

## METHACRYLATE AND ACRYLATE ALLERGY IN DENTAL STUDENTS

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### ABSTRACT

A multitude of acrylic monomers is used in dentistry, and when dental personnel, patients or students of dental medicine become sensitized, it is of great importance to identify the dental acrylic preparations to which the sensitized individual can be exposed. Numerous studies confirm high incidence of sensitization to (meth) acrylates in dental professionals, as well as in patients undergoing dental treatment and exposed to resin-based materials. Quite a few studies are available aiming to evaluate the incidence of sensitization in students of dental medicine

The **purpose** of the study is to evaluate the incidence of contact sensitization to some (meth) acrylates in students of dental medicine at the time of their education, in dental professionals (dentists, nurses and attendants) and in patients, the manifestation of co-reactivity.

A total of 139 participants were included in the study, divided into four groups: occupationally exposed to (meth)acrylates and acrylic monomers dental professionals, 3-4 year-of-education students of dental medicine, 6th year-of-education students of dental medicine and patients with suspected or established sensitization to acrylates, without occupational exposure. All of them were patch-tested with 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), and *tetrahydrofurfuril* methacrylate.

The overall sensitization rates to methacrylates in the studied population are comparative high – from 25.9% for MMA to 31.7% for TREGDMA. Significantly higher incidence of sensitization in the group of 3-4 course students compared to the one in the group of dental professionals for MMA and TREGDMA was observed. Highest was the incidence of sensitization to ethyleneglycol dimethacrylate, BIS-GMA, 2-HEMA and tetrahydrofurfuryl methacrylate in the group of patients, with statistical significance comparing them to the group of dental professionals. More intensive risk management training programs in exposure to

methacrylates and use of proper personal protection among students is recommended.

**Key words:** methacrylates, sensitization, occupational exposure, dental students, skin patch-testing.

### INTRODUCTION

In their everyday activities dental students and dental professionals are exposed to the numerous chemical agents. Their primary source is the used broad range dental materials and medicines. Dental products all contain a number of allergens and irritants that may give rise to health issues both for dental professionals in their occupational exposure, and dental students at the time of their education, as well as for patients to which they have been applied.

**Acrylates** are plastic materials produced by polymerization of monomers derived from acrylic or methacrylic acid. Polymerization may occur at room temperature or with heat [20]. They have been in use since the 1930s, when Rohm and Haas began mass production of Plexiglas, a clear and resistant glass substitute made of polymerized methacrylate. Numerous other acrylates have found applications in paints and adhesives, dental composite resins, printing inks, artificial nails, and medical devices - contact lenses, hearing aids, and bone cement for orthopedic endoprostheses [21].

Methyl methacrylate (MMA) as a small molecular acrylate can permeate thin protective disposable gloves. Methacrylates serve as bases for acrylic resins [14].

Nowadays, numerous (meth)acrylates, mostly used in dental bonding materials, printing inks, and artificial nails, are polymerized by exposure to UV light with help from a priming photoinitiator. The acrylates and, to a lesser extent, methacrylates (2-hydroxyethyl methacrylate (2-HEMA), triethyleneglycol dimethacrylate (TREGDMA), and 2,2-bis[4-(2-hydroxy-3-methacryloxypropoxy) phenyl]propane (bis-GMA) are strong irritants, but they are also notorious allergens. These compounds were found at concentrations of 50 to 90% in unhardened dental adhesives and cements.

Completely polymerized acrylic plastics are inert and harmless. Cured methacrylates also can volatilize, thereby causing respiratory irritation and sensitization and allergic symptoms [5, 21].

Since the 1950s, numerous case reports have documented allergic contact dermatitis to (MMA). In 2012 (meth) acrylates were accessed by the American Contact Dermatitis Society to the rank of “allergen of the year” [21].

A multitude of acrylic monomers is used in dentistry, and when dental personnel, patients or students of dental medicine become sensitized, it is of great importance to identify the dental acrylic preparations to which the sensitized individual can be exposed. Another important aspect is that product declarations of dental acrylic materials should show all acrylic compounds present in the products - even acrylic monomers/impurities with lower concentrations than 1%. This could help to select a product that the sensitized individual could use [11].

