



Should Metamizole sodico be banned in Ecuador due to the increased risk of agranulocytosis?

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Background

Metamizole sodium is an agent used as an anti-pyretic, nonsteroidal anti-inflammatory agent.¹ It is available under names such as Algozone, Algocalmin, Analgin, Dipirona, Optalgin, and Novalgina throughout the world. Despite being banned throughout the world, including in the United States, Metamizole has been used extensively in Latin America due to the fact that its efficacy is the same as Paracetamol and Aspirin but its analgesic effect is higher.¹

In Ecuador, where we spent five weeks this summer, Novalgina is commonly available to treat fever and pain.² In 1973, the American Medical Association issued its first warning against Metamizole as an analgesic, while allowing restricted use as an anti-pyretic. However, in 1979 its use was completely banned due to extensive potential side effects.³ Several cases of neutropenia or leukopenia were reported and were found to be associated with the use of metamizole.

A study conducted in the 1980s found metamizole to be associated with agranulocytosis, but the risk varied by country.⁵ Agranulocytosis and aplastic anemia are the leading causes of drug-induced death. Agranulocytosis is a hematological condition in which the number of circulating neutrophils falls, which thereby increases the risk of bacterial infections and sepsis that may result in a fatality 5-15% of the time.⁶

One of the major drivers of the ban in the United States was observation of a four year old boy who presented with fever, septic arthritis, and persistent neutropenia after the use of metamizole for pain. Further investigation unveiled the fact that the patient's mother was hospitalized previously for sepsis also related to metamizole use.³

Methods

•During our stay in Quito, Ecuador, we rotated through government-funded public hospitals for 5 weeks from June 5-July 15.

•The patients seen in this clinic were the lower to middle class of Quito who did not have private insurance. In Ecuador, the government provides health insurance to all of its citizens; however there is an option to buy private insurance and gain access to private hospitals.

•While there, we observed various prescriptions written for Metamizol. Due to a curiosity in this unknown medication, we researched it and discovered the controversy discussed in the background.

•From there, we observed all the patients that were prescribed Metamizol. In total, 55 patients were prescribed Metamizol during our 5 week stay.

•The reasons for the use of Metamizol ranged from low-grade fever of unknown origin to post-operative pain to colic pain



Results

Of the 55 patients that were prescribed Metamizol, none suffered significant side effects (including agranulocytosis) during our rotations.

This finding is not consistent with other studies, which show Metamizol use causes a significantly higher number of cases of agranulocytosis than other analgesics, as Table 1 below demonstrates.

Table 3 Drug exposures within 10 days prior to the index day* in agranulocytosis patients in Latin America

Drug	Cases, n=30 (%)	Controls, n=120 (%)	Odds ratio (95% CI)	p value
Metamizole	8 (26.7)	0 (0.0)	44.2 (6.8 - infinity)	<0.001
Diclofenac	3 (10.0)	3 (2.5)	4.0 (0.5-29.9)	0.20
Dipyrrone	10 (33.3)	22 (18.3)	2.4 (0.8-6.7)	0.12
Paracetamol	3 (10.0)	7 (5.8)	1.9 (0.3-12.1)	0.64
Acetylsalicylic acid	3 (10.0)	9 (7.5)	1.4 (0.2-6.8)	0.89
Proprenolol	2 (6.7)	7 (5.8)	1.1 (0.1-6.0)	1.00
Furosemide	1 (3.3)	4 (3.3)	1.0 (-0.1-10.1)	1.00
Omeprazole	1 (3.3)	6 (5.0)	0.7 (-0.1-5.5)	1.00
Nifedipine	0 (0.0)	5 (4.2)	0.6 (-0.1-4.4)	0.66
Hydrochlorothiazide	1 (3.3)	9 (7.5)	0.4 (-0.1-3.7)	0.68
Atenolol	0 (0.0)	6 (5.0)	0.4 (-0.1-3.5)	0.46
Captopril	1 (3.3)	12 (10.0)	0.3 (-0.1-2.3)	0.37

CI, Confidence interval.

* Index day was the day of symptom onset (case) or day of hospital admission (controls) for a condition requiring surgery

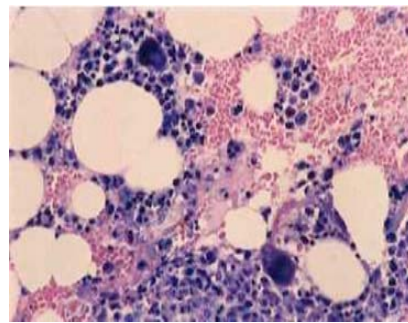
Conclusions

•Ecuador should not ban the use of metamizole due the relatively low risk of agranulocytosis in the population

•However, Ecuador should monitor the use of metamizole closely and further restrict its use.

•Though Metamizole is used much more frequently in Latin American countries than in the rest of the world, one major case study demonstrated that the risk of agranulocytosis is still low in Latin American countries.⁷

•Further research is needed to study the long term effects of metamizole use, specifically case controlled studies centered on patients in Ecuador.



References

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