

A case of anaphylaxis caused by polyethylene glycol analogues

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doi:10.1111/cod.12084

Key words: anaphylaxis; hydroxyethylated starch; poly(oxyethylene)poly(oxypropylene) glycol; polyethylene glycol; polysorbate 80.

PEGs and polysorbates are found in many pharmaceuticals, cosmetics, and foods (1, 2). We report the first patient with anaphylaxis caused by PEGs and polysorbate 80 that were cross-reactive with hydroxyethyl starch.

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Conflicts of interest: The authors have declared no conflicts.

Case Report

A 33-year-old man had undergone surgery for lumbar disc herniation. He went into anaphylactic shock a few minutes after the application of povidone-iodine gel to the dead space resulting from the surgery. He was successfully treated with intravenous corticosteroids and adrenaline. He reported a history of wheezing after using shampoo containing phenothrin. We performed prick tests with the constituents of the povidone-iodine gel and the phenothrin shampoo. A negative saline control and a positive histamine (10 mg/ml) control test were included. The positive wheal was 7×5 mm, and the negative

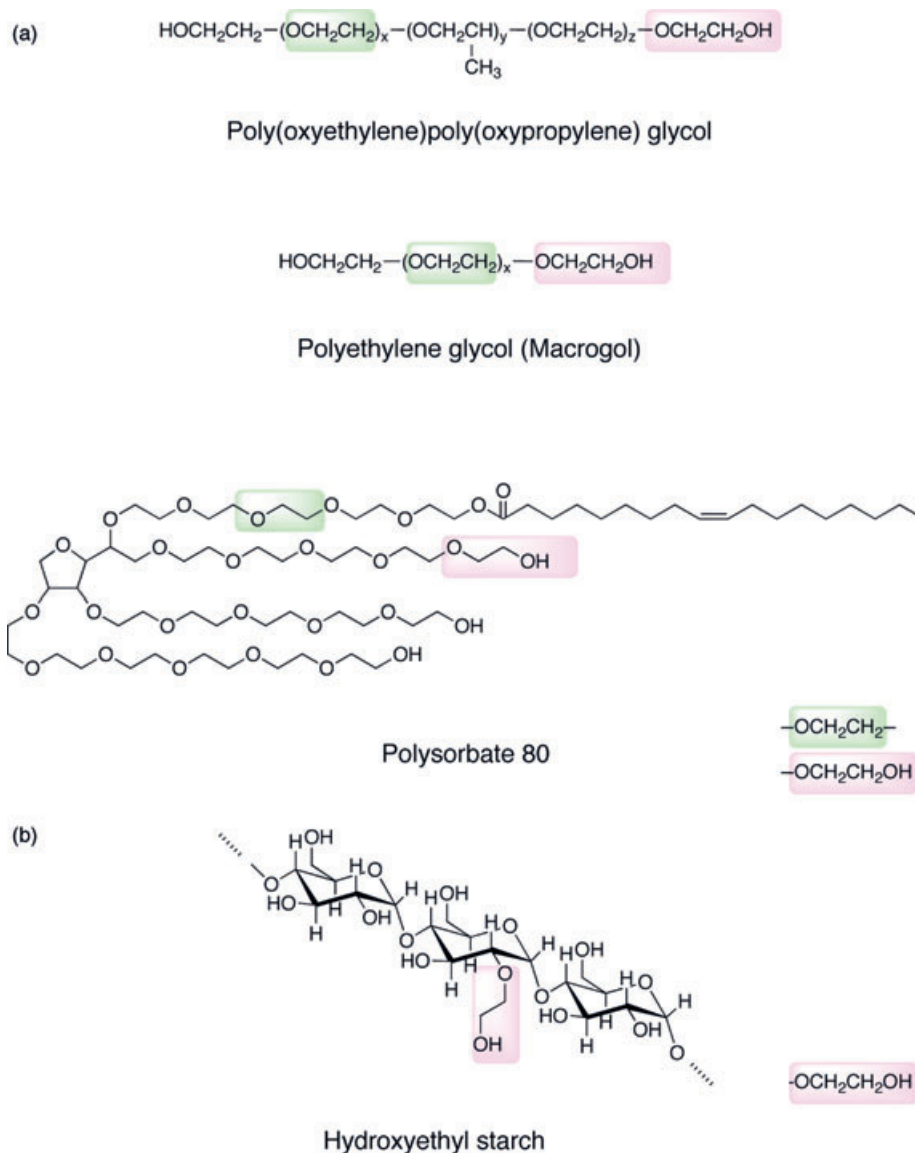


Fig. 1. (a) The chemical moieties of poly(oxyethylene)poly(oxypropylene) glycol, polyethylene glycols, and polysorbate 80. They have the same chemical moiety: $-(\text{CH}_2\text{CH}_2\text{O})_n-$. (b) The hydroxyethylated starch contains the chemical moiety $-\text{OCH}_2\text{CH}_2\text{OH}$.

