



Colombian Journal of Anesthesiology

Revista Colombiana de Anestesiología

www.revcolanest.com.co

OPEN

 Wolters Kluwer

Safe use of dipyrrone

Seguridad en el uso de Dipirona

As relates to the recently published Editorial of the Colombian Journal of Anesthesiology (*Revista Colombiana de Anestesiología*) entitled "Has the time come to restrict the clinical use of dipyrrone?,"¹ we agree with the author regarding the regulatory steps that must be adopted on the use not only of dipyrrone but of the majority of analgesics sold over the counter. There is a need to put an end to the sale of those drugs without an adequate medical prescription based on the absence of risks for the individual patient and a rational time period for use.²

The safety profile of over-the-counter analgesics is difficult to ascertain; however, it has been found that the possibility of renal³ and gastrointestinal⁴ side-effects is more than 1%, while in some instances their use has been associated with increased cardiovascular risk⁵ and severe gastrointestinal bleeding.⁶ As has been reported by the most widely cited studies on pharmacovigilance and dipyrrone, the incidence of agranulocytosis and aplastic anemia ranges between 0.5 and 2.7 cases for every million consumers.⁷ It appears that the incidence of agranulocytosis depends on genetic factors and previous exposure to the medication, which explains the wide variation between studies in Latino⁸ and nordic populations.⁹

The incidence of dipyrrone-associated agranulocytosis is so low that it almost always results in one case report, as is this case. However, risks associated with traditional, commonly used analgesics, are sometimes ignored, although many times they may be lethal.

Dipyrrone has been shown to be as effective as traditional anti-inflammatory agents for the treatment of postoperative pain,¹⁰ renal colic,¹¹ and headaches of all types.^{12,13} It is important to highlight that before the Food

and Drug Administration (FDA) ban, dipyrrone was one of the most popular analgesics in the United States market, with more than 40 commercial brands; the veto came at around the time (late 1960s and early 1970s) of the launch to the market of the anti-inflammatory agents still in use today.¹⁴ The same thing happened with the blackbox imposed on droperidol early in this century, when setrons came to the market.¹⁵ Although we would not want to argue causality, it is quite a regrettable coincidence.

It is highly probable that the close scrutiny to which dipyrrone is subjected will not change and that countries that favor its use will continue to do so even as North America continues to refer to it by the derogatory name of "Mexican aspirin."¹⁶

In short, we are aware of the risk of agranulocytosis associated with the use of dipyrrone but, unfortunately, other options available in the market have not proven to be more effective and are far from being safer for our population. Finally, the mortality risk associated with the use of dipyrrone is, in absolute terms, even lower than that of dying in a collision as we commute to work. Consequently, we should not be deprived of the possibility of the rational use of the drug, just like we should not be deprived of the possibility of driving safely to work.

References

1. Gómez-Duarte OG. Is it time to restrict the clinical use of dipyrrone? *Colombian Journal of Anesthesiology* 2019;47:81-83.
2. Hersh E, Moore P, Ross G. Over-the-counter analgesics and antipyretics: a critical assessment. *Clin Ther* 2000;22:500-548.
3. Whelton A. Renal effects of over-the-counter analgesics. *J Clin Pharmacol* 1995;35:454-463.
4. Bjarnason I. Gastrointestinal safety of NSAIDs and over-the-counter analgesics. *Int J Clin Pract Suppl* 2013;67:37-42.

How to cite this article: Chaparro LE, Giraldo JM. Safe use of dipyrrone. *Colombian Journal of Anesthesiology*. 2020;48:55-56.

Read the Spanish version of this article at: <http://links.lww.com/RCA/A905>.

Copyright © 2019 Sociedad Colombiana de Anestesiología y Reanimación (S.C.A.R.E.). Published by Wolters Kluwer. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Correspondence: Department of Anesthesiology, University of Toronto, 123 Edward Street, Toronto, ON, Canada. E-mail: lechaparro@gmail.com

Colombian Journal of Anesthesiology (2020) 48:1

<http://dx.doi.org/10.1097/CJ9.0000000000000144>

5. Chan AT, Manson JE, Albert CM, et al. Nonsteroidal antiinflammatory drugs, acetaminophen, and the risk of cardiovascular events. *Circulation* 2006;113:1578–1587.
6. Rodríguez LG, Jick H. Risk of upper gastrointestinal bleeding and perforation associated with individual non-steroidal anti-inflammatory drugs. *Lancet* 1994;343:769–772.
7. Benseñor IM. Dipyron and blood dyscrasia revisited: “non-evidence based medicine”. *Sao Paulo Med J* 2005;123:99–100.
8. Hamerschlak N, Maluf E, Biasi Cavalcanti A, et al. Incidence and risk factors for agranulocytosis in Latin American countries—the Latin Study: a multicenter study. *Eur J Clin Pharmacol* 2008;64:921–929.
9. Hedenmalm K, Spigset O. Agranulocytosis and other blood dyscrasias associated with dipyron (metamizole). *Eur J Clin Pharmacol* 2002;58:265–274.
10. Chaparro LE, Lezcano W, Álvarez HD, et al. Analgesic effectiveness of dipyron (metamizol) for postoperative pain after herniorrhaphy: a randomized, double-blind, dose-response study. *Pain Pract* 2012;12:142–147.
11. Edwards JE, Meseguer F, Faura C, et al. Single dose dipyron for acute renal colic pain. *Cochrane Database Syst Rev* 2002;4:CD003867.
12. De Souza Carvalho D, Barea LM, Kowacs PA, et al. Efficacy and tolerability of combined dipyron, isometheptene and caffeine in the treatment of mild-to-moderate primary headache episodes. *Expert Rev Neurother* 2012;12:159–167.
13. Bigal ME, Bordini CA, Tepper SJ, et al. Intravenous dipyron in the acute treatment of migraine without aura and migraine with aura: a randomized, double blind, placebo controlled study. *Headache* 2002;42:862–871.
14. [No authors listed] Risks of agranulocytosis, aplastic anemia. A first report of their relation to drug use with special reference to analgesics. The International Agranulocytosis and Aplastic Anemia Study. *JAMA* 1986;256:1749–1757.
15. Habib AS, Gan TJ. Food and drug administration black box warning on the perioperative use of droperidol: a review of the cases. *Anesth Analg* 2003;96:1377–1379.
16. Hargis JB, La Russa VF, Redmond J, et al. Agranulocytosis associated with “mexican aspirin” (dipyron): evidence for an autoimmune mechanism affecting multipotential hematopoietic progenitors. *Am J Hematol* 1989;31:213–215.

Luis Enrique Chaparro^a, Javier Mauricio Giraldo^b

^aDepartment of Anesthesiology,
University of Toronto, Toronto, ON, Canada

^bDepartment of Anesthesia, University of Western Ontario,
London, ON, Canada.