Anaphylaxis to oral furosemide

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ABSTRACT

Furosemide, one of the most used diuretic drugs, rarely induces type-1 allergic reactions It is included in the non-aromatic sulfonamides but a cross-reactivity mechanism between this group and the sulfonamides antibiotics, has not been clearly demonstrated.

A 24-year-old woman, 10 minutes after the intake of one pill of *Seguril 40mg*® experienced oral itching, generalized urticaria, facial angioedema, dyspnea and hypotension. She recovered after the administration of parental adrenaline, methyl-prednisolone and dyphenhydramine. An skin prick test with furosemide (10 mg/ml) was negative. The intradermal skin tests were positive to furosemide (1 %) as well as sulfamethoxazole (0.03 mg/ml), with 10 atopic and non-atopic negative controls. The patient rejected the performance of an oral challenge test with sulfamethoxazole.

IgE–mediated reactions to furosemide are infrequent, but it could be the cause of life-threatening reactions. We have reported a case of anaphylaxis after the oral administration of furosemide with a demonstrated hypersensitivity mechanism through the positive intradermal skin test. The previous administration of the drug could probably the mechanism of sensitization, but the positive intradermal test to sulfamethoxazole would open the hypothesis of a cross-reactivity between non-aromatic and antimicrobial sulfonamides. It could be necessary an oral challenge test with furosemide in allergic patients to sulfamides.

Key words: Furosemide. Anaphylaxis. Allergic reaction. Hypersensitivity. Sulfamides.

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RESUMEN

La furosemida, uno de los fármacos diuréticos más usados, raramente induce reacciones de hipersensibilidad con un mecanismo de tipo 1, es decir mediado por IgE. Pertenece al grupo de las sulfonamidas no-aromáticas pero no se ha podido demostrar un mecanismo de reacción cruzada entre este grupo y el de las sulfamidas con función antibiótica.

Presentamos el caso de una mujer de 24 años, sin antecedentes alérgicos de interés, que padecía de ovarios poliquísticos. Tras la toma de un comprimido oral de *Seguril 40 mg*®, a los 10 minutos, comenzó con prurito cutáneo, formación de pápulas y máculas generalizadas, angioedema facial, disnea e hipotensión. Se recuperó tras la administración de adrenalina, metil-prednisolona y difenhidramina por vía parenteral. Se realizó una prueba cutánea en prick con furosemida (10 mg/mL) que fue negativa y una prueba cutánea en intradermorreacción que resultó positiva a furosemida (1 %) y a sulfametoxazol (0.03 mg/mL), resultando negativas en 10 sujetos atópicos y no atópicos utilizados como controles. La paciente rechazó la realización de una prueba de provocación oral con sulfametoxazol.

Las reacciones mediadas por IgE debidas al uso de furosemida son infrecuentes, pero no debemos olvidar que puede ocasionar situaciones de riesgo vital para el paciente. Comunicamos un caso de anafilaxia tras la toma de furosemida por vía oral en el que hemos demostrado un mecanismo de hipersensibilidad por pruebas cutáneas. La administración previa del fármaco es, probablemente, el medio de la sensibilización al mismo, pero la positividad de las pruebas intradérmicas al sulfametoxazol, abre la puerta a un mecanismo de reacción cruzada entre las sulfamidas no aromáticas y los antibióticos de dicho grupo, lo que obligaría a realizar una prueba de provocación oral con furosemida en pacientes alérgicos a sulfamidas.

Palabras clave: Furosemida. Anafilaxia. Reacción alérgica. Hipersensibilidad. Sulfamidas.

INTRODUCTION

Furosemide is a widely used Henle's loop diuretic. Although it belongs to the sulfonamides family, a difference in an aryl-amine group at the N_4 position justified its inclusion in the non-aromatic sulfonamides group. Most frequent side effects of furosemide are alterations in the acid-base status and electrolyte disturbances, but some cutaneous reactions have been reported (exanthematic pustulosis[1], bullous dermatosis[2] or lichenoid drug eruption[3]). However, type-1 allergic reactions are exceedingly rare. A case of anaphylaxis after oral administration of furosemide is reported.

CASE REPORT

A 24-year-old woman, without any allergic background, who suffered from a polycystic ovary, shortly after the intake of one pill of *Seguril 40 mg*® (Aventis-Pharma), experienced oral itching, generalized papulae and maculae, facial angioedema, dysphonia, dyspnea and low blood pressure (60/30 mmHg). She was recovered after the administration of parental adrenaline, methyl-prednisolone and dyphenhydramine. The patient was kept at the hospital centre for clinical observation. She had previously taken furosemide one year ago without any reaction and she had not eaten any food and had not being doing exercise in the previous 4 hours.

In the Allergy Unit at our hospital, skin prick tests (SPT) were performed with commercial extracts, *Anisakis simplex* (1 mg/ml), latex, and a common food battery (legumes, nuts, fish, fruits, milk, egg and wheat (IPI, Madrid, Spain and Leti, Barcelona, Spain). They were all negatives with a normal response to the histamine control. A prick test with furosemide (10 mg/ml) was performed and it was negative. The intradermal skin tests were positive to furosemide (1%) as well as sulfamethoxazole (0.03 mg/ml). 5 non-atopic and 5 atopic controls were all negatives to both drugs. To rule out an allergy to the para-amine group[4], epicutaneous test with paraphenylenediamine and parental challenge test with paracetamol (1 g) and procaine (10 mg) were performance and they were both well tolerated with no symptoms or cutaneous reactions 3 and 24 hours after the test. The patient did not consent the performance of an oral challenge test with sulfamethoxazole.

DISCUSSION

Data of immediate anaphylactic reaction after sulfonamide treatment are very scarce and most have been obtained with co-trimoxazol[5]. IgE–mediated reactions to furosemide are infrequent. Although a case of anaphylaxis due to furosemide was previously reported in 1987[6], it seems it occurs very rarely, since no other cases have been communicated. In this patient, immediate hypersensitivity was documented by positive skin tests, but the way of sensitization remains unclear. The previous administration of the drug could probably the mechanism of sensitization, but the positive intradermal test to sulfamethoxazole would open the hypothesis of a cross-reactivity between non-aromatic and antimicrobial sulfonamides[7]. We should not forget that there are enough similarities in chemical structure between both groups to justify a cross-reactivity mechanism between them. Although the patient did not know if she had been ever treated with antimicrobial sulfonamides, we should remember that the use of these drugs to treat paediatric infections was widely extended twenty years ago. Unfortunately, the patient refused the performance of an oral challenge test with sulfamethoxazole.

In conclusion, furosemide is a very well tolerated diuretic but it could rarely be implicated in cases of anaphylaxis through an IgE-mediated mechanism, as it has been demonstrated in this case with a positive cutaneous test, even if the drug is orally administrated. The possible mechanism of cross-reactivity between different drugs of the sulfamides family, could make necessary the performance of an oral challenge test with furosemide in allergic patients to sulfamides.

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