Review Article

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Allergic Reactions to Dental Materials- A Systematic Review

Dentistry Section

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ABSTRACT

Introduction: Utility of various dental materials ranging from diagnosis to rehabilitation for the management of oral diseases are not devoid of posing a potential risk of inducing allergic reactions to the patient, technician and dentist. This review aims to develop a systematic approach for the selection and monitoring of dental materials available in the market thereby giving an insight to predict their risk of inducing allergic reactions.

Materials and Methods: Our data included 71 relevant articles which included 60 case reports, 8 prospective studies and 3 retrospective studies. The source of these articles was Pub Med search done with the following terms: allergies to impression materials, sodium hypochlorite, Ledermix paste, zinc oxide eugenol, formaldehyde, Latex gloves, Methyl methacrylate, fissure sealant, composites, mercury, Nickel-chromium, Titanium, polishing paste and local anaesthesia. All the relevant articles and their references were analysed. The clinical manifestations of allergy to different dental materials based on different case reports were reviewed.

Results: After reviewing the literature, we found that the dental material reported to cause most adverse reactions in patients is amalgam and the incidence of oral lichenoid reactions adjacent to amalgam restorations occur more often than other dental materials.

Conclusion: The most common allergic reactions in dental staff are allergies to latex, acrylates and formaldehyde. While polymethylmethacrylates and latex trigger delayed hypersensitivity reactions, sodium metabisulphite and nickel cause immediate reactions. Over the last few years, due to the rise in number of patients with allergies from different materials, the practicing dentists should have knowledge about documented allergies to known materials and thus avoid such allergic manifestations in the dental clinic.

Keywords: Adverse reaction, Contact dermatitis, Dental setting, Hypersensitivity reaction, Oral-lichenoid lesions

INTRODUCTION

Allergic reactions are becoming prevalent in the general population and the materials used for dental filling, orthodontic instruments etc must satisfy the biocompatibility specifications since they are indicated for a long time in the oral cavity [1]. The first case of dental metal allergy occurred due to amalgam restorations in the oral cavity that resulted in stomatitis and dermatitis around the anus (Fleischmann 1928) [2]. The allergic reactions manifest in the form of urticaria, swelling, rash and rhinorrhea which can also cause life threatening conditions like laryngeal oedema, anaphylaxis and cardiac arrhythmias [3].

Contact allergy of the oral cavity is a T-cell-mediated (delayed) hypersensitivity reaction [3]. The clinical manifestations vary from burning, pain and dryness of mucosa to nonspecific stomatitis and cheilitis [1].

The dental materials suspected with biocompatibility issues are composites, latex gloves, local anaesthetic agents, endodontic materials, impression materials and metals. Now-a-days, due to globalization, liberalization and modernization of dentistry, we are using different dental materials easily available worldwide. However, underreporting of cases is seen in India and therefore individual sensitivity and population sensitivity of dental materials globally available should be considered.

Therefore, this article aims to-

i) Develop a systematic approach for the evaluation and monitoring of the severity of adverse reactions to dental materials available in the market,

ii) Give an insight into the diagnosis and management of allergy to dental materials and

iii) Can help dentists to become aware of incidence of allergy; thereby preventing the progression of these allergies by early recognition and preventive strategies.

MATERIALS AND METHODS

A systematic review according to the PRISMA 2009 Checklist (http://www.prisma-statement.org/2.1.2%20-%20PRISMA%202009%20Checklist.pdf) was performed. A backward search was also performed from the references of relevant studies. A MEDLINE search (PUBMED) of articles published was conducted to summarize the allergies to dental materials encountered in the dental office by the staff and students using the keywords mentioned in [Table/Fig-1].

Eligibility Criteria

i) Any case report or literature facts which were published in the English language only.

ii) Description of allergies manifested with the dental materials were considered for inclusion. The abstracts searched were further screened for compliance with inclusion criteria and full text analyses were performed.

iii) Case reports and literature facts reported from 1928 till 2014 were included in the search criteria.

iv) Allergies reported to personal protective equipment like latex gloves were also included in the systematic review.

Two independent reviewers selected the studies for the systematic reviewing through each phasing of review-screening, eligibility criteria and inclusion criteria.

RESULTS

The search of the term 'allergic reactions to dental materials' used revealed a list of 4919 articles. A total of 4895 articles were excluded based on analyses of abstracts and full texts. A total of 24 articles from the electronic search of the PUBMED database were included while manual search yielded 47 additional publications and the search strategy summarized was arranged in a tabular form as depicted in [Table/Fig-1].

