

CLINICAL RESEARCH

# Prevalence and Risk Factors of Occupational Contact Dermatitis to Formaldehyde and Glutaraldehyde and their Co-Reactivity in Dental Professionals

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## Abstract

**Background:** In dental practice concomitant exposure to formaldehyde and glutaraldehyde is a common occurrence. The objective of the study is to evaluate the incidence of occupational contact dermatitis to formaldehyde and glutaraldehyde in dental professionals and the manifestation of co-reactivity.

**Methods and Results:** This study involved 78 participants (30 dental professionals and 48 referents). A questionnaire survey as well as skin patch testing with formaldehyde and glutaraldehyde was conducted. The incidence of occupational contact dermatitis to formaldehyde among the population investigated was 28.2%, and of glutaraldehyde, 24.4%. Occupational contact dermatitis to formaldehyde was found to be of a significantly higher incidence among dental professionals. A stronger irritant effect of the formaldehyde, with a significantly higher incidence and the relative risk of specifically the upper respiratory tract ( $p = 0.029$ ) and respiratory system ( $p = 0.002$ ) as well as skin ( $p = 0.019$ ) symptoms among the subjects experiencing formaldehyde contact dermatitis was demonstrated. Allergic predisposition plays an important role as a risk factor of sensitization to glutaraldehyde and of co-reactivity.

**Conclusions:** The results indicate high rates of sensitization to formaldehyde and glutaraldehyde. Co-reactivity was found mainly among the non-occupationally exposed people. Atopy does not appear to be a risk factor for formaldehyde-specific allergic contact dermatitis, although it is so for glutaraldehyde-specific allergic contact dermatitis. Screening patch-testing for multiple dental compounds would be beneficial for early diagnosis, as well as for occupational risk assessment and management.

**Keywords:** formaldehyde; glutaraldehyde; allergic contact dermatitis; dental professionals.

## Introduction

Formaldehyde is the simplest aldehyde, an integral part of the general outdoor and indoor working and residential environments [1-3]. It is a common cause of contact allergy [4,5], skin contact being the most important route of exposure for sensitization. Cases of occupational allergic contact dermatitis are described in various industries, the main agents being disinfectants, lubricating and cooling fluids in metal work, chemicals used in

textile finishing and plastics [6-14]. Despite the reduction in its use 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]. Some studies indicate its co-reactivity with glutaraldehyde.

Regardless of the move for restrictions, formaldehyde continues to find use as an ingredient of some dental materials, such as root canal filling materials, formocresol, sealers and cements, polymers etc. Hauman C. and Love R. [18] in a review paper described the composition and biocompatibility of root canal filling materials. 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. Cohen et al.[19] and Koch [13] evaluated the

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release of formaldehyde from some endodontic materials, like root canal filling sealers, and demonstrated that all the materials revealed the highest release of formaldehyde in freshly mixed samples.

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 [2,8,13,20-23]. In the EU the maximum allowed concentration in the finished products is 0.2% (Annex VI of Cosmetics Directive 76/768/EC).

Studies on the sensitization potential of formaldehyde and glutaraldehyde as occupational allergens in dental practice, as well as on the manifestation of co-reactivity, are non-numerous and multidirectional.

**The aim** of the study is to evaluate the up-to-date incidence of occupational contact dermatitis to formaldehyde and glutaraldehyde in dental professionals (dentists, nurses and attendants) exposed to formaldehyde as an ingredient in dental materials, the manifestation of co-reactivity, and to compare their skin-sensitizing and irritating potential.

In the present investigation, we attempted to evaluate the current prevalence of occupational contact dermatitis (positive skin patch test reactions) to formaldehyde and glutaraldehyde among occupationally exposed dental professionals; to identify some possible factors which enhance the risk for occupational sensitization; to assess the possible cross-reactivity between formaldehyde and glutaraldehyde and to evaluate the incidence of subjective symptoms among individuals with contact dermatitis to formaldehyde and glutaraldehyde.

