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Full Length Research Paper

Hard dental tissue lesions in inhabitants of an industrial zone

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The aim of this epidemiological study was to determine the level of hard dental tissue lesions in an air-polluted environment, as well as to evaluate, as one of the factors, the impact of the environment on the occurrence of these lesions and their frequency. An epidemiological study was conducted in the city of Pancevo, which is is one of the most powerful industrial centers in Serbia. 160 patients of both sexes aged 20 years and more, were subjected to routine clinical examinations. The control group consisted of 160 patients of both sexes from Belgrade, the capital of Serbia. The Klein-Palmer DMFT system and SiC index were calculated in assessing the prevalence of dental caries. Also, teeth indicated for extraction, were analyzed for the presence of heavy metals. The average value of the DMFT index in the investigated group and in the control group was 20.41 and 16.52 respectively. A highly statistically significant difference (p=0.0024) was found in the group of patients aged 51 to 60 years, and extremely statistically significant difference (p=0.0005) in the group of patients aged over 60 years. SiC index values were also higher in all age groups from the investigated group than in the control group. In patients of all age groups from the investigated group, a statistically significantly higher value for lead concentration in extracted teeth than in patients from the control group was documented. Noncarious lesions were diagnosed in 44% patients from the investigated group and 24% patients from the control group. The most common lesions in patients from the investigated group were irregular (50%) and wedge-shaped (47%) defects. In patients from the control group a significantly higher percentage of irregular shaped defects (80%) was diagnosed compared to wedge-shaped defects (19%). The results of this study indicate that a polluted environment is one of the factors that cannot be ignored in hard dental tissue lesions etiology, but also requires confirmation by further comprehensive basic research.

Key words: polluted environment, hard dental tissue lesions, noncarious cervical lesions, heavy metals.

INTRODUCTION

The impact of the environment on the population's global health is well-known. Consequently studies dealing with the influence of environmental pollution on human health have become increasingly more important. Unfortunately, establishing a link between environmental geochemistry and human health is not easy. Indeed, the mobility of people and their acquisition of food and drink from many different, often non-local, sources justifies the apparently convincing conclusion that the local geochemical environment must have little influence on health. Dental epidemiology, however, provides some of the most convincing evidence that trace elements can affect the health of communities. Teeth have been extensively used as biological markers of exposure to environmental pollution (Alomary et al., 2006; Appleton et al., 2000; Baranowska et al., 2004; Bayoet al., 2001; Bercovitz and Laufer, 1993; Brudevold et al., 1977; Curzon and Crocker,

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1978; Gdula-Argasinska et al., 2004; Gil et al., 1996; Hernandez-Guerrero et al., 2004; Malara and Kwapulinski, 2005; Nowak and Chmielnicka, 2000; Tvinnereim et al., 2000). Teeth are good biological markers as they are easily available materials and because of the incorporation of elements into the mineral phase of dental tissues. It has been shown that, when present, metals are incorporated into forming hard dental tissue (Alomary et al., 2006; Hernandez-Guerrero et al., 2004). Unlike bone, in which the mineral phase is subject to turnover, teeth, once formed, provide a permanent cumulative and relatively stable record of past environmental exposure (Alomary et al., 2006; Budd et al., 1998). Therefore, the idea arose to conduct an epidemiological study to determine the level of hard dental tissue lesions in an air-polluted environment and to compare the results with those obtained in another area, as well as to evaluate, as one of the factors, the impact of the environment on the occurrence of these lesions and their frequency. A high incidence of tooth-structure damage significantly affects the functional ability of chewing, mental and work capacity of individuals, causes diseases of the digestive tract and other systems and organs and also represents a serious medical, social and economic problem of the global society.