Numerous studies confirm the length promenade incidence of sensitization to (meth) acrylates in dental professionals [3, 7, 9, 12, 16, 17, 19, 22, 23, 25], as well as

in patients undergoing dental treatment and exposed to resin-based materials [8, 24].

Quite a few studies are available aiming to evaluate the incidence of sensitization in students of dental medicine.

### AIM

The purpose of the study is to evaluate the incidence of contact sensitization to some (meth) acrylates in students of dental medicine at the time of their education, in dental professionals (dentists, nurses and attendants) and in patients, the manifestation of co-reactivity.

### PATIENTS AND METHODS

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

Studied groups	No / %	Mean age ± S D	Gender	
			Male	Female
Patients without occupational exposure	29 / 20,9%	47,34 ± 18,21	7 / 24,1%	22 / 75,9%
3-4 year-of-education students of dental medicine	44 / 31,7%	22,05 ± 1,29	17 / 38,6%	27 / 61,4%
6 <sup>th</sup> year-of-education students of dental medicine	28 / 20,1%	26,39 ± 6,79	11 / 39,3%	17 / 60,7%
Occupationally exposed dental professionals	38 / 27,3%	52,32 ± 13,41	8 / 21,1%	30 / 78,9%
<b>Total</b>	<b>139 / 100,0%</b>	-	<b>43 / 30,9%</b>	<b>96 / 69,1%</b>

**Table 1.** General characteristics of studied groups of subjects.

The study was supported by the Medical University - Sofia - Grant No. C-1/2012, and was approved by the Medical Ethics Board at Medical University - 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 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) and *tetrahydrofurfuril* metacrylate was performed, according to the Jadassohn & Bloch classical methods for diagnosis of contact allergy, by placing the allergens (0.2%/pet, Chemotechnique Diagnostics) 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 subjects, 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 vullous)
- 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 by gender was not uniform, with predominance of women in all the investigated groups, but without statistical significance ( $\chi^2=4,5, p=0,212$ ).

Logically, significantly higher was the mean age in the groups of occupationally exposed dental professionals and the unexposed subjects 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 methacrylates in dental practice, data is predictable: 0 years of occupationally unexposed patients, 1-2 years 3-4 course students, 4 years for 6 course students and a number (from 1 to 50 years) for the occupationally exposed 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 statistically significant difference ( $\chi^2=8,741, p=0,033$ ), 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 percentage of individuals with no history of allergic pathology dominated 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 compared with the groups of 3-4 course ( $p=0,044$ ) and 6 course ( $p=0,047$ ) students.

Statistically significant differences in the overall distribution, as well as between the different groups, concerning the history of subjective upper respiratory tract complaints were not proven ( $p=0.324$ ). Except for the group of patient, where the ratio of people with and without such complaints is almost equal, generally higher is the incidence of people without complaints.

Data concerning the history for manifestation of subjective skin complaints were also intentionally collected in the performed questionnaire survey. Summary for the groups of respondents is demonstrated in Table 2.

History of subjective skin complaints	Studied group				Total
	Unexposed patients	Students of Dental Medicine 3 and 4 course	Students of Dental Medicine 6 course	Dental professionals	
No N / %	12 / 48,0%	23 / 53,5%	9 / 32,1 %	24 / 68,6%	68 / 51,9%
Yes N / %	13 / 52,0%	20 / 46,5%	19 / 67,9 %	11 / 31,4%	63 / 48,1%
Total N / %	25 / 100,0%	43 / 100,0%	28 / 100,0%	35 / 100,0%	131 / 100,0

**Table 2.** Distribution of data about history of subjective skin complaints among the studied groups.

Evidently, among the full study population incidence of cases with and without history of subjective skin complaints is almost equal, but in the group of unexposed patients, and more pronounced, in the one of 6 course dental medicine students, people with history of skin subjective complaints prevail. Statistical analysis demonstrated significance in the upper summarized distribution ( $\chi^2=8.471, p=0.037$ ). Also, subjective skin symptoms are more common in the group of 6 course students as compared to dental professionals with a high significance ( $\chi^2=8.276, p=0.004$ ).

