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Aspirin vs. Pravastatin for Prevention of Preterm Delivery in Patients at Risk for Pre-Eclampsia

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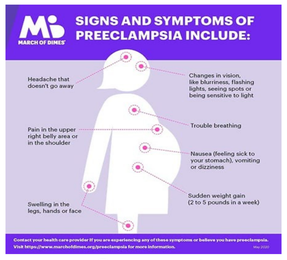
Abstract

•This literature review is an examination of the use of low-dose aspirin therapy versus the use of pravastatin therapy to prevent preterm delivery in women at risk of developing preeclampsia. Preeclampsia is defined as new onset hypertension after 20 weeks of gestation with evidence of maternal organ or uteroplacental dysfunction or proteinuria. Preeclampsia is a serious condition that affects pregnant women and their growing fetuses which may lead to maternal or fetal demise. The Prevention of preeclampsia with the use of low-dose aspirin in the first 12-16 weeks is currently the mainstay of treatment for women with moderate to severe risk factors predisposing them to develop preeclampsia. This literature review looks at the use of low-dose aspirin therapy to prevent preterm delivery and the potential side effects of this therapy on the mother and fetus. Additionally, this review provides some insight into new clinical trials using HMG-CoA reductase inhibitors, specifically pravastatin, and the risk and benefits of this potential treatment option.

•*Keywords: aspirin, pravastatin, preeclampsia prevention, preterm delivery,*

Introduction

Approximately 3-5% of all pregnancies are complicated by preeclampsia (Fox et al, 2019). These pregnancies are at increased risk of having premature births along with other maternal and fetal morbidities. Current guidelines include low-dose aspirin therapy for individuals at moderate to high risk of developing preeclampsia. Low-dose aspirin therapy is the gold standard therapy for preeclampsia with little published research on other medications. However, pravastatin a hydrophilic HMG-CoA reductase inhibitor has been in two published clinical trials researching its safety in pregnancy as well as the potential to prevent preeclampsia and preterm delivery. This review investigates both the risks and benefits of low-dose aspirin therapy and pravastatin therapy in terms of pregnancy and fetal outcomes



Statement of the Problem

Preeclampsia and preterm delivery have continued to plague the healthcare system with no advancements in prevention and minimal improvements to guidelines in the last five years. The study has reviewed clinical trials of aspirin therapy and pravastatin therapy to compare their efficacy in preventing preeclampsia and preterm delivery.

Research Question

In pregnant patients at risk of developing preeclampsia which drug therapy between low dose aspirin and pravastatin is more effective at preventing preterm delivery?

Literature Review

- **Risk reduction of preterm preeclampsia and preterm delivery with pravastatin prophylaxis**
- Costantine et al. (2021) performed a multicenter, blinded, placebo-controlled pilot study that randomized women to a 20mg dose of pravastatin or a placebo to examine the risk vs. benefit of pravastatin therapy
  - The study concluded that pravastatin therapy could be helpful in preventing preeclampsia and its associated effects such as preterm delivery.
- Ahmed et al. (2019) performed a blinded controlled study to determine if women with preeclampsia can lower their elevated circulating levels of soluble fms-like tyrosine kinase-1 by taking pravastatin. Soluble fms-like tyrosine kinase-1 antagonizes vascular endothelial growth factor (VEGF) activity.
  - There was no evidence that pravastatin decreased soluble fms-like tyrosine kinase-1
- **Risk reductions of preterm preeclampsia and preterm delivery with aspirin prophylaxis**
- Hoffman et al. (2020) performed a randomized, placebo-controlled study to determine if low-dose aspirin therapy started before 16 weeks decreased the risk of preeclampsia and subsequent preterm delivery.
  - The study was able to conclude that aspirin therapy started between 6 weeks and 13 weeks reduced the incidence of preterm delivery before 37 weeks and reduced perinatal mortality.
- Rolnik et al 2017 performed a randomized, placebo-controlled study to ascertain whether the intake of low-dose aspirin during pregnancy reduces the risk of preeclampsia
  - It was concluded that low-dose aspirin therapy reduced the risk of preeclampsia in women at high risk
- **The risk of statin therapy and aspirin therapy during pregnancy**
- The retrospective cohort study done by Chang et al. (2021) examined the perinatal outcomes among offspring associated with maternal use of statins during pregnancy. Women who received a diagnosis of hyperlipidemia before pregnancy were considered the statin-exposed group in this study. This literature review looked at the outcomes associated with pravastatin therapy.
  - This study concluded that statins were associated with a greater risk of preterm delivery, however, pravastatin specifically did not seem to increase this risk. Pravastatin during pregnancy to prevent preeclampsia did not show any identifiable safety risks.
- Ofori et al.(2007) assembled a population-based pregnancy registry to examine three women groups, women prescribed aspirin therapy in the first trimester, women prescribed fibrates/nicotinic acid, and women who stopped taking aspirin between 1 month and 1 year of conceiving
  - It was concluded that statin therapy did not show evidence of increased fetal congenital anomalies or evidence of any risk to the fetus of women filling statin prescriptions in the first trimester. The study recommends further research
- Hastie et al 2021 performed a register-based cohort study to investigate whether aspirin therapy during pregnancy was associated with increased bleeding risk
  - The study concludes that aspirin therapy is associated with an increased risk of postpartum bleeding and postpartum hematoma. The study concludes that it may also be associated with neonatal intracranial hemorrhage.

