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"REVIEWING THE EVIDENCE: ASPIRIN IN THE PREVENTION OF PRE-ECLAMPSIA"

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ABSTRACT

Background: Pre-eclampsia is a complex, multisystem disorder affecting pregnant women, often leading to serious maternal and neonatal complications. Aspirin, known for its antiplatelet and anti-inflammatory properties, has been shown a positive effect for the pre- eclampsia in high-risk pregnancies. **Objective:** This review aims to explore the pharmacological mechanism of aspirin in the prevention of pre-eclampsia and evaluate current evidence from clinical trials, systematic reviews, and case reports. **Methods:** A literature review was conducted, including randomized controlled trials, meta- analyses, and case studies that investigated the efficacy and safety of low-dose aspirin in reducing the incidence and severity of pre-eclampsia. Emphasis was placed on dosage, timing of initiation, and maternal risk factors. **Results:** Current evidence indicates that aspirin, particularly in doses of 100–150 mg daily initiated before 16 weeks of gestation, can significantly reduce the risk of preterm pre-eclampsia and improve neonatal outcomes. Meta-analyses suggest that early prophylaxis lowers the risk of adverse outcomes, including foetal growth restriction and perinatal death, without increasing bleeding complications. However, variability in trial design and aspirin regimens contributes to inconsistencies in findings. **Conclusion:** Low-dose aspirin is a promising strategy for pre-eclampsia prevention in high- risk women. Early initiation and appropriate dosing are critical for optimal benefit. Further studies are warranted to refine patient selection criteria and establish universal guidelines.

KEYWORDS: Aspirin, Acetylsalicylic acid, Pre-eclampsia, Low-dose, Pregnancy, Antiplatelet, Prophylaxis, Cyclooxygenase, Neonatal outcomes.

INTRODUCTION

For many years, a substance taken from the bark of the white willow tree has been employed to address different types of fevers and swelling. The key ingredient in white willow, known as salicin or salicylic acid, had a bitter flavour that could upset the stomach lining. However, with a straightforward chemical alteration, a more pleasant option was created. This option is acetylsalicylic acid, commonly referred to as Aspirin[1], the first blockbuster drug.

Medical historians indicate that the origin of aspirin can be traced back to 1897; however, its intriguing story actually goes back over 3500 years. During this time, people in Sumer and Egypt utilized willow bark for its properties as a pain reliever and fever reducer, followed by notable doctors from ancient Greece and Rome. The development of aspirin's precursors, known as salicylates, started in 1763, when Reverend Stone first noted their effects on reducing fevers. Throughout the 19th century, many scientists contributed to isolating and creating these substances chemically. In 1897, chemist Felix Hoffmann from Bayer successfully created aspirin, and seven decades later, pharmacologist John Vane explained how it works by blocking the production of prostaglandins.[2]

USES OF ASPIRIN[3]

Here are several reasons why aspirin might be used

- Preventing chest pain (angina pectoris)
- A type of arthritis (ankylosing spondylitis)
- Lowering heart disease risk
- Colon cancer
- High temperature (fever)
- Stroke caused by lack of blood (ischemic stroke)
- Stroke prevention (ischemic stroke)
- Heart attack (myocardial infarction)
- Joint pain (osteoarthritis)

- Discomfort (pain)
- Preventing procedures to restore blood flow (revascularization)
- Inflammatory arthritis (rheumatoid arthritis)
- An autoimmune disease (systemic lupus erythematosus)
- Antiplatelet
- Cancer-preventing drug

ADVERSE EFFECTS

Aspirin's ability to reduce inflammation comes from its blocking of prostaglandin production. However, this also changes the regular protective roles of prostaglandins, which can have serious outcomes. These can include stomach ulcers, kidney problems, and issues with blood platelets that can lead to bleeding complications.[4]

PRE-ECLAMPSIA

Preeclampsia is a complicated disease that affects multiple systems in the body. It is identified by a sudden increase in blood pressure after 20 weeks of pregnancy, along with at least one other related issue such as excess protein in urine, problems with maternal organs, or issues with the placenta and uterus. This condition occurs only when a placenta is present or was recently present. It can be categorized into three types: preterm (delivery before 37 weeks), term (delivery at 37 weeks or later), and postpartum preeclampsia. This maternal condition is triggered by a poorly functioning placenta, which releases substances into the mother's bloodstream, leading to inflammation throughout the body and significant dysfunction of the blood vessels in the mother.[5]