Keywords	Search results	Excluded based on abstract	Excluded based on full text	Articles manually searched	Included (total)
Allergies to composites	35	32	3	5	5
MMA	148	142	6	10	10
Fissure sealant	12	11	0	0	1
Mercury	717	710	4	3	6
Ni-Cr	377	370	2	2	7
Titanium	268	263	2	3	6
Latex Gloves	1206	16	1185	7	12
Local anaesthesia	738	730	8	5	5
Formaldehyde	1308	1288	20	6	6
Zinc oxide Eugenol	17	13	3	3	4
Ledermix paste	1	0	0	0	1
Sodium hypochlorite	55	55	0	2	2
Impression materials	33	29	0	1	5

[Table/Fig-1]: Search strategy for articles included in the review

ALLERGY TO RESIN MATERIALS COMPOSITES

The maximum exposure concentrations during filling procedures formethyl methacrylate (MMA), 2-hydroxyethyl methacrylate (HEMA), ethylene glycol dimethacrylate (EGDMA), and triethylene glycol dimethacrylate (TEG-DMA) was 0.4 mg/m^3 for MMA, 45 µg/m^3 for HEMA, 13 µg/m for EGDMA and 45 µg/m^3 for TEG-DMA [4].

The dental personnel commonly complain of contact dermatitis and asthma caused by methacrylates. HEMA, EGDMA and TEG-DMA are responsible for occupational contact allergies [4].

A study was reported in which patients had lichenoid-like reactions of lips and patch testing revealed positive reaction to composite components. Antifungal treatment and replacement of existing restorations resulted in improvement [5].

Even though resin-based restorative materials are considered safe, their constituents can leach out and cause allergic contact stomatitis as reported in a patient with mild erythema in the gingiva and buccal mucosa [6,7]. In a study conducted to check patient's reaction to patch testing, only 2 patients showed positive result with BISGMA [8].

Fisher recognized MMA monomer as the main cause of allergic dermatitis in dentists and dental laboratory technicians [9].

The prevalence of contact allergy to methyl methacrylate is 1% [10,11]. Different methods reduce the leachable substances from acrylic dentures such as immersing in hot water (50°C) for one hour prior to inserting into the oral cavity [12] or ultraviolet light [13]. A rare case of a patient with hypersensitivity reaction linked to denture wear has been reported [14].

Hence, optimum room ventilation is necessary and techniques should be employed to reduce patient and dentist exposure to MMA. Dentists must advise patients to avoid wearing dentures overnight, as it may cause mucosal irritation [15].

FISSURE SEALANT

Hallstrom U reported an isolated case in which adverse reactions like asthma and urticaria were reported after fissure sealant placement and the symptoms disappeared after its removal suggesting allergy [16].

ALLERGY TO MERCURY ASSOCIATED WITH AMALGAM RESTORATION

Delayed hypersensitivity reactions to amalgam restorations are seen as erythematous, pruritic lesions on the oral mucosa and skin of the face and neck. The common manifestations of these reactions are oral lichenoid lesions (OLL) [17]. Patch testing done in a study on 29 patients with oral lichen planus revealed that 10 patients showed an allergic reaction to mercury and on replacing the amalgam with composite or glass ionomer, the lesions resolved [18]. Another manifestation of allergy to mercury is burning mouth syndrome (BMS). A study conducted on a patient with BMS revealed positive patch test results and complete remission was achieved after the mercury filling was replaced [19]. The first step in recognizing allergy induced disease is a detailed history of the complaint and its clinical course. In 1976, the Council on Dental materials and devices advised using conventional amalgam condensers instead of ultrasonic amalgam condensers [20]. Air conditioners, proper ventilation of the operating rooms and proper handling of amalgam scraps under sulphide solution can avoid mercury vapor production [18].

ALLERGY TO METALS NICKEL-CHROMIUM

Nickel is the common sensitizer amongst all metals [21]. Nickel was considered as one of the causes of allergic contact dermatitis in women by Fisher [22]. In 1889, Goldman reported the first case of Nickel dermatitis characterized by sensitivity to nickel compounds [23]. The incidence of nickel allergy is 0.1-0.2% [24]. Overall, nickel sensitivity is more common in women (4-10 times) than men [25] whereas, chromium allergy is rare (10% in males and 3% in females) [26]. The clinical signs and symptoms of nickel allergy include burning sensation, gingival hyperplasia, numbness on sides of tongue and the final diagnosis is confirmed by patch test using 5% nickel sulphate in petroleum jelly [27]. In sensitized individuals, nickel exposure leads to systemic allergic contact dermatitis [28].

