

## Allergy to local anaesthetic agents used in dentistry – what are the signs, symptoms, alternative diagnoses and management options?

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### Background

Following administration of a local anaesthetic, a minority of patients may suffer one of a range of unwanted symptoms. Some of these symptoms can be mistaken for allergic reactions and patients may be unnecessarily told they are allergic to the anaesthetic. Mislabelling of patients as allergic to local anaesthetics can lead to problems with patients unable to undergo routine dental treatment [1].

Local anaesthetic agents can be categorised as amide (lidocaine, prilocaine, articaine, mepivacaine) or ester (benzocaine, cocaine, procaine, tetracaine) [2]. True allergy to an amide local anaesthetic is exceedingly rare. Local anaesthetics of the ester type are more likely to produce allergic reactions as they are metabolised to para-aminobenzoic acid (PABA), which is an allergenic compound [3,4 5,6]. The only ester local anaesthetic used in dentistry is benzocaine, which is used in topical preparations applied prior to administration of local anaesthetic injections. Allergy to one ester local anaesthetic contraindicates use of another ester, as metabolism of all esters yields PABA [7]. However, patients are less likely to show cross sensitivity to amide local anaesthetics as these are not metabolised to PABA, although it has been suggested that meta-xylene, present in some amide and ester local anaesthetics, could play a role in cases of cross sensitivity [8]. Allergy to one amide local anaesthetic does not contraindicate use of another amide local anaesthetic but it would be unwise to use another amide local anaesthetic without hypersensitivity testing [4,9,10]. The least allergenic amide local anaesthetics are mepivacaine and plain prilocaine [11].

This Medicines Q&A addresses the signs and symptoms of local anaesthetic allergy, differential diagnoses and management of patients with suspected allergy to local anaesthetics.

### Answer

Local anaesthetics are considered relatively safe but, given the high number of injections that are administered, adverse reactions are inevitable [4]. Adverse systemic reactions to local anaesthetics can be divided into three categories: allergic, psychogenic and toxic [4].

#### 1. Allergic

Genuine allergic reactions to local anaesthetics are extremely rare. It has been estimated that true allergic reactions to local anaesthetics account for less than 1% of all adverse reactions to local anaesthetics [1, 12, 13]. It is unclear where this figure originates from or the number of patients this represents, as the incidence of adverse reactions occurring in patients who have received local anaesthetics is not reported.

#### Signs and symptoms

A true allergy to local anaesthetics may be either type I or type IV [12].

Type I are immediate anaphylactic reactions mediated by IgE antibodies. Signs and symptoms of type I allergy tend to occur within minutes of giving the injection:

- ◆ The lips and periorbital areas swell (angioedema) [12].

- ◆ The patient may become agitated and there is generalised urticaria and pruritus, particularly of hands and feet. Other symptoms include abdominal cramps, nausea and diarrhoea [12, 14].
- ◆ Tightness of the chest, with wheezing and difficulty in breathing may occur [12].
- ◆ There may be a fall in blood pressure and a rapid thready pulse, which may be accompanied by flushing of the skin or rash [12, 14].

Type IV delayed hypersensitivity reactions mediated by sensitised lymphocytes. They are:

- ◆ Usually localised to the injection site.
- ◆ Commonly expressed as a contact dermatitis [12].

### Allergy to other ingredients

Many allergic reactions involving local anaesthetic preparations are due to other constituents in the injection solution rather than to the drug itself. Excipients such as preservatives (e.g. benzoates – used in multidose vials), antioxidants (e.g. metabisulphites – used in local anaesthetic solutions containing adrenaline) and antiseptics (e.g. chlorhexidine) can cause allergic reactions [5, 10, 15].

Allergy to natural rubber latex contained in bungs, gloves, dams and other dental materials should also be considered [5, 17].

Historically, the most sensitising components in local anaesthetic solutions were preservatives such as methylparabens. Parabens are no longer added to dental local anaesthetic solutions available in the UK [4, 18].

## 2. Psychogenic

Psychogenic reactions (originating in the mind, an emotional response) are one of the most common adverse reactions associated with local anaesthetic use in dentistry. They may manifest in many ways, the most common being syncope but other symptoms include panic attack, hyperventilation, nausea, vomiting and alterations in heart rate or blood pressure, which may cause pallor. They can be misdiagnosed as allergic reactions and may mimic them with signs such as flushing of the skin, blotchy red rash, oedema and bronchospasm [4, 14]. All patients have some degree of autonomic response to injections, ranging from slight tachycardia and sweating to syncope [19].

