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Delayed Allergic Reaction to ChloraPrep™ in Foot and Ankle Surgery

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ABSTRACT

Chlorhexidine-based skin preparations are frequently used in orthopaedic surgery. We report 2 recent cases of patients suffering significant allergic reactions to ChloraPrep™ complicating routine foot and ankle surgery. We advise vigilance for this possible issue and recommend thorough removal of all preparation at the end of the procedure.

Chlorhexidine-based skin preparations are frequently used in orthopaedic surgery. Our hospital has recently adopted the use of a prepackaged surgical site preparation system containing chlorhexidine gluconate 2% weight/volume (w/v), isopropyl alcohol 70% w/v, and sunset yellow coloring (E110) (ChloraPrep™ With Tint; CareFusion, San Diego, CA). Chlorhexidine is a bisbiguanide with bacteriostatic and bactericidal activity against a broad range of microorganisms (1,2). Studies have suggested that alcohol-based chlorhexidine surgical preparations have increased efficacy in eliminating bacteria from the foot compared with other preparation solutions (3–5). There is no high-quality evidence of reduced surgical site infection with the use of chlorhexidine-containing preparations (6), and recently published guidelines on prevention of periprosthetic joint infection advocate only that alcohol should be involved in the preparation of surgical sites (7). We report 2 recent cases of allergic reaction to ChloraPrep™ With Tint following foot and ankle surgery. We believe that it is important to raise awareness of this potentially serious issue and suggest strategies to attempt to mitigate it.

Case Report

Case 1

A 40-year-old male underwent a routine hallux metatarsophalangeal joint fusion as a day case in August 2017. The lower extremity was prepared using ChloraPrep™ With Tint from the thigh tourniquet to the toes following the manufacturer's application instructions, including allowing the solution to completely dry for 3 minutes. The tourniquet time was 73 minutes. The patient had no prior history of allergies or contact dermatitis. The patient's foot was washed with saline solution prior to the application of a dressing, orthopaedic wool, and a crepe bandage. From the evening of the surgery, the patient developed a pruritic rash from the mid-thigh to the ankle. Over the following days, the rash intensified; he attended clinic on the fourth postoperative day. On examination, he had an erythematous lower limb with elevated eruptions demonstrating clear demarcation at the tourniquet site and the ankle (Fig. 1). In addition, the medial aspect of the contralateral knee was affected in the area where it contacted the operated leg. Despite taking 4-mg chlorphenamine by mouth 4 times daily, the rash progressed and he was admitted for intravenous flucloxacillin (1 g 4 times daily) for a secondary bacterial infection (Fig. 2). The rash settled over the following 2 weeks with oral flucloxacillin (1 g 4 times daily for 1 week) and betamethasone 0.1% with fusidic acid cream (topical application 2 times daily). His surgical wound was unaffected, and he went on to make a complete recovery with successful fusion.

Case 2

A 71-year-old female underwent a right fifth toe hammer toe correction as a day case in August 2017. The lower extremity was prepared using ChloraPrep™ With Tint from the thigh tourniquet to the toes following the manufacturer's application instructions, including allowing the solution to completely dry for 3 minutes. The tourniquet time was 25 minutes. She had no relevant past medical history. Two days

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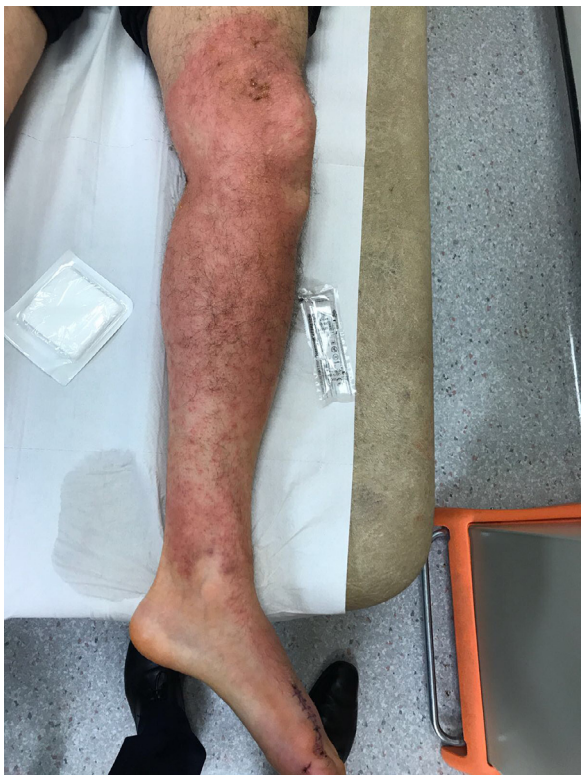

Fig. 1. Case 1: Day 4 postoperative. Allergic reaction with clear lines of demarcation at the ankle and level of thigh tourniquet.