The statistical analysis didn't demonstrate significant differences in the distribution of subjects with history of subjective respiratory system complaints ( $p = 0.318$ ).

The analysis on distribution of clinical findings from upper and lower respiratory tract, skin, cardiovascular, digestive and nervous systems didn't reveal statistically significant differences ( $p > 0.050$ ).

Data concerning the incidence of sensitization to methyl methacrylate (MMA) in the investigated by us population is summarized in Table. 3.

Skin patch test reactions to methyl methacrylate	Studied group				Total
	Unexposed patients	Students of Dental Medicine 3 and 4 course	Students of Dental Medicine 6 course	Dental professionals	
Negative N / %	20 / 69,0%	28 / 63,6%	22 / 78,6 %	33 / 86,8%	103/74,%
Possitive N / %	9 / 31,0%	16 / 36,4%	6 / 21,4 %	5 / 13,2%	36 /25,9%
Total N / %	29 /100,0%	44 / 100,0%	28 /100,0%	38 / 100,0%	139 / 100,0

**Table 3.** Distribution of positive skin patch test reactions to methacrylate among the studied groups.

Individuals with negative skin patch test reactions to MMA prevailed both in the general distribution and in the groups determined by us, without statistical significance in the upper distribution ( $p=0,093$ ). The between-groups analysis revealed significantly higher incidence of

sensitization in the group of 3-4 course students compared to the one in the group of dental professionals ( $\chi^2=5,764$ ,  $p=0,016$ ). No other relevant differences were found.

Results from skin patch testing to triethyleneglycol dimethacrylate (TREGDMA) are presented in Table 4.

Skin patch test reactions to TREGDMA	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%	26 / 59,1%	20 / 71,4 %	31 / 81,6%	95/68,3%
Possitive N / %	11 / 37,9%	18 / 40,9%	8 / 28,6 %	7 / 18,4%	44 /31,7%
Total N / %	29 /100,0%	44 / 100,0%	28 /100,0%	38 / 100,0%	139 / 100,0

**Table 4.** Distribution of positive skin patch test reactions to triethyleneglycol dimethacrylate among the studied groups.

The incidence of sensitization is similar to the one to MMA, with no significant differences in the distribution ( $p=0,141$ ). Highest is the incidence of sensitization in the group of 3-4 course students, with statistical significance

compared to the group of dental professionals ( $\chi^2=4,886$ ,  $p=0,027$ ). No other relevant differences were found.

Results from skin patch testing to ethyleneglycol dimethacrylate are presented in Table 5.

Skin patch test reactions to EGDMA	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%	19 / 67,9 %	32 / 84,2%	101/72,7%
Possitive N / %	11 / 37,9%	12 / 27,3%	9 / 32,1 %	6 / 15,8%	38 /27,3%
Total N / %	29 /100,0%	44 / 100,0%	28 /100,0%	38 / 100,0%	139 / 100,0

**Table 5.** Distribution of positive skin patch test reactions to ethyleneglycol dimethacrylate among the studied groups.

No statistically significant differences concerning the incidence of sensitization to ethyleneglycol dimethacrylate was established in the general distribution ( $p=0,211$ ). The frequency of sensitization in the patients group was found to

be significantly higher than in the one of dental professionals ( $\chi^2=4,258$ ,  $p=0,039$ ).

Skin patch testing results to BIS-GMA are presented in Table 6.

Skin patch test reactions to BIS-GMA	Studied group				Total
	Unexposed patients	Students of Dental Medicine 3 and 4 course	Students of Dental Medicine 6 course	Dental professionals	
Negative N / %	17 / 58,6%	32 / 72,7%	17 / 60,7 %	31 / 83,8%	97/70,3%
Possitive N / %	12 / 41,4%	12 / 27,3%	11 / 39,3%	6 / 16,2%	41 / 29,7%
Total N / %	29 / 100,0%	44 / 100,0%	28 / 100,0%	37 / 100,0%	138 / 100,0

**Table 6.** Distribution of positive skin patch test reactions to (BIS-GMA) among the studied groups.

No statistically significant differences were established in the general distribution ( $p=0,091$ ), but relevantly higher was the sensitization rate in the patient's group ( $\chi^2=5,190$ ,  $p=0,023$ ) and 6 course student's group ( $\chi^2=4,392$ ,  $p=0,036$ )

compared to the one of dental professionals.

