

MULTIPLE OCCUPATIONAL SENSITIZATION IN DENTAL PROFESSIONALS AND DENTAL STUDENTS ALLERGIC TO FORMALDEHYDE AND/OR GLUTARALDEHYDE

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ABSTRACT

Purpose: In dental practice is common concomitant exposure to formaldehyde and glutaraldehyde. Formaldehyde is an ingredient of some dental materials and may be released from methacrylate-based dental materials. A multitude of methacrylic monomers is used in dentistry. In the present study we evaluated the prevalence of multiple contact hypersensitivity to dental allergens (methacrylic monomers, mercury and eugenol) among dental professionals, students of dental medicine and patients, allergic to formaldehyde and/or glutaraldehyde.

Methods: A total of 139 participants were included in the study: occupationally exposed to dental professionals, students of dental medicine and patients without occupational exposure. All of them were patch-tested with formaldehyde, glutaraldehyde, some methacrylic monomers, mercury and eugenol. The results were subject to statistical analysis ($p < 0.05$)

Results: High incidence of contact allergy to formaldehyde and/or glutaraldehyde was revealed. The most vulnerable group in terms of concomitant sensitization to formaldehyde and/or glutaraldehyde and to MMA was the one of students from 6th course; to TREGDMA and EGDMA - students from 3-4 courses; to 2-HEMA and mercury - dental professionals; to tetrahydrofurfuryl methacrylate and to eugenol - students from 3-4 courses and dental professionals. High rates of concomitant sensitization to formaldehyde and/or glutaraldehyde and to the tested dental materials were established both in occupational and non-occupational exposure, suggesting an important role of consumer (patient's) exposure as well.

Conclusions; More effective training and risk management programs in exposure to allergens and use of proper personal protection in dental practice and among dental students could be recommended.

Key words: occupational sensitization; formaldehyde, glutaraldehyde; methacrylic monomers; eugenol; mercury;

INTRODUCTION

Dental practice poses many risks to dental professionals – exposure to various chemical irritant and sensitizing compounds (polymer materials, acrylic resins, eugenol and formaldehyde-containing materials, alloys, ceramics, cements, sealers, etchants, hypochlorite, waxes), unfavorable working posture and ergonomic hazards, occupational stress etc. Studies indicate that one half of dentists reported occupational health complaints such as dermatoses (40%), eye, respiratory and systemic complaints (13%), musculoskeletal problems (3%) [13].

Common occupational contact allergens as biocides (formaldehyde and formaldehyde releasers, glutaraldehyde), plastics and resins (methacrylic monomers), rubber additives, metals (nickel, chromium, cobalt, mercury, gold, platinum) are widely presented in dental practice. In a more recent study (28) was reported that over 40% of dental professionals were affected with hand dermatoses and irritations to eyes, nose, and airways at some point in their career, and women dentists experienced double the chances of allergy occurrence. According to Hamann et al (2004) methacrylates, natural rubber latex proteins, rubber glove allergens, and glutaraldehyde are the predominant allergens in dentistry (9). Reactions range from cell-mediated contact allergy to urticaria and occupational asthma. The degree of risk might depend on several factors including age, personal susceptibility, total daily exposure, exposure measured over the years, and medication.

Dental students are exposed to the listed above physical and chemical factors from the first years of their education, and this way are subjected to risk of early occupational sensitization. Relative few studies are available con-

cerning the prevalence of sensitization to various dental materials among dental students.

The results from our previous study indicate high rates of occupational sensitization to formaldehyde and glutaraldehyde, with co-reactivity manifested mainly among the non-occupationally exposed people, as well as an increased incidence and OR of concomitant sensitization to some methacrylic monomers and formaldehyde mainly among dental students and occupationally unexposed patients [23].

The **purpose** of the present study was to evaluate some health status indicators and the prevalence of multiple contact hypersensitivity to dental allergens (methacrylic monomers, mercury and eugenol) among dental profession-

als (dentists, nurses and attendants), students of dental medicine and non-occupationally exposed patients, all of them with positive skin patch tests to formaldehyde and/or glutaraldehyde.

MATERIAL AND METHODS

A total of 139 participants were included in the study, divided into four groups: occupationally exposed dental professionals, 3-4 year-of-education students of dental medicine, 6th year-of-education students of dental medicine, and patients without occupational exposure, with suspected or established sensitization to dental materials. The general characteristics of studied population are presented in Table 1.

Studied groups	Number of subjects / %	Age mean \pm St D (years)	Gender	
			Male	Female
Patients without occupational exposure	29 / 20,9%	47,34 \pm 18,21	7 / 24,1%	22 / 75,9%
3-4 year-of-education students of dental medicine	44 / 31,7%	22,05 \pm 1,29	17 / 38,6%	27 / 61,4%
6th year-of-education students of dental medicine	28 / 20,1%	26,39 \pm 6,79	11 / 39,3%	17 / 60,7%
Occupationally exposed dental professionals	38 / 27,3%	52,32 \pm 13,41	8 / 21,1%	30 / 78,9%
Total	139 / 100,0%	-	43 / 30,9%	96 / 69,1%

Table 1. General characteristics of studied groups.