If the diagnosis of nickel hypersensitivity is established, the Ni-Ti arch wire should be replaced with stainless steel wire or titanium molybdenum alloy (TMA) [27]. It was observed that orthodontic treatment with stainless steel appliances did not initiate hypersensitivity reaction [29,30]. A case reported by J Noble et al., showed relief of anaesthetic like feeling in a patient after replacement of NiTi wires [27]. The commonly used non-nickel containing orthodontic brackets include ceramic brackets, polycarbonate brackets and gold brackets [27].

Sensitivity to nickel was observed in children treated with old generation SSCs (72% nickel) while on replacing them with new generation SSC (9-12% nickel), no sensitivity was seen [31,32]. Invitro nickel leaching from orthodontic materials, space maintainers and arch wires is maximum within the first week and then declines [33]. Nickel allergy is frequently associated with chromium and cobalt reactivity. Duarte patch tested 1208 patients with contact dermatitis and found that 18.5% had positive reactions to two or three metals [34].

TITANIUM

The first case of delayed hypersensitivity reaction to titanium in the form of local granulomatous reaction was described in patients

wearing cardiac pacemakers [35,36]. Titanium allergy has a low prevalence rate of 0.6% [37] and presents with urticaria, eczema, redness of the mucosa [38,39]. Another case was reported in which patient had eczema on the face after placement of titanium implants in the mandible [40]. More reports were published in which de-keratinized hyperplastic reactions of the peri-implant tissues and drug rash with eosinophilia and systemic symptoms (DRESS) syndrome suggestive of titanium allergy were observed in association with titanium implants [41,42].

Recently, 56 patients developed severe health problems (muscle and joint pain, chronic fatigue syndrome) after receiving titanium dental implants, orthodontic braces or endoprostheses [43]. In a prospective study monitoring 1500 patients with dental implants over a three-year period, titanium allergy appeared following implant placement [37].

It was observed that presence of elements in titanium alloys could cause allergic reactions in dental implant patients such as beryllium (Be), cobalt (Co), chromium (Cr) [44,45]. Patch tests have limited use due to poor sensitivity [46] and the test validated to detect titanium sensitization is MELISA test [43]. Alternate substitutes like Polytheretherketone (PEEK) which offer mechanical properties and bone forming capacity similar to titanium are also under investigation [47].

ALLERGY TO LATEX GLOVES

Nutter reported first case of latex allergy in 1979 [48]. The frequent risk of population for latex allergy includes children with spina bifida (highest risk), patients who underwent surgery before one year of age, latex-fruit syndrome (allergy to various fruits) and healthcare workers (second highest risk) (Kean T) [49] who have higher risk of latex allergy due to sweating and multiple glove changing [48,50,51].

The prevalence of latex allergy in general population is less than 1% [52]. The allergic reactions to latex vary from stomatitis to airway compromise [53] and are reported in 3.8% population [54]. Blinkhorn and Leggate reported a case of angioneurotic edema in a boy due to dental rubber dam. Smart et al., also described three cases of patients with delayed hypersensitivity to rubber [55].

There is no ''gold standard'' for diagnosing latex allergy as no test is 100% accurate [56]. The diagnostic algorithm for latex allergy includes obtaining medical history, skin patch testing for type IV delayed hypersensitivity; measurement of serum IgE for type I immediate hypersensitivity and glove testing when patient's history is not correlating with IgE results [57-59].

The American society of Anaesthesiologists Task Force of Latex Sensitivity recommends patients who have latex allergy to undergo surgical procedures in the morning [50]. The manufacturers of NRL gloves should mention protein levels of gloves on package labels as directed by FDA [60].

ALLERGY TO LOCAL ANAESTHETICS

Although LA are well-tolerated drugs, they precipitate adverse reactions which are related to LA [61,62], doses (toxic reaction or overdosage) [63] or psychogenic factors. Adverse reactions are reported of lignocaine [64], prilocaine [65] mepivacaine [66] or to their components like methylparaben [67] or metabisulphite [68]. The causes of allergic reactions are psychogenic or intravascular injections [69].

