MANAGEMENT HYPERTENSIVE DISORDER IN PREGNANCY UPTODATE 2022

DR TAYEBE NOORI

OBSTETRICIAN & GYNECOLOGIST

THERE ARE 4 MAJOR HYPERTENSIVE DISORDERS RELATED TO PREGNANCY

1)preeclampsia/Eclampsia

2)Chronic /preexisting HTN

3) Preeclampsia superimposed upon chronic hypertension

4) Gestational hypertension

Preeclampsia is a multisystem progressive disorder characterized by

the new onset of hypertension and proteinuria, or of hypertension and significant end-organ dysfunction with or without proteinuria, in the last half of pregnancy or postpartum in a previously normotensive woman. The disorder is *caused* by placental and maternal vascular dysfunction and always resolves after delivery.

INCIDENCE

- **In a systematic review, 4.6 percent of pregnancies worldwide were complicated by preeclampsia .**
- **The incidence in the United States is approximately 5 percent Preeclampsia is less common before 34 weeks of gestation.**

GESTATIONAL HYPERTENSION

- — Gestational hypertension is the most common cause of hypertension during pregnancy. It occurs in 6 to 17 percent of healthy nulliparous women and 2 to 4 percent of multiparous women
- hypertension (systolic ≥140 and <160 mmHg, and/or diastolic ≥90 and <110 mmHg) without proteinuria or other signs/symptoms of preeclampsia-related end-organ dysfunction that develops after 20 weeks
- Some women (10 to 25 percent) with gestational hypertension may ultimately develop signs and symptoms of preeclampsia

PREECLAMPSIA WITH SEVERE FEATURES

INCIDENCE:

the overall incidence of preeclampsia with severe features was approximately 1 percent

Studies limited to nulliparous patients report a 2 to 2.5 percent incidence of preeclampsia with severe features . Approximately 30 percent of cases occur before 34 weeks of gestation

POTENTIAL CONSEQUENCES OF SEVERE DISEASE

Maternal

Serious maternal complications of preeclampsia with severe features include pulmonary edema, hypertensive encephalopathy, stroke, kidney failure, liver failure or rupture, retinal detachment or cortical blindness, DIC, placental abruption, seizures (eclampsia), myocardial infarction, cardiomyopathy, and death

Fetal

Serious fetal complications of preeclampsia with severe features include growth restriction and death. The frequency of these complications depends, in part, on the gestational age at onset: Early onset (variably dened as either second trimester or <34 weeks of gestation) has a poorer prognosis than late onset (variably dened as either third trimester or ≥34 weeks of gestation).

DIAGNOSTIC CRITERIA

PREECLAMPSIA WITH SEVERE FEATURES

- Systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg and proteinuria
- New-onset cerebral or visual disturbance, such as:

-**Photopsia** (flashes of light) and/or **scotomata**

-**Severe headache** (ie, incapacitating, "the worst headache I've ever had") or headache that persists and progresses despite analgesic therapy.

-**Altered mental status**.

Severe, persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by an alternative diagnosis or serum transaminase concentration ≥2 times upper limit of normal for a specific laboratory, or both.

- <100,000 platelets/microL.
- Progressive renal insufficiency (serum creatinine >1.1 mg/dL [97.3 micromol/L]; some guidelines also include doubling of serum creatinine concentration in the absence of other renal disease).
- Pulmonary edema

RISK FACTORS FOR PREECLAMPSIA

1) A **past history of preeclampsia** increases the risk of developing preeclampsia in a subsequent pregnancy eightfold compared with women without this history

- The severity of preeclampsia strongly impacts this risk. Women with severe features of preeclampsia in the second trimester are at greatest risk of developing preeclampsia in **a subsequent pregnancy: Rates *of 25 to 65 percent have been reported***
- . By comparison, women without severe features of preeclampsia in their first pregnancy develop preeclampsia **in 5 to 7 percent** of second pregnancies
- Women who had a normotensive first pregnancy develop preeclampsia in less than 1 percent of second pregnancies

PREEXISTING MEDICAL CONDITIONS

1)**Pregestational diabetes :** This increase has been related to a variety of factors, such as underlying renal or vascular disease, high plasma insulin levels/insulin resistance, and abnormal lipid metabolism.

2)**Chronic hypertension :** Blood pressure ≥130/80 mmHg at the first prenatal visit has also been reported to increase risk . Although chronic hypertension (defined as blood pressure ≥140/90 mmHg) increases the risk of preeclampsia 5fold compared with women without this risk factor,

3)Systemic lupus erythematosus

4)Antiphospholipid syndrome

5)**Prepregnancy BMI>25**

and **(BMI) >30**– The risk of preeclampsia doubles with each 5 to 7 kg/m^2 increase in prepregnancy BMI.