An epidemiological study was conducted in the city of Pancevo, which is located in the South Banat district of Serbia. South Banat is industrially one of the most developed districts in Serbia, second only to the Serbian capital of Belgrade. The city of Pancevo, wedged between two major rivers, is a modern, small-sized city with developed chemical, petroleum refining, agricultural, food and metal industries. It is one of the most powerful industrial centers in Serbia, and this inevitably brings with it the frequent occurrence of air pollution and contamination of water and soil. The existence of these risk factors in the environment has a negative impact on public health. Analysis of morbidity in the adult population of Pancevo, within groups of diseases, showed that this population most often suffers from respiratory diseases. In the period since 1991 to 2001 the concentrations of soot and NH_3 in the air were well above permitted values. In a study completed in 2004 (Cenic-Milosevic and Nikolic, 2004), it was stated that despite the fact that Belgrade is a large and highly developed city with around 2 million residents, pollution in Pancevo (measured by the amount of heavy metals in the stimulated saliva of school children) was significantly higher. In recent years, much effort has been invested to reduce the level of air pollution and the public health institutions carry out daily monitoring of air pollutants. The primary pollutants that are monitored include sulphur dioxide, nitrogen dioxide and soot, while specific pollutants include NH_3, benzene, toluene, xylene and toxic heavy metals (Pb, Cd, Zn, Hg, Ni, Cr). Despite great efforts to lessen the level of air pollution, the results of daily monitoring for the previous year have shown that on 59 days, air quality was not considered as good or moderate regarding the measured concentrations of soot.

Hard dental tissue lesions include caries and noncarious lesions (abrasion, erosion, attrition). The mechanism of caries development was the subject of many studies during previous years and consequently general and local predisposing factors are now well-known (Jakovljevic and Ristic, 2008). In recent years, the subject of many studies has been the connection between environmental conditions and caries, more accurately, the determination of the effects of heavy metals on the occurrence and incidence of caries. In addition, it has been speculated for some time that environmental pollution, especially by acid fumes, could also be one of the factors involved in the occurrence and incidence of noncarious lesions.

The aim of this epidemiological study was to determine the frequency of hard dental tissue lesions in the population of the municipality of Pancevo and, by comparing them to the results from the control group, to evaluate the environmental impact, as one of the factors, on the occurrence of caries and noncarious lesions.

MATERIALS AND METHODS

This epidemiological study was conducted at the Institute of Stomatology, Faculty of Stomatology Pancevo, on a sample of patients referred for dental examination and treatment. 160 patients of both sexes (in further text: investigated group) aged 20 years and more, were subjected to routine clinical examinations. When selecting participants, only individuals that had been living in Pancevo for more than 10 years were considered. The control group consisted of 160 patients of both sexes from Belgrade, the capital of Serbia, also aged over 20 years. Those patients were also examined at the Institute of Stomatology, Faculty of Stomatology Pancevo, by the same observers. Considering that Belgrade is a specific, metropolitan, urban environment, with a dynamic population, heavily influenced by immigration trends, the authors felt that the patients from this city represented an adequate control group. Belgrade is also polluted, but it is a different type of pollution, mainly around the busiest streets of the city, due to heavy traffic during the rush hours, but the level of pollution does not exceed critical values. On the other hand, Pancevo, because of the chemical plants, petroleum refining and metal industries, is often exposed to higher levels of pollution. Participants in the study were divided into five age groups: 1) 20 to 30 years old; 2) 31 to 40 years old; 3) 41 to 50 years old; 4) 51 to 60 years old; 5) over 61 years old.

Data obtained by comprehensive dental history and clinical examinations were entered in a questionnaire developed for this study (Pegoraro et al.,2005). Recorded data related to the general health of patients, problems related to the digestive tract, data about food consumption and consumption of carbonated drinks, as well as the general condition of the mouth and teeth including any changes in intermaxillary relations. Data related to oral hygiene and evaluations of susceptibility to caries based on clinical examination were also included in the questionnaire (Table 6).

Table 1. Mean values of the DMFT in patients from Pancevo and Belgrade.

Experimental group	Number of patients		DMFT		SiC	
	Investigated group	Control group	Investigated group	Control group	Investigated group	Control group
			Mean ± SD	Mean ± SD		
I(20 – 30)	32	32	12.12 ± 6.36	9.56 ± 5.08	19.09	14.27
II(31 – 40)	32	32	19.87 ± 5.30	17.09 ± 5.31	25.09	22.91
III(41 – 50)	32	32	21.44 ± 3.90	18.47 ± 6.10	24.63	24.54
IV(51 – 60)	32	32	23.69 ± 6.07	18.50 ± 7.02	30.00	26.27
V(over 60)	32	32	24.94 ± 6.41	19.00 ± 6.56	28.36	25.27
total	160	160	20.41± 5.03	16.52± 3.96	25.43	22.65

[a]SD= standard deviation.

The patients were clinically examined by a standardised procedure for dental examination, using a dental mirror and a straight dental probe or proximal probe for examination of mesial and distal surfaces of the teeth. Also, radiographic examination was performed on each patient. Radiographic examination included panoramic radiographic survey.

