Allergic reactions to lignocaine

I. A. Ball[1]

True allergic reactions to local analgesics are extremely rare. This case report illustrates the procedures adopted to manage a patient with a history of suspected allergy. A young woman was found to have a true type I hypersensitivity to lignocaine. Another routinely used local analgesic agent, prilocaine, was tested by the same methods and found to give no allergic response. Dental treatment was successfully completed using the latter and the patient advised to wear a medical alert bracelet.

It is widely claimed that adverse reactions to local analgesics are uncommon.[1] It has been estimated that half a million administrations of local analgesic are given each day in the USA,[2] and that around 70 million cartridges of dental local analgesic are given annually in the UK.[3] It has additionally been estimated that true allergic reactions account for less than 1% of all adverse reactions to local analgesic agents.[4,5] Thus genuine allergic reactions to local analgesics are extremely rare.[6] The overwhelming majority of adverse reactions to local analgesics are psychogenic in nature and related to fear.[7,8]

The Committee on Safety of Medicines (CSM) records a total of 702 reported cases (ie patients) showing an adverse reaction to both single and multiconstituent products containing lignocaine, from June 1964 until November 1997 (33 years). In relation to single constituency lignocaine products the CSM lists 8 non-specific allergic reactions, 13 anaphylactic reactions including 2 fatalities; 10 anaphylactoid reactions and one type 1 hypersensitivity reaction during this period, a total of 32 true allergic responses. For multiconstituent products containing lignocaine the CSM reports a total of 41 reactions for the same disorders during the same period. Because the Committee lists all the reactions included on each report, the total number of reactions usually exceeds the number of reports, ie patients. The Committee on Safety of Medicines is also at pains to point out that '...in most situations there is considerable under-reporting of reactions' and 'It has been estimated from various surveys that only 10–15% of serious adverse reactions are reported'. It should be mentioned that the corresponding figures for prilocaine are 217 reported cases with no fatal outcomes for both single and multiconstituent products during the same period. Twenty-seven came into the category of disorders of the immune system: 9 for single constituency products, 18 for multiconstituency products.

Adverse systemic reactions to local analgesics fall into four categories: toxic (drug overdose, rapid absorption, intravascular injection), psychogenic, idiosyncratic, or allergic.[8] True allergy to local analgesics may be either type I — immediate, anaphylactic reactions, mediated by IgE antibodies — or type IV — delayed hypersensitivity reactions mediated by sensitised lymphocytes. The latter type is most commonly expressed as a contact dermatitis and accounts for approximately 80% of all true allergic responses to local analgesics.[9] Type II responses are the result of IgE and IgM interactions with complement, causing a cytotoxic reaction, and type III immune reactions result in vascular or connective tissue oedema and inflammation. Type II and type III hypersensitivity responses have not been observed with local analgesic agents.[10]

In brief

- The overwhelming majority of adverse reactions to local analgesics are psychogenic in nature and related to fear.
- The Committe on Safety of Medicines lists a total of 32 true allergic responses in single constituency Lignocaine products in 33 years.
- Adverse systemic reactions to local analgesics fall into four categories: toxic, psychogenic, idiosyncratic or allergic.

Report of a case

A young woman of 20 years was referred to a community dental clinic for treatment because she had a history of allergy to local anaesthetic. She had been told by her general medical practitioner that she would cross-react with any local anaesthetic and that treatment would need to be under general anaesthesia. She also gave a history of atopy; suffering from hay-fever; asthma; and eczema, and allergies to a variety of antibiotics: Amoxyl, Cefadroxil and Furadantin.

She had been treated 12 months previously by her general medical practitioner for an in-growing toenail during which procedure she had received an injection of 1% lignocaine. She had remained well for 12 hours afterwards but then developed a widespread blotchy itchy rash (urticaria) which persisted for 1 week and was accompanied by asthma and some abdominal discomfort. She had previous experience of local analgesics from her dentist on about eight occasions without any untoward effects.

After examination and assessment in the community clinic the patient was referred to a consultant dermatologist for investigation to determine if the reported reaction was a genuine allergy to the lignocaine itself or to some other chemical in the local analgesic solution, for example a preservative agent, or perhaps even a constituent of the latex plunger. A skin prick test was performed with 1% lignocaine which gave a slight positive reaction. Subsequently an intradermal injection of 0.1% lignocaine was given to which the patient reacted

[1]*Registered Specialist in Paediatric Dentistry and Senior Clinical Dental Officer, Bath & West Community NHS Trust, Dental Department, NHS House, Newbridge Hill, Bath BA1 3QE*