## Patients and Methods

A total of 78 participants were included in the pilot study, divided into two groups: Group E included those dental professionals occupationally exposed to formaldehyde and glutaraldehyde, and Group R involved the referents or control group with no occupational exposure. The general characteristics of the studied population are presented in **Table 1**.

The study was approved by the Medical Ethics Board at Sofia Medical University. All the participants were informed about the purpose of the study and written informed consent was taken from them.

### Sociological methods

Interviews and detailed intentionally conducted questionnaire-based interviews focused on family history, suspected or known allergies to the standard set of household or occupational allergens, on a history of frequent, recurrent respiratory system infections and on subjective symptoms, as well as a review of their medical documentation were conducted.

### Skin patch testing

Skin patch testing with formaldehyde and glutaraldehyde was performed, based on the Jadassohn & Bloch classical methods for diagnosis of contact allergy, by placing the allergens (formaldehyde - 0.1%/aq, Art. nr. F002A and glutaraldehyde 0.2%/pet, Art. nr. G003A, Chemotechnique Diagnostics) in IQ-Ultra hypoallergenic patches of Chemotechnique Diagnostics (IQ Chambers®, Vellinge, Sweden). The obligatory condition was the absence of anti-allergic medication prior to the patches

being placed and during the study. Patches with the allergens were applied and remained on the backs of the tested subjects. Readings of the test were carried out on D2, several hours after removing of the patches, with the control revision on D3.

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

### Medical examinations

The patch-testing of dental professionals was performed during the regular medical examinations. The whole medical documentation of dental professionals and the referents was collected and clinically analyzed.

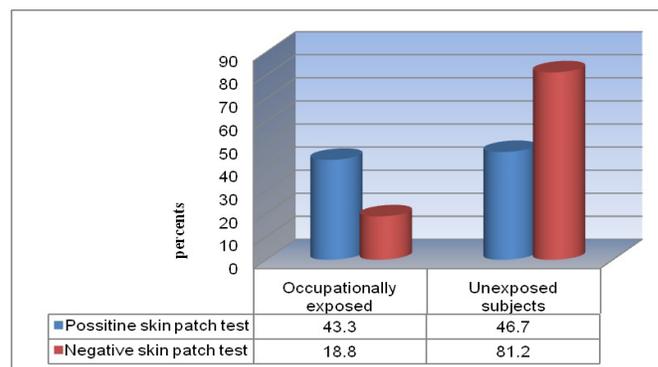
### Statistical methods

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

No statistically significant differences between the investigated groups were found regarding the mean values of age and duration of employment (Table 1). The distribution by gender was also not uniform, with a significant predominance of women in the group of occupationally exposed dental professionals ( $\chi^2 = 6.546$ ,  $p = 0.011$ ). The reason for this uneven distribution is the feminization of most employments in dental medicine.

Regarding smoking habits, 15 (50%) participants were smokers from among the group of dental professionals, whereas there were 19 (39.6%) from among the referents. However, no statistically significant differences were observed ( $p = 0.367$ ). The results from skin patch testing to formaldehyde are presented in Figure 1.



**Figure 1.**

Distribution of positive skin test reactions to formaldehyde (in %) among the dental professionals and the referents (\*  $p = 0.019$ ).

**Table 1.**

General characteristics of the investigated groups

Groups	Number of subjects	By gender		Average age (years)	Duration of employment
		Men n / %	Women n / %		
Occupationally Exposed (Group E)	30 (38.5%)	2 (6.6%)	28 (93.4%)	50.50 ± 9.1	27.70 ± 9.3
Referents (Group R)	48 (61.5%)	15 (31.3%)	33 (68.7%)	49.54 ± 12.5	24.35 ± 11.5
Total	78 (100%)	17 (21.8%)	61 (78.2%)	49.91 ± 11.3	25.64 ± 10.7

Positive skin test reactions were established in 13 (43.3%) of the occupationally exposed dental professionals and in 9 (18.8%) of the referents. Statistical analysis revealed an increased incidence and relative risk of contact dermatitis to formaldehyde among the dental professionals ( $\chi^2 = 5.510$ ,  $p = 0.019$ , OR = 3.314 {1.191 to 9.218}).