Most sensitization reactions are attributed to ester anaesthetics as one of the breakdown products is the antigenicagent p-aminobenzoic acid [70]. Allergic reactions are reported by local anaesthetics including esters and amides [71-77].

A prospective study on patients who received local anaesthesia during dental procedures showed that 25 adverse reactions diagnosed were psychogenic or vasovagal [78]. The most common adverse reaction is syncope (vasovagal type) [79]. The incidence of anaphylaxis is, howeverr are (1 in 6000) [80].

It is important to distinguish true anaphylaxis from other causes of cardiovascular collapse. Hence, the serum-mast cell tryptase test confirms the anaphylactic nature of these reactions [81].

True allergy to LA can be identified with help of skin tests but if the nature of the skin reaction is unclear, challenge test is carried out in which the patient is 'challenged' by subcutaneous injection with graded doses of LA till the therapeutic dose [81]. In a study of 188 cases undergoing such a challenge, only two patients had a positive reaction [82]. There are three cases of death reported in literature; one with prilocaine combined with felypressin; another with lignocaine alone and third with prilocaine combined with adrenaline. In all these cases, the LA agent may be considered as a factor [81]. The management of adverse reactions with LA includes immediate treatment and active prevention. It is important to relieve fear and anxiety, use an aspirating syringe and inject slowly [83].

ALLERGY TO MATERIALS USED IN ENDODONTICS FORMALDEHYDE

Formaldehyde is a common cause of allergic contact dermatitis [84]. It was reported that 40% -60% reactions were due to formaldehyde [85]. There is decrease in the formaldehyde sensitization sine 1980 due to textile finishing resins (release low amounts of formaldehyde) and reduced amount of formaldehyde (1%) used in aqueous patch test solutions [86]. The patients allergic to formaldehyde are usually women who develop eczema on the hands or face [87,88]. In the dental literature 28 patients with immediate symptoms to formaldehyde containing root canal compounds have been described [89].The characteristic features of formaldehyde allergy are anaphylactic reaction [90] or shock [91] and generalized urticaria [89,92]. The most useful and diagnostic tool to determine formaldehyde allergy is the assessment of specific IgE antibodies to formaldehyde [92].

ALLERGY TO ROOTCANAL SEALERS AND OBTURATING MATERIALS

Generally, zinc oxide allergy is rare and only one case of a successful root canal treatment of a patient with zinc oxide allergy is reported [4]. Munaco et al., (1978) and Pascon & Spangberg (1990) reported that Gutta-percha is biocompatible; however, the high content of zinc oxide can contribute to its toxicity. Hence, recently a resin-based filling material (Resilon, Pentron Clinical Technologies, Walling ford, CT, USA) has been introduced as an alternative to gutta-percha which is composed of polyester, difunctional methacrylate resin, bioactive glass and a resin sealer. Studies have shown that resilon is biocompatible and a good alternative for patients allergic to zinc oxide-eugenol based dental materials [4]. Eugenol acts as a contact irritant and induces type IV hypersensitivity reactions and generalized anaphylactic symptoms [93]. Allergic reaction to eugenol was also reported in a patient with gingival inflammation in the mucosal area adjacent to metal-ceramic bridge [93]. Allergic contact stomatitis has also been reported when eugenol was used as a temporary restorative material and on replacement with glass inomer, the lesion healed [94].

LEDERMIX PASTE

No allergy to ledermix paste is reported except for a single case in which a female experienced type I allergy in the form of urticaria, general malaise and fever when a mixture of ledermix paste and calcium hydroxide was used as an intracanal medicament and her symptoms subsided following flushing out of the Ledermix paste and re-dressing the canal with $Ca(OH)_2$ [95].

SODIUM HYPOCHLORITE

Only couple of cases of hypersensitivity to NaOCl are reported in which hypersensitivity to household bleach was confirmed with skin patch tests [96].

Another case report of allergy to sodium hypochlorite is also documented. On irrigating the canals with same, patient had burning sensation and difficulty in breathing and was administered corticosteroids, antibiotics, antihistamines and analgesics for symptomatic relief. After 15 days, positive skin scratch test was seen which confirmed allergy to 1% sodium hypochlorite [97].

