

Toothpaste Allergy as a Cause of Cheilitis in Israeli Patients

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Background: Allergic contact cheilitis may appear after exposure to different substances, including dental materials, toothpastes, cosmetics, foods and medications.

Objective: To compare the rate of toothpaste allergy between patients with and without cheilitis and to examine the yield of our proposed toothpaste patch test kit for use in patients with cheilitis.

Methods: A patch test kit containing 11 substances used in toothpastes was formed. The study sample consisted of 44 patients, 24 with cheilitis (study group) and 20 with contact dermatitis but without cheilitis (control group).

Results: Eleven patients in the study group (45%) were found to be allergic to toothpaste, compared to only one patient (5%) in the control group ($p < .05$).

Conclusion: The rate of toothpaste allergy among patients with cheilitis might be higher than previously reported. Patch-testing with our toothpaste series is recommended in the evaluation of cheilitis.

CHEILITIS is an inflammation of the lips and the vermilion. Many allergens may cause cheilitis, including cosmetics (particularly lipsticks), sunscreen agents, toothpastes, medications, foods, and dental material.¹⁻³ The literature regarding toothpaste allergic contact cheilitis is relatively scarce,⁴ and the subject had never been investigated in Israel.

The main substances in toothpastes that may cause contact dermatitis are flavorings (such as cinnamon and peppermint), fragrances, and preservatives.^{2,3,5-17} The exact prevalence of toothpaste allergic contact cheilitis is not known. Lim and colleagues found that 5 of 27 patients with cheilitis (18.5%) were allergic to toothpaste,¹⁸ and Francalaci and colleagues found 13 of 54 cheilitis patients (24%) to be sensitive to at least one component of toothpastes.⁴

Cheilitis may cause discomfort to patients, and its specific cause often remains unknown.^{3,19} Researchers have suggested that an undiagnosed allergy may cause cheilitis in some patients,^{1,19} and that allergy to toothpaste is an underestimated cause of cheilitis.^{4,7,9,11}

The present study had two main goals: (1) to determine the prevalence of toothpaste allergy among patients with

cheilitis in Israel and (2) to examine the yield of a new toothpaste patch test kit formulated by our department on the basis of earlier studies^{1,2,4-17,20} and our experience.

Materials and Methods

The study sample included 44 patients aged 18 to 76 years (average, 38.06 years), 24 with cheilitis (study group) and 20 as control subjects. All patients in the study group had been referred to the Contact Dermatitis Clinic of Hadassah University Hospital in Jerusalem, Israel, over a period of 1.5 years because of failure to determine the exact cause of their cheilitis. The study group consisted of 4 men (16.67%) and 20 women (83.33%) aged 23 to 76 years (average, 42.87 years). Patients younger than 18 years, pregnant women, and patients who did not use toothpaste were excluded.

The control group included consecutive patients with contact dermatitis who were referred to the same clinic over a 6-week period for patch testing. None of the control subjects had ever had cheilitis. Exclusion criteria for the control group were the same as for the study group. Patients working in dental clinics who were referred for patch testing with the dental series were excluded as well.

All patients completed a questionnaire on medical history, use of medications, atopy background, allergies, characteristics of their cheilitis, and dental treatments. The entire questionnaire appears in Table 1. Relevant information was also obtained from the patients' medical files and by interview.

All patients of both groups were patch-tested with the European Standard series, the dental screening series, a

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Table 1. Toothpaste Allergy Questionnaire

1. Name
2. Age
3. Sex
4. Medical history
5. Medications
6. Atopic trait
7. Family history of atopy
8. Previous rash, location, diagnosis, treatment, any diagnostic tests
9. Cheilitis (if any): exact location, duration, previous diagnostic procedures and treatment, aggravating factors
10. Oral habits: lip licking, lip biting, gum chewing, lipstick use
11. History of recurrent herpes labialis
12. Dental procedures: type, timing, connection with appearance of cheilitis

special toothpaste series formulated by our department (Table 2), and their own personal toothpaste. Patients in whom other causes of contact dermatitis were suspected were patch-tested with other series as well. The allergens for all series were supplied by Chemotechnique Diagnostics (Malmö, Sweden). The patches were applied to the upper back with Transport Surgical Tape (3M Health Care, St Paul, MN). The strips were removed on day 2, and readings were taken on days 2 and 4, according

to the guidelines of the International Contact Dermatitis Research Group.²¹

Statistical analysis was performed with SAS software (SAS Institute, Inc., Cary, NC). The chi-square test, Fisher exact test, and Wilcoxon two-sample test were calculated from the data.

Results

The study group was significantly older than the control group ($p < .05$) and had a significantly higher male-to-female ratio ($p < .05$). There were no statistically significant differences between the groups in the use of medications, atopy background, use of lipsticks, tendency for lip licking, and the other factors examined (see Table 1).

Seven patients in group 1 had 11 positive reactions to allergens in the toothpaste series, compared with 5 patients in group 2, which had a total of 6 positive reactions (see Table 2). Eleven patients in group 1 had a total of 14 positive reactions to at least one of their own personal toothpaste, compared to none of the patients in group 2. A positive reaction either to an allergen in the toothpaste series or to the individual's personal toothpaste was noted in 14 patients (58.3%) in group 1 and 5 patients (25%) in group 2 ($p < .05$). After examining the clinical relevance of the positive reactions, we found that 11 patients (45.8%)

Table 2. Number of Positive Reactions to Allergens in the Toothpaste Series and to Individuals' Own Toothpaste

