

Letter

MACROGOL HYPERSENSITIVITY IN MULTIPLE DRUG ALLERGY

Polyethylene glycols (macrogols) are condensation products of glycols with ethylene oxide and are widely used as excipients in food, cosmetics, and topical and systemic drugs because of their stabilizing properties. Although macrogols are used frequently and extensively, only a few immediate hypersensitivity reactions have been reported, probably because they are poorly absorbed by the gastrointestinal tract. Immediate hypersensitivity reactions have been reported after parenteral and oral administration of products containing macrogols, such as corticosteroids,^{1,2} laxative oral solutions,³ and tablets.^{4,5} We report the first case, to our knowledge, of a positive basophil activation test result after exposure to macrogol in a patient who reported systemic reactions after the oral intake of 2 different drugs in 2 different pharmaceutical preparations (granules and syrup) containing macrogols 4,000 and 6,000.

A 46-year-old man, without a previous history of allergy, was referred to our outpatient clinic for suspected drug reactions. He reported mild urticaria and mouth itching a few minutes after the intake of nimesulide granules (Nimesulide DOC, containing macrogol 4,000; DOC Generici, Milan, Italy). A few months later, after 1 dose of paracetamol syrup (Tachipirina, containing macrogol 6,000; Angelini Farmaceutica, S.A., Barcelona, Spain), he rapidly developed generalized urticaria, face and neck angioedema, and dyspnea, requiring medical assistance in an emergency department, where he recovered after antihistamine and intravenous methylprednisolone. Metamizole, ibuprofen, and acetylsalicylic acid (without macrogol) were well tolerated after these episodes. He also reported skin erythema using some types of bath soap and shaving cream. Standard patch test series (ALK-Abelló, Madrid, Spain), a shaving cream series (cetyl alcohol, stearyl alcohol, cinnamic alcohol, camphor, menthol, sorbitan monolaurate, triethanolamine), and polyethylene glycol patch (F.I.R.M.A., Muggiò, Italy) tests were performed, resulting in positive results for thimerosal, balsam of Peru, and menthol. A prick test with paracetamol syrup 1:1 gave a positive reaction with a wheal that increased in size up to 30 mm in diameter after 30 minutes, when he developed face and neck erythema and a mild throat closure feeling, at which point he was treated with ebastine (20 mg) and methylprednisolone (40 mg) with rapid resolution of symptoms. One month later, skin prick tests with injectable paracetamol (Perfalgan; Bristol-Myers Squibb, New York, New York), which does not contain any macrogol, from 1/10,000 to 1/1 were performed, with negative results. The graduated oral challenge with paracetamol tablets was tolerated up to a cumulative dose of 1 g. Specific ethylene oxide IgE (ImmunoCAP; Phadia, Uppsala, Sweden) test results were negative. Afterward, a skin prick test with macrogol 400 (100 mg/mL starting from 1/10,000 to 1/1) was performed with negative results, whereas skin prick test results with macrogol 4,000 and 6,000 (100 mg/mL at 1/10,000 dilution) were positive (wheal diameter, 6 mm). The results of skin prick tests with paracetamol syrup and macrogols 400, 4,000, and 6,000 were negative in 10 nonatopic controls. The CD203 basophil activation test

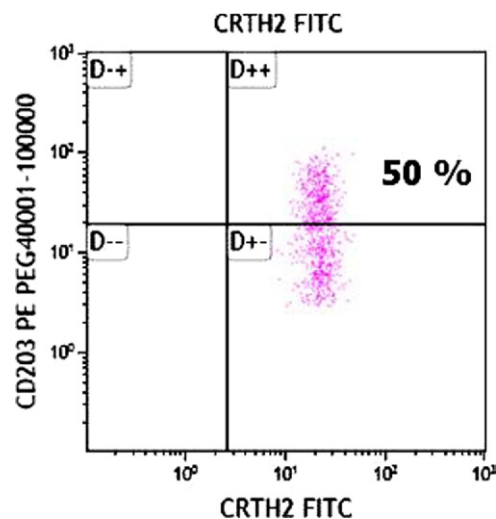


Figure 1. Basophil activation test shows a positive result for macrogol 4,000.

result was positive for macrogol 4,000 and 6,000 at a 1:100,000 dilution and negative for macrogol 400 for all the tested dilutions (Figure 1), in agreement with the cutaneous test results. Low-molecular-weight (200-700) macrogols are liquid and have been reported to cause contact dermatitis or contact urticaria. High-molecular-weight (1,000-7,500) macrogols are solid and, although generally poorly absorbed (approximately 0.2%) by the gastrointestinal tract, have been implicated in some cases of anaphylaxis. A peculiar case of anaphylaxis after oral drug intake and of contact urticaria due to polyethylene glycols of high and low molecular weight, respectively, has been reported.⁵

The systemic reactions reported by our patient seem to be IgE dependent. Positive skin prick test results and a positive basophil activation test result for macrogols 4,000 and 6,000, along with the positive skin prick test result for paracetamol syrup (containing macrogol 6,000), suggest a type 1 reaction. The patient was advised to systematically check drugs and products potentially containing macrogol, including cosmetics and conserved foods. Allergy to excipients should be considered, particularly in cases of multiple allergic reactions to multiple drugs. We suspect that allergic reactions to macrogols may be underreported.

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