



CONTACT SENSITIZATION TO METHACRYLIC MONOMERS AMONG DENTAL TECHNICIAN STUDENTS IN RELATION TO DURATION OF EDUCATIONAL EXPOSURE

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ABSTRACT

Purpose: Sensitization to methacrylic monomers is a significant problem in dental occupational exposures. The purpose of the present study was to evaluate the dynamics in contact sensitization incidence to methacrylic monomers during the educational course of dental technician students.

Material and Methods: Skin patch testing with methyl methacrylate, triethylene glycol dimethacrylate, ethylene glycol dimethacrylate, 4-tolyldiethanolamine, N,N-Dimethyl-4-toluidine, 1,4-butanediol dimethacrylate, tetrahydrofurfuryl methacrylate, formaldehyde and glutaraldehyde was performed among 150 dental technician students (38 – 1st, 40 – 2nd and 38 – 3rd year of education); 34 students without educational exposure to metals served as controls.. Chi square test and Fisher Exact Test were used in data analysis ($p < 0.05$).

Results: The incidence of sensitization to 4-tolyldiethanolamine in the group of dental technician students 2nd and 3rd year of education was significantly higher, if compared with those from the 1st year, as well as with the control group ($P=0.042$). The sensitization rate to 4-tolyldiethanolamine was the highest recorded among all methacrylic monomers tested for the whole tested population. The incidence of positive patch tests to formaldehyde was the highest recorded for all defined groups. Higher were sensitization rates among dental technician students 2nd year of education vs. no cases in the control group.

Conclusions: Our data indicate high and increasing with the duration of educational exposure risk of contact sensitization to 4-tolyldiethanolamine among dental technician students, and this substance could be outlined as a sensitizer of prominent importance. No significant differences were established concerning the other tested methacrylic monomers. We accept the main role of consumer and environmental exposures for the manifestation of formaldehyde sensitization. Adequate preventive measures and information should be provided during the practical educational course of dental technician students. General

population need to be well informed and the European Union regulations to be properly applied.

Keywords: contact sensitization, methacrylic monomers, dental technician students, educational exposure

INTRODUCTION

Dental technicians are occupationally exposed to numerous chemical agents while handling dental materials during their daily activities. Dental materials contain a number of allergens and irritants. The biological reactions can take place close or far away from the site of contact (systemic reactions) [1]. Both dental patients and dental technicians are exposed to potential health risks – the patient as a recipient of restorative materials. The exposure of dental technician starts while being students – during their practical education.

Acrylates are plastic materials produced by polymerization of monomers derived from acrylic or methacrylic acid. Polymerization may occur at room temperature or with heat [2]. Methacrylates serve as a base for acrylic resins [3]. Resin-based dental materials are extensively used today in dentistry. Examples of include general dental applications dentures (bases, liners, tissue conditioners, artificial teeth, temporary restoration, etc.), cavity restorative materials (composites – self / light curing), pulpal, cavity and margin sealants, impression materials (alginate, agar, elastomers, waxes, etc.), resin based cements, dentin bonding agents, orthodontic appliances, habit breaking appliances (nail biting, thumb sucking, etc.), oral and maxillofacial appliances, cleft palate plates maxillary supports, etc. [4]. Acrylic resin dentures contain methyl methacrylate (MMA) as residual monomer [5]. 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 (TEGDMA) are the most frequently occurring methacrylates in composite

resins. The main methacrylate of the glass ionomers is 2-HEMA [6]. Completely polymerized, acrylic plastics are inert and harmless. Cured methacrylates also can volatilize, thereby causing respiratory irritation and sensitization and allergic symptoms [2].

Experimental and clinical studies have documented that methacrylic monomers may cause a wide range of adverse health effects such as irritation to skin, eyes, and mucous membranes, allergic dermatitis, stomatitis, asthma, neuropathy, disturbances of the central nervous system, liver toxicity, and fertility disturbances [7]. The methacrylates are not only strong irritants, but also notorious allergens. Numerous studies confirm the length-promoted incidence of sensitization to methacrylates in dental professionals [8, 9], as well as in patients undergoing dental treatment and exposed to resin-based materials [10].

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

The purpose of the present study was to evaluate the dynamics in the incidence of contact sensitization to **methacrylic monomers** during the course of practical education among students from dental technician school.

METHODS

A total of 150 participants (54 men and 96 women, mean age 23.6±10.8 years), divided into 4 groups, were included in the study: dental technician students from the Medical College – Sofia – 1st, 2nd and 3rd year of education, as well as students from other specialities, non-exposed to metals during their educational course, serving as a control group. The studied groups are presented in table 1.