Among the occupationally exposed dental professionals, positive skin test reactions to glutaraldehyde were established in 8 (26.7%) individuals and in 11 (22.9%) from the subjects from the control group. No statistically significant difference was found ( $\chi^2 = 0.141$ ,  $p = 0.707$ ).

Concerning the data collected from the entire population studied, formaldehyde-specific allergic contact dermatitis was manifested by 22 subjects, which was 28.2% of the 78 participants investigated. Of these, 14 (63.6%) individuals were smokers and 8 were non-smokers. A significantly higher incidence and relative risk for sensitization to formaldehyde were established among the smokers ( $\chi^2 = 5.008$ ,  $p = 0.025$ , OR = 3.150 {1.129-8.791}). Glutaraldehyde-specific allergic contact dermatitis was observed in 19 subjects (24.4% from all investigated), 9 (47.4%) of whom were smokers. However, no significant differences concerning the incidence and relative risk of sensitization to glutaraldehyde were found in relation to smoking habits ( $\chi^2 = 146$ ,  $p = 0.703$ ).

From the whole group of dental professionals, contact dermatitis to formaldehyde was observed only among the women, 13 (46.4%) subjects in all. From the referent group, positive skin path tests were positive in seven women (21.2%) and two men (13.3% from all investigated).

The statistical analysis by gender demonstrated that in the group of women who were occupationally exposed to formaldehyde-containing dental materials, the incidence and the relative risk for sensitization to formaldehyde were significantly higher ( $\chi^2 = 4.371$ ,  $p = 0.037$ , OR = 3.219 {1.053-9.838}). However, no statistically significant differences regarding the incidence and the relative risk for sensitization to glutaraldehyde were observed ( $\chi^2 = 0.013$ ,  $p = 0.910$ ).

A summary of the results obtained by the intentionally conducted questionnaire survey, regarding the subjective symptoms from the upper respiratory tract, respiratory system and skin (systems known to be targets for the immunotoxic action of formaldehyde), as well as a history of atopy among the group of subjects with formaldehyde-specific allergic contact dermatitis, are presented in Table 2.

**Table 2.**

Distribution of subjective symptoms among participants with formaldehyde – specific allergic contact dermatitis

Skin patch test reactions to formaldehyde →	Positive skin patch test reactions		Negative skin patch test reactions		p-value OR
	With symptoms n / %	Without symptoms n / %	With symptoms n / %	Without symptoms n / %	
Subjective symptoms ↓					
Upper respiratory tract	13*/59.1	9/40.9	18/32.1	38 /67.9	*p = 0.029 OR=3.049 (1.102-8.442)
Respiratory system	15*/68.2	7/31.8	17/30.4	39 /69.6	*p = 0.002 OR=4.916 (1.699-14.228)
Skin symptoms	13*/59.1	9/ 40.9	17/30.4	39/69.6	*p = 0.019 OR=3.314 (1.191-9.218)
Atopy	9/40.9	13/59.1	16/28.6	40/71.4	p = 0.293 $\chi^2 = 1.104$

Note: \* - p&lt;0.05

Data from the questionnaire survey, regarding the distribution of subjective symptoms among the participants with glutaraldehyde-specific allergic contact dermatitis are presented in Table 3.

