

Severe maculopapular eruption due to pseudoephedrine in a combination drug, with cross-reactivity to phenylephrine

Alejandro Raúl Gratacós Gómez¹ | Oscar Marcelo González Jimenez² |
Alberto Palacios Cañas² | Lucía Moreno Lozano²  | Miguel Juan Cencerrado³ |
Elisa Gómez Torrijos² 

¹Facultad de Medicina, Universidad de Castilla La Mancha, Ciudad Real, Spain

²Allergy Section, Hospital General Universitario, Ciudad Real, Spain

³Dermatología Médico-Quirúrgica y Venereología UGC, Hospital Universitario "Reina Sofía", Córdoba, Spain

Correspondence

Dr Elisa Gómez Torrijos, Allergy Section. Hospital General Universitario, C/Obispo R. Torija s/n. 13005, Ciudad Real, Spain.

Email: egomez.torrijos@gmail.com

KEYWORDS: case report, cross-reactivity, maculopapular eruption, patch tests, phenylephrine, pseudoephedrine, sympathomimetics

INTRODUCTION

Pseudoephedrine (P-eph) is a sympathomimetic drug and a stereoisomer of ephedrine. It has direct α - and β 2-adrenergic receptor agonist activity. It is, in association with antihistamine drugs, widely used in oral preparations to relieve nasal congestion in adults and children.^{1,2}

Such drugs may, however, cause adverse effects such as nervousness, dizziness, stomach pain, nausea, weakness, palpitation, breathing difficulties, and urinary retention.² Cutaneous adverse drug reactions have also been reported, but despite the frequent use of these drugs, such reactions appear to be rare.³⁻⁵

CASE REPORT

A 48-year-old female patient, with a personal history of hypothyroidism and migraine was referred to our allergy consultation because she had developed—12 hours following the oral intake of Cortafriol (containing paracetamol, P-Eph and ascorbic acid, elaborated by Famar Health Carte Services Madrid SA, Spain)—generalized itching shortly followed by a maculopapular eruption on her trunk, arms, and thighs, together with erythema and edema of the face. In less than 24 hours, the skin lesions progressed rapidly, also affecting her lower legs and ankles, where bullous lesions appeared. She visited the emergency room three times because the cutaneous symptoms were itching so intensely, even though she was already treated with oral corticosteroids (prednisone 60 mg/d, tapering the dose every 3 days until it was withdrawn) and antihistamines (ebastine, 20 mg/12 h). The skin rash

only slowly, but progressively, improved. No general symptoms or mucosal lesions were ever present.

Laboratory analyses only showed a mild leukocytosis (11 000 leukocytes/ μ L with 72% neutrophils), and all the biochemical parameters (glucose, urea, and liver tests) remained normal.

An allergy work-up was performed 3 months after complete resolution of the skin eruption: baseline patch tests with TRUE Test, occluded for 2 days and read on day (D) 2, D4, and D7, all remained negative. However, patch tests with P-Eph and phenylephrine (Ph-I) (2 days occlusion), both diluted in water 30% and petrolatum 30%, were positive (+) to both drugs on D2 and D4, but only to the pet.-based preparations; the aq. dilutions remained completely negative (Figure 1). PT (P-Eph and Ph-I) were negative in three control subjects, both in aq. and in pet.

Patch tests with paracetamol and ascorbic acid, both in water 30% and petrolatum 30%, were negative.

Oral challenge tests with paracetamol and ascorbic acid performed on two different days were equally negative.

DISCUSSION

P-Eph and Ph-I are alkaloids belonging to the phenylamine family,³ which includes two groups, derivatives of phenylpropanolamine (such as ephedrine, P-Eph, and norephedrine), and derivatives of phenylethanolamine (such as Ph-I and epinephrine).⁵

Most allergic reactions to these drugs concern delayed-type (IV) hypersensitivity, with various clinical presentations. There is a published case of a patient with allergic contact dermatitis (ACD) to