REFEREED PAPER
Received 26.08.97; accepted 09.11.98
 186: 224–226

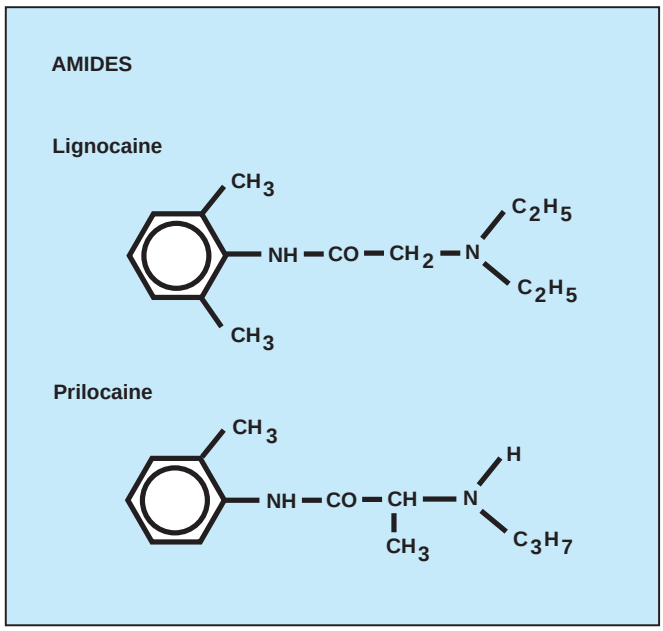

Fig. 1 The similarity between the molecular structure of lignocaine and prilocaine

immediately with a 1 cm diameter erythematous weal, which is a positive sign for a true type I hypersensitivity reaction.

The consultant dermatologist requested that suitable alternative dental local analgesic agents be suggested for testing by this method and therefore advice was sought from the pharmacist at the local district general hospital, who recommended a range of local analgesics both of the amino-amide and amino-ester types. The amino-amides were prilocaine and mepivicaine, and the amino-esters were procaine, amethocaine and meprylocaine. The dermatologist first tested prilocaine, the next most suitable alternative to lignocaine, by the skin prick test and then by intradermal injection and ultimately was able to administer 2 ml of prilocaine intradermally with complete skin analgesia and no reaction.

Routine dental treatment was subsequently carried out painlessly and uneventfully using prilocaine in a variety of injection techniques ranging from a simple infiltration injection, to an intraligamentary injection, and finally a maxillary molar block, which is a modified posterior superior alveolar block injection.[11]

The general medical practitioner and the referring general dental practitioner were then advised of the patient's true allergic status to lignocaine, and the patient was recommended to consider purchasing a medical alert bracelet carrying details of her allergy to lignocaine with information regarding the suitably safe alternative — prilocaine.

Discussion

This case report differs from numerous others including those by Levy and Baker 1986,[6] Bosco *et al.* 1993,[12] Doyle and Goepferd 1989,[13] and Jackson D, Chen A and Bennett C 1994.[1] These showed adverse reactions to local analgesics which mimicked symptoms characteristic of allergic responses, but which on subsequent investigation proved not to be caused by true allergies to local analgesic agents, as was the circumstance here. The adverse reactions reported were ascribed to a variety of causes ranging from an idiosyncratic, very low threshold to toxic side effects of 'caine drugs' entering the circulation in minute quantities; anaphylactoid reaction perhaps involving a psychogenic component; vagal response to local analgesic reaching the trigeminal ganglion; to idiopathic erythematous flush of the patient's face and neck. Tachycardia because of anxiety and overbreathing can also cause what the patient subsequently reports as 'collapse'.

Adverse systemic reactions to local analgesics fall into four categories: toxic, psychogenic, idiosyncratic, or allergic

It has been stated that the amide class of local analgesics is significantly less allergenic than the ester type, and there is also limited cross-reactivity between amide local analgesic agents.[14] However, the molecular structures of the two chemical agents involved in this case report — lignocaine and prilocaine (fig. 1) — are remarkably similar. Even minor variations in molecular structure can make all the difference to their allergenic status, such that cross reactivity will not occur within members of the same group.

The patient had received lignocaine on about eight previous occasions and yet had reported no adverse reaction. The general principle applies that the more contacts made with the allergen the more likely is it to induce an allergic reaction. Allergy does not usually manifest itself on a first exposure to a drug. Most patients who develop a true allergic reaction have had a previous exposure with either no reaction or only a very mild reaction. With each subsequent exposure the reaction becomes more severe.

In cases where there is a proven allergy to a large number of local analgesic agents, alternative methods of providing pain-free operative treatment must be sought, and these may include sedation, both conscious (relative analgesia) and intravenous, general anaesthesia, hypnosis or electronic dental analgesia.[15]

It is perhaps pertinent to conclude with a brief mention of the clinical signs and symptoms of allergy and its treatment in the context of what one might observe in one's surgery and the actions one should take in such an emergency. Signs and symptoms of type I allergy tend to occur within minutes of giving the injection. The lips and periorbital areas swell; the patient becomes agitated and there is generalised itching, particularly of the hands and feet. Tightness of the chest, with wheezing and difficulty in breathing, may occur, and a fall in blood pressure and a rapid thready pulse causes pallor. A true anaphylaxis would cause laryngeal oedema, bronchospasm and hypotension. Other distinctive signs and symptoms include urticaria, angioedema, sneezing and pruritus.