6)**Chronic kidney disease (CKD)** . In some studies, as many as 40 to 60 percent of women with advanced CKD (stages 3, 4, 5) were diagnosed with preeclampsia

- ✓ **Multifetal pregnancy**– The risk increases with increasing numbers of fetuses
- ✓ **First pregnancy (nulliparity)**– It is unclear why the nulliparous state is consistently found to be a significant predisposing factor for preeclampsia.
- ✓ **A family history of preeclampsia** in a first-degree relative

suggesting a heritable mechanism in some cases . The occurrence and severity of the disease appears to be influenced primarily by maternal factors, but the paternal contribution to fetal genes may have a role in defective placentation and subsequent preeclampsia

- ✓ **Prior pregnancy complications associated with placental insufficiency** – Fetal growth restriction, abruption , or stillbirth

- ✓ **Advanced maternal age** (maternal age ≥35

  Older women tend to have additional risk factors, such as diabetes mellitus and chronic hypertension, that predispose them to developing preeclampsia

- ✓ **Use of assisted reproductive technology(ART)**

  - ➢ Of note, women who smoke cigarettes have a **lower** risk of preeclampsia than nonsmokers.

CLINICAL (ALARM FINDING) PRESENTATION

- Persistent and/or severe headache
- Visual abnormalities (scotomata, photophobia, or temporary blindness [rare])
- Upper abdominal or epigastric or retrosternal pain
- Altered mental status(confusion, altered behavior [agitation])
- New dyspnea, orthopnea

INITIAL ASSESSMENT AND MANAGEMENT OF PREGNANCIES WITH PREECLAMPSIA WITH SEVERE FEATURES:

- Admission to the labor and delivery unit
- – The patient may need to be monitored in an intensive care type setting for as long as 48 hours.

- Administration of antenatal corticosteroids to preterm pregnancies if delivery is not imminent

PREECLAMPSIA: MANAGEMENT AND PROGNOSIS

the definitive treatment is delivery to prevent development of maternal or fetal complications from disease progression. Delivery leads to eventual resolution of the disease.

- Timing of delivery is based on a combination of factors, including disease severity, maternal and fetal condition, and gestational age. Pharmacotherapy does not prevent disease progression, but low-dose aspirin can reduce the occurrence of preeclampsia, antihypertensive therapy can prevent and treat severe hypertension, and magnesium sulfate can prevent seizures.

PREECLAMPSIA WITHOUT FEATURES OF SEVERE DISEASE

❑ **Term pregnancies:**

- **Delivery** — Experts consistently recommend delivery of patients with preeclampsia at ≥37wof gestation, even without features of severe disease (previously called "mild preeclampsia") .
- The benefits of this approach are best supported by a multicenter trial (HYPITAT) that randomly assigned 756 women with mild preeclampsia or gestational hypertension at 36+0 to 41+0 weeks of gestation to induction of labor within 24 hours of randomization or expectant management with maternal/fetal monitoring . Intervention had favorable efects on maternal outcome, without incurring an increase in cesarean delivery or neonatal morbidity.

- ✓ **Induction resulted in a 30 percent reduction in a composite of serious maternal outcomes. The composite included maternal mortality, maternal morbidity (eclampsia, HELLP syndrome , pulmonary edema, thromboembolic disease, placental abruption), progression to severe hypertension or proteinuria, and major postpartum hemorrhage.**
- ✓ **Induction resulted in a lower rate of cesarean delivery (14 versus 19 percent).**
- ✓ **Induction did not result in statistical diferences between groups in any neonatal outcome measure, even though the induced group delivered, on average, 1.2 weeks earlier than the control group. The possibility of small diferences in newborn outcomes could not be denitively excluded because of the small number of adverse outcomes.**

MANAGEMENT :PREECLAMPSIA WITH FEATURES OF SEVERE DISEASE

indication for delivery in pregnancies ≥34 weeks of gestation .

Delivery minimizes the risk of serious maternal complications, such as cerebral hemorrhage, hepatic rupture, renal failure, pulmonary edema, seizure, bleeding related to thrombocytopenia, myocardial infarction, stroke, acute respiratory distress syndrome, retinal injury, or abruptio placentae, and fetal complications, such as growth restriction and fetal demise . With the exception of fetal growth restriction, any of these life-threatening complications can occur suddenly

- **Expectant management** rather than delivery is reasonable for selected preterm pregnancies with preeclampsia with features of severe disease to reduce neonatal morbidity from immediate preterm birth, even though the mother and fetus are at risk from disease progression. Expectant management allows administration of a course of antenatal corticosteroids and may provide time for further fetal growth and maturation.

