CASE REPORT

An unexpected positive hypersensitive reaction to eugenol

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Dr Praveen Tammannavar,
Praveenst79@gmail.com**SUMMARY**

Eugenol is an active, principal aromatic liquid responsible for several pharmacological activities. It is widely used in dental practice to relieve pain arising from various sources, such as pulpitis and dentinal hypersensitivity. As a primary irritant and sensitizer, it is known to cause contact urticaria as well as chronic urticaria. However, eugenol causes allergic contact dermatitis, possibly because it can react directly with proteins to form conjugate and reactive haptens. It is found that eugenol in various dental preparations—especially in the case of some zinc oxide—contains preparations such as periodontal dressings and root canal cements. This can cause hypersensitivity when it comes in contact with gingiva or teeth. This article presents a case of immediate allergic contact urticaria to eugenol during dental treatment.

BACKGROUND

Eugenol is a para-substituted phenolic compound contained in several plants including clove and bay leaves and has been widely used as an analgesic and anti-inflammatory drug to treat tooth ache and pulpitis in the dental clinic.¹ It is used not only in combination with zinc oxide as a pulp-capping agent, temporary filling and a root canal sealer but also as a fragrant and flavouring agent in a variety of cosmetics and food products.² The joint Food and Agriculture Organisation/WHO committee on food additives has permitted an acceptable daily intake of eugenol of 2.5 mg/kg body weight for humans.³ It is considered non-carcinogenic and non-mutagenic and is generally recognised as safe by the Food and Drug Administration.⁴ On the other hand, there are many studies about the cytotoxicity of eugenol.^{5–7} Generally, low concentrations of eugenol are known to act as an antioxidant and anti-inflammatory agent, whereas its high concentrations act as a pro-oxidant resulting from the enhanced generation of tissue damaging free radicals.^{6, 8, 9} However, the mechanism responsible for the cytotoxicity of eugenol, especially for that of photo damage to cells, is not yet well understood.²

Eugenol in its unrefined form is mixed with zinc oxide to form zinc oxide eugenol.¹⁰ The setting reaction between zinc oxide and eugenol produces zinc eugenolate, which is highly unstable in the presence of water. The surface of this material undergoes hydrolysis, releasing free eugenol, which has been reported to induce type IV hypersensitivity reactions as well as generalised anaphylactic symptom.¹¹ Adverse reactions to eugenol range

from localised irritation of the skin to allergic contact dermatitis.⁴

However, there have been rare reports of immediate hypersensitivity reaction to eugenol. We report a case of type I immediate hypersensitivity reaction to eugenol in a paediatric patient referred for dental treatment.

CASE PRESENTATION

An 8-year-old boy reported to a private dental clinic with pain in the maxillary right first molar. After clinical and radiographic evaluation, a diagnosis of chronic irreversible pulpitis was made and pulpectomy was indicated. Medical history revealed no episodes of allergic responses to any drug.

After adequate preparation of the patient, isolation of the tooth was accomplished with a 5×5 inch rubber dam. An infiltration of local anaesthetic to the area to be treated was given. An extirpation was performed, and the root canal was medicated with sodium hypochlorite and sealed with zinc oxide eugenol dressing.

About 1 min after the zinc oxide eugenol placement the patient was anxious and excited, with evident erythema on the face, neck, torso, upper limbs, lower limbs and itchiness and redness extending behind the ear (figures 1–5). Cutaneous examination revealed extensive weals of various

Figure 1 Evident erythema involving back region.

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Figure 2 Erythematous weals seen on the face region.

sizes and shapes. There was no angio-oedema or mucosal involvement. Owing to the fact that the erythema was noticed after the placement of zinc oxide eugenol, it was thought that the patient could have had a reaction to zinc oxide eugenol or some others disinfectants used during the procedure.

A provisional diagnosis of immediate hypersensitivity reaction to eugenol was made due to rapid onset of urticaria clinically within few minutes after application of zinc oxide eugenol.

INVESTIGATIONS

The patient was referred to a consultant dermatologist for investigation to determine if the reported reaction was a genuine

Figure 3 Erythematous weals seen on the scapular region.

Figure 4 Erythematous lesion seen on the neck region.

allergy to the zinc oxide eugenol itself or to any other medications administered during the procedure. The patient underwent skin prick test for various chemicals which were found to be contained in the root canal disinfectants and zinc oxide eugenol including formaldehyde. The patient showed positive response for eugenol (10%) and negative responses for zinc oxide (10%), formaldehyde (1% aq) and sodium hypochlorite.