Risk Factors

1. First time pregnancy
2. Carrying multiple babies at once
3. A past occurrence of preeclampsia
4. Having obesity
5. Diabetes (whether it's existed before or develops during pregnancy)
6. Disorders of the vascular and connective tissues (such as systemic lupus erythematosus and antiphospholipid syndrome)
7. Being over 35 years old during the first pregnancy
8. Engaging in smoking
9. Identifying as African American
10. A family record of preeclampsia
11. Genetic factors (in certain instances)

These factors are the primary risks frequently linked to preeclampsia.[6]

MECHANISM OF ASPIRIN IN PRE-ECLAPSIA

Aspirin, when taken in doses under 300 mg, permanently and selectively inhibits the cyclooxygenase-1 enzyme which causes decreased. This action decreases the production of both prostaglandins and thromboxane, leading to reduced inflammation and lower platelet aggregation. Due to this pharmacological trait, researchers suggest that aspirin might contribute to lowering the likelihood of developing preeclampsia. This property has led researchers to believe that aspirin may help in preventing preeclampsia. The initial suggestion of a relationship between aspirin use and preeclampsia prevention came from a case report in 1978, soon followed by the first randomized controlled trial in 1985. Since that timefollowing that, many randomized trials have been conducted, showcasing the safety of aspirin during pregnancy and the varied impacts of aspirin on preeclampsia rates. Many inconsistencies in the results can werebe attributed to different factors, including how trial participants were chosen, the initial risk levels of the women involved, the specific aspirin dosage, when the prophylaxis started during pregnancy, and how preeclampsia is defined. A metanalysis focusing on individual patient data has shown a slight 10% decrease in preeclampsia rates due to aspirin use. However, later metanalysis that looked at combined data indicated a dose response relationship regarding aspirin's impact on preeclampsia rates, with the most significant effects achieved when treatment begins before the 16th week of pregnancy. Recently, findings from the Aspirin for Evidence Based Preeclampsia Prevention trial demonstrated that a daily dose of 150 mg of aspirin, started before reaching 16 weeks of pregnancy and taken at night by a high-risk group identified through first trimester screening, can lower the rate of preterm preeclampsia by 62%. Additionally, a secondary analysis of this trial's results showed a 68% decrease in neonatal intensive care unit stays compared to placebo, primarily due to fewer births occurring before 32 weeks of pregnancy involving preeclampsia.[7]

CASE STUDIES

Brielle Demuth et al 8 conducted a systemic review where aim of the study was to estimate whether a dose of 75 to 81 mg daily aspirin could help prevent pre term pre eclampsiapre-eclampsia. A comprehensive search was performed using various databases and meta-analyses of randomized controlled trials (RCTs) that assessed the effects of aspirin started in the early stages of pregnancy compared to a placebo or no intervention, in line with the PRISMA guidelines and the Cochrane tool for evaluating bias. Findings:The study included Eleven 11 RCTs involving a total of 13,981 participants were identified., Aamong these, five RCTs displayed a low risk of bias, one had an unclear risk, and five were classified as having a high risk of bias. A combined analysis indicated that aspirin doses ranging from 75 to 81 mg did not lead to a notable decrease in the occurrence of preterm pre-eclampsia when compared to a placebo or no treatment (eight studies; 12,391 participants; relative risk 0. 66; 95% confidence interval: 0. 27 to 1. 62; p = 0. 36). Nonetheless, the studies showed considerable variability. The systemic review concluded that it was not possible to determine if taking 75 to 81 mg of aspirin each day lowers the chances of developing preterm pre-eclampsia. However, because the studies showed a lot of

differences, the actual impact of this aspirin dose on pregnancy results could not be precisel yassessed.