Bearing in mind that the results of epidemiological studies are highly dependent on the criteria in the diagnosis of certain diseases, dental caries lesions were diagnosed by standard criteria and marked in universal templates for dental status. The Klein-Palmer system DMFT (Decayed Missing Filled Teeth) was applied in assessing the prevalence of dental caries. Also, for each of the age groups of patients, a SiC index was calculated (Significant Caries Index), which represents the mean values of the DMFT index for one third of respondents with the highest DMFT-values, using tables recommended by World Health Organisation (WHO, 2011a). This index was introduced in 2000 in order to bring attention to those individuals with the highest caries values in each population under investigation and is used as a supplement to the DMFT index. Information related to clinically diagnosed loss of enamel and dentin of a noncarious etiology, the so-called noncarious lesions, was entered in the second part of the questionnaire. These lesions were systematised by: 1) distribution;

2) functional group of tooth; 3) localization, that is, the tooth surface on which the lesion occurred; 4) size and shape of lesion; 5) mode of lesion propagation.

Considering the fact that in the same facility within the project entitled "The Effects of a Chemically Polluted Environment on Oral Tissues and Teeth of Patients from Pancevo, Serbia", supported by The Ministry of Science and Technological Development, Republic of Serbia, (Project Number 21045), teeth indicated for extraction in some of the patients (who were additionally included in this study), were analyzed for the presence of heavy metals, some of those results were also used in this study. The sample included teeth from 32 patients from both cities, both sexes and different age groups. In most cases, the cause for extraction was either subsequent orthodontic therapy or progressive periodontal disease. The weight of each sample was at least 0.5 g which is a cut-off value for a valid chemical analysis. Samples of extracted teeth were prepared for analysis by microwave digestion by Milestone SK-10 (Milestone, Sorisole, Italy). The concentrations of heavy metals in the final digested solution of samples were determined by the PS control system for voltmetry 797 VA Computrace (Metrohm, Herisau, Switzerland), in the Department for Ecotoxicology, Institute of Public Health, Pancevo. All investigations in this study, i.e. the complete medical history, dental examination of patients, as well as taking the necessary samples, were carried out after approval by the Ethics Committee for Research (Approval Protocol No. 1323/1 to 2008, according to Resolution sections 3, 7, and 8 of the National Commission of Ethics in Research). Additionally, all participants in the study signed an informed consent form prior to any involvement in the study.

After data collection, coding and sorting of the material was carried out. Statistical significance of data was calculated using Student's t-test and the results of numerical variables are presented in tables and graphs that contain the relevant statistical parameters necessary for the conclusions of this epidemiological study.

RESULTS

Table 1 shows the mean values of the DMFT index for each of the five groups of patients from the investigated and control groups, as well as SiC index values. The average value of the DMFT index in the investigated group and in the control group was 20.41 and 16.52 respectively. It is notable that the index value increased with the age of patients, as had been expected, and that it was higher in each group of patients from the investigated group, compared to the control group. In the group of patients aged 20 to 30 years the difference was not statistically significant ($p>0.05$), while in the second and third group of patients, the difference between the coefficient of DMFT patients from the investigated group and the control group was statistically significant ($p<0.05$). The most striking differences were in the group of patients aged 51 to 60 years, where the recorded value of the DMFT index in the investigated group were 23.69 versus 18.50 in the control group, which was a highly statistically significant difference ($p = 0.0024$), and in the group of patients aged over 60 years, where the recorded values of the DMFT index in the investigated group were 24.94 versus 19.00 in the control group, which was an extremely statistically significant difference

