

## Severe anaphylaxis to the antiseptic polyhexanide

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An 81-year-old female patient experienced symptoms of a grade III anaphylaxis with palmar pruritus, flush, swelling of the lips, swallowing difficulties, hypotension and loss of consciousness while

using a new brand of wet toilet paper containing polyhexanide as disinfectant.

The detailed allergy history revealed that the patient had experienced three similar

anaphylactic episodes (grade II) during wound care of an existing leg ulcer, once when using a new wound dressing that contained polyhexanide (Suprasorb PHMB) and twice after wound cleansing with two different polyhexanide disinfectants (Lavanid 1 and Pronto-san). The patient had no known allergies or atopic diseases. Total IgE was elevated (411 kU/l), there were no specific IgE detected for common seasonal and perennial inhalation allergens, base line mast cell tryptase was normal (3.07 µg/l). Skin prick tests

(SPT) were positive for Lavanid 1 in a 1 : 10 dilution corresponding to 20 µg/ml polyhexanide. Except for polyethylene glycol (PEG) 4000, Lavanid 1 contains no other additives. SPT performed with PEG 4000 was negative. SPT with chlorhexidine in different commercial preparations was positive. None of five healthy volunteers tested positive using the same test preparations for polyhexanide and chlorhexidine. Analysis of specific IgE (ImmunoCAP; Phadia, Uppsala, Sweden) revealed specific IgE to chlorhexidine (0.88 kU<sub>A</sub>/l) and polyhexanide (16.5 kU<sub>A</sub>/l) (a result  $\geq 0.35$  kU<sub>A</sub>/l was considered positive). The polyhexanide ImmunoCAP was an experimental prototype, and the chlorhexidine ImmunoCAP was the

regular product c8 (ImmunoCAP; Phadia).

Polyhexanide is a poly-biguanide antiseptic, which is widely used, for example, in contact lens solutions, wound dressings, pool cleaners and in cosmetics. It is reported to have an excellent tissue compatibility, to be non-cytotoxic, nonirritating and nonsensitizing (1). Only two reports about allergic reactions to polyhexanide exist, in each case anaphylactic reactions during surgery are described (2, 3). Allergic reactions to another biguanide antiseptic, chlorhexidine, are well known (4), and an IgE-mediated mechanism has been established (5, 6). The diagnosis of polyhexanide allergy in previous reports was based on history and SPT

### First report of anaphylaxis to polyhexanide, a widely used antiseptic, with confirmed IgE-mediated mechanism.

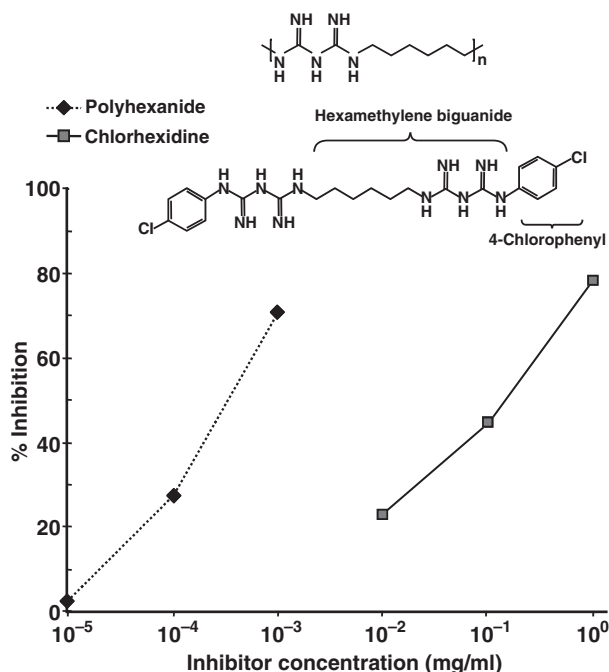


**Figure 1** Inhibition of sIgE binding to polyhexanide ImmunoCAP prototype by preincubation of patient's serum with increasing concentrations of polyhexanide (diamonds) or chlorhexidine (squares).

(2) or history alone (3). To our knowledge, the patient presented here is the first case of anaphylaxis to polyhexanide with a confirmed IgE-mediated mechanism.

The way of sensitization in the presented case is unclear. The use of the polyhexanide containing wound dressing, which led to anaphylaxis, was the first documented contact to polyhexanide. It may be speculated that the former use of chlorhexidine sensitized the patient. No studies on the allergenic determinants of polyhexanide have been performed. Polyhexanide is a hexamethylene biguanide polymer. With chlorhexidine, it shares the hexamethylene biguanide, but lacks the 4-chlorophenyl aromatic ring present in chlorhexidine (Fig. 1). Therefore, a partial cross-reactivity with chlorhexidine could be expected. To address this question, we performed inhibition studies: varying concentrations of polyhexanide and chlorhexidine digluconate were added to the patient serum, and a 50% inhibition of the assay response was achieved at a polyhexanide concentration of 0.34 µg/ml and a chlorhexidine concentration of 145 µg/ml (Fig. 1). The results from this inhibition study indicate a limited *in vitro* cross-reactivity between polyhexanide and chlorhexidine, with a higher relative avidity of the patient's IgE antibodies

to polyhexanide compared with chlorhexidine. As a clinical consequence, patients with known chlorhexidine allergy could be at risk for anaphylactic reactions to polyhexanide.

However, sera from three patients with a history of chlorhexidine allergy and sIgE to chlorhexidine ranging from 1.0 to 28.1 kU<sub>A</sub>/l tested negative for sIgE to polyhexanide, suggesting that the earlier reported patient displayed a genuine polyhexanide sensitization. Patients and health care workers should be aware of polyhexanide as a potential allergen and need to be informed that polyhexanide is often also declared as polyhexamethylenebiguanide or as polyaminopropylbiguanide. This work was in part funded by a research grant from Phadia to TJ.

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