

Macrogol hypersensitivity reactions during cleansing preparation for colon endoscopy

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Clinical Implication

- Anaphylaxis during bowel-cleansing preparation due to macrogol allergy is a possibility that should be taken into account by both gastrointestinal endoscopists and allergists, who should collaborate more closely to improve the safety of the endoscopic diagnostic procedure.

TO THE EDITOR:

Macrogols are polymers of ethylene glycol (PEG) that are widely used as laxatives (higher-weight variants) or as excipients in pharmaceutical products (lower-weight variants), for example, as solvents in oral liquids and soft capsules. In colon endoscopy or surgery and in radiologic examinations of the large and small intestines, macrogols are used as osmotic laxatives to minimize fecal contamination. Generally, PEG preparations are well tolerated and safe, although the National Patient Safety Agency¹ issued a report that alerted health care providers to the potential risk of adverse reaction to all oral bowel-cleansing preparations. With regard to macrogols, risks are frequently associated with electrolyte disturbances, whereas hypersensitivity reactions are rarely reported.²⁻⁸

Herein, we describe the case of a 55-year-old man referred to our outpatient allergy clinic for a suspected reaction to an osmotic preparation for colon endoscopy. He reported a runny nose, sneezing, and mild urticaria several minutes after intake of approximately half of a liter of the conventional dose of 4 L of PEG 4000 (SELG; Promefarm, Milan, Italy). His symptoms rapidly improved after fexofenadine 180 mg and prednisone 25 mg administration. The colon endoscopy was rescheduled, and it was suggested that the patient use a different bowel preparation with a smaller volume (2 L) of liquid. However, unfortunately, the preparation still contained PEG 4000 (Lovel-esse; Promefarm, Milan, Italy). Ten minutes after intake of the first glass of the solution, the patient reported a feeling of moderate throat closure, together with chest tightness, dyspnea, face erythema, and near fainting. The patient was admitted to the emergency department, where he recovered after receiving a saline solution infusion, intramuscular epinephrine 0.5 mg, and intravenous methylprednisolone 125 mg.

One month after the last suspected hypersensitivity reaction, the patient underwent an allergologic evaluation, which consisted of skin prick tests with macrogol 4000 (100 mg/mL) at different dilutions (1/1000, 1/100, and 1/10), which yielded a positive result at a 1/10 concentration (14-mm wheal diameter; histamine, 8 mm; control solution, 2 mm). Five healthy subjects without atopy and 5 subjects with atopy served as controls for the skin prick test with Macrogol 4000 at a 1/10 dilution, all of whom tested negative.

The patient reported a previous adverse drug reaction 2 years earlier, which consisted of the rapid onset of generalized urticaria soon after intake of a soft capsule that contained nimesulide (Mesulid; Helsinn Birex Pharmaceuticals Ltd, Dublin, Ireland), which also contains macrogol (cetomacrogol 1000). An *in vivo* oral tolerance test with a nimesulide formulation that did not contain macrogol was well tolerated by the patient. Colonoscopy was subsequently safely performed after the patient used a sodium phosphate solution for bowel preparation.

In conclusion, herein, we reported a case of 2 consecutive episodes of hypersensitivity reactions after intake of a bowel preparation that contained PEG 4000 in a patient with a previous hypersensitivity reaction to a soft capsule that contained macrogol. The systemic reactions reported by our patient seemed to be IgE dependent, because his positive skin prick test results suggested a Type 1 reaction. The patient was advised to systematically check drugs and products that potentially contained macrogol, including cosmetics and preserved foods.

We suspect that allergic reactions to macrogols may be underreported. Different types of macrogols are widely used in pharmaceutical preparations, softening agents, and lubricants, according to their molecular weight (which range from 200 to 20000 g/mol). In the literature, severe adverse allergic reactions to PEG have been reported after intake of tablet or pill drug formulations³ or of topical⁴ or injectable corticosteroids.⁵ Anaphylactic reactions due to electrolyte lavage solutions that contained Macrogol 4000 have been described since the 1990s.⁶ Belsey et al⁷ systematically reviewed all adverse reactions to PEG and oral sodium phosphate (another laxative) reported in the literature. In this study, 5 of 28 adverse events (17.8%) reported for PEG were clearly hypersensitivity reactions (ie, anaphylaxis, urticaria, and angioedema), whereas none of the adverse events reported for oral sodium phosphate were due to an allergic reaction. Moreover, when considering governmental databases of reported adverse events, the prevalence of suspected hypersensitivity reactions to PEG is similar to what has been reported by Belsey et al.⁷ As an example, the Adverse Reaction Database of Health Canada⁸ received reports of 111 cases of adverse reactions to PEG from 1971 to October 2013, 23 (20.7%) of which were due to allergic reactions, whereas none of the reported adverse reactions to oral sodium phosphate were a hypersensitivity reaction.

A diagnostic allergy workup provides the opportunity to investigate possible sensitization to PEG by *in vivo* skin prick tests and/or intradermal tests or *in vitro* analysis (ie, the basophil activation test).³ Certainly, the symptoms reported by our patient after the first bowel preparation should have suggested prompt allergologic evaluation. Therefore, we suggest that a closer collaboration between gastrointestinal endoscopists and allergists is desirable to improve the safety of the endoscopic diagnostic procedure. This collaboration may be particularly important in light of a recent report on the poor effectiveness of premedication and desensitization for hypersensitivity reactions to PEG.⁹ It is well known that premedication is not expected to be completely successful against presumed IgE-mediated reactions.

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