For consideration of this approach, **both the mother and fetus should be stable**, closely monitored in a hospital with an appropriate level of newborn care, and cared for by, or in consultation with, a maternal-fetal medicine specialist. **We favor limiting expectant management to pregnancies ≥24 weeks and <34 weeks of gestation**.

In studies of expectant management of preeclampsia with severe features with onset in the second trimester, 25 to 63 percent of patients developed serious complications, including HELLP syndrome , renal insuciency, placental abruption, pulmonary edema, and eclampsia

Perinatal mortality

Studies of expectant management of preeclampsia with severe features with onset in the second trimester describe high perinatal mortality (PNM) :

Onset <22+6 weeks –-- PNM %98

Onset 23+0 to 23+6 weeks---– PNM %87

Onset 24+0 to 24+6 weeks ---– PNM %67

Onset 25+0 to 26+0 weeks ---– PNM %40

PRETERM PREGNANCIES: EXPECTANT MANAGEMENT

- **At preterm gestational ages, the risks for serious sequelae from disease progression needs to be balanced with the newborn risks resulting from preterm birth. When mother and fetus are stable and have no findings of serious endorgan dysfunction, an expectant approach with close monitoring for evidence of progression to the severe end of the disease spectrum is reasonable to achieve further fetal growth and maturity.**
- **However, at any gestational age, evidence of severe hypertension, serious maternal end-organ dysfunction , or nonreassuring tests of fetal well-being are generally an indication for prompt delivery. Before 34 weeks**

34+0 TO 36+6 WEEKS

- **management of preeclampsia without features of severe disease and stable maternal and fetal condition at 34+0 to 36+6 weeks. Although there are serious maternal risks with expectant management, we believe expectant management until 37+0 weeks is reasonable in fully informed patients because the absolute maternal risk of a serious adverse outcome is low, and there are modest neonatal benfits from delivery at 37+0 weeks rather than earlier.**

COMPONENTS OF EXPECTANT MANAGEMENT ✓ INPATIENT VERSUS OUTPATIENT CARE

- **Close maternal monitoring** upon diagnosis of preeclampsia is important to establish disease severity and the rate of progression.
- **Hospitalization** is useful for making these assessments and facilitates immediate intervention in the event of rapid deterioration. After the initial in-hospital diagnostic evaluation, outpatient care is a cost-eective option for patients found to be stable over a period of several days and with no severe features of preeclampsia
- **Patients** oered **outpatient** monitoring should be well-informed and understand the importance of calling for symptoms/signs of worsening disease, able to comply with modied activity at home, live close to a hospital, have someone at home at all times to call in the event of an unexpected adverse event, able to have blood pressure measured twice daily, and willing to come in for antenatal visits twice a week for fetal monitoring and blood tests. Readmission is indicated for progression of disease

Compared with expectant management, planned early delivery:

- **Reduced adverse maternal composite** outcome (maternal morbidity or systolic blood pressure ≥160 mmHg .
- **Increased adverse perinatal composite** outcome (**perinatal death or neonatal unit admission**.

