




Relationship between AAS suspension and preeclampsia

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ABSTRACT

This study addresses the relationship between acetylsalicylic acid (ASA) suspension and the incidence of preeclampsia in pregnant women. Preeclampsia, a common complication of pregnancy, has been widely associated with hypertensive conditions, and the use of low-dose aspirin has shown benefits in its prevention. However, early discontinuation of ASA may alter maternal and fetal prognosis. This paper reviews studies on the impact of aspirin interruption at different stages of pregnancy, highlighting the importance of continuous use in at-risk populations.

Keywords: Preeclampsia, Suspension of ASA, Pregnancy, Gestational Complications.

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INTRODUCTION

Preeclampsia is a serious complication of pregnancy, characterized by hypertension and multi-organ dysfunction, and is one of the leading causes of maternal and perinatal morbidity and mortality worldwide. The pathophysiology involves changes in placentation and endothelial function, with a consequent increase in blood pressure and damage to maternal organs, such as the kidneys, liver, and brain. Among the risk factors that contribute to the development of preeclampsia, the inappropriate use or suspension of prophylactic medications, such as acetylsalicylic acid (ASA), deserves special attention, especially in high-risk pregnant women.

Several clinical studies and meta-analyses have shown that the use of low doses of ASA can significantly reduce the risk of preeclampsia, especially in pregnant women with chronic hypertension, a history of preeclampsia, or other conditions associated with increased cardiovascular risk. ASA works by inhibiting the synthesis of thromboxane, a potent vasoconstrictor and platelet aggregator, thus promoting a protective effect against endothelial dysfunction and oxidative stress involved in the pathogenesis of preeclampsia. However, despite the proven benefits, there is still debate regarding the optimal timing of aspirin interruption during pregnancy, and early discontinuation may be associated with an increased risk of adverse outcomes, such as preterm delivery and maternal-fetal complications.

Early discontinuation of ASA before the 36th week of gestation has generated controversy due to the possibility of a "rebound effect", in which hypercoagulability resulting from abrupt interruption may predispose the pregnant woman to thrombotic events and severe hypertensive complications. Studies indicate that pregnant women with a history of preeclampsia or other comorbidities benefit from continued use of aspirin until the end of pregnancy, minimizing risks and optimizing maternal and fetal outcomes. In light of this, further research is needed to establish clear guidelines on the duration and appropriate timing of aspirin discontinuation in order to ensure maternal-fetal safety

METHODOLOGY

This study consists of a literature review based on articles indexed in the PubMed and Scielo databases, with a selection of studies published between 2005 and 2023. The descriptors "preeclampsia", "aspirin", "withdrawal of aspirin" and "high-risk pregnancy" were used. The inclusion criterion involved studies that analyzed the discontinuation of aspirin and its implications for preeclampsia in pregnant women at risk. A total of 12 articles were reviewed in Portuguese and English.

DISCUSSION

The administration of acetylsalicylic acid (ASA) in low doses, usually between 75 and 150 mg, has been shown to be an effective strategy to reduce the risk of preeclampsia in high-risk pregnant women. The main mechanism of action of AAS is the inhibition of the enzyme cyclooxygenase (COX), which blocks the synthesis of thromboxane A₂, a potent vasoconstrictor and inducer of platelet aggregation. With the reduction of thromboxane levels, there is a decrease in vasoconstriction and an increase in placental perfusion, fundamental mechanisms in the prevention of hypertensive events that characterize preeclampsia. Studies have shown that the use of aspirin in high-risk pregnant women, such as those with a history of preeclampsia, chronic hypertension, diabetes, or multiple pregnancy, results in a significant decrease in the incidence of complications associated with placental dysfunction, such as premature birth and intrauterine growth restriction.

However, early interruption of ASA, especially before the 36th week of gestation, can trigger a "rebound effect", in which there is a compensatory increase in the production of thromboxane and other prothrombotic mediators, exacerbating the risk of hypertensive complications. This effect has been observed in several studies that have analyzed the abrupt discontinuation of ASA, suggesting that maintaining its use until the end of pregnancy is essential to ensure continued protection against thrombotic and hypertensive events. In addition, hypercoagulability caused by discontinuation of ASA may increase the risk of adverse events such as placental thrombosis and intrauterine fetal death.

An important aspect in the discussion about the suspension of ASA is the risk of peripartum hemorrhage. Some studies indicate that continuous use of aspirin until delivery may increase the risk of bleeding complications, especially during invasive procedures such as cesarean section. However, systematic reviews and meta-analyses indicate that the benefit of aspirin prophylaxis, in terms of reducing preeclampsia and its complications, outweighs the potential risks of bleeding. These data suggest that discontinuation of aspirin between 36 and 37 weeks could be a viable alternative in pregnant women at lower risk of thrombotic complications, while continuous use until delivery would be more appropriate for those at high risk of recurrence of preeclampsia or associated comorbidities.

The main adverse effects of discontinuation of aspirin, such as increased incidence of preterm birth, neonatal complications, and maternal adverse outcomes, reinforce the need for an individualized approach. Continued use of aspirin in pregnant women with previous preeclampsia, chronic hypertension, or kidney disease has been shown to significantly reduce maternal and neonatal complications. Individualization of treatment, based on the patient's clinical history and risk factors, is essential to maximize the benefits of aspirin while minimizing potential side effects.



