

Chlorhexidine-induced IgE-mediated allergy in a 6-year-old child

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Clinical Implications

- There is a global lack of recognition regarding chlorhexidine as a potential allergen leading to unfortunate re-exposures. Practitioners need to be aware of potential IgE-mediated allergy after topical chlorhexidine application on mucosae or wounds, even in children.

TO THE EDITOR:

Chlorhexidine is a synthetic chlorophenyl-bis-biguanide widely used as an antiseptic in both medical and nonmedical settings. Immediate chlorhexidine allergy has been reported, mainly in adulthood, since the 1980s. However, it remains relatively unknown despite previous governmental warnings on hypersensitivity reactions to chlorhexidine-impregnated central venous catheters (CVCs) and other products containing chlorhexidine in Japan, the United States, and more recently in Australia.¹ In addition, chlorhexidine is also increasingly recognized as a cause of perioperative allergy in the United Kingdom² and Denmark,³ although not in France. We report here an uncommon pediatric case of IgE-mediated chlorhexidine allergy.

Within minutes of a 2% aqueous chlorhexidine application on a hip wound, a 6-year-old boy, with no history of atopy, experienced a grade I reaction according to the Ring and Messmer scale,⁴ consistent with a widespread itching erythema with subsequent edematous fingers and lower limbs. Clinical signs subsided within 30 minutes after desloratadine.

During the previous 6 months, this young patient had already experienced, on 3 separate occasions, immediate hypersensitivity after topical chlorhexidine application on abraded skin. These events were handled by our pediatric emergency department. The third of these occasions occurred 1 month previously, in the following manner. Within minutes of a topical chlorhexidine application on a cheek wound, a localized urticaria occurred and expanded along with hemifacial and palpebral angioedema (Figure 1). At the time, the emergency practitioners did not advocate chlorhexidine-induced allergy due to the global lack of recognition regarding chlorhexidine as a potential allergen. These 4 clinical events were all characterized by the onset of the first symptoms around the wound bed and an increasing severity during subsequent topical chlorhexidine applications.

Chlorhexidine-induced allergy was suggested by the emergency medical practitioner in charge after this fourth clinical event. Serum tryptase exhibited a 6-fold increase (24.5 µg/L; normal <13.5) 60 minutes after the onset of clinical features, when compared with baseline tryptase (3.9 µg/L) measured

when skin testing was performed 4 weeks later. A prick-test with 0.2% (2 mg/mL) aqueous chlorhexidine was strongly positive leading to a 5-mm-diameter wheal surrounded by an itching erythema, whereas the serum-specific chlorhexidine IgE level (ThermoFisher Scientific, Uppsala, Sweden) was markedly increased (54.3 kUA/L; normal <0.1).

IgE-mediated chlorhexidine allergy was therefore evidenced according to the criteria recently suggested by Opstrup et al.⁵ These criteria are consistent with at least one or more previous relevant clinical reactions to chlorhexidine combined with increased specific IgE and a positive prick-test with chlorhexidine. Our young patient and his mother were advised to avoid all formulations containing chlorhexidine. An emergency kit including desloratadine and betamethasone was delivered. The mother informed the school staff and provided the school nurse with medical documentation. Nine months after this allergological assessment, the child fell at school with a subsequent skin knee wound. Despite stating that he was allergic to chlorhexidine, his complaint was not taken seriously and chlorhexidine spray was applied. Within minutes, he experienced highly pruriginous urticaria beginning around the wound bed that spread to the corresponding leg. The clinical signs subsided after desloratadine and betamethasone.

Immediate chlorhexidine allergy has been widely reported in adults³ because IgE-mediated drug allergy is more likely to occur in adulthood.⁴ Only 3 cases of chlorhexidine allergy have been published in children for whom the diagnosis was supported by a suggestive clinical presentation and positive skin tests with chlorhexidine as specific chlorhexidine IgE measurement was not available at that time. The last case was published 25 years ago.⁶

Immediate chlorhexidine allergy has been primarily reported after chlorhexidine-coated-CVC insertion or during surgery, after surgical site or mucosae, or wound surfaces application.³ The mucosal route seems to be overrepresented and the products mostly reported to cause allergic reactions are the urethral gels containing chlorhexidine.³ Three decades ago, the lowest concentration (0.05%) of chlorhexidine was recommended to be used on wound surfaces, whereas its use on mucosae was prohibited in Japan. However, this latter recommendation is not implemented in other countries.³ In France, alcoholic chlorhexidine or povidone iodine solutions are recommended for use before surgical procedures, on unbroken skin only, whereas the chlorhexidine concentration to be used (2% vs 0.5%) has not been defined as further studies are required.⁷ In addition, different aqueous or alcoholic chlorhexidine solutions, 0.05%, 0.2%, 0.5%, and even 2%, are available over-the-counter in our country.

However, the lack of knowledge about allergy to chlorhexidine among health care personnel and the population at large leads to unfortunate re-exposures to chlorhexidine both before and after a diagnosis is made. This emphasizes the need for effective risk communication. Opstrup et al.⁸ recently reported that 35% of patients diagnosed with chlorhexidine allergy experienced accidental re-exposures, and that the highest risk of re-exposure seems to be in the perioperative setting. Most of these re-exposures elicited symptoms and were followed by an



FIGURE 1. Within minutes of a topical chlorhexidine application on a cheek wound, a localized urticaria occurred and expanded along with hemifacial and palpebral angioedema.

increase in specific IgE. In our patient, this fifth clinical event was still consistent with a grade I reaction (ie, cutaneous-mucous signs),⁴ whereas the specific IgE level was not measured after chlorhexidine re-exposure. The delivered emergency kit therefore did not include an epinephrine autoinjector as this young patient had only mild reactions all responding to antihistamines and/or steroids. Thus, epinephrine should be restricted to the treatment of severe cardiovascular disturbances including allergic cardiovascular collapse or circulatory arrest, that is, anaphylaxis.⁴ In addition, the dangers of intravenous or intramuscular epinephrine administration outside the context of anaphylaxis have even been highlighted by the report of serious adverse outcomes.⁹

In conclusion, despite the 6-year-old child being aware of the need to avoid all contact with chlorhexidine, it was not enough to prevent re-exposure. Allergy to chlorhexidine remains largely unknown among health care providers and the population at large. Chlorhexidine allergic patients should

always be advised to avoid all contact with chlorhexidine, whereas practitioners need to be informed about potential IgE-mediated allergy after topical chlorhexidine on mucosae or wounds, even in children.

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