control gave no reaction. A minimal wheal diameter of ≥ 3 mm at 15 min was considered to be positive (3). POEPOP, polysorbate 80 and PEG 6000 (CAS no. 9003-11-6, 9005-65-6, and 25322-68-3) elicited positive reactions (Table 1). As they have a common structure, $-(\text{CH}_2\text{CH}_2\text{O})_n-$ (Fig. 1a), we attributed the patient's anaphylaxis to these PEG analogues. We prescribed an epinephrine auto-injector, and instructed him to avoid PEG analogues when taking new, over-the-counter drugs.

Six months later, he had a traffic accident and required surgery under general anaesthesia for a clavicle fracture.

On the basis of the information that we provided, his physicians ascertained the absence of PEG analogues in all drugs used to treat this patient. However, he went into anaphylactic shock intraoperatively, and required extubation 3 hr after the operation, because his vital signs became unstable. We subsequently found that the hydroxyethylated starch solution (Hespander[®]) used has a chemical moiety $(-\text{OCH}_2\text{CH}_2\text{OH})$ similar to $-(\text{CH}_2\text{CH}_2\text{O})_n-$ (Fig. 1b). The prick test for hydroxyethylated starch was positive (Table 2).

Table 1. Results of the first prick tests

Tested substance	Concentration (%)	Reading
Phenothrin shampoo		
Phenothrin	–	Not tested
Alkyl dimethylamine oxide	0.01	–
POEPOPG	0.01	+
Polysorbate 80	0.1	+
Edetic acid sodium	1	–
Fragrance	1	–
Povidone-iodine gel		
Povidone iodine	1	–
PEG 400	1	–
PEG 4000	1	–
PEG 6000	0.01	+

PEG, polyethylene glycol; POEPOPG, poly(oxyethylene)-poly(oxypropylene) glycol.

Discussion

Allergic reactions to PEG, polysorbate 80, and hydroxyethylated starch solution, but not to POEPOPG, have been reported (1, 2, 4, 5). We present here the first case of anaphylaxis showing cross-reactivity with PEG analogues, including POEPOPG and hydroxyethyl starch. Although these compounds are present in many foods, cosmetics, and pharmaceuticals, the mechanism(s) of PEG allergy is not entirely clear. Shah et al. (2), who reported on a patient with hypersensitivity to PEG 3350, suggested that multivalent PEG polymers may be large enough to be complete allergens without haptentation,

Table 2. Results of the second prick tests

Tested substance	Concentration (%)	Reading
Hespander®	0.10	+
Hydroxyethyl starch	0.01	+
Hespander® without hydroxyethyl starch	0.01	–
Lidocaine jelly	'as is'	–

and that larger PEG polymers are more immunogenic. The results of our prick tests support their suggestion.

The reactions to PEG analogues are diverse. Our patient experienced anaphylaxis in response to laxatives containing PEG 4000, although the test for this compound gave a negative result. On the other hand, anaphylaxis was not elicited by oral antibiotics containing PEG 6000 as an excipient, although the prick test for PEG 6000 gave a positive result.

Sohy et al. (4) reported on a patient who suffered anaphylaxis in response to PEG 4000 introduced by intra-articular injection. They orally challenged their patient with PEG 4000, delivered at a dose of 1 mg initially, and with the dose then being increased at 30-min intervals. Palmo-plantar pruritus developed 30 min after the ingestion of a cumulative dose of 7.1 g, which is equivalent to the minimal dose in osmotic laxatives. Subsequently, oedema of the lips, eyelids, feet and hands appeared. They concluded that the amount of ingested PEG is critical for eliciting hypersensitivity.

Anaphylactic reactions to PEG analogues may be dependent on both dose and route. We must be alert to the cross-reactivity between PEG analogues and hydroxyethylated starch.

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