## 3. Toxic

Toxic reactions may occur if high levels of anaesthetic enter the blood stream. Local anaesthetics can reach the systemic circulation as a result of repeated injections, inadvertent intravascular administration or overdose in those patients who have problems eliminating or metabolising the anaesthetic [4, 19, 20]. Toxic side effects are predominantly neurological and include excitability or agitation, sedation, light headedness, slurred speech, mood alteration, diplopia, disorientation and muscle twitching. Higher blood levels may result in tremors, respiratory depression and seizures [4, 20].

Vasoconstrictor agents such as adrenaline may also cause adverse effects. Adrenaline toxicity can result in symptoms such as anxiety, restlessness, trembling, pounding headache, palpitations, sweating, pallor, weakness, dizziness and respiratory distress [9].

Toxic reactions can be minimised by staying within safe dose ranges and using safe injection techniques [19].

### Management options to prevent adverse effects occurring

When a patient experiences signs and symptoms suggestive of local anaesthetic allergy, possible alternative causes should be considered such as contact with other common allergens, psychogenic or toxic reactions. The possible causes of symptoms experienced should be discussed with the patient. Use of the terms 'allergic' and 'allergy' should be avoided when discussing any adverse event as this term is recognised by patients and readily adopted as the explanation [21].

Adverse psychogenic or toxic reactions can be minimised by:

- ◆ Administering injections with an aspirating syringe to avoid intravascular injection [16, 21].
- ◆ Relaxing nervous patients to relieve their anxiety. For extremely anxious patients, sedation may be required [21].
- ◆ Treating patients in a supine position to prevent fainting [21].
- ◆ Giving injections slowly to reduce discomfort and improve localisation of solution [21].
- ◆ Restricting the total dose given to the patient to prevent toxic effects occurring by overdose [21]. The maximum dose for the individual patient can be calculated using dosage information contained in the package insert or recognised dental resources on local anaesthesia, and taking into account age and weight of the patient, any concomitant drug therapy and underlying medical conditions.

### Management of a patient who suffers an adverse reaction in the surgery

**Psychogenic reaction:** If a fall in blood pressure occurs or the patient feels faint, laying the patient flat and elevating the legs should be sufficient to help restore blood pressure [22]. Any tight clothing around the neck should be loosened [23]. Once conscious, the patient should be given a glucose drink [22]. Calm the patient and reassure them.

**Toxic reaction:** Symptoms caused by toxicity will be short-lived in most patients. The pharmacokinetics of local anaesthetic agents used in dentistry suggest that the drug will be eliminated from the blood stream within a couple of hours, but this may be as long as 12 hours in some individuals. Reassure the patient that they will feel better after several hours and inform them that, although the reaction is unpleasant, it should not happen again and it is not necessary to avoid that local anaesthetic in the future.

### Management of a patient when local anaesthetic allergy is strongly suspected

If symptoms suggestive of a true allergic reaction occur (localised reaction consisting of swelling, erythema, an itchy rash or systemic features such as dyspnoea, wheezing, widespread skin rash or circulatory collapse), the patient should be given emergency treatment following the 'Emergency treatment of anaphylaxis guidelines' (see 'Medical emergencies in dental practice' in the 'Prescribing in dental practice' section of the current BNF or [www.resus.org.uk/quality-standards/primary-dental-care-quality-standards-for-cpr-and-training](http://www.resus.org.uk/quality-standards/primary-dental-care-quality-standards-for-cpr-and-training) for details). If the patient feels unwell, their condition is deteriorating or they are very distressed, they should be transferred to hospital [17].

The patient should be referred for further investigation to confirm if the local anaesthetic or another possible allergen (e.g. excipient, natural rubber latex) was responsible for the adverse effects [21, 22]. If the cause of symptoms is uncertain, dentists should contact the local dental hospital to discuss referring the patient for further investigation. Alternatively, if a true allergic reaction is suspected, patients can be referred by the dentist or GP directly to the allergy clinic at their local hospital, if this service is available [14]. Location and contact details for allergy clinics can be found via the British Society for Allergy and Clinical Immunology website: [www.bsaci.org](http://www.bsaci.org).