Results about the sensitization rates to 2-hydroxyethyl methacrylate are demonstrated in Tabl. 7.

Skin patch test reactions to 2-HEMA	Studied group				Total
	Unexposed patients	Students of Dental Medicine 3 and 4 course	Students of Dental Medicine 6 course	Dental professionals	
Negative N / %	17 / 58,6%	30 / 68,2%	20 / 71,4 %	30 / 78,9%	97/70,3%
Possitive N / %	12 / 41,4%	14 / 31,8%	8 / 28,6 %	7 / 21,1%	41 / 29,7%
Total N / %	29 / 100,0%	44 / 100,0%	28 / 100,0%	37 / 100,0%	138 / 100,0

**Table 7.** Distribution of positive skin patch test reactions to 2-HEMA among the studied groups.

No statistically significant differences were established in the general distribution ( $p=0,255$ ), but again relevantly higher was the sensitization rate in the patient's group ( $\chi^2=4,001$ ,  $p=0,045$ ) compared to the one of dental

professionals. No other significant differences were found.

Different is the distribution of positive skin patch reactions to tetrahydrofurfuryl methacrylate (Tabl. 8).

Skin patch test reactions to tetrahydrofurfuryl methacrylate	Studied group				Total
	Unexposed patients	Students of Dental Medicine 3 and 4 course	Students of Dental Medicine 6 course	Dental professionals	
Negative N / %	15 / 51,7%	31 / 70,5%	19 / 67,9 %	32 / 86,5%	97/70,3%
Possitive N / %	14 / 48,3%	13 / 29,5%	9 / 32,1 %	5 / 13,5%	41 / 29,7%
Total N / %	29 / 100,0%	44 / 100,0%	28 / 100,0%	37 / 100,0%	138 / 100,0

**Table 8.** Distribution of positive skin patch test reactions to tetrahydrofurfuryl methacrylate among the studied groups.

Statistical significance was established for the overall distribution ( $\chi^2=9,514$ ,  $p=0,023$ ). Except from the relevantly higher sensitization rate in the patients compared to dental professionals ( $\chi^2=9,583$ ,  $p=0,002$ ), no other significant differences were found.

## DISCUSSION

A total of 139 subjects, divided into four groups, according to presence and duration of occupational exposure to methacrylates, 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.

Since non-smokers significantly predominated in the whole studied population generally, we consider that tobacco smoking should not have serious impact on the investigated health status parameters. We should only take into account the discovered significant inter-group differences.

The intentionally conducted questionnaire survey

aimed to collect data about allergic predisposition, subjective symptoms from upper respiratory tract, respiratory system and skin, as well as history for atopy among the investigated population.

Generally, a crucial role of allergic pathology and predisposition as a risk factor for the sensitization to methacrylates should not be presumed in this study. Both occupational and during the education of Dental Medicine exposure to methacrylates didn't result in an increased incidence of subjective upper respiratory system symptoms. This observation is in contrast with other findings about increased incidence of respiratory sensitization [4, 10, 13, 18], as among the most common causes are the methacrylates.

Attention should be paid to the fact that over two thirds (61.9%) of all subjects with history of subjective skin complaints is constituted by 3 and 4 course students and trainees. On the other hand, somewhat surprisingly, in the group of dental professionals clearly prevail subjects without subjective skin complaints. More detailed causal evaluation of these data will be carried out below.

The exposure to methacrylates didn't result in increased incidence of subjective symptoms from the respiratory, as well as from the other systems.

The analysis on distribution of objective clinical findings from upper and lower respiratory tract, skin, cardiovascular, digestive and nervous systems also didn't reveal statistically significant differences.