Choi YJ et al 9 performed a systematic review and meta-analysis to thoroughly examine how aspirin prophylaxis affects outcomes for mothers and newbornsnew-borns during pregnancy, considering the dosage and when treatment starts through a stratified approach. The research analyzed 35 randomized trials that included a placebo control, encompassing 46,568 expectant mothers. The findings indicated that aspirin prophylaxis was associated with a decreased likelihood of experiencing pre-eclampsia, premature birth, perinatal death, and restricted growth in the womb, with no increased bleeding complications. The use of low-dose aspirin notably improved the birth weight of infants but didn't lower the incidence of gestational hypertension. Subgroup analysis showed that women who started aspirin before reaching 20 weeks gestation had a significantly lower risk of pre-eclampsia, along with increased birth weight and gestational age at delivery (RR=0. 76, 95% CI=0. 64, 0. 90, p=0. 001). Nonetheless, the influence of aspirin dosage on pregnancy results was not statistically significant and demands additional research. The study concluded that starting low-dose aspirin treatment prior to 20 weeks of gestation significantly reduces the occurrence of pre-eclampsia and improves neonatal outcomes without raising the risk of bleeding.

G Boog et al[10] reported a case that highlights the clinical results from two pregnant women who received treatment with corticosteroids and aspirin for long-term placental inflammation issues—, specifically, chronic villitis of unknown cause (CVUE) and chronic intervillositis of unknown cause (CIUE)— which had previously resulted in negative pregnancy results. Findings: The first patient was a gravida 3, who had previously experienced fetal loss and asphyxia during labor, and she was diagnosed with CVUE. The second patient, a gravida 4, had suffered three losses around the time of birth and was later found to have CIUE. In both instances, using aspirin and corticosteroids during their pregnancies showed positive outcomes for both the mothers and their babies. The study concluded that CVUE is seen in 7 to 33 percent of placentas and is often connected to issues like intrauterine growth restriction, preeclampsia, premature births, perinatal asphyxia, and intrauterine fetal demise. The less common CIUE, which occurs in 0. 6 to 0. 9 out of 1,000 pregnancies, is associated with repeated pregnancy losses. It is believed that both cases are related to an immune response against the fetal allograft. The reports on these two cases indicate that using corticosteroids and aspirin could help manage these issues. Nevertheless, more research with larger groups of patients is needed to confirm these results.

CASE REPORTS

Min Ming et al[11] reported a case of a 32-year-old expectant mother who had several risk factors for preeclampsia, which included being overweight, experiencing negative pregnancy results in the past, and having a previous pregnancy of hydatidiform mole. She was advised to take low-dose aspirin (100 mg daily) to help prevent preeclampsia, starting after 12 weeks into her pregnancy. Throughout her pregnancy, she had regular check-ups with her obstetrician and did not experience gestational hypertension or other health issues. At 33 weeks and 5 days into her pregnancy, she suddenly had a severe headache, which was also accompanied by vomiting, confusion, and clammy hands and feet. She stated that she had no previous head injuries. Initially, she was assessed at a local hospital and later moved to a specialized medical center. An emergency CT scan showed a brain bleed in the left frontal lobe that extended into the ventricles. After a discussion among a team of specialists, an emergency cesareancaesarean delivery was conducted to bring the baby into the world, while the mother’s brain bleed was treated conservatively. Both the mother and the baby did well after the surgery. The study concluded that Bleeding in the brain and within the brain's ventricles in expectant mothers who use aspirin daily is a very uncommon yet dangerous condition for both the mother and the baby. An accurate diagnosis significantly depends on computed tomography. To manage these situations effectively, it is essential to have a team of healthcare professionals, to perform a timely cesarean section for the baby's safety, and to customize the treatment for the bleeding in the brain.

