

Symptomatic oral lesions may be associated with contact allergy to substances in oral hygiene products

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Received: 6 July 2016 / Accepted: 5 January 2017
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Abstract

Objective Dental materials and oral hygiene products may be responsible for oral contact allergic reactions. We aimed to determine the occurrence of allergies in patients with symptomatic oral lichen planus (OLP), oral lichenoid lesions (OLLs) and stomatitis and investigate if patch testing could identify contact allergies to dental materials and oral hygiene products in these patients.

Methods Forty-nine patients (7 men, 42 women) aged 31 to 77 years (61 ± 10.3 years) with symptomatic OLP, OLL or stomatitis and 29 healthy age- and gender-matched control subjects were included. They underwent an interview, clinical examination, oral mucosal biopsy and epicutan testing to the European baseline series, a toothpaste and dental material series.

Results Nineteen patients had OLP, 19 OLL and 11 stomatitis. Oral burning/itching was the most common symptom (83.7%), and 65.3% patients had more than one symptom. Patients visited their dentist more often than the healthy subjects and had statistically higher DMF-T and DMF-S scores. Nineteen patients (38.8%) and 10 healthy control subjects

(34.5%) had allergic contact reactions primarily to fragrance ingredients. No differences could be found between OLP, OLL, stomatitis and healthy controls with regard to allergic contact reactions. However, contact allergy to aroma substances differed significantly between the patients and the healthy control subjects ($p = 0.02$). This type of contact allergy was most common in patients with OLP and OLL ($p = 0.01$). Avoidance cleared symptoms in all cases.

Conclusion/clinical relevance Allergic reactions to aroma substances in oral hygiene products are common in patients with symptomatic OLP, OLL and stomatitis.

Keywords OLP · Contact allergy · Dental materials · Oral hygiene products

Introduction

The oral cavity and the lips are repetitively exposed to various irritants and allergens including oral hygiene products and materials used in diagnosing and treating oral diseases (in the following referred to as dental materials). Both dental materials and oral hygiene products are established as potent sensitizers, and they may be responsible for sensitization and allergic reactions in the oral mucosa [1–7]. It is assumed that the persistent antigenic stimulation from dental materials and/or oral hygiene products may lead to oral mucosal changes [8]. The clinical manifestations of oral contact allergic reactions are diverse comprising localised lichenoid lesions, diffuse widespread erythema and swellings including stomatitis and cheilitis, perioral dermatitis, vesicles and blisters as well as ulcerations [9]. Symptoms may include burning, stinging and/or tingling sensations in the oral mucosa, xerostomia, dysgeusia and other sensory disturbances [10]. As the oral allergic reactions may resemble changes seen in other oral

Electronic supplementary material The online version of this article (doi:10.1007/s00784-017-2053-y) contains supplementary material, which is available to authorized users.

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mucosal diseases, diagnosing and treating the patients may often be challenging [11]. Only a limited number of studies have investigated the occurrence of contact allergic reactions to both dental materials and oral hygiene products in patients with oral lichen planus (OLP) and oral lichenoid lesions (OLLs), respectively [4, 12]. According to a large Scandinavian questionnaire study from 1991, adverse reactions to dental materials were estimated to occur in one out of 300 patients in prosthodontic practices, in one out of 2600 patients treated in public dentistry and in one out of 100 undergoing orthodontic treatments [13–15]. In this line of questionnaire-based studies, adverse patient reactions were encountered at a frequency of 1 every other year per periodontist [16]. The prosthodontists, the orthodontists and the public dentists primarily reported type IV allergic reactions whereas the periodontists primarily reported type I allergic reactions [13–16]. This difference is explained by the type of materials the patients are exposed to and the type of allergic reactions the different materials elicit.

The aims of this cross-sectional study were therefore to determine the occurrence of contact allergies in patients with symptomatic OLP, OLL and stomatitis with and without close proximity to dental restorations and to examine the extent to which patch testing of patients with symptomatic and potentially allergy-induced oral lesions may identify actual contact allergies to dental materials and oral hygiene products. We hypothesised that patients with symptomatic OLP, OLL and stomatitis would display positive patch test reactions (in terms of contact allergies to dental materials and/or oral hygiene products) more often than healthy control subjects.