The study was approved by the supported by the Medical University of Sofia - Grant No. S-1/2012 Medical Ethics Board at Medical University of Sofia. All participants were informed about the purpose of the study and gave their written informed consent.

Sociological methods

Interviews and detailed and intentionally conducted questionnaire-based interview with an emphasis on family history, suspected or known allergies to standard set of household or occupational allergens, on history of frequent, recurrent respiratory system infections and on subjective symptoms, as well as review of medical documentation were performed.

Skin patch testing

Skin patch testing with formaldehyde (0.1%/aq, Art. nr. F002A, Chemotechnique Diagnostics), glutaraldehyde, methyl methacrylate (MMA), triethyleneglycol dimethacrylate (TREGDMA), ethyleneglycol dimethacrylate (EGDMA), 2,2-bis[4-(2-hydroxy-3-methacryloxypropoxy)phenyl]propane (bis-GMA), 2-hydroxyethyl methacrylate (2-HEMA), *tetrahydrofurfuril* metacrylate, mercury and eugenol (0.2%/pet, Chemotechnique Diagnostics) was performed, according to the Jadassohn & Bloch classical methods for diagnosis of contact allergy, by placing the aller-

gens in IQ-Ultra hypoallergenic patches of Chemotechnique Diagnostics (IQ Chambers®, Vellinge, Sweden). Obligatory condition was lack of anti-allergic medication before placing the patches and during the study. Patches with allergens were applied and stayed on the back of the tested individuals, reading of the test was carried out on day 2, several hours after removing of the patches, with control revision on day 3. For the interpretation of the test result the following scheme was used (International Contact Dermatitis Research Group - ICDRG):

(-)	Negative reaction
?	Doubtful reaction
+	Weak reaction (non-vesicular)
++	Strong reaction (oedematous or vesicular)
+++	Extreme reaction (ulcerative or bullous)
IR	Irritant reaction

Statistical methods

The statistics were calculated with SPSS 19.0. Available for cross-tabulation statistics were used: chi-square test, Fisher Exact Test for statistical significance, testing of the ratio of two probabilistic ones OR (Odds ratio). Values of $p < 0,05$ were accepted as statistically significant.

RESULTS

The distribution of the studied population by gender was not uniform, with predominance of women in all investigated groups, but without statistical significance ($\chi^2=4,5$, $p=0,212$).

The mean age in the groups of occupationally exposed dental professionals and the unexposed subjects was logically, significantly higher compared to the groups of 3-4 course and 6th course students of dental medicine. In respect of the indicator, characterizing the years of exposure to chemical compounds in dental practice, data is predictable: 0 years of occupationally unexposed patients, 2-3 years 3-4 course students, 4 years for 6 course students and a number (from 1 to 50 years) for the occupationally exposed dental personnel.

Concerning smoking habits, smokers were 24,1% of the unexposed patients, 27,3% of the 3-4 course students,

57,1% of 6 course students and 26,3% from the group of dental professionals. Non-smokers predominated in the whole studied population with statistical significance ($\chi^2=8,741$, $p=0,033$), but the number of smokers in the group of 6 course students was significantly higher compared with the unexposed patients ($p=0,016$), the 3-4 course students ($p=0,017$) and the group of dental professionals ($p=0,022$).

The individuals with no history of allergic pathology predominated in all the studied groups, with no reliable differences in the overall distribution. Significantly lower was the number of subjects without history for atopy in the group of dental professionals if compared to the groups of 3-4 course ($p=0,044$) and 6 course ($p=0,047$) students.

Data concerning the distribution of positive skin patch test reactions to formaldehyde and/or glutaraldehyde are presented in Table 2.

Skin patch test reactions to formaldehyde and/or glutaraldehyde	Studied group				Total
	Unexposed patients	Students of Dental Medicine 3 and 4 course	Students of Dental Medicine 6 course	Dental professionals	
Negative N / %	18/62,1%	32/72,7%	16/57,1%	30/78,9%	96/74,%
Positive N / %	11/37,9%	12/27,3%	12/42,9%	8/21,1%	43/25,9%
Total N / %	29/100,0%	44/100,0%	28/100,0%	38/100,0%	139 /100,0

Table 2. Distribution of positive skin patch test reactions to formaldehyde and/or glutaraldehyde among the studied groups.

High incidence of positive skin patch test reactions to formaldehyde and/or glutaraldehyde was revealed, highest being in the group of students of dental medicine – 6 course and in the one of occupationally unexposed patients.

The role of the allergic predisposition for sensitization to the investigated compounds was analyzed,

and no significant difference found ($\chi^2=0,001$, $p=0,971$).

Below (Table 3) is presented the distribution of sensitized to formaldehyde and/or glutaraldehyde subjects from the studied groups as defined by occupational exposure and smoking habits.