Aja-Okorie U et al[12] reported a case that shares an unusual occurrence of preeclampsia to highlight the necessity for healthcare professionals to be more vigilant for early recognition and prompt treatment in order to avoid serious problems for both the mother and the fetus. Case Description: A of a 29 yr old woman aged 29, who was pregnant for the third time and had delivered once before while experiencing one miscarriage, started her prenatal care at 10 weeks into her pregnancy. The only noted risk factor for preeclampsia was being a first-time mother, as revealed through her medical history and physical assessment. She had one ultrasound in the middle of her pregnancy, but no thorough screening in the first trimester was carried out using ultrasound or biomarkers to evaluate the risk of developing preeclampsia. At 18 weeks pregnant, she visited a primary care clinic reporting a headache and pain in her upper abdomen, with a blood pressure reading of 169/71 mmHg. An alpha- methyldopa prescription was given, and she was treated as an outpatient. However, the next day, she had two seizures and was moved to a specialized care hospital, where she was diagnosed with atypical eclampsia and HELLP syndrome. After receiving magnesium sulfatesulphate treatment and achieving stability, the pregnancy was ended without any issues, and the patient fully recovered. It was concluded

that Thorough thorough screening during the first trimester for preeclampsia, which includes a review of medical history, a physical check-up, ultrasound imaging, and testing for biomarkers, can assist in spotting women who are at a high risk for this condition. Recognizing the risk early allows for prompt implementation of preventive strategies, like the use of aspirin, which may help avoid the onset of preeclampsia.

TRIALS

Nguyen-Hoang L[13] conducted a multicenter stepped wedge cluster-randomized trial conducted across 10 regions in Asia between August 1, 2019, and February 28, 2022 to evaluate the efficacy, acceptability, and safety of a first-trimester screen-and-prevent strategy for preterm preeclampsia in Asia. Women underwent first trimester screening for preterm preeclampsia using a Bayes theorem-based triple-test. In the study 88.04% of women (42,897 of 48,725) agreed to undergo screening and 82.39% of high-risk women (2,919 of 3,543) received aspirin. As per the study, among high-risk women in the intervention phase, aspirin prophylaxis was associated with- 41% reduction in preterm preeclampsia incidence (aOR, 0.59 [95% CI, 0.37–0.92]), 54% reduction in preeclampsia with delivery <34 weeks (aOR, 0.46 [95% CI, 0.23–0.93]), 55% reduction in spontaneous preterm birth <34 weeks (aOR, 0.45 [95% CI, 0.22–0.92]) and 64% reduction in perinatal death (aOR, 0.34 [95% CI, 0.12–0.91]). Additionally, no significant difference in aspirin-related severe adverse events was noted. The study concluded that the screen-and- prevent strategy did not significantly reduce the overall incidence of preterm preeclampsia. However, aspirin prophylaxis in high-risk women was associated with substantial reductions in severe pregnancy complications, including preterm birth and perinatal death.

Amro FH et al[14], conducted a Open-label randomized trial conducted between May 2019 and November 2022 to determine whether 162 mg of aspirin is more effective than 81 mg in reducing preeclampsia with severe features among high-risk obese pregnant individuals. The study included pregnant individuals at 12–20 weeks gestation with BMI ≥30 kg/m² and at least one high-risk factor- History of preeclampsia in a prior pregnancy, stage I hypertension in the index pregnancy and Pregestational or gestational diabetes diagnosed before 20 weeks. Participants received either 162mg or 81mg of aspirin daily until delievery. A total of 220 of 343 individuals were randomized. The primary outcome was observed in 37 of 107 (35%) in the 162 mg group vs 41 of 102 (40%) in the 81 mg group (posterior relative risk, 0.88 [95% CI, 0.64–1.22]). As per the Bayesian analysis, it was noted that the 162mg aspirin group reduced the severe preeclampsia by 78% probability. Other findings such as rates of preterm birth due to preeclampsia (21% vs 21%), small for gestational age (6.5% vs 2.9%), placental abruption (2.8% vs 3.0%), and postpartum hemorrhage (10.0% vs 8.8%) were comparable. The study concluded that the 162mg aspirin showed a potential benefit over 81mg in recuding thee severe preeclampsia suggesting that the higher doses of aspirin maybe beneficial for preeclampsia.

DISCUSSION

Pre-eclampsia remains a major contributor to maternal and foetal morbidity and mortality, especially in low- and middle-income countries. The pathological basis of the condition is rooted in abnormal placentation and systemic endothelial dysfunction, often triggered by inflammatory and thrombotic pathways. Aspirin, by irreversibly inhibiting cyclooxygenase-1 (COX-1), reduces thromboxane A2 levels, thereby decreasing platelet aggregation and promoting vasodilation mechanisms crucial in preventing the vascular complications seen in pre-eclampsia.