Materials and methods

Study group

One hundred and thirty-four patients referred to the Clinic for Oral Medicine, Department of Odontology, University of Copenhagen, in the period 2013–2015 for investigation of oral mucosal symptoms and lesions, were screened. Caucasian patients with oral symptoms and mucosal changes that were compatible with OLP or stomatitis could be included. Fifty-two patients were eligible for inclusion. Forty-nine patients (94.2%) completed the study. Two patients stated living too far from the hospital as the reason for not completing the study, and the third patient gave no reason for dropping out of the study (Fig. 1). All patients had oral symptoms and clinical signs of OLP, OLL or stomatitis. A total number of 29 age- and gender-matched healthy control subjects were recruited using a Danish online volunteer webpage (www.forsoegsperson.dk). The exclusion criteria for this group were current or past medical history of systemic disease, oral mucosal diseases or symptoms and intake of medication.

The study was approved by the Regional Ethics Committee, Copenhagen, Denmark (Protocol No. H-3-2013-033), and performed in accordance with the Helsinki declaration. The study participants were both informed by letter and gave oral and written consent.

One examiner (KRL) conducted the interviews and oral clinical examinations. All procedures were carried out in the same order and same time of the day, i.e. between 9:00 and 11:00 a.m. Each participant underwent a standardised interview including inquiries regarding oral symptoms and medical and dental history, including history of allergy, intake of medication, tobacco and alcohol consumption and dietary and oral hygiene habits.

An oral smear was taken from all participants in order to eliminate oral candidiasis as the cause of the oral symptoms, including sensations of mucosal soreness, itching, burning and dryness [17]. The smear was stained with *Periodic acid-Schiff* (PAS) and evaluated cytologically for presence of yeast hyphae and spores. Five patients with OLP, four patients with OLL and two patients with stomatitis were diagnosed with oral candidiasis and treated with nystatin for 4 weeks, prior to inclusion in the study. After treatment, hyphae were not present in repeated smears; the symptoms, however, persisted after treatment indicating their relation to OLP, OLL and stomatitis. None of the healthy control subjects had oral candidiasis.

