# IgE hypersensitivity mediated to lysine clonixinate

Villalón García AL, Pérez Pimiento A, López San Martín MG, Iglesias Cadarso A

Allergy Department, University Hospital Puerta de Hierro, Madrid, Spain

**Corresponding:**

Allergy Department

University Hospital Puerta de Hierro

Majadahonda-Madrid, Spain.

Calle Manuel de Falla,1.

28222 Majadahonda-Madrid. Spain.

E-mail: anluvillalon@yahoo.es



This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.18176/jiaci.0613

**Key words:** Lysine clonixinate. Drug allergy. Anti inflammatory analgesics. Urticaria. IgE hypersensitivity mediated

**Palabras clave:** Clonixinato de lisina, Alergia a medicamentos, Analgésicos antiinflamatorios, Urticaria, Hipersensibilidad mediada por IgE.



Lysine clonixinate is a drug belonging to the nicotinic acid family, a family of non-steroidal anti-inflamatory analgesics (NSAIDs) and an antiprostaglandinic drug which, at therapeutic doses, acts mainly by inhibiting cyclooxygenase-2 (COX-2); while at lower doses, it inhibits cyclooxygenase-1 (COX-1). It is indicated as an analgesic and anti-inflamatory in patients with acute or chronic pain. It has been proven effective in various algic syndromes such as renal colic, nerve compression, muscular pain and odontalgias [1]. Generally, it is used orally but it also effective and well tolerated intravenously in the treatment of severe migraine attacks [1-3]. The cross-reactivity among nicotinic acid family anti-inflamatories (lysine clonixinate, morniflumate, isonixin and niflumic acid) is not well known in acute allergic reactions. Most of them are used as an useful alternative in patients with NSAID hypersensitivity [4]. There are numerous studies about the efficacy and tolerance of lysine clonixinate orally when compared to other analgesics/NSAIDs [5-8]. Allergic reactions to lysine clonixinate are very rare and there are no studies thereof in the medical literature.

A 70-year-old female had been prescribed lysine clonixinate for headache, and 30 minutes following the first 250 mg intake, she developed itching in ears, armpits and arms and, progressively, generalized rash without angioedema. She did not develop dyspnea, stomach pain or other systemic symptoms. In emergencies, she was treated with antihistamines and intramuscular corticosteroids, improving completely in 2 hours.



doi: 10.18176/jiaci.0613

A month later, she reported a similar reaction following the first 250 mg intake. At a later moment, a 2 gr paracetamol per day dose was well tolerated. Skin prick test and single-blind-placebo-controlled oral challenge with lysine clonixinate, morniflumate, isonixin and niflumic acid and acetylsalicylic acid were performed, after 2-3 months of the reaction and once written consent had been obtained.

Skin prick test using lysine clonixinate dissolved in saline, was positive with 4x4mm, histamine control: 4x4mm and saline serum: 0mm (Figure). We performed skin prick test with lysine clonixinate, dissolved in saline, in 10 atopic patients and in 10 patients with diagnostic of hypersensitivity to NSAIDS, and all prick test were negative. Oral challenge with lysine clonixinate was not performed. Skin prick test using morniflumate, isonixin and niflumic acid and acetylsalicylic acid, dissolved in saline, was negative. Oral challenge with acetylsalicylic acid 1g was well tolerated. Oral challenges with morniflumate, isonixin and niflumic acid were not performed as these were not authorized by the patient.

Lysine clonixinate is a NSAID with only few adverse effects [9]. Like all medicines, Lysine clonixinate can cause side effects, although not everybody gets them. Common (may affect up to 1 in 10 people): discomfort, stomach ache, sickness, vomiting, diarrhea and minimal intestinal bleeding. Rare (may affect up to 1 in 1,000 people): Stomach inflammation, vomiting with blood. Very rare (may affect up to 1 in 10,000 people): dizziness, hypersensitivity reactions (allergy) with rash and itchy skin, spotted eczema, skin disorders, bronchospasm, breathing difficulties, insomnia, suffocation, tremor, pharyngitis, fever, fatigue, lack of appetite and blood disorders such as agranulocytosis, anemia or thrombocytopenia. It has to be noted that Kramer et al. described that lysine clonixinate did not induce changes in platelet count or function when administered to healthy volunteers at the commonly used therapeutic doses [10].