Studied groups according to occupational exposure and smoking habits			Contact hypersensitivity to formaldehyde (F) and/or glutaraldehyde (G)		N
			Negative	Positive	
Occupationally unexposed patients	Non-smokers	N	11	11	22
		% within F and/or G negative/ positive	100,0%	61,1%	
	smokers	N	0	7	7
		% within F and/or G negative/ positive	0,0%	38,9%	
Total N		11	18	29	
Students of Dental Medicine 3 and 4 course	Non-smokers	N	13	19	32
		% within F and/or G negative/ positive	68,4%	76,0%	
	smokers	N	6	6	12
		% within F and/or G negative/ positive	31,6%	24,0%	
Total N		19	25	44	

Students of Dental Medicine 6 course	Non- smokers	N	6	6	12
		% within F and/or G negative/ positive	66,7%	33,3%	
	smokers	N	3	12	15
		% within F and/or G negative/ positive	33,3%	66,7%	
Total N		9	18	27	
Dental professionals	Non- smokers	N	19	8	27
		% within F and/or G negative/ positive	76,0%	66,7%	
	smokers	N	6	4	10
		% within F and/or G negative/ positive	24,0%	33,3%	
Total N		25	12	37	
Total	Non- smokers	N	50	44	94
		% within F and/or G negative/ positive	76,9%	60,3%	
	smokers	N	15	29	44
		% within F and/or G negative/ positive	23,1%	39,7%	
Total N		65	73	138	

Tabl. 3. Distribution of positive skin patch test reactions to formaldehyde and/or glutaraldehyde and smoking habits among the subjects from the studied groups.

As evidenced above, all the smokers from the control group were sensitized, while among the non-smokers the ratio was 50:50. Smokers were 39,7% of all sensitized subjects. No crucial role of smoking habits in the occurrence of sensitization to those chemical agents could be considered since non-smokers significantly predominated in the overall distribution ($\chi^2=5,639$; $p=0,018$).

Data obtained from the intentionally conducted questionnaire-based interviews, concerning the incidence of subjective symptoms, was statistically analyzed. No statistically significant differences concerning the distribution of subjective symptoms from the upper respiratory tract ($\chi^2=0,027$, $p=0,311$) the skin ($\chi^2=0,696$, $p=0,404$) and respiratory system ($\chi^2=0,003$, $p=0,955$) were established. Interestingly, 100% from sensitized to F and/or G and 56,5% from non-sensitized subjects from the group of dental professionals reported about subjective complaints of the nervous system ($\chi^2=7,304$, $p=0,007$). No significant differences were found regarding the prevalence of subjective symptoms from the other organs and systems.

The between-groups analysis didn't reveal significant differences between sensitized and non-sensitized individuals from the studied groups regarding the objectively diagnosed lesions in the upper respiratory tract. Even in the

group of 3-4 students course no pathological findings were diagnosed among the subjects with positive skin patch test reactions; such were observed among 45,5% of non-sensitized. There is a statistical significance in the latter distribution ($\chi^2=5,968$, $p=0,015$). A trend for asymptomatic sensitization to formaldehyde and/or glutaraldehyde was observed.

This trend was confirmed in terms of objectively diagnosed skin pathology. In the group of occupationally unexposed patients only 16.7% of sensitized individuals demonstrated objectively diagnosed skin pathology, while 66.7% from the non-sensitized subject suffered from skin pathology. A statistical significance was established in the latter distribution ($\chi^2=4,500$, $p=0,034$). Also, no significant differences regarding objectively diagnosed pathology of other organs and systems was found.

A statistical analysis of data concerning the incidence of sensitization to the other included in our study occupational allergens among sensitized to formaldehyde and/or glutaraldehyde individuals was performed. Data regarding the prevalence of sensitization to MMA among subjects with positive skin patch tests to formaldehyde and/or glutaraldehyde from the defined by occupational exposure groups are presented in Table 4.

Studied groups according to occupational exposure and sensitization to MMA			Contact hypersensitivity to formaldehyde (F) and/or glutaraldehyde (G)		N
			Negative	Positive	
Occupationally unexposed patients	Negative	N	8	12	20
		% within F and/or G negative/ positive	72,7%	66,7%	
	Positive	N	3	6	9
		% within F and/or G negative/ positive	27,3%	33,3%	
Total N			11	18	29
Students of Dental Medicine 3 and 4 course	Negative	N	12	16	28
		% within F and/or G negative/ positive	63,2%	64,0%	
	Positive	N	7	9	16
		% within F and/or G negative/ positive	36,8%	36,0%	
Total N			19	25	44
Students of Dental Medicine 6 course	Negative	N	10	12	22
		% within F and/or G negative/ positive	100,0%	66,7%	
	Positive	N	0	6	6
		% within F and/or G negative/ positive	0,0%	33,3%	
Total N			10	18	28
Dental professionals	Negative	N	23	9	32
		% within F and/or G negative/ positive	92,0%	75,0%	
	Positive	N	2	3	5
		% within F and/or G negative/ positive	8,0%	25,0%	
Total N			25	12	37
Total	Negative	N	54	49	103
		% within F and/or G negative/ positive	81,8%	67,1%	
	Positive	N	12	24	36
		% within F and/or G negative/ positive	18,2%	32,9%	
Total N			66	73	139

Tabl. 4. Distribution of positive skin patch test reactions to formaldehyde and/or glutaraldehyde and to MMA among the subjects from the studied groups.