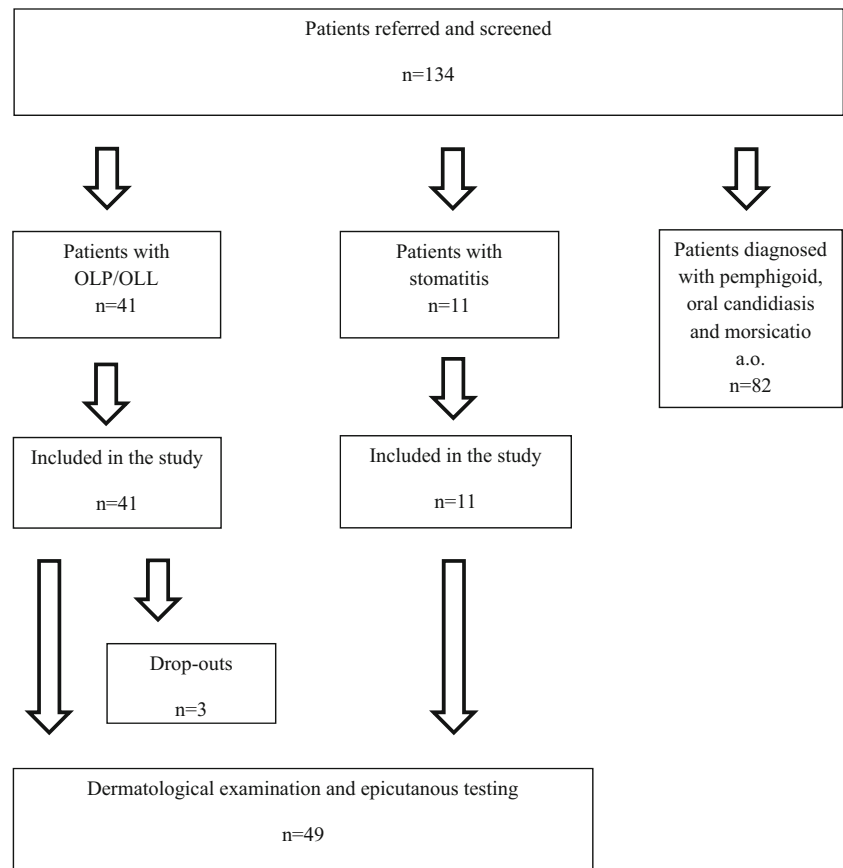
Clinical examination

The number of decayed, missing and filled teeth and surfaces (DMFT/–S) was recorded excluding third molars as previously described in details [18]. Plaque and gingival indices were determined at four sites per tooth on six index teeth (16, 12, 21, 36, 32 and 41) [19]. Presence, localization, relation to dental materials and types of oral mucosal changes were registered and photographed.

Oral mucosal biopsies and histopathological evaluation

Incisional biopsies were taken from areas with oral mucosal changes, mainly the buccal mucosa from the patients and from normal buccal mucosa from the control subjects. The biopsies were taken under infiltration anaesthesia (30 mg/ml Citanest® Dental Octapressin®, Dentsply Pharmaceutical, Surrey, England). One part of the biopsy was fixed in 10% neutral buffered formalin (pH 7.3, 24 h, at room temperature), embedded in paraffin and routinely processed and stained with haematoxylin and eosin and PAS. The specimens were then analysed by an experienced oral pathologist (JR), who was blinded regarding clinical data. The histopathological analysis was performed according to the WHO standards [20]. The other part of the biopsy was transferred to RNAlater®

Fig. 1 Flowchart showing the number of patients referred to the Clinic for Oral Medicine with symptoms and signs suggestive of OLP, OLL or stomatitis and potential allergic reactions. They were all screened for eligibility



Stabilization Reagent (Qiagen®) and stored at -80°C until further analysis.

The diagnosis of OLP was established when the lesions met all the criteria established by van der Meij and van der Waal [21]. When the clinical and histopathological features of the lesions met most of these criteria, the diagnosis was established as OLL, i.e. patients with typical OLP clinically but not histologically [20, 21]. The diagnosis of stomatitis was based on is a more diffuse reaction that varied from a barely visible erythema to a bright red erythema anywhere in the oral cavity. Erosions and hyperkeratosis could also be seen [5].

Allergy testing

All participants were referred to the University Hospital of Copenhagen, Gentofte, for allergy testing. Epicutan testing to the European baseline series as well as to toothpaste and dental material series was performed according to the European Society of Contact Dermatitis (ESCD) guidelines (Appendix 1). The allergens were applied to the upper part of the back in Finn Chambers® and were occluded with Scanpore tape®. The Finn Chambers were removed after 48 h. The tests were read at days 2, 4 and 7 according to the European Society of Contact Dermatitis reading criteria,

assessing reactions by inspection and palpation of the morphology (erythema, infiltrate, papules and vesicles). Contact allergy was defined as a +1 reaction at the least. In a patient, a doubtful positive patch test reaction could be judged relevant based on the patients' individual history [22]. Skin prick tests were performed on the volar part of the forearm with chlorhexidine and latex. A positive histamine control and a negative saline control were included [23].

Statistics

The statistical analyses were made using SPSS Version 22 (IBM). The significance level was set at $p < 0.05$. Pearson's chi-square test and Fischer's exact test were used when evaluating the differences between the patients and the healthy control subjects with regard to contact allergy. A negative binomial test and a Poisson regression test were used for evaluating the differences between the patients, the different patient groups and the healthy control subjects with regard to DMF-T, DMF-S, PI, GI and contact allergy to the individual groups of substances. Values are given in means, standard deviations (SD) and medians.

Results

Demographics

The study included 7 male and 42 female patients aged 31 to 77 years (61 ± 10.3 years) as well as 4 male and 25 female healthy controls aged 23 to 73 years (58.2 ± 12.1 years). Recruitment of healthy participants above showed to be challenging, and that is why we ended with 29 subjects. Table 1 shows the characteristics of the study population. Fourteen patients (28.6%) reported a suspicion of allergic reactions to certain food items due to an aggravation of their oral symptoms when consuming the suspected food item. However, none of them had been confirmed by allergy testing. Six patients had pollen allergy, 7 had contact allergy to nickel and 5 had allergy to fragrance ingredients. These allergies were all medically proven.

