Severe Skin Hypersensitivity Reaction to Local Infiltrating Anaesthetic Agent

ABSTRACT

Although the incidence of allergic reactions to local anaesthetics has decreased, they are still documented. Allergic reactions may consist of cutaneous lesions, urticaria, oedema or anaphylactic reactions. Severe hypersensitive reaction to local infiltration resulting in thin, charred and parchment-like skin with subsequent granuloma formation requiring debridement has not been reported earlier. We report a case of severe local skin reaction to lignocaine which is known to contain methylparaben as a preservative.

KEYWORDS hypersensitivity reaction, local anaesthetic agent, methylparaben

CASE REPORT

A female patient aged 24 years, having 3 children with the last child birth being 6 months, was admitted in the hospital for conventional tubal ligation. The patient had no history of systemic disease or allergic reaction. Her general condition was fair, and abdomen was soft on examination. Vaginal bleeding was not present. Her pulse rate was 70/min and regular; her blood pressure reading was 120/82 mm of Hg.

Laboratory investigations

Haemoglobin was 11.1 g/dl, leucocyte count was 6000/mm³, differential white blood cell count revealed 76% polymorphs, 20% lymphocytes, 2% monocytes, 2% eosinophils and 0% basophils. Further, total red blood cell (TRBC) was 5.13 × 10¹²/mm³, packed cell volume (PCV) was 33.8% and platelet count was 231 × 10³/mm³. HIV spot, HbsAg spot and Venereal Disease Research Laboratory (VDRL/RPR) are nonreactive. Further, total red blood cell (TRBC) was 5.13 × 10¹²/mm³, packed cell volume (PCV) was 33.8% and platelet count was 231 × 10³/mm³. Total serum bilirubin was 0.7 mg/dl, that is, direct 0.45 mg/dl and indirect 0.25 mg/dl. Further, serum glutamic oxaloacetic transaminase (SGOT) was 29 IU/l and serum glutamic-pyruvic transaminase (SGPT) was 18 IU/l. Serum proteins: total 6.11 g/dl, that is, albumin (A) 3.2 g/dl and globulin (G) 2.91 g/dl, and the A/G ratio was 1:09. Blood urea was 34 mg/dl and serum creatinine was 0.74 mg/dl. Random blood sugar was 83 mg/dl. Blood group: ‘A’ positive, sickling of red blood cell (RBC) was negative. Urine pregnancy test was negative and pelvic ultrasound was normal. Urinalysis: Routine and microscopic urinalyses were normal. X-ray of chest: Normal

The patient was taken for a conventional tetanus toxoid (TT) tubal sterilization. Local infiltration of 2% lignocaine was done (Fig. 1); an incision was made and within few minutes it was detected that the skin around the incision became black and charred (Fig. 2). The skin was excised before closure of the operative wound but the charring extended around the wound and sloughed resulting in gaping of the wound. Resuturing of the wound was done with debridement. Daily dressing was carried out. Fortunately, the patient did not develop signs and symptoms of systemic toxicity and was discharged after 4 weeks in normal condition.
DISCUSSION

Methylparaben has been used as a preservative in the food, cosmetic and pharmaceutical industries for over 50 years. It is commonly used as a preservative not only in many cosmetic and pharmaceutical products but also in some food stuff. Further, it has been shown to be an effective antimicrobial agent, and is used primarily as a bacteriostatic agent to maintain the sterility of some dental anaesthetic solutions. The local anaesthetic solutions usually contain 0.1% methylparaben.

Parabens are allowed as preservatives in food stuff and the maximum daily ingestion for humans has been estimated as 4–6 mg/kg. In cosmetics, parabens are allowed in concentrations up to 1%. The local anaesthetic solutions usually contain 0.1% methylparaben.

The Cosmetic Ingredient Review (CIR) reviewed the safety of methylparaben, propylparaben and butylparaben in 1984 and concluded that they were safe for use in cosmetic products at levels up to 25%. Typically, parabens are used at levels ranging from 0.01% to 0.3%.

Methylparaben may be found naturally in fruits like blueberries where it has antimicrobial activity. It is completely absorbed through the skin or after ingestion, thence is hydrolyzed to parahydroxybenzoic acid and the resultant metabolites are rapidly excreted in the urine. However, there is no evidence of accumulation. Methylparaben has not been shown to be teratogenic, carcinogenic, mutagenic or embryotoxic. It does not appear to be irritating when used topically.

Local anaesthetic agents are commonly used in day-to-day practice. Occasionally a patient is found to have hypersensitive reaction and mostly the sensitivity test is not done.