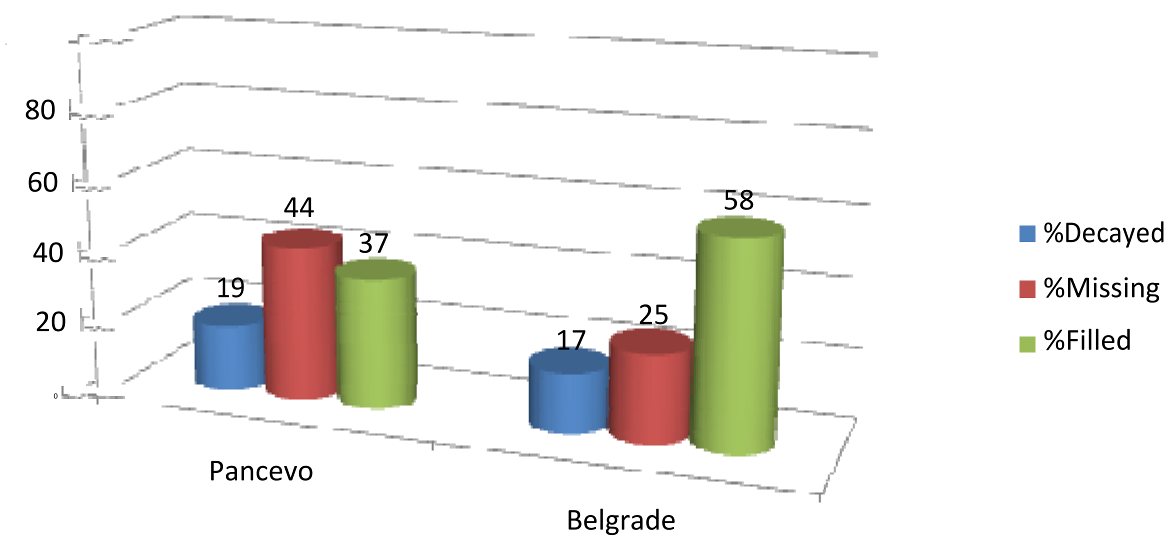

Figure 1. DMFT components among patients from Pancevo and Belgrade.

Table 2. Mean values of lead, nickel and mercury concentrations in hard dental tissues of extracted teeth.

Experimental group	Lead		Nickel		Mercury	
	Investigated group	Control group	Investigated group	Control group	Investigated group	Control group
	Mean ± SE[a]	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE
I(20 – 30)	1.57 ± 0.35	0.61 ± 0.14	/[b]	2.20 ± 0.46	/	/
II(31 – 40)	4.48 ± 1.12	0.39 ± 0.09	/	/	/	/
III(41 – 50)	4.60 ± 0.78	0.80 ± 0.22	/	/	2.78 ± 0.27	/
IV(51 – 60)	11.10 ± 2.43	4.15 ± 1.76	2.17 ± 0.87	/	5.14 ± 1.25	/
V(over 60)	26.61 ± 3.89	4.86 ± 2.00	/	/	1.66 ± 0.57	/

[a]SE=standard error; [b] /=undetectable.

(p=0.0005). SiC index values, more precisely, values of the most vulnerable patients, were also higher in all age groups from the investigated group than in the control group, but this difference is considered to be not statistically significant on such a sample of patients.

The structure, more precisely the percentage representation of the components of the DMFT index for the investigated group and the control group, are shown in Figure 1. The most frequent component of the DMFT index in the investigated group was extracted teeth, with the proportion of 44%, versus 25% in the control group. On the other side, the most frequent component of the DMFT index in the control group was filled teeth (58%).

Table 2 shows the presence of heavy metals in teeth indicated for extraction, from patients of different age groups from the investigated and the control group. The values are presented in µg/g. The cadmium level in patients from both groups studied, failed to reach the threshold value of 0.02 µg/g.

Statistically significantly higher value for lead concentration in extracted teeth of patients from investigated group than in patients from the control group was documented. Those results count for all age groups of patients. It should also be noted that the concentration of lead in teeth was rapidly increasing with age in patients from both areas, which means that the concentration of lead is in correlation with age. Positive correlation between age and concentration of lead in hard dental tissue was found also by other authors (Baranowska et al., 2004; Nowak and Chmielnicka, 2000).

Also, significantly higher concentrations of mercury were recorded in patients aged over 41 years, from the investigated group. This finding could be partly a result of the use of amalgam, which was very often a material of

Table 3. Frequency of noncarious lesions.