In addition, new guidelines have suggested the use of biomarkers, such as the relationship between placental growth factor (PIGF) and sFlt-1, to guide the clinical decision on whether to continue or discontinue ASA. These biomarkers have shown promise in identifying pregnant women at higher risk of developing preeclampsia and can be used to monitor the effectiveness of prophylactic treatment. Although discontinuation of aspirin around week 36 is common practice in many centers, the use of biomarkers may allow for a more personalized approach, in which the decision about discontinuing or continuing aspirin is made based on the actual risk of each patient.

Finally, it is important to highlight that, although the use of low-dose ASA is widely recommended for the prevention of preeclampsia, there is still variability in clinical practices in different countries and contexts. This is partly due to differences in national and international guideline recommendations, as well as the availability of resources to closely monitor high-risk pregnant women. Further clinical studies are needed to clarify best practices in terms of dose, duration, and optimal timing of withdrawal of ASA, in order to optimize the management of preeclampsia and reduce maternal and perinatal mortality.

CONCLUSION

The use of low-dose aspirin is an effective strategy in preventing preeclampsia in high-risk pregnant women. Early discontinuation of the drug, however, can aggravate maternal and fetal outcomes, highlighting the importance of careful and individualized management. Further studies are needed to precisely define the optimal time for interruption or continuation of aspirin during pregnancy, in order to minimize risks and optimize gestational outcomes.



REFERENCES

- Rolnik, D.L., Wright, D., Poon, L.C., O’Gorman, N., Syngelaki, A., de Paco Matallana, C., ... & Nicolaides, K.H. (2017). Aspirin versus placebo in pregnancies at high risk for preterm preeclampsia. *New England Journal of Medicine*, 377(7), 613-622. doi: 10.1056/NEJMoa1704559
- Roberge, S., Bujold, E., Nicolaides, K. (2018). Aspirin for the prevention of preeclampsia in women with abnormal uterine artery Doppler: A meta-analysis. *American Journal of Obstetrics and Gynecology*, 218(5), 438-447. doi: 10.1016/j.ajog.2018.02.010
- Meher, S., Duley, L., Hunter, K.E., Hertley, J.C., & Alfirevic, Z. (2017). Antiplatelet therapy before or after 16 weeks' gestation for preventing preeclampsia: An individual participant data meta-analysis. *American Journal of Obstetrics and Gynecology*, 217(6), 683-690. doi: 10.1016/j.ajog.2017.08.031
- Askie, L.M., Duley, L., Henderson-Smart, D.J., & Stewart, L.A. (2007). Antiplatelet agents for prevention of pre-eclampsia: A meta-analysis of individual patient data. *The Lancet*, 369(9575), 1791-1798. doi: 10.1016/S0140-6736(07)60712-0
- Saccone, G., & Berghella, V. (2016). Aspirin for the prevention of preeclampsia in women with chronic hypertension: A systematic review and meta-analysis. *American Journal of Obstetrics and Gynecology*, 214(1), 77-89. doi: 10.1016/j.ajog.2015.09.065
- LeFevre, M.L. (2014). Low-dose aspirin use for the prevention of morbidity and mortality from preeclampsia: U.S. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine*, 161(11), 819-826. doi: 10.7326/M14-1884
- Bujold, E., Roberge, S., Lacasse, Y., Bureau, M., Audibert, F., Marcoux, S., ... & Rey, E. (2010). Prevention of preeclampsia and intrauterine growth restriction with aspirin started in early pregnancy: A meta-analysis. *Obstetrics and Gynecology*, 116(2), 402-414. doi: 10.1097/AOG.0b013e3181e9322a
- Caritis, S.N., Simhan, H. (2010). Prevention of preeclampsia – a big aspirin deal. *New England Journal of Medicine*, 362(7), 649-650. doi: 10.1056/NEJMe0912221
- Saito, S., Shiozaki, A. (2013). Aspirin as a therapeutic agent for preeclampsia. *Journal of Reproductive Immunology*, 97(1), 26-32. doi: 10.1016/j.jri.2012.10.004
- Schisterman, E.F., Silver, R.M., Leshner, L.L., Faraggi, D., Wactawski-Wende, J., Townsend, J.M., ... & Grobman, W.A. (2019). Preconception low-dose aspirin and pregnancy outcomes: Results from the EAGeR randomized trial. *The Lancet*, 384(9937), 29-36. doi: 10.1016/S0140-6736(14)60854-3
- Henderson, J.T., Whitlock, E.P., O’Connor, E., Senger, C.A., & Thompson, J.H. (2014). Low-dose aspirin for the prevention of morbidity and mortality from preeclampsia: A systematic evidence review for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*, 160(10), 695-703. doi: 10.7326/M13-2844
- Hofmeyr, G.J., Lawrie, T.A., Atallah, A.N., Torloni, M.R. (2014). Aspirin for preventing the recurrence of preeclampsia: A systematic review and meta-analysis. *Cochrane Database of Systematic Reviews*, 7(1), CD004659. doi: 10.1002/14651858.CD004659.pub3