Aspirin &Pregnancy

Dr.Nooshin Eshraghi

Perinatologist –Assistant professor

IUMS

Pharmacologic Category

- Analgesic, Nonopioid
- Antiplatelet Agent
- Nonsteroidal Anti-inflammatory Drug (NSAID) Oral
- Salicylate

Pathophysiology

- Aspirin (acetylsalicylic acid) is a nonsteroidal antiinflammatory drug (NSAID) that works primarily through its inhibition of two cyclooxygenase isoenzymes (COX-1 and COX-2), which are necessary for prostaglandin biosynthesis.

- The COX-1 isoform is present in the vascular endothelium and regulates the production of prostacyclin and thromboxane A_2, prostaglandins with opposing regulatory effects on vascular homeostasis and platelet function. Prostacyclin is a potent vasodilator and inhibitor of platelet aggregation, whereas thromboxane A_2 (TXA2) is a potent vasoconstrictor and promotes platelet aggregation.

- Low-dose aspirin has been used during pregnancy, most commonly to prevent or delay the onset of preeclampsia

Evidence of efficacy

- At least four large randomized trials, as well as several small trials, have demonstrated a reduction in the incidence of preeclampsia in patients treated with low-dose aspirin prophylaxis compared with placebo/no treatment.

High Risk

- -History of preeclampsia ,especialy when accompaired by an adversed outcome
- Multifetal Gestation
- -chronic HTN
- -Type 1or 2 Diabets
- -Renal Disease
- -Autoimune Disease(SLE)

Moderate Risk

- -Nuliparity
- -Obesity(BMI>30)
- -FH of preeclampsia(mother or sister)
- -Personal history factor (LBW-SGA-previouse pregnancy adverse outcome –
- interval pregnancy>10 y)
- Age ≥35 years
- Sociodemographic characteristics (African American race, low socioeconomic level)

- Even though nulliparous women are the group comprising the largest proportion of preeclampsia cases, nulliparity alone is not an indication for prophylaxis, as major trials limited to unselected nulliparous women have found little or no benefit from prophylactic low-dose aspirin therapy

unexplained prior sillbirth

- Low-dose aspirin prophylaxis is not recommended solely for the indication unexplained prior stillbirth, in the absence of risk factors for preeclampsia.

prevention of fetal growth restriction

- Low-dose aspirin prophylaxis is not recommended for prevention of fetal growth restriction, in the absence of risk factors for preeclampsia

prevention of spontaneous preterm birth

- Low-dose aspirin prophylaxis is not recommended for the prevention of spontaneous preterm birth, in the absence of risk factors for preeclampsia.

Contraindications

- Hypersensitivity to NSAIDs; patients with asthma, rhinitis, and nasal polyps.
- Exposure to low-dose aspirin in patients with nasal polyps may result in life-threatening bronchoconstriction and should be avoided.

- Relative contraindications to low-dose aspirin include a history of gastrointestinal bleeding, active peptic ulcer disease, other sources of gastrointestinal or genitourinary bleeding, and severe hepatic dysfunction.

hemorrhagic complications

- The majority of systematic reviews of randomized controlled trials (RCTs) have found no increase in hemorrhagic complications associated with low-dose aspirin during pregnancy

- The decision to continue low-dose aspirin in the presence of obstetric bleeding or risk factors for obstetric bleeding should be considered on a case-by-case basis .

placental abruption

- low-dose aspirin for prevention of preeclampsia identified no increased risk of placental abruption .

Fetal Risks

- Several systematic reviews of trials using low-dose aspirin for prevention of preeclampsia have shown no increased risk of congenital anomalies

- concern has been raised about a possible association between aspirin use during pregnancy and gastroschisis

Safety

there is no apparent risk of fetal/neonatal intracranial bleeding and no difference in developmental outcomes at 18 months of age

adverse effects

- Many adverse effects of aspirin are dose related, and are rare at low dosages. Other serious reactions are idiosyncratic, related to allergy or individual sensitivity.
- Cardiovascular: Cardiac arrhythmia, edema, hypotension, tachycardia