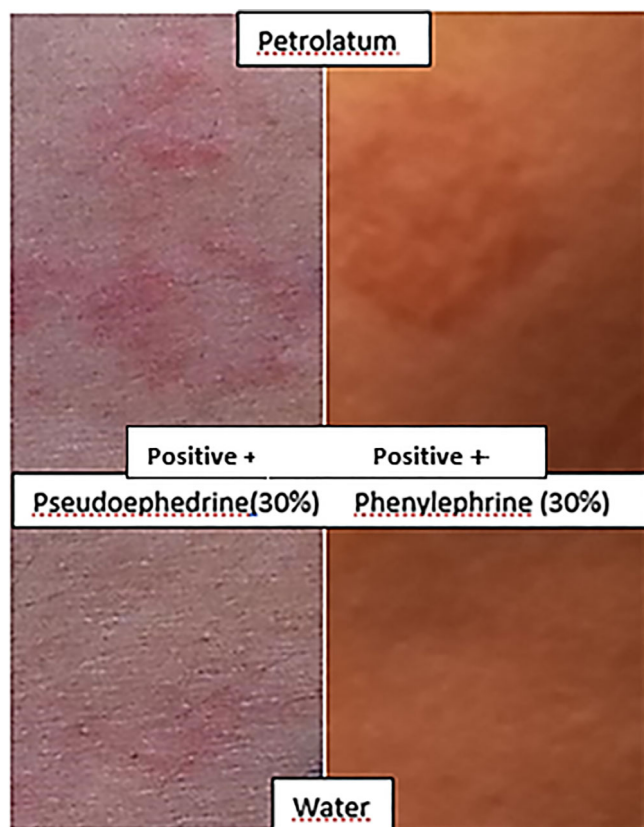


FIGURE 1 Reading at 96 hours of patch tests with patch tests pseudoephedrine (30%) and phenylephrine (30% in petrolatum, both positive, and in water, both negative)

Ph-I, who subsequently developed an erythroderma to P-Eph.³ In our patient, a maculopapular eruption first appeared following the oral intake of P-Eph, and subsequently cutaneous sensitization to Ph-I was detected. This was relevant as our patient was scheduled to undergo an ophthalmological examination 2 months later, a procedure during which typically Ph-I may be used. Due to the positive patch test to Ph-I it was reasonable to counsel our patient to avoid its future use and to use alternatives instead. In fact, cyclopentolate hydrochloride 1% eye drops were eventually used without any problem.

Cross-reactivity may exist among the drugs of the phenylamine family, but the reported data are inconclusive.³ Some studies have shown that patients who develop a generalized rash following the oral administration of P-Eph have a stronger response to, and more cross-reactivity with, other sympathomimetic drugs during patch testing, as opposed to those who only experience ACD.⁴ A similar phenomenon occurred in our patient, who had a generalized eruption caused by orally administered P-Eph, with patch tests also showing sensitization to Ph-I.

In conclusion we presented a case of a severe, maculopapular eruption due to P-Eph, with cross-reactivity to Ph-I, showing that such patients may need to undergo a full allergy workup in order to prevent potentially adverse reactions resulting from cross-reactivity.

CONFLICT OF INTEREST

The authors have no conflict of interest to declare and all give their permission for the publication of this article.

AUTHOR CONTRIBUTIONS

Alejandro Raul Gratacos Gomez: Methodology (lead); validation (lead). **Oscar Marcelo Gonzalez Jimenez:** Data curation (equal); resources (equal). **Alberto Cañas:** Investigation (equal); software (equal). **Lucia Moreno Lozano:** Data curation (equal); writing - original draft (equal). **Miguel Juan Cencerrado:** Methodology (supporting); writing-review & editing (equal). **Elisa Gomez Torrijos:** Investigation (lead); visualization (lead).

ORCID

Lucia Moreno Lozano  <https://orcid.org/0000-0003-3147-9774>

Elisa Gómez Torrijos  <https://orcid.org/0000-0002-4532-2498>

REFERENCES

1. Gelotte CK, Albrecht HH, Hynson J, Gallagher V. A multicenter, randomized, placebo-controlled study of pseudoephedrine for the temporary relief of nasal congestion in children with the common cold. *J Clin Pharmacol*. 2019;59(12):1573-1583.
2. Shao IH, Wu CC, Tseng HJ, Lee TJ, Lin YH, Tam YY. Voiding dysfunction in patients with nasal congestion treated with pseudoephedrine: a prospective study. *Drug Des Devel Ther*. 2016;10:2333-2339.
3. Gonzalo-Garjio MA, Pérez-Calderón R, de Argila D, Rodríguez-Nevado I. Erythrodermia to pseudoephedrine in a patient with contact allergy to phenylephrine. *Allergol Immunopathol*. 2002;30(4):239-242.
4. Barranco R, Rodríguez A, de Barrio M, et al. Sympathomimetic drug allergy: cross-reactivity study by patch test. *Am J Clin Dermatol*. 2004; 5(5):351-355.
5. Tanno LK, Fillard A, Landry Q, et al. Ephedrine-induced erythrodermia: clinical diagnostic procedure and cross-sensitivity. *Contact Dermatitis*. 2018;79(1):43-44.

How to cite this article: Gratacós Gómez AR, González Jimenez OM, Palacios Cañas A, Moreno Lozano L, Juan Cencerrado M, Gómez Torrijos E. Severe maculopapular eruption due to pseudoephedrine in a combination drug, with cross-reactivity to phenylephrine. *Contact Dermatitis*. 2021; 1-2. <https://doi.org/10.1111/cod.13951>