In the group of students of dental medicine - 6 course, all subjects who were allergic to formaldehyde and/or glutaraldehyde were sensitized to MMA as well, with statistical significance established ($\chi^2 = 4,242$, $p = 0,039$).

The prevalence of sensitization to TREGDMA and among subjects with positive skin patch tests to formaldehyde and/or glutaraldehyde are presented in Table 5.

Studied groups according to occupational exposure and sensitization to TREGDMA			Contact hypersensitivity to formaldehyde (F) and/or glutaraldehyde (G)		N
			Negative	Positive	
Occupationally unexposed patients	Negative	N	8	10	18
		% within F and/or G negative/ positive	72,7%	55,6%	
	Positive	N	3	8	11
		% within F and/or G negative/ positive	27,3%	44,4%	
Total N			11	18	29
Students of Dental Medicine 3 and 4 course	Negative	N	12	13	25
		% within F and/or G negative/ positive	63,2%	52,0%	
	Positive	N	7	12	19
		% within F and/or G negative/ positive	36,8%	48,0%	
Total N			19	25	44
Students of Dental Medicine 6 course	Negative	N	9	11	20
		% within F and/or G negative/ positive	90,0%	61,1%	
	Positive	N	1	7	8
		% within F and/or G negative/ positive	10,0%	38,9%	
Total N			10	18	28
Dental professionals	Negative	N	22	9	31
		% within F and/or G negative/ positive	88,0%	75,0%	
	Positive	N	3	3	6
		% within F and/or G negative/ positive	12,0%	25,0%	
Total N			25	12	37
Total	Negative	N	52	43	95
		% within F and/or G negative/ positive	78,8%	58,9%	
	Positive	N	14	30	44
		% within F and/or G negative/ positive	21,2%	41,1%	
Total N			66	73	139

Tabl. 5. Distribution of positive skin patch test reactions to formaldehyde and/or glutaraldehyde and to TREGDMA among the subjects from the studied groups.

The results from statistical analysis indicate increased incidence and OR of contact sensitization to TREGDMA among subjects with positive skin patch tests to formaldehyde and/or glutaraldehyde in the overall distribution of the studied population ($\chi^2=6,334, p=0,012$; OR=2,591, CI=1,22–5,50).

The statement above is valid also regarding the incidence and OR of contact sensitization to EGDMA among subjects with positive skin patch tests to formaldehyde and/or glutaraldehyde in the overall distribution of the studied population ($\chi^2=5,034, p=0,021$; OR=2,489, CI=1,132–5,473). Data are presented in Table 6.

Studied groups according to occupational exposure and sensitization to EGDMA			Contact hypersensitivity to formaldehyde (F) and/or glutaraldehyde (G)		N
			Negative	Positive	
Occupationally unexposed patients	Negative	N	8	9	17
		% within F and/or G negative/ positive	72,7%	50,0%	
	Positive	N	3	9	12
		% within F and/or G negative/ positive	27,3%	50,0%	
Total N			11	18	29
Students of Dental Medicine 3 and 4 course	Negative	N	15	17	32
		% within F and/or G negative/ positive	78,9%	68,0%	
	Positive	N	4	8	12
		% within F and/or G negative/ positive	21,1%	32,0%	
Total N			19	25	44
Students of Dental Medicine 6 course	Negative	N	7	12	19
		% within F and/or G negative/ positive	70,0%	66,7%	
	Positive	N	3	6	9
		% within F and/or G negative/ positive	30,0%	33,3%	
Total N			10	18	28
Dental professionals	Negative	N	23	9	32
		% within F and/or G negative/ positive	92,0%	75,0%	
	Positive	N	2	3	5
		% within F and/or G negative/ positive	8,0%	25,0%	
Total N			25	12	37
Total	Negative	N	54	47	101
		% within F and/or G negative/ positive	81,8%	64,4%	
	Positive	N	12	26	38
		% within F and/or G negative/ positive	18,2%	35,6%	
Total N			66	73	139

Tabl. 6. Distribution of positive skin patch test reactions to formaldehyde and/or glutaraldehyde and to EGDMA among the subjects from the studied groups.

With regard to results from the overall, as well as the between-groups analysis of the distribution of subjects sensitized to formaldehyde and/or glutaraldehyde and bis-GMA, no statistically significant differences were established ($\chi^2=0,052$, $p=0,820$).

Data regarding the prevalence of sensitization to 2-HEMA among subjects with positive skin patch tests to formaldehyde and/or glutaraldehyde from the groups defined by occupational exposure are presented in Table 7.