TREATMENT

Intravenous injection of 100 mg of hydrocortisone hemisuccinate was administered immediately and zinc oxide eugenol temporary dressing was replaced with non-eugenol containing material. The patient was kept under observation. Forty-five minutes later the patient presented reduced erythema on the face, neck, hands, torso and the limbs. After 2 h he completely recovered.

OUTCOME AND FOLLOW-UP

No relapse or recurrence was observed during 3 months follow-up.

DISCUSSION

Eugenol is a major volatile constituent of clove essential oil obtained through hydrodistillation of mainly *Eugenia caryophyllata* (= *Syzygium aromaticum*) buds and leaves. Its vast range of pharmacological activities has been well-researched and includes antimicrobial, anti-inflammatory, analgesic, anti-oxidant and anticancer activities, among others.¹²

Eugenol was first isolated in 1929 and commercial production started in the USA in the 1940s.¹³ Chisholm in 1873 described

Figure 5 The outer part of the arm was also affected.

its mixture with zinc oxide to form a polymerised eugenol cement used for surgical dressings, temporary fillings, pulp capping agents and cavity liners.⁴

Several adverse effects related to the use of dental products containing eugenol have been observed and include localised irritation of the skin, ulcer formation, allergic contact dermatitis, tissue necrosis, reduced healing and in rare cases even anaphylactic-like shock.⁴ According to Barkin, therapeutic action on the pulp is cytotoxic and three reaction types may be promoted by eugenol; direct tissue damage due to the nature of the medication, contact dermatitis and true allergic reaction.¹⁴ However, eugenol causes allergic contact dermatitis, possibly because it can react directly with proteins to form conjugates and reactive haptens.^{4 15}

Hypersensitivity reactions according to Gell and Coombs classification may be type I (immediate hypersensitivity reaction mediated by IgE antibodies), type II (cytotoxic reactions), type III (immune complexes) or type IV (delayed hypersensitivity reaction mediated by sensitised T-lymphocytes).¹⁶

Allergic reactions associated with dental materials are generally delayed hypersensitive reactions that are usually not associated with circulating antibodies. The delayed hypersensitive reaction is not manifested clinically until several hours of exposure.¹⁰ Eugenol is known to cause contact urticaria, characterised clinically by development of an immediate weal and flare response on intact skin coming into direct contact. The immediate reactions are based on the release of active mediators by interaction between the IgE immunoglobulin in the mast cells, eosinophils and platelets and the intruding allergen. The present patient showed type I immediate hypersensitive reaction to eugenol which is very rare in dentistry. The signs and symptoms clinically manifested within minutes after placement of eugenol are characterised by agitation, urticaria, generalised itching of face, neck, hands, limbs, torso and redness extending behind the ears.

Although eugenol allergy is uncommon, proper history is needed in order to prevent a situation as described above. The history includes asking about allergy to substances like dental materials, preservatives and flavouring agents, as eugenol is considered as common oral flavouring allergens. Identification and elimination of the allergen that initiated the reaction is essential to treat the condition, as well as to prevent recurrences.¹⁷ When the skin symptoms are present the patient should be referred to a dermatologist for consultation. The epicutaneous test should be undertaken by a dermatologist. Once positive test has been confirmed by the dermatologist, the offending material should be withdrawn. Rapid remission of the symptoms will confirm the positive allergy test and the patient should be made aware of his or her allergic status and be advised to report it to future dental practitioners. A repeat test may be necessary for the true confirmation of allergy, but because of ethical considerations, may not be clinically possible.¹⁰

Diagnosis of type I drug allergy includes a complete medical history and history of atopy. The commonest diagnostic test for drug allergy is skin prick test. IgE mediated reaction can be demonstrated by a positive skin prick test and/or intradermal test.¹⁸ In this case report, the diagnosis of type I eugenol allergy was made based on the suggestive clinical finding and demonstration of specific IgE by skin prick test.

Type I immediate hypersensitivity reaction can be controlled by avoiding non-allergens, and by hyposensitisation and drug therapy. Some newer approaches include treating with interferon and allergoids.¹⁹ Dentist forms an important link in the differential diagnosis of allergy.¹⁰

Learning points

- Our case, reports that type I immediate hypersensitive reaction to eugenol is very rare and most of the adverse reaction tend to occur within minutes after placement of eugenol and may present with lip, tongue and periorbital swelling, agitation, generalised itching particularly of the hands and feet, urticaria and wheezing.
- To diagnose and manage these cases properly, a complete history must be taken to determine the nature of the reaction, as well as a proper allergological testing.
- However, it is important for the practitioner to be aware of the presence of allergic reactions that may occur after placing eugenol, but the physician and the dentist should be able to reassure their patients and to prepare them to minimise the frequent fears that are built around the use of any dental materials.

Contributors All authors helped in diagnosis and treatment planning for the patient.

Competing interests None.

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