The mainstay of treatment, which must be immediate, is adrenaline. The dose is 0.01 ml per kilogram body weight up to a maximum of 1 ml of 1:1000 adrenaline solution (usually between 0.3 and 0.5 ml) which may be injected submucosally beneath the tongue so that rapid systemic absorption is assured from this highly vascular area, or alternatively intramuscularly. This is supplemented by antihistamine treatment with agents such as 10–20 mg chorpheniramine, or 50 mg hydroxyzine hydrochloride, or 50 mg promethazine hydrochloride given slowly by intravenous injection. Hydrocortisone 100 mg may also be given by intravenous injection.

During these procedures the airway must be secured and oxygen administered continuously to compensate for compromised ventilation. If the patient continues to deteriorate, immediate medical help must be summoned, as cardiac massage and intravenous infusion of plasma expanders may be required. One should record all drugs given, routes of administration and times of clinical signs and symptoms for future reference.

Although extremely rare, generalised anaphylaxis is rapid and life threatening, with sudden onset of syncope, hypotension, respiratory failure, and cardiac arrest, and death can occur within minutes of exposure to an insignificant amount of a drug.

The important point to make in any suspected case of allergy is to gain a clear and precise history of the patient's experiences from which to make a tentative diagnosis, even to the extent of persuading the patient to write down details of times and reactions as accurately as they can remember.

The author is indebted to Professor John Burton for his invaluable assistance in proof reading this manuscript and for his helpful suggestions for its improvement.

1 Jackson D, Chen A H, Bennett C R. Identifying true lidocaine allergy. *J Am Dent Assoc* 1994; **125**: 1364-1366.
2 Milam S B, Giovannitti J A, Bright D. Hypersensitivity to amide local anesthesia? *Oral Surg* 1983; **56**: 593-596.
3 Cawson R A, Curson I, Whittington D R. The hazards of dental local anaesthetics. *Br Dent J* 1983; **154**: 253-258.
4 Giovannitti J A, Bennett C R. Assessment of allergy to local anesthetics. *J Am Dent Assoc* 1979; **98**: 701-706.
5 Bennett C R. *Monheim's local anesthesia and pain control in dental practice.* 7th ed. St. Louis: Mosby 1984; 225-237.
6 Levy S M, Baker K A. Considerations in different diagnosis of adverse reactions to local anesthetic: report of a case. *J Am Dent Assoc* 1986; **113**: 271-273.
7 Verrill P J. Adverse reactions to local anaesthetics and vasoconstrictor drugs. *Practit* 1975; **214**: 380-385.
8 Malamed S F. *Handbook of local anesthesia*. 3rd ed. Chicago: Mosby, 1990.
9 Adriani J. Etiology and management of adverse reactions to local anesthetic. *Int Anesth Clin* Spring 1972; **10**: 127-151.
10 Canfield D W, Gage T W. A guideline to local anesthetic allergy testing. *Anesth Prog* Sept-Oct 1987; **34**: 157-163.
11 Adatia A K. Regional nerve block for maxillary permanent molars. *Br Dent J* 1976; **140**: 87-92.
12 Bosco D A, Haas D A, Young E R, Harrop K L. An anaphylactoid reaction following local anesthesia: a case report. *Anesth Pain Control Dent* 1993; **2**: 87-93.
13 Doyle K A, Goepferd S J. An allergy to local anesthetics? The consequences of a misdiagnosis. *ASDC J Dent Child* 1989; **56**: 103-106.
14 Glinert R J, Zachary C B. Local anesthetic allergy. Its recognition and avoidance. *J Dermatol Surg Oncol* 1991; **17**: 491-496.
15 Malamed S F, Quinn C L. Electronic dental anesthesia in a patient with suspected allergy to local anesthetics: a case report. *J Am Dent Assoc* 1988; **116**: 53-54.

BDJ Reduces Publication Times

We are delighted to announce that the time between acceptance of a research paper and publication is now (on average) between 1 and 2 months.

This reduction in waiting time is largely due to the efforts of the editorial team in streamlining our refereeing system over the last 2 years. A number of improvements have been included in our editorial process, including redesigning the refereeing form, updating our manuscript-tracking software and constantly reviewing and updating our administration. It is especially gratifying that we have reduced this waiting time from 6–8 months down to 1–2 months at a time when the number of manuscripts received at the *BDJ* office has doubled.

We hope to maintain this improvement in publication times for research papers in the future, and are now working on a similar plan to help reduce the waiting time for papers for the practice section as well.

Mike Grace, Editor