

RISK OF AGRANULOCYTOSIS ASSOCIATED WITH METAMIZOLE: A REAL-WORLD PHARMACOVIGILANCE STUDY IN NORTHERN EUROPEAN POPULATIONS

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BACKGROUND

Metamizole is a widely used non-opioid analgesic and antipyretic. Although effective, its association with agranulocytosis led to withdrawal in several countries, while its use remains common in Southern Europe. Possible ethnic or genetic susceptibility has been suggested, particularly among Northern Europeans, but real-world evidence is limited. Clarifying this risk is important to improve pharmacovigilance and ensure safe analgesic use.

AIM AND OBJECTIVES

To estimate the incidence and relative risk of metamizole-induced agranulocytosis or neutropenia and to explore potential ethnic differences in adverse reactions between Northern and Southern European adults using real-world hospital and outpatient data.

MATERIAL AND METHODS

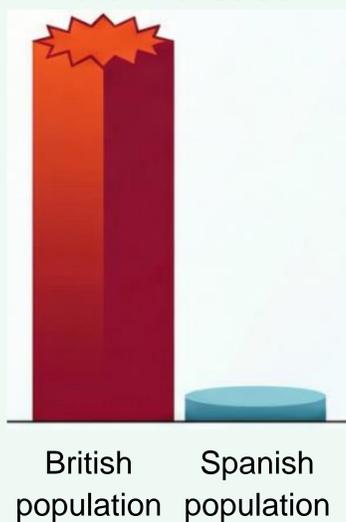
A retrospective observational study was performed in five regional health departments with a high Northern European population. Hospital admissions (2016–2017) were identified through CMBD using ICD-10 codes for drug-induced neutropenia or agranulocytosis. Patients >45 years exposed to metamizole within one month prior to admission were included, excluding alternative causes. Cases were individually reviewed, and incidence was calculated per 100,000 DDD and per 1,000 treated patients.

RESULTS

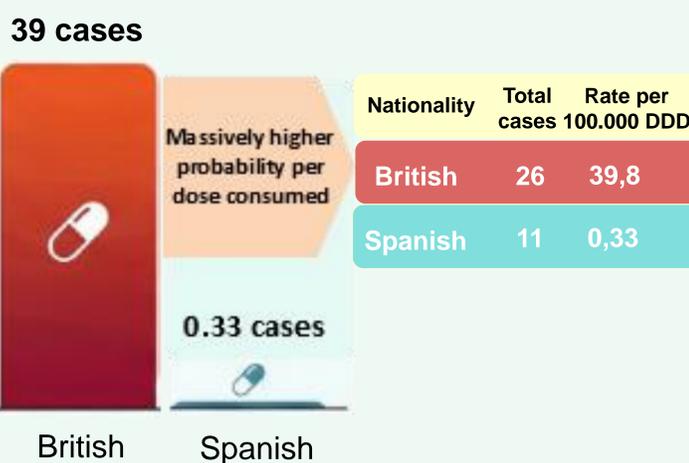
Among 555 hospitalizations identified, 41 met inclusion criteria. Twenty-six cases occurred in Northern European patients and eleven in Southern Europeans. The incidence of agranulocytosis was 39.8 vs. 0.33 cases per 100,000 DDD (RR = 120.6). Nine deaths were reported, seven in Northern European patients.

Risk Disparity: British vs. Spanish Population

Relative risk: **120-fold increase**



Incidence per 100.000 DDD



Genetic Susceptibility (HLA): The variability suggests an ethnic predisposition linked to specific alleles of the HLA system

Clinical Impact and Patient Safety

Disproportionate Mortality



AEMPS Recommendation: The use of metamizole should be avoided in patients for whom monitoring cannot be carried out.



At-Risk Population: The risk is higher in elderly patients and in treatments lasting more than one week.

CONCLUSION AND RELEVANCE

Among 555 hospitalizations identified, 41 met inclusion criteria. Twenty-six cases occurred in Northern European patients and eleven in Southern Europeans. The incidence of agranulocytosis was 39.8 vs. 0.33 cases per 100,000 DDD (RR = 120.6). Nine deaths were reported, seven in Northern European patients.