Table 1. Characteristics of the studied population.

Group	Total [n I(%)]
Dental technician students – 1 st year	38 (25.3%)
Dental technician students – 2 nd year	40 (26.7%)
Dental technician students – 3 rd year	38 (25.3%)
Students without exposure to metals	34 (22.7%)
Total	150 (100.0)

The study was granted by the Medical University of Sofia, Contract No 101/2018, and approved by the Medical Ethics Board at Medical University – Sofia. All the participants were informed about the purpose of the study and gave their written informed consent before its commencement.

Skin patch testing

Skin patch testing with methyl methacrylate (2.0% pet), triethylene glycol dimethacrylate (2.0% pet), ethylene glycol dimethacrylate (2.0% pet), 4-tolyldiethanolamine (2.0% pet), N,N-Dimethyl-4-toluidine (5.0% pet), 1,4-butanediol dimethacrylate (2.0% pet), tetrahydrofurfuryl methacrylate (2.0% pet), formaldehyde (2.0% pet) and glutaraldehyde (0.2% pet) – Chemotechnique Diagnostics was performed according to the Jadassohn & Bloch classical methods for diagnosis of contact allergy, by placing the allergens in IQ-Ultra hypoallergenic patches of Chemotechnique Diagnostics (IQ Chambers®, Vellinge, Sweden). Lack of anti-allergic medication constituted a mandatory condition before placing the patches and during the testing. Patches with allergens were applied on the back of the tested individuals; reading of the test was performed after 48 hours, several hours after removing the patches, with control revision after 72 hours.

Interpretation of reaction sites was based on the method and the interpretation key recommended by the International Contact Dermatitis Research Group (ICDRG) - table 2.

Table 2. Interpretation key of skin patch test results based on International Contact Dermatitis Research Group.

Symbol	Meaning
(-)	negative reaction
?	doubtful reaction
+	weak positive reaction (non-vesicular)
++	strong positive reaction (oedematous or vesicular)
+++	extreme positive reaction (ulcerative or bullous)
IR	irritant reaction

Statistical methods

The statistics were calculated with SPSS 19.0. The following statistics available for cross-tabulation were used: Chi-square (χ^2) test, Fisher's Exact Test for statistical significance. Values of $p < 0.05$ were accepted as statistically significant.

RESULTS

The distribution by gender was not uniform, with a predominance of women in all the investigated groups, but without statistical significance [$\chi^2(3)=1.96$, $p=0.582$]. Individuals without a history of allergic pathology and skin complaints prevailed in all the studied groups, with no reliable differences in the overall distribution.

Data on the incidence of sensitization to the selected metals in the defined groups are summarized in table 3.

Table 3. Incidence of sensitization to the selected metals in the defined groups.

Target group	Positive reactions to:								
	MMA	TEGDMA	EGDMA	4-tolyl-diethanl-amine	N,N-dimethyl4-toluidine	1-4-butanediol dimethacrylate	THFDMA	FA	GLU
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Dental technician students 1st year	4 (10.5)	3 (7.9)	3 (7.9)	4 (10.5)	2 (5.3)	4 (10.5)	4 (10.5)	8 (21.1)	3 (7.9)
Dental technician students 2nd year	5 (12.5)	2 (5.0)	4 (10.0)	8 (20.0)	0 (0.0)	8 (20.0)	5 (12.5)	14 (35.0)	7 (17.5)
Dental technician students 3rd year	2 (5.3)	5 (13.2)	3 (7.9)	9 (23.7)	5 (13.2)	2 (5.3)	5 (13.2)	7 (18.4)	3 (7.9)
Students without exposure to metals	3 (8.8)	5 (14.7)	2 (5.9)	1 (2.9)	2 (5.9)	2 (5.9)	2 (5.9)	8 (23.5)	0 (0.0)
Total	14 (9.3)	15 (10.0)	12 (8.0)	22 (14.7)	9 (6.0)	16 (10.7)	16 (10.7)	37 (24.7)	13 (8.7)

The statistical analysis revealed a significantly higher incidence of sensitization to **4-tolyldiethanolamine** in the group of dental technician students 2nd and 3rd year of education, if compared with those from 1st year, as well as with the control group ($p=0.042$). Moreover, the sensitization rate to **4-tolyldiethanolamine** was the highest recorded among all methacrylic monomers tested for the tested population as a whole. No other significant differences were revealed.

Data on the incidence of sensitization to the selected methacrylic monomers, formaldehyde and glutaraldehyde according to gender characteristics of the studied population are presented in table 4.

Table 4. Incidence of positive skin patch tests to the selected methacrylic monomers, formaldehyde and glutaraldehyde according to gender.

