlated to a more westernized diet.

Italy was in the middle of the evaluation. They reported a more equilibrated occurrence of oral diseases: the severity of caries was moderated in relationship to the other countries and the prevalence or erosion was in association with the consumption of acidic foods as vinegar. They had a modest sweet taste threshold and this was proportional to the taste preference. Bad dietary habits (excessive use of soft drinks and sweets) were reported mainly at school.

Both caries and dental erosion are associated to diet and diet is a decisive factor both in homogeneous and heterogeneous societies. Being diet likewise a risk factor for overweight, the reported significant relationship between body mass index and caries experience in the adolescent population indicate the preventive measures that need to be implement in countries with different backgrounds to reduce the incidence of both oral and general health conditions. Oral health strategies can make a decisive change in the current and future quality of life of adolescents worldwide.

Stage III. Informative Phase

The aim of this phase was to develop and promote an adequate intervention approach to strengthen public health awareness and disclose the prevention of oral diseases.

The results have been exhibited and divulged in scientific meetings. As well, in each country, awareness and promotion of education at the school was given priority and the corresponding authorities as well as the parents were urged to apply preventive tactics. Each student was communicated with their oral health status and the Dean of each school was given a report about the findings, the impact of them and the corresponding strategies.

The outcomes have been presented in the International Association for Dental Research meetings as the IADR/PER Congress 2014 in Dubrovnik, Croatia and the 93th General Session & Exhibition of the IADR, 44th Annual Meeting of the AADR and 39th Annual Meeting of the CADR in Boston, Mass., USA. The results have been as well shown at the 9o Summer School from the W.H.O. Collaboration Center For Epidemiology and Community Dentistry of Milan in Alghero. Simultaneously, the research has lead to further international cooperation as a Cariology research collaborator at the Department of Public Health of the University of Leeds, England under the guidance of Prof. Gail Douglas and to a grant for the Biological Research in Dentistry Summer School of the University of Goettingen, Germany in 2015.

We plan to continue on promoting the results obtained during this three-year evaluation of the oral status of the adolescents in all three different parts of the world. This cooperation permitted a large number of people to get involved, practitioners and not, that at the end of the study were able to learn something new and to apply a bit of it into their personal activities.

We hope that the children involved in the study were able to understand the importance of dental diseases, the relationship with the everyday life and the ways to prevent their development and as well, the options of treatment.

We wish the parents were able to learn from their own children about proper oral hygiene techniques and frequency, the relationship between diet and oral health and that the children as well, will be able in the future to make a difference in their own sons and daughters.

We thank the personal of the schools that got involved and put great interest in the project to help us to collect the data.

The investigation of dental health seems to be less important when we think about the extreme poverty that is found in some countries in Latin America like Mexico, the main problematic in Middle East countries, and we give it for granted in European countries like Italy. Yet it is; it is fundamental and a priority for us all. Our dental health represents our general health status, it permits us to communicate, to nourish ourselves to grow up and grow old and as well, it allow us to smile: to smile without shame and without fear.

I am very honored to be part of a small piece that can make a huge difference in other's life.

THANK YOU

Cynthia Lara Capi

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