Ester local anaesthetics are associated with higher incidence of allergic reactions due to one of their metabolites, paraaminobenzoic acid (PABA). Interestingly, PABA is structurally similar to methylparaben. Amide local anaesthetics do not metabolize to PABA and therefore hypersensitivity to amide methylparaben is rare.

Antioxidants (sodium metabisulphite, bisulphate, etc.) are added to local anaesthetic products that contain vasoconstrictors (epinephrine, levonordefrin, etc.) to prevent biodegradation by oxygen. Some patients may also be allergic to sulphites. It is rare that a patient would be allergic to both an ester and amide local anaesthetic. It may be difficult to determine the cause of allergy in the patient and therefore skin testing can be utilized.

A clinical study of 273 consecutive patients with chronic dermatitis who were patch tested to 5% paraben in petrolatum, had 0.8% overall incidence of paraben allergy.
Parabens are practically nonirritating and nonsensitising in the population with normal skin. Even when patients with chronic dermatitis are patch tested to a paraben mix, parabens generally induce sensitization in less than 4% of such individuals. Although parabens do penetrate the stratum corneum, metabolism of parabens takes place within viable skin, which is likely to result in only 1% non-metabolized parabens available for absorption into the body.1

Similar to ester anaesthetics, methylparaben also produces PABA as a metabolite, which is a highly allergenic substance related to various cases of hypersensitivity.1

A study revealed the lack of information regarding methylparaben concentration in the drug insert package, thus preventing the feasibility of avoiding the allergic reaction to methylparaben in susceptible patients.

Paraben mix sensitivity produces the classic allergic contact dermatitis reactions. Sometimes, it may be seen as a flare or spread of an existing treated rash. Paraben allergic hypersensitivity is common although rare in relation to its widespread use. Paraben mix allergy is diagnosed from the clinical history and by performing special allergy tests, that is, patch tests. Patch testing with 15% paraben mix in petrolatum is used.5

Allergic reactions to local anaesthetic agents may occur as a result of sensitivity to (1) either the ester or amide component, (2) the methylparaben used as a preservative in the multiple dose vials or (3) the antioxidants used in some formulations.

A cause of local toxicity is allergic reaction to PABA. PABA is a metabolic product of the degradation of ester class of local anaesthetics, such as procaine (novocaine), benzocaine and to a lesser degree amide class anaesthetics such as lidocaine and prilocaine.1 It is also a metabolic by-product of methylparaben, a preservative in multidose vials of lidocaine. When allergic response to injected anaesthetics does occur, it is most likely due to ester class of local anaesthetics. The amide class of local anaesthetics is far less likely to produce an allergic reaction.1

The toxicity reactions range from urticaria to anaphylaxis.1

The three basic immediate allergic reactions include anaphylaxis, serum sickness and the Arthus reaction. The Arthus reaction is a serious localised destructive response characterized by redness and oedema and later inductions with haemorrhage and necrosis. A common example of this allergic response is the dermatitis. Because the allergic response due to local anaesthetics and methylparaben is similar, it is easy to overlook the possibility of the somewhat obscure chemical, methylparaben, being the causative agent and assume that an observed hypersensitivity is due to the local anaesthetic.1

Systemic toxicity of local anaesthetics can be described by the direct effects on the immune system, blood (methaemoglobinemia), central nervous system (CNS) (tinnitus, tingling or numbness in mouth, motor twitching, grand mal seizures, coma, respiratory arrest and cardio-vascular system (CVS; bradycardia, cardiac arrhythmia, hypotension and cardiovascular collapse).5

The traditional classification for hypersensitivity reactions is that of Gell and Coombs6 and is currently the most commonly known classification system. It divides the hypersensitivity reactions into the following four types:

- Type I reactions (i.e., immediate hypersensitivity reactions)
- Type II reactions (i.e., cytotoxic hypersensitivity reactions)
- Type III reactions (immune complex reactions)
- Type IV reactions (i.e., delayed hypersensitivity reactions, cell-mediated immunity)

Although allergic dermatitis is termed an ‘allergic’ reaction (which usually refers to type I hypersensitivity), its pathophysiology actually involves a reaction that more correctly corresponds to types of T cells (CD4+) that destroy target cells on contact as well as activated macrophages that produce hydrolytic enzymes.7

Intravenous lipid emulsions, termed as lipid rescue by Dr. Guy Weinberg in 1998, may be useful for cardiotoxicity, as they act as a sink allowing for the removal of lipophilic toxins from the affected tissues. There is one published case report of successful treatment of refractory cardiac arrest in cases of bupropion and lamotrigine overdose using lipid emulsion.8

REFERENCES