

Title Useful alternative drugs before the use of opioids in patients with allergy to NSAIDs

Authors

Ruth Barranco, MD ^{1,4}
Cristina Alava, MD ²
Ismael Garcia-Moguel, MD ¹
Elena Mederos, MD ²
Javier Iglesias-Souto, MD, PhD ³
Paloma Poza-Guedes, MD, PhD ²
Ruth Mielgo, MD ¹
Victor Matheu, MD, PhD ²

¹ Hospital Universitario 12 de octubre, Madrid, Spain

² Hospital Universitario de Canarias, La Laguna, Spain

³ Hospital Universitario NS Candelaria, Tenerife, Spain

⁴ RETIC ARADyAL, Instituto de Salud Carlos III, Madrid, Spain

Corresponding author

Víctor Matheu, MD, PhD
Allergy Service, Hospital Universitario de Canarias,
Floor -2, Outpatient Building
Ctra. Cuesta s/n
38320 La Laguna. SPAIN
Email: victor.matheu@gmail.com

Keywords

nonsteroidal anti-inflammatory drug (NSAID); Nabumetone; hypersensitivity; drug allergy; adverse drug reaction; opioid use disorder; analgesics; drug challenge

Key message: Meloxicam and Nabumetona could be safely proven in patients with NSAID allergy before opioids treatment

Type of manuscript: Correspondence

Authors: RB & VM have the idea, prepared, and wrote the manuscript. CA made the epidemiological and statistical analysis. IGM, EM, JIS, PPG & RM performed all the clinical work

The authors declare that they have no conflict of interest regarding this manuscript.

There are no funders to report for this submission

Data are available with request.

Dear Editor,

The use of analgesics for chronic pain in insidious pathologies such as osteoarthritis (OA)¹ or chronic back pain (CBP) is a global problem. In those cases, the first step is usually prescribed NSAIDs and acetaminophen. However, a notable percentage of patients may refer symptoms of hypersensitivity to NSAIDs in their anamnesis. Very recently, a UK study about relative incidence of a first gabapentinoid prescription showed that patients with OA have a higher risk of being prescribed a gabapentinoid². Some authors have reported that adults with reported nonsteroidal anti-inflammatory drugs (NSAIDs) “allergy” are at a higher risk of developing opioid use disorder since they are receiving opioid analgesics instead. Authors also consider allergy evaluation as critical for potential de-labeling of patients with reported NSAID allergies and chronic pain³ and the use of celecoxib in adult patients with NSAID⁴.

The objective of the study was to demonstrate the degree of tolerance to both nabumetone and meloxicam in patients with a true diagnosis of allergy to NSAIDs.

We have collected, 450 patients (315 women) with a mean age of 44.3 years and with a true diagnosis of NSAID allergy in the last 3 years. The diagnosis was demonstrated by anamnesis of at least two cutaneous or respiratory reactions with two or more different NSAIDs and at different time points. When there was doubt in the diagnosis by medical history, the diagnosis was made by a positive oral provocation test with acetyl-salicylic acid or ibuprofen. One hundred thirteen out of 450 patients had had reactions with at least two different NSAIDs and the other 337 patients had had reactions with three different or more NSAIDs, the most frequent being ibuprofen, followed by dexketoprofen and, remotely, naproxen. The mean latency time since drug was taken until first symptoms were noticed was 52,3 minutes and the principal sign was palpebral edema.

Subsequently, we performed oral challenge tests with meloxicam 15 mg in these patients after being informed and signing the informed consent. On a second day, the patients were cited for a single-blind oral challenge test with nabumetone 1000 mg. All the patients remained in the Allergy consultation, supervised by the nursing team. In all cases, vital signs were monitored, and the patients were discharged at least two hours after the last dose. The study was approved by the Ethics Committee (H12O-CEI17/115).