Discussion

Aspirin therapy is recommended by ACOG and the United States Preventative Services Task Force as the treatment for individuals at moderate to high risk of developing preeclampsia. Aspirin therapy has numerous studies reinforcing its efficacy and its benefit in the prevention of preeclampsia and the study by Hoffman et al. (2020) provided data that aspirin therapy administered between 6 weeks and 13 weeks of gestation reduced the risk of delivery before 37 weeks.

Pravastatin is a hydrophilic HMG-CoA reductase inhibitor used to treat hyperlipidemia. Statin use is considered a category X medication and is not advised to use during pregnancy however several studies performed in this literature review provide evidence that this medication can be safe and efficacious during pregnancy. The study by Constantine et al. (2021) found pravastatin to have some beneficial properties that decreased the risk of preeclampsia in at-risk populations and prevent preterm delivery. Evidence was provided that support that pravastatin is efficacious and safe to use during pregnancy

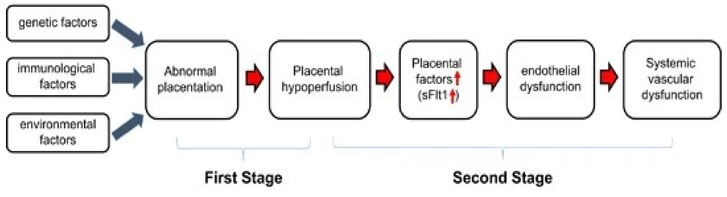
The question that must be discerned is: Is there any comparison between aspirin and pravastatin when it comes to the ability to prevent preterm delivery?

- Low-dose aspirin therapy has been deemed a safe therapy for pregnant patients and has been the gold standard of care. Studies have shown support that the benefits of therapy far outweigh the risks of associated bleeding.
- Although pravastatin has limited studies the articles observed in this literature review would suggest that therapy with 20mg of pravastatin can help prevent preeclampsia and prevent the risk of preterm delivery (Costantine et al 2021), without increasing the risk of congenital anomalies (Ofori et al 2007).

The intrigue with pravastatin therapy is that young patients wanting to have children would no longer have to stop their statin therapy while trying to get pregnant or while pregnant. The studies for pravastatin could prove the safety of the medication while also helping to reduce hyperlipidemia and its increase in coronary artery disease and heart attack risk.

The difficulty with this literature review is that there are no direct studies comparing these two therapies against one another. Aspirin therapy has been around for a decade or two and has studies to back the treatment while pravastatin has recently been in the eyes of academics as treatment. Currently, the guidelines remain that aspirin therapy is the main choice when it comes to preeclampsia, however, pravastatin will continue to be studied and maybe there will be a new preventative treatment on the horizon or a conjoined therapy in the future.

Two Stage Theory of Preeclampsia



Applicability to Clinical Practice

The clinical implications of this literature review are important as preeclampsia continues to be a dangerous complication of pregnancy and can detrimentally affect the mother and the fetus. Currently, guidelines continue to push aspirin therapy for prevention starting at 12 to 16 weeks. Aspirin therapy is considered safe and effective at this time and should be continued to be prescribed. Perhaps in the future new medications, such as pravastatin, will move on from clinical trials and be proven advantageous to individuals at risk for preeclampsia. As always it is important for blood pressure to be monitored at every prenatal visit and observation for swelling.

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