Gender	Positive reactions to:								
	MMA	TEGDMA	EGDMA	4-tolyl-diethanl-amine	N,N-dimethyl4-toluidine	1-4-butanediol dimethacrylate	THFDMA	FA	GLU
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Men	6 (11.1)	3 (5.6)	6 (11.1)	6 (11.1)	3 (5.6)	7 (13.0)	5 (9.3)	12 (22.2)	3 (5.6)
Women	8 (8.3%)	12 (12.5)	6 (6.3)	16 (16.7)	6 (6.2)	9 (9.4)	11 (11.5)	25 (26.0)	10 (10.4)
Total	14 (9.3)	15 (10.0)	12 (8.0)	22 (14.7)	9 (6.0)	16 (10.7)	16 (10.7)	37 (24.7)	13 (8.7)

No statistically significant differences were revealed.

The results on the distribution of sensitization incidence to the selected methacrylic monomers, formaldehyde and glutaraldehyde regarding the age characteristics (below and above 30 years) of the studied population are presented below – table 5.

Table 5. Incidence of positive skin patch tests to the selected methacrylic monomers, formaldehyde and glutaraldehyde according to age.

Age	Positive reactions to:								
	MMA	TEGDMA	EGDMA	4-tolyl-diethanl-amine	N,N-dimethyl-4-toluidine	1-4-butanediol dimethacrylate	THFDMA	FA	GLU
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
≤ 30 y.	11 (8.9)	11 (8.9)	7 (5.6)	16 (12.9)	7 (5.6)	10 (8.1)	11 (8.9)	29 (23.4)	10 (8.1)
>30 y.	3 (11.5)	4 (15.4)	5 (19.2)	6 (21.3)	2 (7.7)	6 (23.1)	5 (19.2)	8 (30.8)	3 (38.5)
Total	14 (9.3)	15 (10.0)	12 (8.0)	22 (14.7)	9 (6.0)	16 (10.7)	16 (10.7)	37 (24.7)	13 (8.7)

Significantly higher was the incidence of contact sensitization to ethylene glycol dimethacrylate and to 1,4-Butanediol dimethacrylate ($p=0.036$) in the group of individuals above 30 years ($p=0.036$).

DISCUSSION

Numerous chemical substances, many of which allergens being ingredients of various dental materials impose serious health risk for dental technicians. Their occupational exposure starts as early as during the course of their practical education.

Nowadays, (meth) acrylates have found applications in a variety of dental resin-based materials as well as in consumer products such as paints and adhesives, printing inks, artificial nails, medical devices - contact lenses, hearing aids, etc. [2]. Due to the specificity and the chemical composition of the used materials dental technicians during their education and work are mostly exposed to MMA and to a less degree to dental composites. Resin-based dental materials are not inert in the oral environment of dental patients, and may release numerous components, including methacrylic monomers. For dental patients everyday consumer's exposure is of importance as well [11].

Numerous studies confirm increased incidence of sensitization to (meth) acrylates in dental professionals [8, 9], as well as in patients undergoing dental treatment and exposed to resin-based materials [10]. Quite a few studies are available aiming to evaluate the incidence of sensitization in dental technician students.

Methyl methacrylate (MMA) as a small molecular acrylate can permeate thin protective disposable gloves. Since the 1950s, numerous case reports have documented allergic contact dermatitis to MMA. In 2012 (meth) acrylates were accessed by the Amercian Contact Dermatitis Society to the rank of "allergen of the year" [12]. Dental personnel are at risk when handling acrylic monomers manually while at work.

No specific group was identified to be at risk of sensitization to methacrylic monomers. Basing on literature data, we expected the incidence of sensitization to MMA to be highest observed. The obtained results were at some extent surprising – MMA was not identified as a sensitizer of prominent importance for dental technician

students. Highest was the recorded sensitization incidence among the students 2nd year of education. A possible explanation of these data is the fact that their most intensive exposure to methacrylates starts at the second year of their education. According to the data collected in the interviews, at that time they were uninformed and unaware of the fact that they should protect themselves by using gloves at work. Also, man and individuals above 30 years were found to be at increased risk of sensitization manifestation.

Triethyleneglycol dimethacrylate (TEGDMA) is a common monomer in composites, fissure sealants, bonding agents. The probability of release of TEGDMA from composite resins is high, and the risk of allergies and cytotoxicity has been recognized [13]. In our study, highest were the sensitization rates among dental technician students 3rd year of education, as well as among the controls, women and subjects over 30 years. We can't consider the role of exposure to TEGMA during the educational process of dental technician students as a factor contributing for the sensitization onset.