Oral mucosal lesions and oral symptoms

The diagnosis of OLP was established in 19 patients, and another 19 patients were diagnosed with OLL. Thus, a total number of 38 (77.6%) patients had OLP or OLL. The diagnosis of stomatitis was made in 11 patients (22.4%). Details about the oral mucosal lesions including the localization are shown in Table 2. Table 3 provides an overview of the various oral symptoms reported by the patients. Thirty-two (65.3%) patients reported more than one symptom. There was no

difference in the type and severity of symptoms reported by the patients with OLP, OLL or stomatitis, respectively.

Dental examination

In the healthy control group, the DMF-T score was 17% lower and the DMF-S score 50% lower than in the patient group ($p = 0.03$ and $p = 0.01$, respectively) (Table 4). The DMF-T and DMF-S scores were characterised by a high number of filled teeth and surfaces in all patients groups and to a lower extent missing teeth. A more detailed analysis revealed that the patients with stomatitis had higher DMF-T score ($p < 0.001$) and DMF-S score ($p < 0.001$) than the patients with OLP and OLL.

The plaque index score was lower in the patient group than in the healthy control group (0.14 ± 0.33 vs. 0.30 ± 0.36 , $p = 0.01$), whereas the gingival index score was higher in the patients than in the healthy control subjects (0.88 ± 1.15 vs. 0.22 ± 0.30 , $p < 0.001$). However, 69.4% of the patients also had lichenoid lesions on their gingiva resulting in pronounced inflammation and spontaneous bleeding. Twenty-one patients had oral lesions in close contact with dental restorations, whereas 28 patients had more widespread lesions. In eight patients diagnosed with OLP, nine patients with OLL and four patients with stomatitis, the mucosal lesions were localised close to a dental restoration. Furthermore, the patients and the healthy control subjects differed with regard to regular visits to their dentist. Thus, the patients with OLP, OLL and stomatitis visited their dentist significantly more

Table 1 General information about the participants

	Patients with OLP/OLL ($n = 49$)	Healthy controls ($n = 29$)
Age, years	61.0 ± 10.3 (range 31–77)	58.2 ± 12.1 (range 23–73)
Gender female/male ratio	42:7	25:4
Chronic medical conditions (no. given in %)		
Hypertension	24.5%	6.9%
Herpes simplex	40.8%	41.4%
Hypercholesterolaemia	10.2%	6.9%
Allergic rhinitis	12.2%	0%
Asthma	14.3%	3.4%
Arthrosis	24.5%	6.9%
Smoking, percentage (smoking pack year)		
Non	55.1% (0)	37.9% (0)
Former	38.8% (21.2)	48.3% (12.8)
Current	6.1% (21.5)	13.8% (17.3)
Alcohol consumption, percentage		
Never	61.2%	17.2%
Occasionally	24.5%	44.8%
Daily	14.3%	37.9%

Data are given in mean and SD

Table 2 Diagnoses (based on clinical and histopathological features), localization of oral mucosal changes and relation to dental restoration(s) in the patient groups

Total no. of ptt. with OLP lesions	19/49 (38.8%)
Erosive/reticular OLP lesions ^a	15/19 (78.9%)
Reticular OLP lesions	4/19 (21.1%)
OLL	19/49 (38.8%)
Stomatitis	11/49 (22.4%)
Localization of oral mucosal changes	
Buccal	38/49 (77.6%)
Gingiva	34/49 (69.4%)
Palate	10/49 (20.4%)
Tongue	18/49 (36.7%)
Alveolar buccal sulcus	22/49 (44.9%)
Floor of the mouth	2/49 (4.1%)
Lips	18/49 (36.7%)
Relation to dental material	
Yes	21/49 (42.9%)
No	28/49 (57.1%)

^a At time of present examination

often than the healthy control subjects (2.67 ± 1.10 visits per year vs. 1.8 ± 0.74 visits per year, $p < 0.001$). This difference is a result of a statistical significant difference in the OLP/OLL group ($p = 0.001$) and the stomatitis group ($p = 0.01$), respectively.