Four hundred and twenty patients (93.3%) tolerated meloxicam without clinical incidents and were discharged. Likewise, and with an interval of at least 72 hours, 423 patients (93%) tolerated nabumetone without any adverse effect. Among the 30 patients who did not tolerate meloxicam because they had symptoms like those that initially complained in their medical history, the 27 patients who did not tolerate nabumetone were

included. Twenty four out of these 27 patients were women, and the median age was 36 years. Three patients had allergic rhinitis as comorbidity, 9 had asthma (6 of them allergic asthma) and another 9 had rhinitis and asthma (8 with allergy). All patients were treated appropriately and were discharged to their homes without symptoms.

As mentioned, patients with OA not only have a higher risk of being prescribed a gabapentinoid but, once prescribed a gabapentinoid, are also at greater risk of opioid co-prescription². Furthermore, a significant number of adults with chronic pain self-manage the use of NSAIDs. Many of them when they have an adverse reaction do not contact their primary care provider and therefore avoid the use of NSAIDs and go to the next step of analgesia by labeling themselves a NSAID allergy. This leads to a high consumption of other types of analgesia such as the use of minor opioids. The problem of high opioid use is a global issue since opioid use disorder is a public health problem^{1, 2, 5}. Strict restriction of opioid prescription, and improved access to, and uptake of, effective non-pharmacological and surgical alternatives for OA are required². Due to the high frequency of self-report of allergy to NSAIDs⁶ it would be a promising proposal for primary care physicians, and before using coxibs or prescribing opioids, to try the tolerance to these two drugs in these patients in an Allergy medical office or in a specialized medical office, with registered nurses (RN), and trained in the assessment and management of possible reactions, which are rare and generally mild. Giving the patient nabumetone 1000mg or meloxicam 15mg in the consultation office and being monitored for 2 hours under the supervision of the RN would be enough to check tolerance to the drug and thus drastically reduce the use of other second and third-line medications. Although they have remained in the forgetfulness of the pharmacopoeia of many physicians, nabumetone and meloxicam are very well tolerated in a very high percentage of patients⁷.

References

- 1.- van den Driest J, Schiphof d, de Wilde M, Bindels PJE, van der Lei J, Bierma-Zeinstra SMA Opioid prescriptions in patients with osteoarthritis: a population-based cohort study. *Rheumatology*, 2020: 59 (9): 2462–2470,
- 2.- Yu D, Appleyard T, Cottrell E, Peat G. Co-prescription of gabapentinoids and opioids among adults with and without osteoarthritis in the United Kingdom between 1995 and 2017. *Rheumatology (Oxford)*. 2020 Nov 7:keaa586. doi: 10.1093/rheumatology/keaa586. Epub ahead of print. PMID: 33159800.
- 3.- Li L, Chang Y, Song S, Losina, E, Costenbader K.H., Laidlaw T.M. Impact of reported NSAID “allergies” on opioid use disorder in back pain *J Allergy Clin Immunol* 2020: Published:September 08, 2020DOI:https://doi.org/10.1016/j.jaci.2020.08.025
- 4.- Li L, Laidlaw T. Cross-reactivity and tolerability of celecoxib in adult patients with NSAID hypersensitivity. *J Allergy Clin Immunol Pract*. 2019; 7: 2891-2893.e2894
- 5.- Maher C, Underwood M, Buchbinder R. Non-specific low back pain. *Lancet*. 2017 Feb 18;389(10070):736-747. doi: 10.1016/S0140-6736(16)30970-9. Epub 2016 Oct 11.
- 6.- Blanca-Lopez N, Soriano V, Garcia-Martin E, Canto G, Blanca M. NSAID-induced reactions: classification, prevalence, impact, and management strategies. *J Asthma Allergy*. 2019 Aug 8;12:217-233. doi: 10.2147/JAA.S164806.
- 7.- Prieto A, De Barrio M, Martín E, Fernández-Bohórquez M, de Castro FJ, Ruiz FJ, et al. Tolerability to nabumetone and meloxicam in patients with nonsteroidal anti-inflammatory drug intolerance. *J Allergy Clin Immunol*. 2007 Apr;119(4):960-4. doi: 10.1016/j.jaci.2006.12.616. Epub 2007 Feb 9.