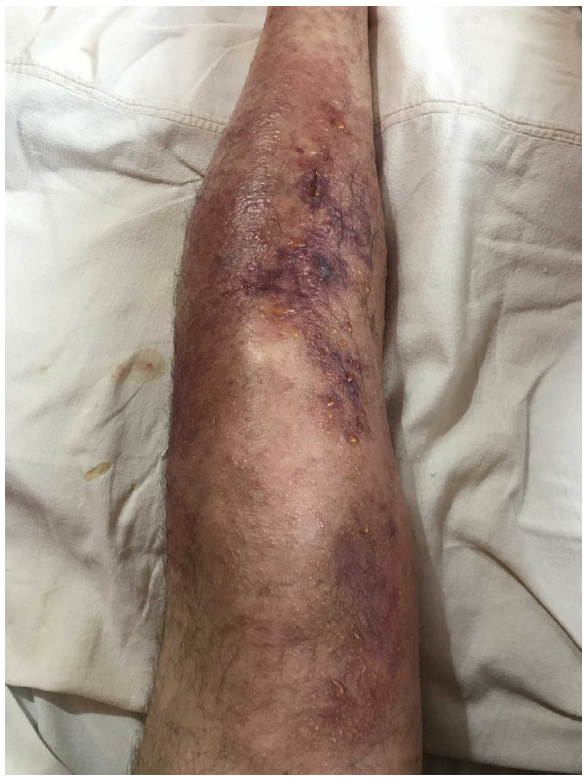

Fig. 2. Case 1: Day 6 postoperative. Secondary bacterial skin infection.

following surgery, she developed a raised erythematous rash across the entire operated lower limb (Fig. 3). She went to the emergency department, where she was diagnosed with an allergic reaction and treated with chlorphenamine 4 mg by mouth 4 times daily. Further treatment was required from her general practitioner with a single dose of prednisolone 30 mg by mouth, cetirizine 10 mg by mouth 1 time daily, betamethasone 0.1% cream (topical application 2 times daily), and topical emollients. The rash settled after 2 weeks, and she went on to have an uncomplicated postoperative recovery.

Discussion

Hypersensitivity to chlorhexidine has been reported in various forms, including contact dermatitis (8), urticaria (9), and anaphylaxis (10,11). The exact incidence of allergy to chlorhexidine is unknown—patch testing has been reported as positive for chlorhexidine in 2% of patients (12) and in up to 5% of those with eczema (13). The manufacturers report a <1 in 10,000 rate of allergic or irritated skin reactions with ChloraPrep™ (14). In 2012, the United Kingdom Medicines and Healthcare products Regulatory Agency issued a medical device alert about the risk of anaphylactic reaction owing to chlorhexidine allergy (15).

To reduce the risk of complications from the use of ChloraPrep™, the manufacturer advises using it only on intact skin with the avoidance of an overvigorous application technique in those with frail skin. The product should be avoided in those with a known or suspected allergy to chlorhexidine. The manufacturer advises that the preparation can be left on the skin after the procedure (14). The sparing of the foot from allergic reaction in Case 1 may be the result of this area being thoroughly washed with saline prior to the application of dressings. We believe that inadequate removal of the preparation following surgery may contribute to a postoperative allergic reaction. Prolonged exposure to chlorhexidine is felt to be related to the development of contact sensitization (8).

In hindsight, we would advise the thorough and complete removal of all skin preparation at the end of the procedure with the use of copious amounts of sterile saline or water, but we do not know whether this would reduce the risk of late allergy. This is especially relevant in extremity surgery, where large areas of skin distant to the operative site are routinely prepared to allow for appropriate sterile draping. Fig. 4 provides strategies to attempt to reduce the risk of allergic reactions to ChloraPrep™ and potential management options.

One of our gravest concerns is that the manufacturer suggests an allergy incidence of 1 in 10,000; however, based on our own findings, it would be

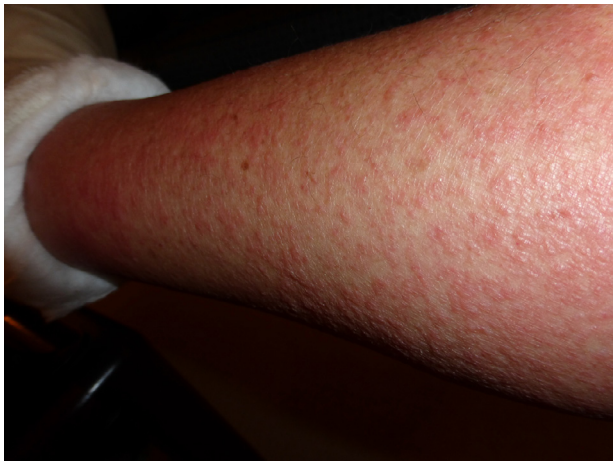

Fig. 3. Case 2: Day 4 postoperative. Raised erythematous rash across leg.

Prior to surgery

- Ask patient if known history of allergy to chlorhexidine or other constituents of ChloraPrep ™
- Ask patient if history of atopic diseases including eczema

Intra-operative

- Thorough and complete removal of all skin preparation with copious sterile saline solution at the end of procedure

Post-operative

- Inform patient of symptoms of allergic reaction and importance of seeking urgent medical advice if they occur
- If allergy occurs for immediate treatment with chlorphenamine and urgent referral to dermatologist for further assessment and management

Fig. 4. Strategies to reduce risk of allergic reaction to ChloraPrep™ skin preparation.

>1 in 1000. We have reported the reactions to the United Kingdom Medicines and Healthcare products Regulatory Agency and would advise others encountering similar reactions to report them to the appropriate organization, such as the US Food and Drug Administration.

In conclusion, each 26-mL ChloraPrep™ With Tint applicator costs $8.98 (16)—a minimum of 2 are required per case. In comparison, a 500-mL bottle of povidone-iodine 10% alcoholic tincture (Videne; Ecolab UK, Northwich, UK]) costs $8.93 (17). Our recent experiences of postoperative allergy from ChloraPrep™ have increased our awareness of potential issues with chlorhexidine-based preparations; this together with its increased cost has led us to reconsider our routine use of the product.

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