Patch testing

All patients and healthy control subjects completed the patch testing. Nineteen patients (38.8%) and 10 healthy control subjects (34.5%) displayed positive patch test reactions to tested allergens. Fifteen patients with OLP/OLL (39.5%) and four patients with stomatitis (36.4%) had positive patch test reactions, and they did not differ with regard to symptoms, clinical and histopathological characteristics or relation to dental restorations. There were no statistically significant differences with respect to positive patch test reactions between the patients and healthy subjects or between the patient groups. The

Table 3 Oral symptoms reported by the patients

Symptoms	No. of patients
Stinging, stabbing and/or burning sensation	41/49 (83.7%)
Roughness of the oral mucosa	32/49 (65.3%)
Abrasion of the oral mucosa	25/49 (51.0%)
Ulcerations	23/49 (46.9%)
Blisters in the oral mucosa	15/49 (30.6%)
Peeling of the surface of the oral mucosa	13/49 (26.5%)

Table 4 Characteristics of patient group ($n = 49$) and healthy control group ($n = 29$) with regard to the number of dental visits, the plaque index (PI) and the gingival index (GI), the number of decayed-missed-filled teeth and surfaces and the number of teeth with the particular dental material in the patient group and the healthy control group

	Patients with OLP, OLL or stomatitis	Healthy control subjects	<i>p</i> value
Dental visits per year	2.67 ± 1.05	1.85 ± 0.86	0.0005
PI	0.14 ± 0.33	0.30 ± 0.36	0.01
GI	0.88 ± 1.15	0.22 ± 0.30	0.0001
DMF-T	18.29 ± 5.98	15.14 ± 6.14	0.033
DMF-S	56.96 ± 30.14	41.1 ± 22.48	0.010
Composite	6.78 ± 4.56	8.17 ± 4.86	
Amalgam	3.90 ± 3.92	3.66 ± 3.90	
Gold	0.84 ± 1.39	0.97 ± 1.65	
Metal ceramic	3.39 ± 4.46	1.72 ± 2.35	
Porcelain	0.67 ± 2.13	0.14 ± 0.34	
Titanium	0.22 ± 0.97	0.03 ± 0.18	
Glass ionomer cement	0.06 ± 0.24	0.03 ± 0.18	
Acrylics	1.22 ± 3.41	0 ± 0	
Metals, others	0.16 ± 0.37	0.03 ± 0.18	

Data given in mean and SD

most common allergen was fragrance among both patients ($n = 7$) and healthy controls ($n = 4$). Of the 19 patients with a positive patch test reaction, 12 (63.2%) had a positive reaction to more than one allergen. In the healthy control group, 3 of the 10 (30%) subjects displayed more than one positive patch test reaction.

There was no statistically significant difference in the occurrence of contact allergy towards dental materials and oral hygiene products, as a whole, between the patients and the healthy control subjects, or between patients with OLP, OLL and stomatitis. Furthermore, no statistically significant difference in contact allergy to dental materials could be observed between the patients and the healthy control group, or between patients with OLP, OLL and stomatitis.

Regarding contact allergy towards the metals used in dentistry, no statistically significant difference could be observed between the patients and the healthy control group, or between patients with OLP, OLL and stomatitis. In the patient group, the most common allergens were nickel and mercury, whereas it was nickel in the healthy control group.

Contact allergy to aroma substances differed significantly between the patients and the healthy control subjects ($p = 0.02$). This type of contact allergy was most common in patients with OLP and OLL ($p = 0.01$). Spearmint was the most common allergen in the patients, whereas it was cassia oil in the healthy control group.

Figure 2 shows the number of patients with positive reactions to some of the allergens tested.

Doubtful positive patch test reactions were observed in 31 (63.3%) patients and in 16 (55.2%) healthy control subjects ($p = 0.06$). This difference was statistically significant between patients with stomatitis (but not OLP/OLL) and healthy control subjects ($p = 0.03$). The most common doubtful positive patch tests reactions were to nickel, perfume, balsam of Peru and linalool.