Studied groups according to occupational exposure and sensitization to 2-HEMA			Contact hypersensitivity to formaldehyde (F) and/or glutaraldehyde (G)		N
			Negative	Positive	
Occupationally unexposed patients	Negative	N	7	11	18
		% within F and/or G negative/ positive	63,6%	61,1%	
	Positive	N	4	7	11
		% within F and/or G negative/ positive	36,4%	38,9%	
Total N			11	18	29
Students of Dental Medicine 3 and 4 course	Negative	N	13	17	30
		% within F and/or G negative/ positive	68,4%	68,0%	
	Positive	N	6	8	14
		% within F and/or G negative/ positive	31,6%	32,0%	
Total N			19	25	44
Students of Dental Medicine 6 course	Negative	N	6	14	20
		% within F and/or G negative/ positive	60,0%	77,8%	
	Positive	N	4	4	8
		% within F and/or G negative/ positive	40,0%	22,2%	
Total N			10	18	28
Dental professionals	Negative	N	22	6	28
		% within F and/or G negative/ positive	88,0%	54,5%	
	Positive	N	3	5	8
		% within F and/or G negative/ positive	12,0%	45,5%	
Total N			25	11	36
Total	Negative	N	49	48	97
		% within F and/or G negative/ positive	74,2%	66,7%	
	Positive	N	17	24	41
		% within F and/or G negative/ positive	25,8%	33,3%	
Total N			66	72	138

Tabl. 7. Distribution of positive skin patch test reactions to formaldehyde and/or glutaraldehyde and to 2-HEMA among the subjects from the studied groups.

Significant differences were established in the group of dental professionals, where the prevalence of persons sensitized to formaldehyde and/or glutaraldehyde and to 2-hydroxyethyl methacrylate is higher ($\chi^2=4,946$, $p=0,026$).

Interesting results were obtained with regard to the prevalence of subjects, sensitized to formaldehyde and/or glutaraldehyde and to **tetrahydrofurfuryl methacrylate**. Data are presented in Table 8.

Studied groups according to occupational exposure and sensitization to tetrahydrofurfuryl methacrylate			Contact hypersensitivity to formaldehyde (F) and/or glutaraldehyde (G)		N
			Negative	Positive	
Occupationally unexposed patients	Negative	N	8	7	15
		% within F and/or G negative/ positive	72,7%	38,9%	
	Positive	N	3	11	14
		% within F and/or G negative/ positive	27,3%	61,1%	
Total N			11	18	29
Students of Dental Medicine 3 and 4 course	Negative	N	17	14	31
		% within F and/or G negative/ positive	89,5%	56,0%	
	Positive	N	2	11	13
		% within F and/or G negative/ positive	10,5%	44,0%	
Total N			19	25	44
Students of Dental Medicine 6 course	Negative	N	7	12	19
		% within F and/or G negative/ positive	70,0%	66,7%	
	Positive	N	3	6	9
		% within F and/or G negative/ positive	30,0%	33,3%	
Total N			10	18	28
Dental professionals	Negative	N	25	6	31
		% within F and/or G negative/ positive	100,0%	54,5%	
	Positive	N	0	5	5
		% within F and/or G negative/ positive	0,0%	45,5%	
Total N			25	11	36
Total	Negative	N	58	39	97
		% within F and/or G negative/ positive	87,9%	54,2%	
	Positive	N	8	33	41
		% within F and/or G negative/ positive	12,1%	45,8%	
Total N			66	72	138

Tabl. 8. Distribution of positive skin patch test reactions to formaldehyde and/or glutaraldehyde and to tetrahydrofurfuryl methacrylate among the subjects from the studied groups.

The statistical analysis established, with high statistical significance, prevalence of subjects sensitized to formaldehyde and/or glutaraldehyde and tetrahydrofurfuryl methacrylate in the group of students 3-4 course ($\chi^2=6,252$, $p=0,012$). Similar results were obtained in the group of dental professionals – all subjects with positive skin patch tests to formaldehyde and/or glutaraldehyde demonstrated contact sensitization to tetrahydrofurfuryl methacrylate as well ($\chi^2=13,196$, $p=0,001$). The analysis of the whole studied

population categorically evidenced statistically significant increased incidence and OR of manifestation of contact sensitization to tetrahydrofurfuryl methacrylate among subjects sensitized to formaldehyde and/or glutaraldehyde ($\chi^2=18,740$, $p<0,001$; $OR=6,135$, $CI=2,56-14,68$).

Data concerning the manifestation of sensitization to mercury in subjects with positive skin patch tests to formaldehyde and/or glutaraldehyde are summarized in Table 9.