We describe a patient with allergy to lysine clonixinate, acute urticaria, with positive prick test and good tolerance to acetylsalicylic acid, discarding hypersensitivity to NSAIDs. Cross-reactivity between drugs of the nicotinic group could not be demonstrated as authorization therefor by patient could not be obtained. Prick test to lysine clonixinate is a useful tool for the diagnosis of immediate acute urticaria allergy due to sensitization to lysine clonixinate. To our knowledge, this is the first skin prick



doi: 10.18176/jiaci.0613

test positive to lysine clonixinate described in medical literature, strongly suggesting an IgE mediated mechanism.

**Funding**

The authors declare that no funding was received for the present study.

**Conflicts of Interest**

The authors declare that they have no conflicts of interest.

**REFERENCES**

1. Krymchantowski AV, Barbosa J. Intravenous lysine clonixinate for the treatment of migraine: an open pilot study. Arq Neuropsiquiatr. 1999.57(3A):606-9.

2. Krymchantowski AV, Silva MT. Intravenous lysine clonixinate for the acute treatment of severe migraine attacks: a double-blind, randomized, placebo-controlled study. Curr Ther Res Clin Exp. 2003;64(8):505-13.

3. Krymchantowski AV, Barbosa JS, Cheim C, Alves LA. Oral lysine clonixinate in the acute treatment of migraine: a double-blind placebo-controlled study. Arq Neuropsiquiatr. 2001;59(1):46-9.

4. Mero F, Nettis E, Aloia AM, Di Leo E, Ferranini A, Vacca A. Short-term tolerability of morniflumate in patients with cutaneous hypersensitivity to non-steroidal anti-inflammatory drugs. Int J of Immunopathology and Pharmacology 2013;26(1):247-50.

5. Perez-Urizar J, Martínez-Rider R, Torres-Roque I, Garrocho-Rangel A, Pozos-Guillen A. Analgesic efficacy of lysine clonixinate plus tramadol versus tramadol in



doi: 10.18176/jiaci.0613

multiple doses following impacted third molar surgery. Int J Oral Maxillofac Surg. 2014;43(3):348-54.

6. Noronha VR, Gurgel GD, Alves LC, Noman-Ferreira LC, Mendonça LL, Aguiar EG, et al. Analgesic efficacy of lysine clonixinate, paracetamol and dipyrone in lower third molar extraction: a randomized controlled trial. . Med Oral Patol Oral Cir Bucal. 2009;14(8):e411-5.

7. Krymchantowski AV, Peixoto P, Higashi R, Silva A Jr, Schutz V. Lysine clonixinate vs naproxen sodium for the acute treatment of migraine: a double-blind, randomized, crossover study. MedGenMed. 2005;7(4):69.

8. De los Santos AR, Di Girolamo G, Martí ML. Efficacy and tolerance of lysine clonixinate versus paracetamol/codeine following inguinal hernioplasty. Int J Tissue React. 1998;20(2):71-81.

9. Franchi A[1], Di Girolamo G, Farina M, de los Santos AR, Martí ML, Gimeno MA. Differential action of non-steroidal antiinflammatory drugs on human gallbladder cyclooxygenase and lipoxygenase. Medicina (B Aires). 2000;60(5 Pt 1):580-6.

10. Kramer EH[1], Sassetti B, Kaminker AJ, De Los Santos AR, Martí ML, Di Girolamo G. Effects of lysine clonixinate on platelet function. Comparison with other non-steroidal anti-inflammatory agents. Medicina (B Aires). 2001;61(3):301-7.





doi: 10.18176/jiaci.0613