The evidence supporting aspirin's prophylactic use is robust, yet heterogeneous. While some trials (e.g., ASPRE trial) showed up to a 62% reduction in preterm pre- eclampsia when 150 mg of aspirin was started before 16 weeks of gestation, others using lower doses (75–81 mg) did not demonstrate significant benefits. This supports the hypothesis of a dose-response relationship and highlights the importance of timing of aspirin initiation.

Moreover, subgroup analyses consistently reveal that high-risk women — those with a history of pre-eclampsia, multiple gestations, chronic hypertension, or autoimmune disorders — derive the most benefit. Importantly, safety data suggest that low-dose aspirin does not significantly increase the risk of major haemorrhagic events in either the mother or neonate.

Case reports and observational studies also reveal aspirin's potential in improving outcomes in pregnancies complicated by immune-mediated placental inflammation (e.g., CVUE, CIUE). However, rare but serious adverse events, such as intracranial haemorrhage, underscore the need for careful patient selection and monitoring.

The lack of standardization in dosing, definitions of high-risk pregnancies, and inconsistent first-trimester screening tools limits the generalizability of findings. Furthermore, the variability in aspirin bioavailability and individual response necessitates further pharmacogenomic exploration.

CONCLUSION

Low-dose aspirin represents a well-tolerated, cost-effective intervention to reduce the incidence and severity of pre-eclampsia, especially when initiated before 16 weeks of gestation in high-risk pregnancies. While current evidence suggests its routine use in selected populations, standardized guidelines regarding dose, initiation timing, and screening for eligibility are needed. Further research should focus on optimizing

personalized prophylactic strategies, understanding pharmacokinetic variability, and ensuring global accessibility to improve maternal and neonatal outcomes.