Studied groups according to occupational exposure and sensitization to mercury			Contact hypersensitivity to formaldehyde (F) and/or glutaraldehyde (G)		N
			Negative	Positive	
Occupationally unexposed patients	Negative	N	9	9	18
		% within F and/or G negative/ positive	81,8%	50,0%	
	Positive	N	2	9	11
		% within F and/or G negative/ positive	18,2%	50,0%	
Total N			11	18	29
Students of Dental Medicine 3 and 4 course	Negative	N	16	15	31
		% within F and/or G negative/ positive	84,2%	60,0%	
	Positive	N	3	10	13
		% within F and/or G negative/ positive	15,8%	40,0%	
Total N			19	25	44
Students of Dental Medicine 6 course	Negative	N	7	11	18
		% within F and/or G negative/ positive	70,0%	61,1%	
	Positive	N	3	7	10
		% within F and/or G negative/ positive	30,0%	38,9%	
Total N			10	18	28
Dental professionals	Negative	N	22	4	26
		% within F and/or G negative/ positive	88,0%	33,3%	
	Positive	N	3	7	10
		% within F and/or G negative/ positive	12,0%	66,7%	
Total N			25	11	36
Total	Negative	N	55	39	94
		% within F and/or G negative/ positive	83,3%	53,4%	
	Positive	N	11	34	41
		% within F and/or G negative/ positive	16,7%	46,6%	
Total N			66	73	139

Tabl. 9. Distribution of positive skin patch test reactions to formaldehyde and/or glutaraldehyde and to mercury among the subjects from the studied groups.

Increased (with high significance) incidence of contact sensitization to mercury among subjects with positive skin patch tests to formaldehyde and/or glutaraldehyde was established for the group of dental professionals ($\chi^2=11,599$, $p=0.001$). Summarizing the results for the whole population studied by us, categorically was established a statistically significant increased incidence and OR of manifestation of contact sensitization to mercury among subjects sensitized to formaldehyde and/or glutaraldehyde ($\chi^2=14,162$, $p<0,001$; OR=4,359, CI=1,97-9,64).

Below (Table 10) are presented data on the distribution of subjects with positive skin patch tests to formaldehyde and/or glutaraldehyde, manifesting contact hypersensitivity to eugenol.

Studied groups according to occupational exposure and sensitization to eugenol			Contact hypersensitivity to formaldehyde (F) and/or glutaraldehyde (G)		N
			Negative	Positive	
Occupationally unexposed patients	Negative	N	7	10	17
		% within F and/or G negative/ positive	63,6%	55,6%	
	Positive	N	4	8	12
		% within F and/or G negative/ positive	36,4%	44,4%	
Total N			11	18	29
Students of Dental Medicine 3 and 4 course	Negative	N	18	13	31
		% within F and/or G negative/ positive	94,7%	52,0%	
	Positive	N	1	12	13
		% within F and/or G negative/ positive	5,3%	48,0%	
Total N			19	25	44
Students of Dental Medicine 6 course	Negative	N	7	13	20
		% within F and/or G negative/ positive	70,0%	72,2%	
	Positive	N	3	5	8
		% within F and/or G negative/ positive	30,0%	27,8%	
Total N			10	18	28
Dental professionals	Negative	N	21	5	26
		% within F and/or G negative/ positive	84,0%	41,7%	
	Positive	N	4	7	11
		% within F and/or G negative/ positive	16,0%	58,3%	
Total N			25	11	36
Total	Negative	N	54	41	95
		% within F and/or G negative/ positive	81,8%	56,2%	
	Positive	N	12	32	44
		% within F and/or G negative/ positive	18,2%	43,8%	
Total N			66	73	139

Tabl. 10. Distribution of positive skin patch test reactions to formaldehyde and/or glutaraldehyde and to eugenol among the subjects from the studied groups.

Increased was the incidence (with high statistical significance) of subjects sensitized to formaldehyde and/or glutaraldehyde and eugenol in the group of students from 3-4 course ($\chi^2=10,001$, $p=0,002$). The same results and statistical significance were revealed in the group of dental professionals as well ($\chi^2=6,955$, $p=0,008$). The analysis of the overall distribution categorically established significantly increased prevalence and OR for sensitization to eugenol among subjects with positive skin patch tests to formaldehyde and/or glutaraldehyde ($\chi^2=10,544$, $p=0,001$; OR=3,512, CI=1,614-7,645).

DISCUSSION

Formaldehyde is the simplest aldehyde, an integral part of the general outdoor and indoor working and residential environments [2]. It is a common cause of contact allergy [21], skin contact being the most important route of

exposure for sensitization. According to the reported patch test results for 2007-2008 from the North American Contact Dermatitis Group, formaldehyde ranked among the top 15 most frequently positive allergens, irrespective of the significant decreases in positivity rates [6].

Formaldehyde or formaldehyde-releasers (agents that release formaldehyde when used) may occur in several cosmetics, household products such as washing and cleaning agents and in a great number of industrial applications (16, 30). In the EU the maximum allowed concentration in the finished products is 0.2% (Annex VI of Cosmetics Directive 76/768/EC).

Regardless of the move for restrictions in use of formaldehyde in disinfection procedures and substitution by other chemical substances from the aldehyde group (glutaraldehyde and glyoxal, formaldehyde still finds numerous applications in medical science and practice [15, 17, 19].