**Table 3.**

Distribution of subjective symptoms among participants with glutaraldehyde-specific allergic contact dermatitis

Skin patch test reactions to glutaraldehyde →	Positive skin patch test reactions		Negative skin patch test reactions		p-value OR
	With symptoms n / %	Without symptoms n / %	With symptoms n / %	Without symptoms n / %	
Subjective symptoms ↓					
Upper respiratory tract	8/42.1	11/57.9	23/39	36/61	p = 0.809 $\chi^2 = 0.059$
Respiratory system	10 /52.6	9/47.4	22/37.3	37/62.7	p = 0.237 $\chi^2 = 1.398$
Skin symptoms	8/42.1	11/57.9	22/37.3	37/62.7	p = 0.707 $\chi^2 = 0.141$
Atopy	10*/52.6	9/47.4	15/25.4	44/74.6	*p = 0.027 OR=3.259 (1.113-9.544)

Note: \* - p&lt;0.05

A history of frequent, recurrent respiratory system infections was reported by 54.5% from among subjects with formaldehyde-specific allergic contact dermatitis, and by 57.9% from those with glutaraldehyde-specific allergic contact dermatitis. No significantly increased incidence of the infectious respiratory system pathology among the subjects with formaldehyde ( $\chi^2 = 1.496$ ,  $p = 0.221$ ) and glutaraldehyde-specific ( $\chi^2 = 2.090$ ,  $p = 0.148$ ) allergic contact dermatitis was established.

Both formaldehyde and glutaraldehyde-specific allergic contact dermatitis was observed in a total of 9 individuals from among all the subjects investigated, of whom 2 were men and 7 women. Only 3 subjects of this group were from among those who were occupationally exposed to the chemical agents investigated. The general characteristics of this group of participants include: average age  $46.11 \pm 15.4$  years, average duration of employment  $24.00 \pm 15.8$ . Smoking habits appear to be a risk factor for sensitization among the latter group thus defined (66.7% of the participants with double-positive patch skin test reactions were smokers), but no statistical significance has been established ( $\chi^2 = 2.203$ ,  $p = 0.138$ ).

No statistically significant differences were established in any of the indicators used to evaluate the overall health status (recurrent upper respiratory tract infectious pathology, atopy or subjective symptoms) among the group of subjects with both formaldehyde and glutaraldehyde-specific allergic contact dermatitis. Although no statistical significance was presented, women once again emerged as the more vulnerable group with respect to the risk of sensitization ( $\chi^2 = 0.001$ ,  $p = 0.974$ ).

## Discussion

Studies focused on evaluating the incidence of occupational contact dermatitis to formaldehyde and glutaraldehyde in dental practice and their co-reactivity, as well as the subjective symptoms of the affected subjects, are few and multidirectional.

Fransway et al. [24] reported patch test results for 2007-2008 from the North American Contact Dermatitis Group, from a total of 5085 patients tested. Formaldehyde ranked among the top 15 most frequently positive allergens, irrespective of the significant decreases in positivity rates.

A study conducted involving more than 2000 healthcare workers established that some of the most common occupational contact allergens were disinfectants such as formaldehyde, glutaraldehyde and glyoxal. 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 [25,26]. Among nurses, and particularly dental nurses, an increased risk for occupational sensitization to glutaraldehyde as well as to glyoxal was established. An investigation was performed to evaluate the incidence of allergy to aldehydes (formaldehyde, glutaraldehyde, glyoxal) among 280 health care workers suffering from skin lesions. Allergic contact dermatitis was diagnosed in 22.8% of patients, the majority of them (85.9%) being sensitive to only one aldehyde. Formaldehyde was found to cause allergy slightly more frequently (13.9%) than the glutaraldehyde (12.4%) [25, 27, 28].

The surveys regarding the sensitizing effects of formaldehyde and glutaraldehyde in dental practice are relatively few and multidirectional [29-31]. Data from a four-year study on the incidence of occupational allergic contact dermatitis in dental nurses, when summarized, showed up in 66.7% of the cases investigated, and the most frequent sensitizing agent was glutaraldehyde, followed by formaldehyde and glyoxal [12]. Gawkrödger [31] included formaldehyde in the list of agents causing contact allergy the most often, in dental staff. According to the author, occupational irritant problems causing

hand dermatitis are probably more common in dental personnel than is dermatitis caused by contact allergy. The results obtained by Ravis et al. [25] 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).