ALLERGY TO IMPRESSION MATERIALS

Allergic reactions are reported to polyether impression materials which manifests as swelling, itching and redness. It was seen on patch testing that a component of the catalyst paste caused the allergy and on replacement of this component, no allergic reactions were observed [98,99]. Another retrospective study documented results of multiple allergy tests with polyether impression material and its components (between 2007 and 2009). The results of patch tests showed a positive reaction to mixed polyether impression materials, base paste or to the base component [100].

There is only a single allergic case reported in which a patient developed hypersensitivity reaction to polysulfide material in the form of redness, itching and oedema following secondary impression for upper and lower complete dentures and on treatment with topical corticosteroids (Betamethasone valerate ointment 0.1%) she recovered [101]. A retrospective case report of fatal anaphylactic shock to alginate impression material has also been documented [102]. Because of the isolated allergic cases reported to alginate and polysulphide materials, there is inconclusive evidence of the incidence of these reactions.

DISCUSSION

During dental treatment, various materials are used which can have side effects on patients and dental staff; hence it is necessary to use them with caution.

In 2006, Khamaysi et al., conducted a research of allergens in dental practice which are related to contact reactions and observed that patch testing of 134 patients showed cheilitis and perioral dermatitis as the most common oral manifestations (25.6%) followed by burning mouth syndrome (15.7%), lichenoid reaction (14%) and orofacial granulomatosis (10.7%). The common contact allergens were sodium thiosulfate (14%), nickel sulfate (13.2%), mercury (9.9%), palladium chloride (7.4%) and 2-hydroxyethyl methacrylate (5.8%) [56].

According to Khamaysi et al.,, allergy to mercury did not contribute to oral lichenoid reactions. Although 35% of patients with lichenoid reaction were positive to mercury [56], positive reaction to mercury was also seen in patients with orofacial granulomatosis [57,103-105].

While dental patients exhibit symptoms mainly on the oral mucosa, dental staff usually has hand dermatitis. The most common cause of contact allergies in dental workers are metals, rubber, antimicrobial drugs, preservatives and methacrylates [56]. Studies in dental workers have shown the incidence of skin diseases to range from 30% to 50% [106,107]. Khamaysi et al., observed that dental workers with hand dermatitis have a high incidence of allergies to metals [56] while reports from Europe and USA suggest that the most common cause of allergies are gloves and dental restorative materials [108,109].

When a patient is suspected of allergy, a thorough history taking and clinical examination should be done. Prick method (prick test) and scratching of the skin (scratch test) are used to confirm immediate hypersensitivity while patch test confirms delayed hypersensitivity [110]. Patch testing should be done according to the criteria from the International Contact Dermatitis Research Group (ICDRG) [2]. Patch testing includes the application of a specific allergen at a specific concentration in a particular vehicle which has the ability to induce a cutaneous inflammatory reaction when administered to a sensitized person. The results are then read at 48 and 72 hours and any skin reaction with erythema and papulovesicles is taken as positive [111]. For decades, the Lymphocyte Stimulation Test (LST) has been used for diagnosis of delayed hypersensitivity reaction [112]. But, MELISA (memory lymphocyte immuno-stimulation assay test) is used to measure the sensitization induced by metals [113,114].

After reviewing the literature, we found that dental personnel have higher risk of allergy from latex gloves while patients have increased risk from metals. Metal reactions can be caused by amalgam, base metal and precious metals. The symptoms are intra-oral lichenoid reactions or a burning sensation and/or swelling of the buccal mucosa. The dental material that causes most adverse reactions in patients is amalgam. The degree of adverse reactions ranges from mild to moderate which shows that adverse reactions are not life threatening except in rare cases.

LIMITATIONS

The current review is not devoid of inherent information bias limitations as it did not cover grey literature, non-English language articles and articles related to medical field.

CONCLUSION

The oral cavity is constantly exposed to sensitizing substances that cause allergic reactions and contributes to rise in healthcare expenditures annually. The common allergic reactions in dental staff are allergies to latex, acrylates and formaldehyde. While polymethylmethacrylates and latex trigger delayed hypersensitivity reactions, sodium metabisulphite and nickel cause immediate reactions. For establishing diagnosis, it is essential to obtain proper history related to allergy, clinical examination and confirmatory tests like patch tests and MELISA. Thus, due to rise in number of patients with allergies from different materials, the practicing dentists should be aware about the allergies documented to known materials and thus prevent allergic manifestations in the dental clinic.

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