Allergen	Patients with Cheilitis	Patients without Cheilitis*
Balsam of Peru (25% in petrolatum)	2	—
Birch tar (3% in petrolatum)	—	1
Benzyl alcohol (1% in petrolatum)	1	—
Cinnamic alcohol (2% in petrolatum)	1	—
Cinnamic aldehyde (1% in petrolatum)	1	—
Eugenol (2% in petrolatum)	1	—
Formaldehyde (1% in water)	1	—
Fragrance mix (8% in petrolatum)	2	4
L-carvone (5% in petrolatum)	1	—
Menthol (5% in petrolatum)	—	—
Paraben mix (16% in petrolatum)	1	1
Personal toothpaste	14	—
Homeodent (Boiron, Lyon, France)	1	—
Meridol (GABA, Therwil, Switzerland)	3	—
Crest (Proctor & Gamble)	2	—
Gum'v'gum (Careline, Israel)	1	—
Aquafresh (GlaxoSmithKline, Brentford, UK)	2	—
Colgate (Colgate-Palmolive Company, New York)	3	—
Parodontax (GlaxoSmithKline, Brentford, UK)	2	—

*Contact dermatitis but not cheilitis.

in group 1 were allergic to either an allergen of the toothpaste series or to their personal toothpaste, in contrast to only 1 patient (5%) in group 2 ($p < .05$).

Eighteen patients (75%) in group 1 had a total of 33 positive reactions to allergens in the dental series, compared to 4 patients (20%) with a total of 5 positive reactions in group 2 ($p < .05$). However, after checking the clinical relevance of the positive reactions, we found no significant difference between the groups.

Eleven patients (46%) in group 1 had a total of 20 positive reactions to allergens in other series (not the toothpaste or dental series), compared to 13 patients (65%) with a total of 26 positive reactions in group 2 ($p > .05$). It should be noted, however, that these patients had different causes of their dermatitis.

Overall, the patients in the study group had a higher average number of positive reactions than the controls of group 2 when the results of the standard series, dental screening series, and toothpaste series (without personal toothpaste) were taken into account. The average number of positive reactions per patient was 2.33 in group 1 and 1.25 in group 2 ($p < .05$). However, only an average of 0.79 positive reactions were relevant in group 1, and only an average of 0.6 positive reactions were relevant in group 2 ($p > .05$).

In the study group, there was a significant difference in the average number of positive reactions to the standard series and the dental screening series between those who were allergic to toothpaste and those who were not (3.45 vs 1.38 positive reactions per patient, $p < .01$).

Discussion

This study examined the prevalence of toothpaste allergy as a cause of cheilitis among Israeli patients. We added the use of a toothpaste patch test to lower the rates of false-positive and false-negative reactions. The results showed a 45% rate of clinically relevant toothpaste allergy in the patients with cheilitis, which is higher than previously reported. This difference may be explained by the different focuses of the studies. We specifically investigated toothpaste allergy whereas most earlier studies simply searched for different causes of cheilitis. Accordingly, Francalaci and colleagues, who also studied toothpaste allergy, found a relatively higher frequency of toothpaste allergy than other studies found.⁴ Of their 54 patients with cheilitis who were patch-tested with a special toothpaste series and the standard series, 13 (24%) were sensitive to at least one

allergen in the toothpaste series. Of the 32 patients patch-tested with their personal toothpastes, 11 were found to be sensitive.

Another reason for the high rate of toothpaste allergy in the present study is our inclusion of patients from a tertiary clinic who had already undergone attempts in primary clinics to find a cause for their cheilitis. If toothpaste allergy is indeed an underestimated and unfamiliar cause of cheilitis among dermatologists, it is likely that it would not have been identified outside of a special contact dermatitis clinic. It should also be emphasized that establishing clinical relevance when reading positive patch-test results is often difficult and needs to be done by experts (with the proper knowledge and skills) who may not be available in primary clinics. Determination of the cause also requires thorough questioning of the patient about the use of different substances and the connection of such substances to the positive allergic reaction. The patch test kit we created may therefore serve as a useful tool in screening for toothpaste allergy, even in primary clinics.

The possibility that the positive response to a toothpaste patch placed on the skin of the back is actually an irritant reaction is refuted by the absence of such a response to personal toothpastes in any of the control group patients.

The much higher frequency of positive reactions to the dental series allergens in the cheilitis patients is also worthy of mention. In the study group, of the 33 positive reactions to this series among 18 patients, only 3 were found to have clinical relevance, whereas none of the 5 reactions in 4 patients in the control group were clinically relevant. However, establishing relevance in the study group was complicated because all the patients had undergone dental procedures in the past. Although most of them did not directly connect these procedures with the appearance of the cheilitis, we could not rule out prolonged exposure to materials in dental fillings, prostheses, and other dental materials as a possible cause.

Patients with cheilitis who were found to be allergic to toothpaste had a higher average number of positive reactions than those who were not. This finding may suggest that allergy to toothpaste is indeed rare in the general population but does appear among people who have a tendency to develop allergic contact reactions.²²

The study group had a higher percentage of women ($p < .05$). We attribute this to former sensitization to substances found in cosmetics, especially lipsticks,¹⁹ with an overlap with substances in toothpastes.

Conclusion

We believe that patients with idiopathic cheilitis have a high rate of toothpaste allergy, perhaps greater than previously reported. The toothpaste kit formulated by our group contains a small number of allergens, but it yielded sensitive, specific, and relevant results. We recommend its use (in addition to the standard dental and cosmetics series) in cases of unexplained cheilitis. Further studies are required to standardize its ingredients and concentrations. The number of positive reactions might have been greater if other allergens were included (such as spearmint or peppermint^{14,16}). Patch-testing with the dental series is also important, and doctors should try to find relevance when positive reactions appear, even though doing so might be difficult. In all cases, a detailed history of dental procedures and the use of toothpastes and cosmetics should be taken.

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