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Readers' comments

Use of non-steroidal anti-inflammatory drugs for pericarditis in pregnancy

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Dear Editor,

In response to the recent review “Noninvasive Multimodality Imaging and Special Treatment Considerations for Pericarditis in Pregnancy” published by Karmali et al.(1), we respectfully suggest that the review adopts an overly cautious approach regarding the use of non-steroidal anti-inflammatory drugs (NSAIDs) during pregnancy.

During the preconception period, NSAID use has been associated with an increased risk of luteinized unruptured follicle (LUF) syndrome. This condition is characterized by anovulation resulting from the failure of the follicular wall to rupture, despite normal follicular development and elevated serum progesterone levels. Cyclooxygenase-2 (COX-2), an enzyme essential for ovarian follicular development, is hypothesized to play a crucial role in this process, and its inhibition by COX-2 inhibitors is thought to contribute to the development of LUF. Notably, the risk appears to be higher in patients taking these drugs in the quiescent phase of disease, and with the selective COX-2 inhibitor etoricoxib—which is not commonly used for the management of pericarditis—compared to nonselective COX inhibitors, such as ibuprofen. This effect is reversible upon discontinuation of the drug(2,3). Current guidelines from European Alliance of Associations for Rheumatology (EULAR) and American College of Rheumatology (ACR) recommend considering NSAIDs discontinuation only in cases of infertility, if disease control can be maintained(4,5).

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Regarding the risk of miscarriage, as highlighted by the authors of the review, studies investigating the association between NSAID exposure during the preconception period and the first trimester of pregnancy have produced conflicting results. Notably, studies reporting a positive association exhibit significant methodological limitations(6,7). Drug exposure was inadequately assessed, with medication dispensing assumed to equate to actual consumption, and over-the-counter NSAID use not accounted for. Moreover, the indication for NSAID use was not clearly specified or adequately controlled. Furthermore, when positive associations were observed, they were generally stronger for diclofenac and indomethacin compared to ibuprofen, and more pronounced when NSAID were used close to the time of conception(3).

Regarding the risk of congenital malformations, current evidence does not indicate an increased rate associated with NSAIDs use during the preconception period or pregnancy. The few studies suggesting a potential association often lacked statistical significance or were limited by methodological flaws (3,8).

The use of NSAIDs after 20 weeks' gestation is contraindicated due to the risk of fetal renal dysfunction, which can lead to oligohydramnios and, in some cases, neonatal renal impairment and premature closure of the fetal ductus arteriosus(9,10).

In conclusion, leading scientific societies in rheumatology consider aspirin and nonselective NSAIDs as appropriate options during the first and second trimesters of pregnancy, up to 20 weeks, when necessary to control disease activity(4,5,10). These agents are considered the first-line therapeutic choice for managing acute and recurrent pericarditis during this period. In cases of acute pericarditis, high-dose aspirin or full dosages of nonselective NSAIDs should be considered, with aspirin often preferred due to greater clinical experience with its use(11). We used NSAIDs with success in women with recurrent pericarditis(12) Gradual tapering should begin at least two weeks after clinical resolution of the episode and normalization of C-reactive protein levels(13). Indeed, active inflammation poses significant risks to both mother and fetus, whereas well-controlled disease activity is associated with significantly better pregnancy outcomes. It is crucial for pregnant women to fully understand the benefits and risks of pharmacological treatment during

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this critical period. Therefore, a collaborative treatment approach involving healthcare providers and the patient is essential to ensure optimal care.

Declaration of Competing Interest

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CRediT authorship contribution statement

Lisa Serati: Conceptualization, Writing − original draft, Writing − review & editing

Antonio Brucato: Conceptualization, Writing − review & editing

Other authors: Writing − review & editing

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Declaration of Interests

☐ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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