Doubtful positive patch test reactions to dental materials including metals used in dentistry did not differ between the patients and the healthy control subjects or between the patients with OLP, OLL and stomatitis.

Doubtful positive patch test reactions to aroma substances did not differ between the patients (the whole group, patients with OLP/OLL and stomatitis, respectively) and the healthy controls. However, in 17 of the 31 (54.8%) patients, the doubtful reaction was interpreted as relevant to their oral symptoms and in some patients more than one doubtful positive reaction was interpreted as relevant. Figure 3 shows the doubtful positive reactions being relevant to the patients' oral symptoms. In the healthy control group, none of the doubtful positive reactions were considered relevant to the oral cavity.

Positive patch test reactions to acrylates were only seen in three patients and in none of the healthy controls. These were all patients with OLL and OLP. Using binary cross tabulation and Fischer's exact test, with estimated 0.5% risk of acrylate allergy in the background population [20], it was estimated that patients with stomatitis had an increased risk of contact allergy to acrylates of 0–27%. Doubtful positive patch test reactions to dental acrylates were very sparse, and the difference between the patients and the healthy control group was insignificant. Finally, none had positive skin prick test reactions to chlorhexidine or latex.

Discussion

The purpose of this cross-sectional study was to determine whether mucosal lesions due to OLP, OLL or stomatitis could be related to allergy to dental materials or substances in oral hygiene products and whether these allergies primarily could be detected in those with lesions in close proximity to dental restorations, and also whether OLP, OLL and stomatitis display differences in terms of allergies to dental materials and substances in oral hygiene products. Thus, at present, it may be difficult to discriminate between OLP, OLL and stomatitis and to decide when to refer the patient for allergy testing [9].

The vast majority of patients included in this study were females. This not only reflects the fact that more women than men are referred to medical clinics as they more often seek care for their oral and general symptoms but also the fact that OLP/OLL is more prevalent in women. There is an increasing amount of evidence pointing towards a role of gender hormones in the development and exacerbation of various diseases, especially autoimmune diseases but also various allergies [24]. The age of onset of OLP also indicates that gender hormones may be involved in the pathogenesis via immunological and endocrinological changes affecting the oral mucosa and the immunological response and making the mucosa more susceptible to oral diseases like OLP and allergic reactions. However, the literature in this field is still very sparse [25]. Furthermore, the majority of men screened for inclusion in this study were not eligible.

The diagnosis of OLP and OLL was established in 38 patients (77.6%) based on the recommendations of WHO and van der Meij and van der Waal [20, 21]. Although the latter seeks to differentiate between OLP and OLL based on clinical and histopathological criteria, the value of distinction between them is still debatable. In this study, the patients with OLP fulfilled all the clinicohistopathological criteria whereas those characterised as OLL only partly fulfilled the criteria.

Fig. 2 Number of patients ($n = 19$) and healthy control subjects ($n = 10$) who reacted positive to a tested allergen