Experimental group	Number of patients		Patients with noncarious lesions		Frequency of patients with noncarious lesions (%)		Number of teeth affected with noncarious lesions	
	IG	CG	IG	CG	IG	CG	IG	CG
I(20 – 30)	32	32	6	2	18.75	6.25	6	2
II(31 – 40)	32	32	16	3	50.00	9.37	69	10
III(41 – 50)	32	32	11	6	34.37	18.75	33	33
IV(51 – 60)	32	32	14	8	43.75	25.00	133	78
V(over 60)	32	32	24	20	75.00	62.50	259	213
total	160	160	71	39	44.37	24.37	500	336

IG: Investigated group; CG: Control group.

choice for the fillings on posterior teeth. It is interesting that in patients aged 20 to 30 years from the control group a significantly higher value of nickel in extracted teeth was recorded compared to patients from the investigated group, while in the age group of 51 to 60 years, a significantly higher concentration of nickel was recorded in patients from the investigated group. Nickel has been detected in different media in all parts of the biosphere. Humans are constantly exposed to this ubiquitous element, though in variable amounts. Nickel is used to make everything from fashion jewelry to pens and paper clips, to bra snaps, batteries, coins and eyeglasses. Humans can be exposed to nickel by eating legumes, spinach, lettuce, nuts, shellfish, chocolate milk or beans. Soft drinking-water and acid beverages may dissolve nickel from pipes and containers. Researchers blame such habits as biting on paper clips and pens, and the surge of body piercing as the cause of allergic reactions to nickel. People can also be exposed to nickel when drinking water from the faucet. The high level of nickel in hard dental tissues of young patients from the control group (20 to 30 years) could also be the consequence of fixed orthodontic appliance therapy, while the high level of nickel in hard dental tissues of older patients from the investigated group could be the consequence of the presence of removable partial dentures.

Noncarious lesions were diagnosed in 71 (44%) patients from the investigated group and 39 (24%) patients from the control group (Table 3). The most frequent lesions were the ones found on anterior teeth and premolars in both jaws with the incidence more than three times higher than in the molar region (Table 4). Also, the most common lesions in patients from the investigated group were irregular (50%) and wedge-shaped (47%) defects, affecting both the enamel and dentin, on occlusal and incisal surfaces of teeth (49%) and on vestibular surfaces (50%). Only 1% of noncarious lesions were diagnosed on oral tooth surfaces. In patients from the control group a significantly higher percentage of irregular shaped defects (80%) was diagnosed compared to wedge-shaped defects (19%) (Tables 5, 6 and Figure 2). These findings support the results of preliminary studies by the same group of authors and point to a very significant and consistent clinical picture of patients with noncarious lesions (Kolak et al.,2010). Patients from this study, who were diagnosed with noncarious lesions, denied the presence of parafunctions and problems with regurgitation, while an insignificant number stated that they often drank carbonated beverages and ate acidic food in larger quantities.

DISCUSSION

The DMFT and SiC index values, both in Pancevo and Belgrade, must be considered as extremely high, given some of the values that WHO has defined as acceptable (WHO, 2011b). Namely, as expressed by DMFT index, 6 is theacceptable value of oral health for members of the group aged between 35 to 44 years, while in the investigated group of this study this value was as much as 20 and in the control group it was 17. These results are worse than in many well-developed countries (Turkey 12.62, Austria 14.7, Germany 16.1, UK 16.6, Denmark 16.7), but however, they are similar to, for example, Norway (20.5) and Canada (20.0) (Namal et al., 2008; Nishi et al., 2002). For people over 65 years of age, WHO considers acceptable DMFT to be 12, while in the investigated group this value was as much as 25 and in the control group it was 19. This low level of oral health in patients aged over 60 years resulted from the high DMFT index values in all age groups and also from a large number of extracted teeth.

An alarming fact is that the most frequent component of the DMFT index in the investigated group was extracted teeth, with the proportion of 44%, versus 25% in the control group (which is also a high percentage). A large

Table 4. Frequency of noncarious lesions in relation to the localization.

Tooth group						Dental tissue					
Frontal		Premolars		Molars		Enamel		Enamel with dentin transparencis		Dentin	
IG	CG	IG	CG	IG	CG	IG	CG	IG	CG	IG	CG
225	175	210	124	65	37	75	20	5	7	420	309
45%	52%	42%	37%	13%	11%	15%	6%	1%	2%	84%	92%

IG: Investigated group; CG: Control group.

Table 5. Frequency of noncarious lesions in relation to form and localization of defect.

Defect form						Defect localization					
Wedge shaped		Plate shaped		Irregular shape		Vestibular		Oral		Oclusal (incisal)	
IG	CG	IG	CG	IG	CG	IG	CG	IG	CG	IG	CG
235	64	15	3	250	269	250	64	5	7	245	265
47%	19%	3%	1%	50%	80%	50%	19%	1%	2%	49%	79%

IG: Investigated group; CG: Control group.