REFERENCES

1. Early drug discovery and the rise of pharmaceutical chemistry - Jones - 2011 - Drug Testing and Analysis - Wiley Online LibraryJones AW. Early drug discovery and the rise of pharmaceutical chemistry. Drug Test Anal. 2011 Jun; 3(6): 337-44. doi: 10.1002/dta.301. PMID: 21698778.
2. The first 3500 years of aspirin history from its roots – A concise summary - ScienceDirect Montinari MR, Minelli S, De Caterina R. The first 3500 years of aspirin history from its roots - A concise summary. Vascul Pharmacol. 2019 Feb; 113: 1-8. doi: 10.1016/j.vph.2018.10.008. Epub 2018 Nov 2. PMID: 30391545.
3. Salicylic Acid (Aspirin) - StatPearls - NCBI Bookshelf Arif H, Aggarwal S. Salicylic Acid (Aspirin). 2023 Jul 5. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–.PMID: 30085574.
4. Aspirin | Circulation Awtry EH, Loscalzo J. Aspirin. Circulation. 2000 Mar 14; 101(10): 1206-18. doi: 10.1161/01.cir.101.10.1206. PMID: 10715270.
5. Pre-eclampsia | Nature Reviews Disease PrimersDimitriadis E, Rolnik DL, Zhou W, Estrada-Gutierrez G, Koga K, Francisco RPV, Whitehead C, Hyett J, da Silva Costa F, Nicolaides K, Menkhorst E. Pre-eclampsia. Nat Rev Dis Primers. 2023 Feb 16; 9(1): 8. doi: 10.1038/s41572- 023-00417-6. Erratum in: Nat Rev Dis Primers. 2023 Jul 3; 9(1): 35. doi: 10.1038/s41572-023- 00451-4. PMID: 36797292.
6. Preeclampsia 2012 - Eiland - 2012 - Journal of Pregnancy - Wiley Online Library Eiland E, Nzerue C, Faulkner M. Preeclampsia 2012. J Pregnancy. 2012; 2012: 586578. doi: 10.1155/2012/586578. Epub 2012 Jul 11. PMID: 22848831; PMCID: PMC3403177.
7. Prevention of preeclampsia with aspirin - ScienceDirectRolnik DL, Nicolaides KH, Poon LC. Prevention of preeclampsia with aspirin. Am J Obstet Gynecol. 2022 Feb; 226(2S): S1108-S1119. doi: 10.1016/j.ajog.2020.08.045. Epub 2020 Aug 21. PMID: 32835720.
8. Aspirin at 75 to 81 mg Daily for the Prevention of Preterm Pre-Eclampsia: Systematic Review and Meta-Analysis - PubMedDemuth B, Pellan A, Boutin A, Bujold E, Ghesquière L. Aspirin at 75 to 81 mg Daily for the Prevention of Preterm Pre-Eclampsia: Systematic Review and Meta- Analysis. J Clin Med. 2024 Feb 10; 13(4): 1022. doi: 10.3390/jcm13041022. PMID: 38398335; PMCID: PMC10888723.
9. Aspirin Prophylaxis During Pregnancy: A Systematic Review and Meta-Analysis - ScienceDirectChoi YJ, Shin S. Aspirin Prophylaxis During Pregnancy: A Systematic Review and Meta-Analysis. Am J Prev Med. 2021 Jul; 61(1): e31-e45. doi: 10.1016/j.amepre.2021.01.032. Epub 2021 Mar 30. PMID: 33795180.
10. Combining corticosteroid and aspirin for the prevention of recurrent villitis or intervillositis of unknown etiology] Boog G, Le Vaillant C, Alnoukari F, Jossic F, Barrier J, Muller JY. Association des corticoïdes à l'aspirine pour la prévention des récidives de villite ou d'intervillite chroniques d'étiologie indéterminée [Combining corticosteroid and aspirin for the prevention of recurrent villitis or intervillositis of unknown etiology]. J Gynecol Obstet Biol Reprod (Paris). 2006 Jun; 35(4): 396-404. French. doi: 10.1016/s0368-2315(06)76411-0. PMID: 16940908.
11. Ming M, Han W, Peng J, Zhang R. Intracranial Hemorrhage in a Pregnant Woman on Low-Dose Aspirin: A Case Report. Am J Case Rep. 2025 Apr 11; 26: e946179. doi: 10.12659/AJCR.946179. PMID: 40215213; PMCID: PMC11997900. Intracranial Hemorrhage in a Pregnant Woman on Low-Dose Aspirin: A Case Report.
12. Aja-Okorie U, Ngene NC. Atypical preeclampsia-eclampsia syndrome at 18 weeks of gestation: A case report. Case Rep Womens Health. 2022 Nov 25; 36: e00470. doi: 10.1016/j.crwh.2022.e00470. PMID: 36467289; PMCID: PMC9712551. Atypical preeclampsia- eclampsia syndrome at 18 weeks of gestation: A case report.
13. Nguyen-Hoang L, Dinh LT, Tai AST, Nguyen DA, Pooh RK, Shiozaki A, Zheng M, Hu Y, Li B, Kusuma A, Yapan P, Gosavi A, Kaneko M, Luewan S, Chang TY, Chaiyasit N, Nanthakomon T, Liu H, Shaw SW, Leung WC, Mahdy ZA, Aguilar A, Leung HHY, Lee NMW, Lau SL, Wah IYM, Lu X, Sahota DS, Chong MKC, Poon LC; FORECAST Collaborators. Implementation of First-Trimester Screening and Prevention of Preeclampsia: A Stepped Wedge Cluster-Randomized Trial in Asia. Circulation. 2024 Oct 15; 150(16): 1223-1235. doi: 10.1161/CIRCULATIONAHA.124.069907. Epub 2024 Jun 26. PMID: 38923439; PMCID: PMC11472904.
14. Amro FH, Blackwell SC, Pedroza C, Backley S, Bitar G, Daye N, Bartal MF, Chauhan SP, Sibai BM. Aspirin 162 mg vs 81 mg for preeclampsia prophylaxis in high-risk obese individuals: a comparative effectiveness open-label randomized trial (ASPREO). Am J Obstet Gynecol. 2025 Mar; 232(3): 315.e1-315.e8. doi: 10.1016/j.ajog.2024.06.038. Epub 2024 Jul 6. PMID: 38977068.