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Aspirin and pregnancy: A comprehensive review

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Abstract

Aspirin (acetylsalicylic acid) is a widely used nonsteroidal anti-inflammatory drug (NSAID) with increasing application in obstetrics, and most importantly, for the prevention of placental-mediated complications. The aim of this review is to discuss the use of low-dose aspirin (LDA) in pregnancy, focusing on its advantages of reducing the occurrence of preeclampsia and fetal growth restriction (FGR). Its mechanism involves the irreversible inhibition of cyclooxygenase (COX) enzymes, thus enhancing uteroplacental blood flow and reducing placental ischemia. Clinical trials, such as the ASPRE trial, demonstrated that aspirin, initiated before 16 weeks of gestation, significantly lowers the risk of preterm preeclampsia. Aspirin has also been found to be beneficial in antiphospholipid syndrome (APS), recurrent pregnancy loss, and preterm birth prevention. Despite its benefits, there are still challenges in optimizing patient selection, dosing, and guideline compliance. Future research must address individualized medical strategies, long-term neonatal outcomes, and access to care in low-resource environments. This review documents the changing role of aspirin in the management of pregnancy and reinforces the call for ongoing research to maximize its clinical application.

Keywords: Low-dose aspirin; Preeclampsia; Fetal growth restriction; Pregnancy complications; Antenatal care

1. Introduction

Aspirin (acetylsalicylic acid), a nonsteroidal anti-inflammatory drug (NSAID), has been widely utilized in obstetrics for its antiplatelet and anti-inflammatory properties. Initially recognized for its role in cardiovascular disease prevention, its application in pregnancy has expanded, particularly in mitigating placental-mediated complications such as preeclampsia and fetal growth restriction (FGR) (Roberge et al., 2017). Despite its established benefits, uncertainties persist regarding optimal dosing, timing, and patient selection. This review synthesizes current evidence on aspirin's efficacy, safety, and clinical applications in pregnancy, emphasizing high-risk populations. Additionally, emerging research on its potential to reduce preterm birth and its long-term neonatal effects is explored (Henderson et al., 2022).

The role of aspirin in pregnancy is multifaceted, extending beyond its well-documented effects on preeclampsia and FGR. Research is increasingly exploring its impact on conditions such as recurrent miscarriage, gestational hypertension, and even the prevention of stillbirth. While its benefits in these areas remain under investigation, aspirin's ability to improve vascular function and placental development positions it as a promising therapeutic agent. The challenge remains in refining clinical guidelines to ensure maximum benefit while minimizing risks associated with inappropriate use.

2. Mechanisms of Action

Aspirin exerts its effects by irreversibly inhibiting cyclooxygenase (COX) enzymes, thereby reducing thromboxane A2 (TXA2) synthesis—a potent vasoconstrictor and platelet aggregator. In pregnancy, this mechanism enhances uteroplacental blood flow by preventing placental ischemia and thrombosis, which are implicated in preeclampsia and

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FGR (Visser et al., 2021). Low-dose aspirin (LDA; ≤150 mg/day) selectively inhibits platelet TXA2 while preserving endothelial prostacyclin (PGI2), a vasodilator, thus maintaining vascular homeostasis (Schrör, 2020). Higher doses (>150 mg/day) may non-selectively inhibit both COX-1 and COX-2, increasing the risk of adverse effects without providing additional efficacy (Wright et al., 2019).

Beyond its vascular effects, aspirin also modulates immune function and inflammation. It reduces oxidative stress and enhances nitric oxide production, contributing to endothelial stability. Some studies suggest aspirin may also downregulate inflammatory cytokines involved in placental dysfunction, which could explain its protective effects in high-risk pregnancies. This immunomodulatory role remains an area of active research, with implications for conditions such as recurrent pregnancy loss and chronic placental insufficiency.

3. Indications for Use

3.1. Preeclampsia Prevention

Preeclampsia, a hypertensive disorder affecting 2–8% of pregnancies, remains a leading cause of maternal and perinatal morbidity. LDA is recommended for high-risk women, including those with a history of preeclampsia, chronic hypertension, diabetes, or multifetal gestation (ACOG, 2020). The 2019 ASPRE trial demonstrated that 150 mg/day aspirin initiated before 16 weeks reduces the incidence of preterm preeclampsia by 62% (Rolnik et al., 2017). Meta-analyses support these findings, showing a 24% overall risk reduction in preeclampsia with LDA (Duley et al., 2019).

Despite these benefits, real-world adherence to aspirin recommendations remains suboptimal. Barriers include inconsistent clinician prescribing patterns, patient concerns about medication safety, and limited healthcare access in low-resource settings. Efforts to improve education and guideline implementation are crucial to maximizing aspirin's impact on maternal and fetal health.

3.2. Fetal Growth Restriction (FGR)

FGR, commonly linked to placental insufficiency, affects 5–10% of pregnancies. LDA improves placental perfusion, reducing FGR incidence by 20% in high-risk populations (Roberge et al., 2018). A 2020 Cochrane review emphasized that early initiation (<16 weeks) is more effective than later administration (Meher et al., 2020). However, its benefits in low-risk populations remain inconclusive, necessitating individualized risk assessment (O'Gorman et al., 2021).

Emerging research suggests aspirin may also influence fetal programming, with potential implications for long-term cardiovascular and metabolic health. While the mechanisms remain speculative, some studies indicate aspirin-exposed infants may have improved endothelial function and lower rates of metabolic syndrome in childhood. Further research is needed to elucidate these effects.

3.3. Antiphospholipid Syndrome (APS)

For pregnant individuals with APS, aspirin combined with heparin reduces pregnancy loss by 54% (Mak et al., 2020). The ALIFE2 trial supports this regimen, though the optimal aspirin dose (81 mg vs. 150 mg) remains a subject of debate (de Jong et al., 2022).

Given APS's complexity, future trials should explore the role of personalized dosing strategies, incorporating biomarkers of coagulation activity to optimize treatment efficacy. The integration of low-molecular-weight heparin with aspirin continues to be refined, with ongoing trials investigating its role in recurrent pregnancy loss beyond APS.

4. Knowledge Gaps and Future Directions

- **Personalized Medicine:** Biomarkers (e.g., placental growth factor [PlGF]) may improve patient selection (Poon et al., 2020).
- **Long-Term Outcomes:** Data on aspirin's impact on childhood cardiovascular health are limited (Groom et al., 2022).
- **Low- and Middle-Income Countries (LMICs):** The feasibility of LDA implementation in LMICs requires further study (Smith et al., 2021).
- **Recurrent Pregnancy Loss (RPL):** Future studies should investigate aspirin's role in unexplained RPL, particularly in women without APS.

- **Pharmacogenomics:** Genetic variations in aspirin metabolism may influence efficacy and side effects, warranting further investigation.

5. Conclusion

Low-dose aspirin is a cornerstone of antenatal care for high-risk pregnancies, significantly reducing preeclampsia and FGR when initiated early. Its role extends beyond these conditions, with potential benefits in recurrent pregnancy loss, preterm birth prevention, and long-term offspring health. Ongoing research aims to optimize dosing, validate biomarkers, and expand accessibility in underserved populations. Clinicians must integrate evidence-based guidelines with individualized risk assessments to enhance maternal and fetal outcomes (Magee et al., 2023).

Efforts to improve adherence, address knowledge gaps, and refine clinical protocols will be essential in fully harnessing aspirin's benefits in obstetric care. As our understanding of aspirin's mechanisms and applications continues to evolve, its role in pregnancy management is likely to expand, offering new avenues for improving maternal and perinatal health outcomes.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflict of interest.

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