Table 6. Questionnaire.

1. Do you brush your teeth, and if so, how many times daily?
2. How often do you visit your dentist?
3. Do you have any parafunctional habit such as tooth clenching or grinding, tongue biting, lip biting, gum chewing, cheek biting, biting objects or nail biting?
4. Do you chew unilaterally?
5. Have you had orthodontic treatment?
6. Do you drink acidic beverages such as colas or orange juice?
7. Have you/have you had any regurgitation problem?
8. Do you have any health problems?
9. Have you taken any drugs for long periods?
10. Do you regard yourself as a nervous person?

number of people prefer to have teeth extracted rather than undergo some kind of conservative treatment, partly due to fear and partly for financial reasons, more precisely, because of low income. Besides caries, reasons for the large number of extracted teeth can also be found in a low level of health education, that is, lack of information in terms of oral health care, and lack of regular oral hygiene habits. In smaller towns in Serbia, socio-economic standard and level of education are, more or less, at a lower level than in Belgrade, which might also be one of the factors that contribute to differences between the overall dental health conditions in those two groups of patients.

Many researchers have analysed the connection of the presence of heavy metals in hard dental tissues and dental caries (Anderson and Davies, 1980; Bercovitz and Laufer, 1993;Bowen, 2001; Brudevold et al., 1977; Campbell et al., 2000; Curzon and Crocker,1978;Davies and Anderson, 1987; Duggal et al., 1991; Gemmel et al., 2002; Gil et al., 1996; Malara et al., 2006; Moss et al., 1999; Youravonget al., 2006). The relationship between environmental fluoride, especially in drinking water, and dental caries is probably one of the best established links between environment and disease. Al, Fe, Se, Sr are associated with a low rate of caries, while Pb, Mn, Cu and Cd are concommitant with a high rate (Curzon and Crocker, 1978). The mechanism through which these trace elements act is still not completely clear. Since

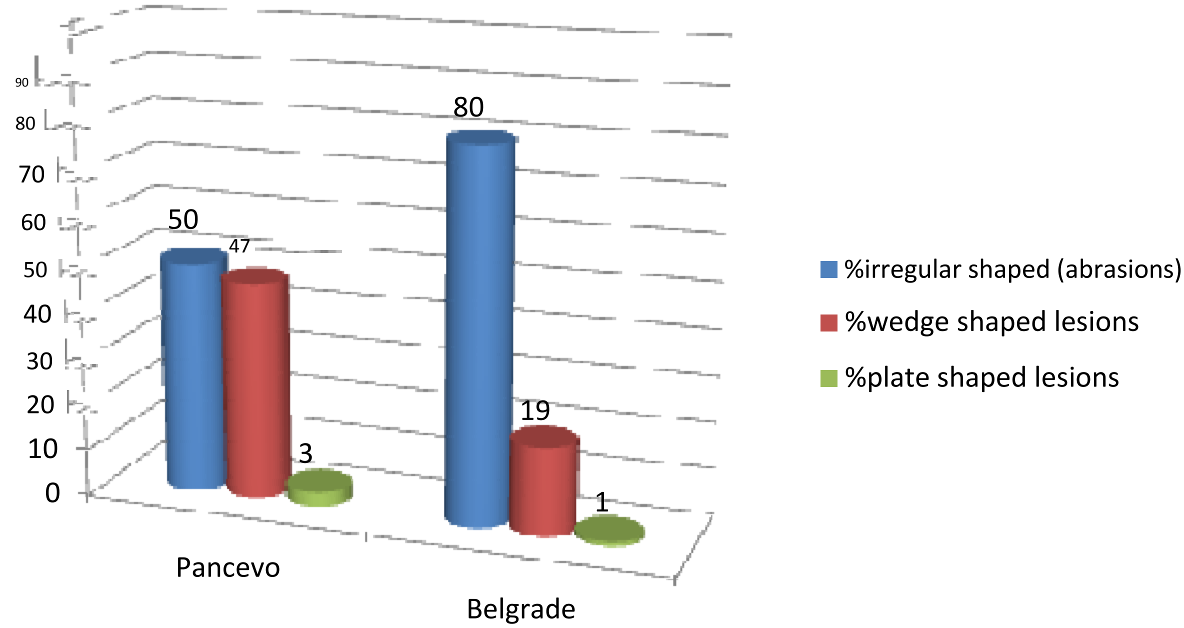

Figure 2. The frequency of noncarious lesions based on defect form.