- Central nervous system: Agitation, cerebral edema, coma, confusion, dizziness, fatigue, headache, hyperthermia, insomnia, lethargy, nervousness, Reye's syndrome
- Dermatologic: Skin rash, urticaria
- Endocrine & metabolic: Acidosis, dehydration, hyperglycemia, hyperkalemia, hypernatremia (buffered forms), hypoglycemia (children)

- Gastrointestinal: Gastrointestinal ulcer (6% to 31%), duodenal ulcer, dyspepsia, epigastric distress, gastritis, gastrointestinal erosion, heartburn, nausea, stomach pain, vomiting
- Genitourinary: Postpartum hemorrhage, prolonged gestation, prolonged labor, proteinuria, stillborn infant

- Hematologic & oncologic: Anemia, blood coagulation disorder, disseminated intravascular coagulation, hemolytic anemia, hemorrhage, iron deficiency anemia, prolonged prothrombin time, thrombocytopenia

- Hepatic: Hepatitis (reversible), hepatotoxicity, increased serum transaminases
- Hypersensitivity: Anaphylaxis, angioedema
- Neuromuscular & skeletal: Acetabular bone destruction, rhabdomyolysis, weakness

- Otic: Hearing loss, tinnitus
- Renal: Increased blood urea nitrogen, increased serum creatinine, interstitial nephritis, renal failure (including cases caused by rhabdomyolysis), renal insufficiency, renal papillary necrosis

- Respiratory: Asthma, bronchospasm, dyspnea, hyperventilation, laryngeal edema, noncardiogenic pulmonary edema, respiratory alkalosis, tachypnea
- Miscellaneous: Low birth weight

LOW-DOSE ASPIRIN

- Low-dose aspirin reduces the frequency of preeclampsia, as well as related adverse pregnancy outcomes (preterm birth, growth restriction), by approximately 10 to 20 percent when given to women at moderate to high risk of the disease. It has an excellent maternal/fetal safety profile in pregnancy; thus, it is a reasonable preventive strategy for these wome .

Timing of Use During Pregnancy

- low-dose aspirin during pregnancy have initiated between 12 weeks and 16 weeks of gestation. Some investigators have reported optimal results only when treatment is started before 16 weeks .

- . Study protocols specific to pregnancy have varied, with some discontinuing low-dose aspirin at 36 weeks of gestation and others continuing low-dose aspirin until delivery .

- Some believe that aspirin may be more effective if taken at bedtime; however, specifying timing of administration is not standard practice and night-time dosing may increase gastric irritation.

Dose

- The optimal dose of aspirin for preeclampsia prevention is controversial.
- use 81 mg daily.
- Randomized trials of aspirin for preeclampsia prevention have used doses ranging from 50 to 150 mg daily .
- trial, 150 mg aspirin was used with a significant risk reduction of preterm preeclampsia

- A 2018 meta-analysis in which subgroup analyses of preterm and term preeclampsia were available found that aspirin reduced the risk of preterm preeclampsia, but not term preeclampsia, and only when it was initiated at ≤16 weeks of gestation and at a daily dose of ≥100 mg .
- Based on these data, some practitioners have advocated a higher dose of aspirin (100 to 150 mg) daily rather than the lower dose of 75 to 81 mg.

- As opposed to higher dose aspirin therapy, low-dose aspirin (60 to 150 mg/day) diminishes platelet thromboxane synthesis while maintaining vascular wall prostacyclin synthesis .Although not well studied, the beneficial effect of low-dose aspirin for prevention of preeclampsia may also be partly related to modulation of inflammation, which is exaggerated in women with preeclampsia

- The combination of low-dose aspirin and unfractionated or low-molecular-weight heparin has been shown to reduce the risk of early pregnancy loss in women with antiphospholipid syndrome .

Conclusions

- Daily low-dose aspirin use in pregnancy is considered safe and is associated with a low likelihood of serious maternal, or fetal complications, or both, related to use. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine support the USPSTF guideline criteria for prevention of preeclampsia.

- . Low-dose aspirin (81 mg/d) prophylaxis is recommended in women at high risk of preeclampsia and should be initiated between 12 weeks and 28 weeks of gestation (optimally before 16 weeks) and continued daily until delivery


THANK
YOU