Ethyleneglycol dimethacrylate (EGDMA) is a common monomer in composites and bonding agents. We can't consider the role of exposure during education of dental technician students as a main factor for sensitization, though its incidence among dental technician students was higher, without significance.

Occupational exposure doesn't seem to be the main factor for the onset of sensitization to ethyleneglycol dimethacrylate since we established a higher sensitization rate in the group of patients when compared to the dental professionals.

Acrylic resins are produced by inducing polymerization of a mixture of MMA monomer a and polymethyl methacrylate powder. At room temperature the reaction needs an accelerator (activator). **4-Tolyldiethanolamine** is an amine accelerator for the polymerization of e.g. dental acrylic composite restorative materials [14].

N,N-dimethyl-p-toluidine is used as an amine accelerator for the polymerization of dental methacrylic restorative materials and a chemical bond for polyesters, acrylate, and epoxy resins. It is also used as a hardener for dental cements and in adhesives. It has also been used for the preparation of acrylic denture material for the past

50 years [15]. It can be found in dental products, photographic materials, colorants, and pharmaceuticals.

Quite a few data in the available literature was found regarding the sensitization rates to the discussed above amine accelerators, so we decided to include them in our patch-test set of haptens. The results obtained were intriguing.

The sensitization incidence to 4-tolyldiethanolamine was the highest one recorded for dental technician students 2nd and 3rd year of education, with significance if compared with students 1st year of education and the control group. A clear tendency of its increase in parallel with exposure duration was also observed. Since no significant relation with age was found, we could state that the exposure to 4-tolyldiethanolamine during the process of practical education of dental technician students plays an important role for sensitization onset.

In contrast, the incidence of positive patch tests to N,N-dimethyl-p-toluidine was the lowest established, with no positive results among students 2nd year of education and single cases among the control group. Basing on our results, we could evaluate N,N-dimethyl-p-toluidine as a non-significant sensitizing substance in exposures during process of practical education of dental technician students.

1,4-Butanediol dimethacrylate is used as a cross-linking methacrylic monomer of polymers. They are present in dental composite materials, sealants and inks. In our study, the incidence of positive patch tests to this chemical compound was among the highest recorded among dental technician students 2nd year of education, but decreasing up to 4 times and equaling with the one in the control group during the 3rd year of education, though without statistical significance. Since the sensitization rates were significantly higher among the individuals above 30 years, we could suggest again the importance of consumer exposures.

Tetrahydrofurfuryl methacrylate (THFMA) is common in crowns and bridges; used in the formulation of ultraviolet light-curable adhesives, coatings, paints, and printing inks; found in artificial nails. According to our results, the incidence of sensitization to this substance was about twice higher among dental technician students if compared with the control group, and slightly increasing in parallel with the duration of exposure. We could suggest the leading role of consumer's exposure in the case of sensitization to tetrahydrofurfuryl methacrylate. This statement seems to be confirmed by the increased rates among individuals above 30, supposed to have more dental restorations.

Other important sensitizers in dental practice are the

disinfectants, such as glutaraldehyde and formaldehyde [16]. 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 [17].

Formaldehyde is a ubiquitous chemical agent, a part of our general outdoor environment, as well as of our indoor working and residential environment. It is believed that whole civilized population is exposed to formaldehyde [18]. Formaldehyde is still used as an ingredient of some dental materials – root-canal-filling materials, formocresol, etc. [19]. Formaldehyde is formed as an oxidation product of the residual methylmethacrylate monomer and may be released from methacrylate-based dental materials, such as composites and denture bases [20].

The results obtained in the present study confirm our previous findings – the sensitization rates to formaldehyde were the highest recorded for all the groups defined in our study. Since no significant differences were established during the statistical analysis, we categorically accept the important role of consumer and environmental exposures for sensitization manifestation.

Glutaraldehyde doesn't seem to be among the leading allergens for the population included in the present study. Higher were sensitization rates among dental technician students 2nd year of education vs. no cases in the control group. Nevertheless, we can't give a categorical statement about the role of the exposure during the practical education of dental technician students. Women and subjects above 30 years were identified as groups at increased risk sensitization.

CONCLUSIONS:

Our data indicate high and increasing with the duration of educational exposure risk of contact sensitization to 4-tolyldiethanolamine among dental technician students, and this substance could be outlined as a sensitizer of prominent importance. No significant differences were established concerning the other tested methacrylic monomers. We accept the main role of consumer and environmental exposures for the manifestation of formaldehyde sensitization. Adequate preventive measures and information should be provided during the practical educational course of dental technician students. General population need to be well informed and the European Union regulations to be properly applied.

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