cavity formation probably involves localised dissolution of the enamel surface caused by the influence of organic acids, it is tempting to hypothesise that the incorporation of trace elements into the apatite structure or into the protein matrix alters the physical properties of enamel, such as solubility and thereby renders it more or less susceptible to attack by organic acids (Davies and Anderson, 1987). It is evident that within the patients from the investigated group significantly higher DMFT index values were recorded than in patients from the control group. Bearing in mind, the results of the studies of the previously mentioned researchers, as well as the fact that patients from the control group and the investigated group had relatively similar oral hygiene habits and frequency of visits to the dentist's, one can suspect that prolonged exposure to a polluted environment, particularly in patients older than 40, was one of the factors that led to poor oral health condition.

Unusually, large percentage of noncarious lesions (44%) were diagnosed in patients from the investigated group. Abrasions of anterior teeth and premolars and wedge-shaped erosions, where the loss of tooth substance extends to both the enamel and dentin, were the most frequently diagnosed noncarious lesions in patients from the investigated group, while abrasions were the most frequently diagnosed noncarious lesions in patients from the control group (Figure 2). The explanation for this result, when it comes to the representation of abrasions, could be related to the early loss of molar teeth, that is, a large number of missing posterior teeth, and, therefore, over-loading of the remaining teeth during mastication (Jakovljevic et al., 2009).

However, the most obvious difference was observed in the prevalence of wedge-shaped lesions among the two groups of patients (47% to 19%). The etiology of such lesions is still not fully understood (Bishop et al., 1997; Grippo and Simring, 1995; Hattab and Yassin, 2000; Litonjua et al., 2003). The most frequently cited etiological factor in forming cervical erosions is chemical etching, more precisely, acid dissolution of hard dental tissues (Leviteh et al., 1994). Studies have confirmed that cervical erosions are more frequent in people who are exposed to acids in the workplace or living environment, in competitive swimmers whose teeth are in contact with chlorinated water in pools, or in people who frequently consume acidic drinks and drinks containing vitamin C, or use chemicals for oral hygiene which chelate calcium. Due to frequent vomiting, a significant frequency of dental erosive lesions was noticed in patients with gastrointestinal problems, in pregnant women and alcoholics. The same problem was noticed in bulimia and anorexia neurosa (Chikte et al., 1998; Dülgergil et al., 2007; Jarvinen et al., 1991; Mayhew et al., 1998; Ten Bruggen Cate, 1968).

Many different studies in recent years, have confirmed that "bendin" or "flexing" of teeth caused by eccentric occlusal forces is one of the factors which could explain the occurrence of cervical lesions (Bishop et al., 1997; Estafan et al., 2005; Grippo and Simring, 1995; Hattab and Yassin;2000; Litonjua et al., 2003; Mayhew et al., 1998; Pegoraro et al.,2005; Telles et al., 2000). Numerous epidemiological studies consider inappropriate teeth brushing technique as one of the reasons for cervical erosions etiology (Bishop et al., 1997; Hattab and Yassin, 2000; Litonjua et al., 2004; Zivkovic et al., 2006).There is a good basis for the theory that the environment also has an impact on the occurrence of noncarious lesions, bearing in mind the following:

1. Most of the patients have negatively responded to questions from the questionnaire;
2. In most cases apart form multiple wedge-shaped lesions, signs of occlusal wear of hard dental tissues have not been diagnosed;
3. 50% of lesions were localized on vestibular surfaces of frontal teeth, which are directly exposed to environmental influences, among patients from the investigated group, compared to 19% in patients from the control group.

Conclusions

This epidemiological study found a high incidence of hard dental tissue lesions, both in the investigated group and the control group. In the investigated group significantly higher values of DMFT index and higher frequency of noncarious lesions were recorded. Also, the analysis of the presence of heavy metals in the extracted teeth showed a higher incidence in patients living in Pancevo, especially when it came to lead. Although, hard dental tissue lesions, of both carious and noncarious etiology are multifactorial, none of the factors that lead to these conditions can be considered separately. In this epidemiological study evident differences in their representation in the two groups of patients were found. This fact leads to the conclusion that a polluted environment is one of the factors that cannot be ignored, but also requires confirmation by further comprehensive basic research.

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