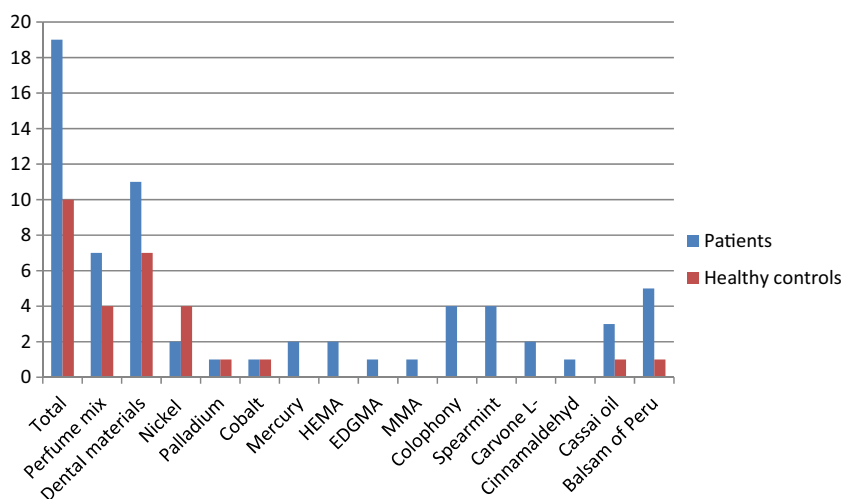
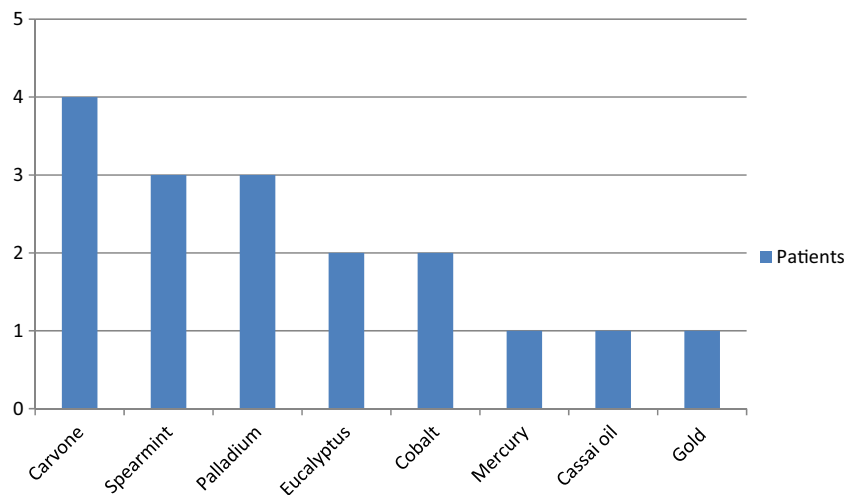


Fig. 3 Substances interpreted as being relevant to the patients' oral symptoms



However, a clear distinction between OLP and OLL with respect to the symptoms and positive allergic reactions was not found. The diagnosis of stomatitis was made in 11 patients (22.4%), based on more diffuse, widespread erythematous lesions. The distribution of systemic diseases/medical conditions reflects that of the general population [26].

The patients with OLP, OLL and stomatitis visited their dentist more frequently, had a higher number of DMF-T and DMF-S and had a higher degree of gingival inflammation, but lower scores of dental plaque than the healthy control subjects. These findings reflect that these patients have an increased need of dental treatment and regular dental follow-up, due to their oral mucosal conditions including problems with gingival inflammation despite good oral hygiene in terms of lower plaque index than healthy subjects. In this respect, they may also be more exposed to substances in oral hygiene products that could lead to contact allergies.

In this study, we found almost similar rates of contact allergy in patients with OLP, OLL and stomatitis and in healthy persons with no prior history of allergy, 38.8 and 34.5%, respectively. These rates are comparable to the results of a review from 2007 that finds that contact allergy to at least one allergen was 21.2% (range 12.5–40.6%) based on data collected between 1966 and 2007 [27]. We also found that patients with OLP and OLL have a larger number of contact allergies to aroma substances than healthy control subjects which may be ascribed to more thorough oral hygiene procedures and thereby exposure to aroma substances. Positive allergic reactions to acrylates were only seen in few patients with OLP/OLL.

Previous studies on adverse reactions to materials used in dentistry have focussed on either the dental materials or the aroma substances. A retrospective study in which 46 patients with OLP were patch tested, 54% displayed positive reactions and 39% had positive reactions to an allergen anticipated to exacerbate the OLP lesions [28]. In another retrospective

study from 2009, the results of patch testing with metals used in dentistry were analysed in 206 patients with suspected contact allergy. They found that 13.6% patients displayed positive reactions to metals used in dentistry, primarily to gold, palladium and nickel. Fourteen of the patients had clinically relevant contact allergy [29]. Laine et al. found that 67.8% of their patients with OLP had a positive patch test reaction to metals used in dentistry, primarily to mercury compounds [30]. Hosoki and co-workers found that in a population with suspected allergy to metals used in dentistry, 69.8% had one or more positive patch test reactions, primarily to nickel (25.0%), palladium (24.4%), chromium (16.7%) and cobalt (15.9%) [31].

