Incidence of Metamizole-Induced Agranulocytosis: A Systematic Review of Post-2015 Publications

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Introduction. Metamizole is preferred as a nonopioid analgesic due to its efficacy as an antipyretic and spasmolytic. There is concern over metamizole's safety profile, emphasizing agranulocytosis as a rare, yet serious, adverse effect. This study aims to update the current understanding of metamizole-induced agranulocytosis (MiA) using literature published after 2015, quantifying MiA incidence.

Methods. This systematic review examines literature from January 2015 through December 2023 that quantifies MiA. Literature was gathered in adherence to Preferred Reporting Items for Systematic Reviews and Meta-Analysis standards from PubMed, Cochrane Library, Embase, OVID, and Web of Science. Studies published before 2015, originally in a non-English language, or not quantifying metamizole incidence, were excluded. Incidence rates, metamizole dosages, study design, use (in person-days), and fatalities were extracted.

Results. This study yielded 5,816 abstracts and 31 publications for full-text analysis. There were 1,619 cases of MiA and 60 reported fatalities. MiA incidence ranged from 0 to 166,667 cases per million person-days. The highest rates of MiA were observed in pharmacovigilance studies and case series. However, 7 of the 31 included studies included cancer patients in their populations.

Conclusions. MiA remains a rare but serious adverse effect of metamizole use. This study presents varied results, probably due to differences in study design and the inclusion of higher-risk patients. Compared to other medications that list agranulocytosis as an adverse effect, like clozapine and methimazole, MiA incidence may be comparable. The risk of MiA should be weighed against the impact of opioids in post-operative pain tolerance.