Very rarely allergy to local anaesthetic is confirmed. In these cases immunological testing should be extended to other local anaesthetics in order to identify a safe alternative for future dental procedures [13].

### Management of patients who report they are allergic to local anaesthetic agents

New patients who claim to have had an allergic reaction to a local anaesthetic should be carefully questioned to obtain a history of past events [6]. These details may be more reliably obtained from the patient's previous dentist.

Questions to ask the patient or dentist include:

- ◆ What symptoms did the patient experience?
- ◆ What explanation for the symptoms was given at the time? Who told them this?
- ◆ Have they ever had any other dental treatment or surgery in the past that required them to have a local anaesthetic agent – what happened?
- ◆ Do they have any other allergies?
- ◆ Have they ever been tested for a local anaesthetic allergy? If so, what was the result? (The allergy specialist should be contacted for confirmation and further information.)

### Management

- ◆ If further information obtained strongly suggests an allergy but no details are available, refer the patient for allergy testing.
- ◆ If further information strongly suggests a psychogenic reaction, proceed with care and address the patient's anxiety.
- ◆ If further information strongly suggests toxicity, proceed with care starting with low doses of local anaesthetic/vasoconstrictor.
- ◆ If no information is available from the patient or dentist, contact the GP who may have information about previous local anaesthetic exposure or other relevant knowledge.
- ◆ If it is strongly suspected that the patient has previously suffered an allergic reaction to a local anaesthetic and emergency dental treatment is required, consider contacting a local hospital dental department to discuss management and referral to a unit that has full resuscitation facilities available.

### Summary

- ◆ Allergy to amide local anaesthetics is rare. Allergic reactions are most likely to occur with ester local anaesthetic agents; these are not used routinely in dentistry.
- ◆ Adverse effects experienced after administration of local anaesthetics may be mistaken for allergic reactions, but often there is another explanation for the symptoms.
- ◆ True allergic reactions to local anaesthetics are either immediate hypersensitivity reactions (type I – angioedema, urticaria, pruritus, chest tightness, wheezing, fall in blood pressure) or delayed hypersensitivity reactions (type IV – localised reaction at the injection site, contact dermatitis).
- ◆ Due to the rarity of local anaesthetic allergy, if a patient experiences signs and symptoms suggestive of an allergic response, consideration should be given to other possible causes of the symptoms e.g. toxicity (sedation, light headedness, slurred speech, mood alteration, diplopia, disorientation and muscle twitching) or a psychogenic reaction (anxiety, skin flushing, blotchy red rash, bronchospasm, sweating, tachycardia, syncope, hyperventilation, nausea and vomiting).
- ◆ Where local anaesthetic allergy is strongly suspected, patients should be referred for allergy testing for confirmation.

### Limitations

None.

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### Search strategy

1. Embase 1974 to date – (exp HYPERSENSITIVITY/si AND ("ADRENALIN HYDROGEN TARTRATE PLUS ARTICAINE"/ OR "ADRENALIN HYDROGEN TARTRATE PLUS LIDOCAINE"/ OR "ADRENALIN HYDROGEN TARTRATE PLUS PRILOCAINE"/ OR "ADRENALIN PLUS LIDOCAINE"/ OR ARTICAINE/ OR BENZOCAINE/ OR LIDOCAINE/ OR PRILOCAINE/ OR "DENTAL ANESTHESIA"/)) [DT 2015-2019]".
2. Medline 1950 to date – (exp "DRUG HYPERSENSITIVITY"/ OR exp "HYPERSENSITIVITY, DELAYED"/ OR exp "HYPERSENSITIVITY, IMMEDIATE"/ OR "LATEX HYPERSENSITIVITY"/) AND (exp "ANESTHESIA, DENTAL"/ OR "ANESTHESIA, INTRAVENOUS"/ OR exp "ANESTHETICS, LOCAL"/)) [DT 2015-2019]".
3. Clinical experts – contacted in 2008 when developing the first issue of this Medicines Q&A:
  - Dr Lesley Longman, Consultant/Hon Senior Lecturer in Restorative Dentistry. Liverpool University Dental Hospital and School of Dentistry, Liverpool.
  - Dr Tina Dixon, Consultant Allergist. Royal Liverpool and Broadgreen University Hospitals, Liverpool.
4. In-house database/ resources.