Among the most important adverse effects from formaldehyde exposure are respiratory tract irritation and sensitization [32-34]. The irritant action of formaldehyde on the 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 [35-38].

To achieve the purpose of the present study, we performed a comparative estimation of the subjective symptoms of individuals with formaldehyde and glutaraldehyde-specific allergic contact dermatitis.

An increased incidence (43.3%) and relative risk of occupationally-induced contact dermatitis to formaldehyde were established among the dental professionals. The incidence is nearly twice higher compared with the results of other cited authors.

No significantly higher incidence and risk of occupationally-induced contact dermatitis to glutaraldehyde in dental professionals were established. Our results suggest a much stronger skin-sensitizing action of formaldehyde in dental practice, compared with glutaraldehyde.

From among the entire group of dental professionals, occupational contact dermatitis to formaldehyde was observed only among the women. The statistical analysis by gender demonstrated that women as a defined group in terms of occupational exposure to formaldehyde in dental practice, showed a significantly higher incidence and relative risk of allergic contact dermatitis to formaldehyde. However, no reliable differences were established regarding the frequency and relative risk of occupational contact dermatitis to glutaraldehyde.

On evaluating the incidence of formaldehyde and glutaraldehyde-specific allergic contact dermatitis among the 78 participants investigated, high rates of positive skin test reactions to formaldehyde (28.2%) and glutaraldehyde (24.4%) were established.

Concerning the role of smoking habits as a risk factor, significantly higher incidence and relative risk for sensitization to formaldehyde among the smokers was established. No significantly higher risk for sensitization to glutaraldehyde with respect to smoking habits was established.

To confirm the statement given above, results are given regarding the increased (with very high significance) incidence and relative risk for subjective symptoms of the respiratory system among the individuals with formaldehyde-specific allergic contact dermatitis. This group of subjects reported a significantly increased incidence of subjective dermal symptoms as well. The latter statistical dependencies were not established among the individuals with glutaraldehyde-specific allergic contact dermatitis.

According to the results of our pilot study, atopy does not appear to be a risk factor for formaldehyde-specific allergic contact dermatitis. On the contrary, the incidence of atopy among subjects with glutaraldehyde-specific allergic contact dermatitis was significantly higher.

One of the objectives of our study was to evaluate the risk for

formaldehyde and glutaraldehyde co-reactivity in occupational and non-occupational exposure in dental practice. Positive skin test reactions to both chemical agents were diagnosed in 11.5% of all the tested individuals, although only 3 from among them had been occupationally exposed. Only those with a relatively long employment history were affected. Double-sensitized women predominated, however, with no statistical significance. The role of smoking habits as a risk factor for dual sensitization was not established. Also, no significantly increased incidence of the subjective symptoms was found for those individuals with contact dermatitis to both aldehydes.

In conclusion, our results provide strong evidence for the skin-sensitizing effect of formaldehyde in dental professionals, with higher sensitizing and irritant effects compared with glutaraldehyde. No immunotoxic effects expressed as decreased resistance to upper respiratory tract infectious diseases were established among the subjects with contact dermatitis.

According to the results achieved, atopy does not appear to be a risk factor for formaldehyde-specific allergic contact dermatitis. On the contrary, the incidence of atopy among individuals with glutaraldehyde-specific allergic contact dermatitis was significantly higher.

Women could be highlighted as a group at risk, but because of the fewer number of men investigated in the present pilot study, a definite conclusion may not be justified.

Based on the results achieved in this study, we would recommend skin patch-testing, with more numbers of compounds of dental materials to be conducted among dental professionals during regular medical examinations. This would be beneficial for early the diagnosis of contact allergy, as well as to accomplish more effective risk assessment and management programs.

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