Formaldehyde continues to find use as an ingredient of some dental materials, such as root canal filling materials, formocresol, sealers and cements, polymers etc. A large group of sealer/cements, including the commonly used Endomethasone, Riebler's paste, N2, etc. contain substantial amounts of paraformaldehyde and release formaldehyde into water in amounts sufficient to cause local allergic reactions [10]. Endodontic materials, like root canal filling sealers, revealed the highest release of formaldehyde in freshly mixed samples [4].

Among the most important adverse effects from formaldehyde and glutaraldehyde exposure are respiratory tract irritation and sensitization. Their irritant action on eyes (watery, itchy eyes), upper respiratory tract (itchy, runny, or stuffy nose, sinus fullness, dry or sore throat) and skin (irritation and dermatitis) is well documented [5].

In dental practice it is most common to have concomitant exposure to formaldehyde and glutaraldehyde. In this context, of practical significance is the problem regarding possible co-reactivity between formaldehyde and other aldehydes, which cannot be entirely attributed to simultaneous exposure [18, 26]. Studies focused on this problem are few and multidirectional.

A four-year study on the incidence of occupational allergic contact dermatitis in dental nurses, showed that the most frequent sensitizing agent was glutaraldehyde, followed by formaldehyde and glyoxal [16]. Formaldehyde was included in the list of agents causing contact allergy most often in dental staff [7]. The results obtained by Ravis et al. [26] contradict the prior findings; they found no significantly increased incidence of occupational sensitization from formaldehyde in dental personnel (significantly higher was the incidence of sensitization from glutaraldehyde). Our previous studies indicate high prevalence of sensitization to both formaldehyde and glutaraldehyde (41% of all investigated participants) [22].

A multitude of acrylic monomers is used in dentistry as well. Acrylic resin dentures contain methylmethacrylate (MMA) as residual monomer. Commercial dental restorative materials (for example, bonding materials, composite resins and glass ionomers) were also shown to contain methacrylates. The most frequently occurring methacrylates in bonding materials are 2-hydroxy-ethyl methacrylate (2-HEMA) and 2,2-bis-[4-(2-hydroxy-3-methacryloxypropoxy) phenyl]-propane (bis-GMA). Bis-GMA and triethyleneglycol dimethacrylate are the most frequently occurring methacrylates in composite resins. The main methacrylate of the glass ionomers is 2-HEMA or trimethylolpropane trimethacrylate [11].

Formaldehyde is formed as oxidation products of the residual methylmethacrylate monomer and may be released from methacrylate-based dental materials, such as composites and denture bases [20]. It is responsible for allergic inflammation in acrylic denture wearers and it is necessary to

study its leaching from denture-base materials. Both MMA and formaldehyde have been often associated with allergic local reactions in the patients' oral mucosa in contact with prosthetic and orthodontic devices [14]. Other adverse reactions reported include contact dermatitis and occupational respiratory hypersensitivity in dental professionals because of volatilization [8, 12].

Numerous studies confirm the length promenade incidence of sensitization to methacrylates in dental professionals [8, 24], as well as in patients undergoing dental treatment and exposed to resin-based materials [3]. Such reactions could be observed in dental students exposed to methacrylic monomers and formaldehyde during their practical education. Quite a few studies are available aiming to evaluate the incidence of sensitization in students of dental medicine.

Basing on our previous finding on manifestation of co-reactivity between formaldehyde and glutaraldehyde, and the persistent combined exposure to numerous chemical compounds in dental practice, in the present study we aimed to evaluate the prevalence of concomitant sensitization to other dental materials (mainly methacrylic monomers) among dental professionals and students of dental medicine with positive skin patch tests to formaldehyde and/or glutaraldehyde.

A total of 139 subjects, divided into four groups, according to presence and duration of occupational exposure to dental materials participated in our study. Due to the feminization of most occupations in dental medicine, the distribution of participants by gender was not uniform, with predominance of women in all the investigated groups, but without statistical significance.

Basing on the irritant action of most tested by us and widely used in dental practice chemical compounds, we conducted intentionally questionnaire-based interviews to evaluate the incidence of subjective symptoms mainly from the upper respiratory tract, skin and respiratory system. No statistically significant differences were established. A trend for asymptomatic sensitization to formaldehyde and/or glutaraldehyde was observed in the investigated by us groups. This trend is confirmed in terms of results about clinically diagnosed pathology from skin and other organs and systems.

High incidence of positive skin patch test reactions to formaldehyde and/or glutaraldehyde was revealed (21,1% – 42,9%), highest being in the group of students of dental medicine from 6 course and in the one of occupationally unexposed patients. No significant role of allergic predisposition or smoking habits was established.

Methyl methacrylate (MMA) as a small molecular acrylate can permeate thin protective disposable gloves. Several studies have indicated high prevalence of skin symptoms and incidence of sensitization to methacrylates among dental professionals as well as in patients. In our

study relatively high sensitization rates to MMA among individuals with positive skin patch tests to formaldehyde and/or glutaraldehyde were observed. According to our results, the most vulnerable group was the one of students of dental medicine - 6 course, being exposed to combined action of MMA and aldehydes for 4-5 years in their practical education.