These research groups all found more positive patch test reactions to metals used in dentistry in their patient groups than we found in our patient group. This is most likely due to the fact that different inclusion criteria were used. Hosoki et al. included patients that were suspected of having a contact allergy [31]; Laine et al. only included patients with a close topographical relation between the mucosal reaction and dental metal [30]. Raap et al. and Yiannias et al. both made retrospective studies where the included patients had already been patch tested [28, 29]. None of these research groups had a healthy control group included.

In 2009, Lavy et al. compared the incidence of contact allergy to oral hygiene products in patients with cheilitis and patients with contact dermatitis. They found that 45% of patients with cheilitis had a contact allergy to an oral hygiene product compared to only 5% in the dermatitis group [32]. In a study on the association of cheilitis and toothpaste allergy, 13 out of 54 patients reacted to allergens in toothpaste, especially spearmint [33]. In a more recent study, 73 out of 1467 tested patients had a positive reaction to spearmint. In 19 of the 73 patients with positive reactions to spearmint, the reactions were interpreted as relevant. Fourteen of the 19 patients had concomitant erosive OLP [4]. Thus, these studies report

higher numbers of contact allergic reactions to oral hygiene products than we do, which can be due to the fact that in the previous studies contact allergy was already suspected in the included patients [4, 32, 33].

In 2014, Ahlgren et al. investigated the relationship between OLL and contact allergy to both dental materials and oral hygiene products. Among 83 patients with OLL, there were more positive patch test reactions to carvone and to mercury than in patients with dermatitis [12]. They also found that the rate of contact allergy to gold was 28.9% in patients with OLP compared to 18.2% in patients selected from files and 22.9% in the clinically examined control patients [34].

The rate of positive patch test varies tremendously from one study to the other. In general, the rate is often very high in a study population already suspected to have contact allergy to dental materials and oral hygiene products.

Our study is primarily comparable to that of Ahlgren et al. [12, 34]. They also reported that patients with OLL had more dental surfaces with amalgam and composite restorations and an increased incidence of contact allergy to carvone. However, we could not substantiate their finding of a high number of contact allergies to gold. This may be due to our patients having few dental restorations in gold [35]. In the present study, multiple positive patch test reactions were common probably due to cross-reactions such as that between nickel and palladium.

One of the strengths of this study is that the patients are not selected on the basis of suspected allergy as they were referred to the Clinic for Oral Medicine for examination of oral symptoms. If contact allergy is already suspected, a higher incidence of positive patch test reactions can be expected. Therefore, our study gives a more accurate picture of the incidence of contact allergy in patients with symptomatic OLP, OLL and stomatitis. The limitation of our study is the number of patients and the number of healthy controls included. On the other hand, all participants were thoroughly characterised.

The seven patients with a positive reaction and the six patients with a doubtful positive reaction to aroma substances were advised on and instructed in avoidance. Their oral symptoms disappeared without further treatment within 1–3 months, and the improvement persisted for a minimum of 1 year (own unpublished data). All patients with other contact allergies besides aroma substances were also advised on and instructed in allergen avoidance. All patients with other contact allergies besides aroma substances ($n = 12$) were also advised on and instructed in allergen avoidance. In some patients ($n = 4$), this also led to an improvement in the oral symptoms (own unpublished data).

Conclusion

Our findings suggest that sensitization to aroma substances in oral hygiene products is common in patients with

symptomatic OLP and OLL. Follow-up also showed that all of these patients were cleared of their oral symptoms after avoidance. Although based on a limited number of patients, our findings suggest that patch testing may be indicated in patients with symptomatic oral lesions.

Acknowledgements We gratefully wish to thank laboratory technician Louise Rosgaard Duus for her assistance with the laboratory work, project nurse Anne Marie Topp for helping with the coordination of the participants and assistant professor Kasper Rosing for assistance with the statistical analyses.

Compliance to ethical standards

Conflicts of interest The authors declare that they have no conflicts of interest.

Funding We gratefully thank the Faculty of Medical and Health Sciences, University of Copenhagen, the Danish Dental Association and Toyota Fonden, Denmark, for the financial support.

Ethical approval The study was approved by the Regional Ethics Committee, Copenhagen, Denmark (Protocol No. H-3-2013-033) and performed in accordance with the Helsinki declaration.

Informed consent The study participants were both informed by letter and gave oral and written consent.

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