The most commonly positive allergens in dentists and dental nurses were to 2-hydroxyethyl methacrylate (2-HEMA), ethyl acrylate (EA), triethyleneglycol dimethacrylate (TREGDMA), and 2,2-bis[4-(2-hydroxy-3-methacryloxypropoxy) phenyl]propane (bis-GMA). 2-HEMA is considered to be the most important allergen in dentists and dental nurses, and MMA and EGDMA in dental-technicians. Reactions to bis-GMA, DEGDA, TREGDA, EMA and EA were relevant in some patients [1, 2, 6]. We performed patch-testing with methacrylated, included in Dental Materials Staff (DMS-1000) series.

The overall sensitization rates to methacrylates in the studied population are comparative high - from 25.9% for MMA to 31.7% for TREGDMA.

Generally, lowest was the incidence in the group of dental professionals, and highest levels varied for different allergens and studied groups.

For example, significantly higher was the incidence of sensitization in the group of 3-4 course students compared to the one in the group of dental professionals for MMA and TREGDMA. This could be related to their recent and intensive exposure to these substances in the second year of education at dental technician laboratories. There, according to data obtained from the students during the interviews, they didn't use and were unaware about the role of proper protective gloves at work. This is a possible

explanation for the high sensitization rates, corresponding with previously discussed finding that 61.9% of all subjects with history of subjective skin complaints is constituted by 3 and 4 course students and trainees, with clear prevalence of subjects without subjective skin complaints in the group of dental professionals.

Interesting were the results concerning the distribution of sensitization incidence to ethyleneglycol dimethacrylate, BIS-GMA, 2-HEMA and tetrahydrofurfuryl methacrylate.

Regarding the distribution of positive skin patch test reactions to ethyleneglycol dimethacrylate among the studied groups, highest were the rates in the group of patients, with statistical significance compared to the group of dental professionals. The latter is valid for sensitization rates to BIS-GMA, 2-HEMA and tetrahydrofurfuryl methacrylate - highest incidence in the group of patients, with statistical significance comparing them to the group of dental professionals.

A possible explanation of relatively higher incidence of sensitization to the listed above methacrylates among occupationally unexposed patients is the specificity of the investigated group - with mean age 47,34 years, with a history for multiple exposures to resin-based materials while undergoing dental treatment, and suspected or previously diagnosed sensitization to dental materials.

One more observation was the relatively higher incidence of sensitization to *BIS-GMA* in the group of trainees - with significant differences compared to the dental professionals.

Contrary to previous studies, the relative sensitization rates among relatively lower compared to the other studied groups. We could suggest that it is due to improved working conditions, effective educational programs and strict use of proper personal protective equipment.

Acrylic monomers often cross-react - that is, allergic sensitization induced by one acrylic compound extends to one or more other acrylic compounds. Therefore, sensitized individuals are often multiallergic and, accordingly, cannot be exposed to any of the compounds [2, 6, 9, 12, 16].

The results from our study also confirm manifestation of cross-reactivity of acrylic compounds - 66.3% of all individuals, sensitized to (meth)acrylates were allergic to more than one of the tested compounds.

More intensive risk management training programs in exposure to methacrylates and use of proper personal protection among students is recommended.

## CONCLUSIONS

1. A crucial role of allergic pathology and predisposition as a risk factor for the sensitization to methacrylates should not be presumed in our study.

2. The exposure to methacrylates didn't result in increased incidence of subjective symptoms and objective

clinical findings from the respiratory cardiovascular, digestive and nervous systems. Over two thirds (61.9%) of all subjects with history of subjective skin complaints is constituted by 3 and 4 course students and trainees, with clear prevalence of subjects without subjective skin complaints in the group of dental professionals.

3. The overall sensitization rates to methacrylates in the studied population are comparative high – from 25.9% for MMA to 31.7% for TREGDMA.

4. Significantly higher incidence of sensitization in the group of 3-4 course students compared to the one in the

group of dental professionals for MMA and TREGDMA was observed.

5. Highest was the incidence of sensitization to ethyleneglycol dimethacrylate, BIS-GMA, 2-HEMA and tetrahydrofurfuryl methacrylate in the group of patients, with statistical significance comparing them to the group of dental professionals.

6. More intensive risk management training programs in exposure to methacrylates and use of proper personal protection among students is recommended.

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