The probability of release of **TEGDMA** from composite resins is high, and the risk of allergies and cytotoxicity has been recognized [3]. Most probably, due to the ubiquitous occurrence of formaldehyde, the wide use of composite resins and bonding agents containing TREGDMA, as well as of biocides containing glutaraldehyde in dentistry, we revealed an increased incidence and OR of contact sensitization to TREGDMA among the total studied population of 139 subjects. The rates of sensitization to formaldehyde and/or glutaraldehyde and to TEGDMA ranged from 25% in the group of dental professionals (surprisingly lowest) to 48% in the group of students of dental medicine from 3 and 4 courses (surprisingly highest due to the shortest exposure period). Similar were the subtracted conclusions regarding the incidence and the OR of contact sensitization to **EGDMA** among individuals with positive skin patch tests to formaldehyde and/or glutaraldehyde. No significant differences were established regarding the overall, as well as the between-groups analysis of the distribution of individuals, sensitized to formaldehyde and/or glutaraldehyde and **bis-GMA**.

2-HEMA is the main monomer in many dentin-bonding agents and light cured glass-ionomers. The only known consumer exposure to HEMA in its monomeric form is through to be its use in dentistry (11). The results from our study demonstrate high rates of concomitant sensitization to formaldehyde and/or glutaraldehyde and 2-HEMA among all the investigated groups, highest being among the dental professionals – 45.5%, with statistical significance. However, a prominent role of occupational exposure could be definitely stated.

Tetrahydrofurfuryl methacrylate is reactive monomer, used in the formulation of ultraviolet light-curable adhesives, coatings, paints, and printing inks. It is used in dental materials such as crowns and bridges. It is also found in artificial nails [27].

Data obtained in our study indicate high prevalence of sensitization to later methacrylic monomer among individuals with positive skin patch tests to formaldehyde and/or glutaraldehyde - lowest being in the group of 6th course students of dental medicine - 33,3%, and highest in the group of occupationally non-exposed participants - 61,1%. On other hand, the within-group analysis established, with high statistical significance, prevalence of individuals with concomitant sensitization to these allergens in the group of students from 3-4 course and, especially, the one of dental professionals. Since the statistics categorically revealed an

increased incidence and OR of concomitant contact sensitization among the total studied population, we could consider an equally significant role of both exposures - occupational and consumer.

The role of occupational and non-occupational (patient's) exposures for sensitization to **mercury** is well evidenced [1, 25]. In the present study we investigated the incidence of possible concomitant sensitization to mercury among individuals with positive skin patch tests to formaldehyde and/or glutaraldehyde.

Taking into consideration the observed increased incidence of concomitant contact sensitization in the group of dental professionals and the categorically established increased incidence and OR of manifestation of contact sensitization to mercury among subjects sensitized to formaldehyde and/or glutaraldehyde among the whole studied by us population again we accept the importance of both occupational and consumer exposures.

Eugenol is widely used in dental practice to relieve pain arising from various sources. It presents in various dental preparations - some zinc oxide preparations such as periodontal dressings and root canal cements As a primary irritant and sensitiser, it is known to cause contact urticaria as well as chronic urticaria and allergic contact dermatitis [29].

We established significantly increased incidence of individuals with positive skin patch tests to formaldehyde and/or glutaraldehyde and to eugenol in the groups with shortest and longest duration of exposure - the ones of students from 3-4 course and of dental professionals. Once again increased prevalence and OR of concomitant sensitization was categorically established for the whole tested population.

Dental professionals and their physicians frequently do not recognize, accurately diagnose or appropriately manage occupational allergies. Dental students, as a whole, are insufficiently aware about the risks arising from their exposure to chemical hazards, starting during their practical education, as well as about the proper personal and general prevention.

The basic goal of occupational health specialists is to educate employers and employees about the work place hazards, risk assessment, and risk management strategies. Better information and improved cooperation between dental workers, their clinicians and occupational health services is needed.

Basing on the results of the present study, more efficient risk management and training programs about use of proper personal protection, especially among students, and limitations of general exposure to the studied chemical allergens could be recommended.

CONCLUSIONS

1. High incidence of sensitization to formaldehyde and/or glutaraldehyde was revealed, without crucial role of

allergic predisposition or smoking habits as risk factors.

2. A trend for asymptomatic sensitization to formaldehyde and/or glutaraldehyde was observed in the investigated population, confirmed in terms of prevalence of subjective symptoms and the objective clinical findings.

3. The most vulnerable group in terms of concomitant sensitization to formaldehyde and/or glutaraldehyde and to MMA seems to be the students from 6th course; to TREGDMA and EGDMA - the students from 3-4 course; to 2-HEMA and to mercury - the dental professionals; to

tetrahydrofurfuryl methacrylate and to eugenol - the students from 3-4 course and dental professionals.

4. As a whole, high rates of concomitant sensitization to formaldehyde and/or glutaraldehyde and the studied dental materials were established, suggesting also an important role of consumer (patient's) exposure.

5. More effective training and risk management programs in exposure to allergens and use of proper personal protection in dental practice and among dental students could be recommended.

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