Indications for Delivery in Women <34 Weeks' Gestation Managed Expectantly

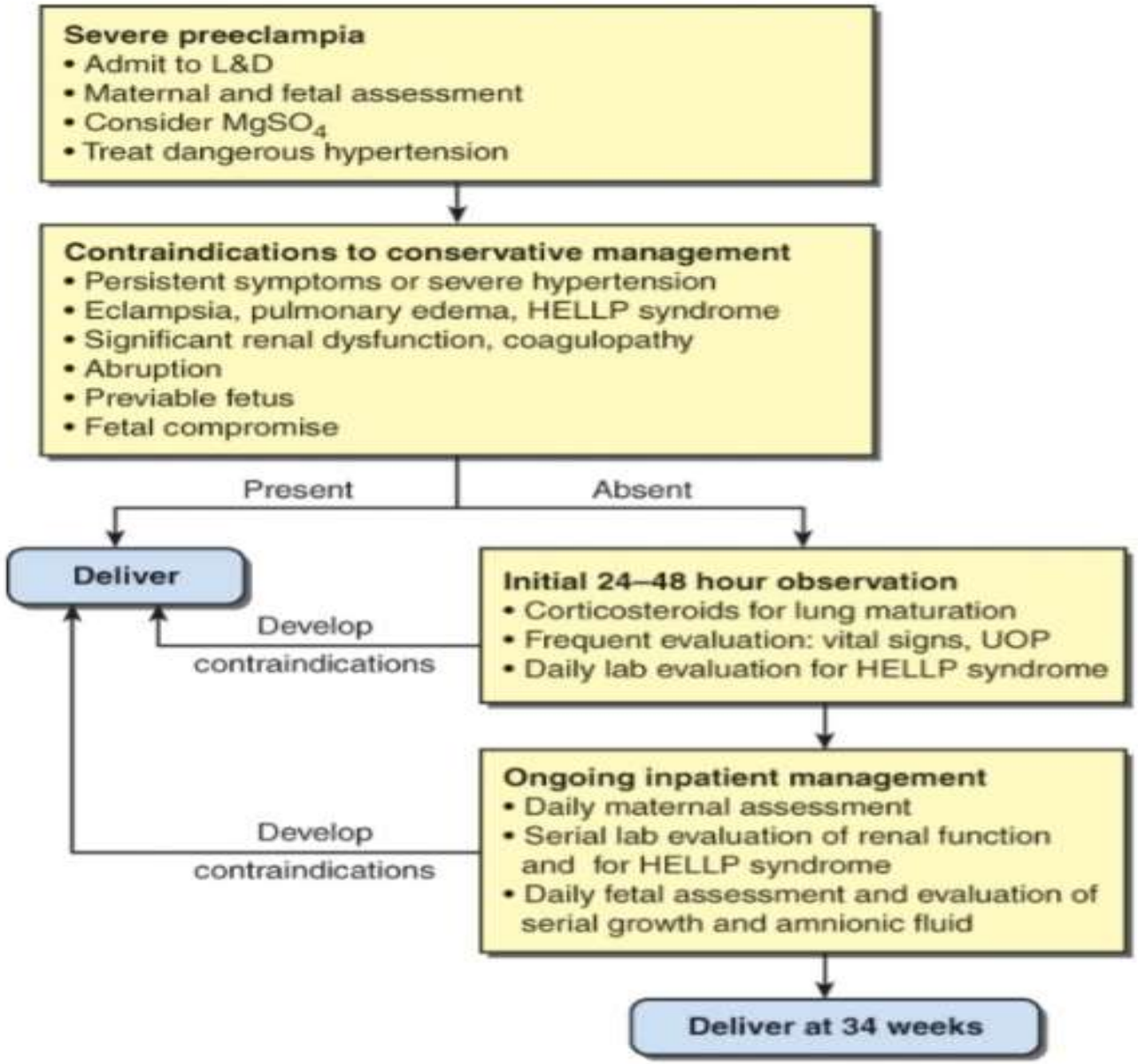
Corticosteroid Therapy for Lung Maturation[a] and Delivery after Maternal Stabilization:

- Uncontrolled severe hypertension
- Eclampsia
- Pulmonary edema
- Placental abruption
- Disseminated intravascular coagulation
- Nonreassuring fetal status
- Fetal demise

Corticosteroid Therapy for Lung Maturation—Delay Delivery 48 hr If Possible:

- Preterm ruptured membranes or labor
- Thrombocytopenia <100,000/μL
- Hepatic transaminase levels twice upper limit of normal
- Fetal-growth restriction
- Oligohydramnios
- Reversed end-diastolic Doppler flow in umbilical artery
- Worsening renal dysfunction

$MgSO_4$= magnesium sulfate; UOP = urine output. (Adapted from the Society for Maternal-Fetal Medicine, 2011.)



Source: F. Gary Cunningham, Kenneth J. Leveno, Steven L. Bloom, Catherine Y. Spong, Jodi S. Dashe, Barbara L. Hoffman, Brian M. Casey, Jeanne S. Sheffield: *Williams Obstetrics*, 25th Edition
Copyright © McGraw-Hill Education. All rights reserved.

- **Patient education** — All women with preeclampsia should be aware of the signs and symptoms at the severe end of the disease spectrum and should monitor fetal movements daily.
- If a woman develops a severe or persistent headache (ie, does not respond to one dose of acetaminophen), visual changes, new shortness of breath, or right upper quadrant or epigastric pain, she should notify her health care provider immediately. Women who self-monitor blood pressure should be instructed about the correct procedure.
- As with any pregnancy, decreased fetal movement, vaginal bleeding, abdominal pain, rupture of membranes, or uterine contractions should be reported immediately, as well.
- **Activity** — Strict bedrest is unnecessary as there is no evidence that bedrest improves pregnancy outcome or delays progression of the disease Furthermore, strict bedrest in hospitalized pregnant women has been associated with an increased risk of venous thromboembolism

- **Monitoring blood pressure and treatment of hypertension** — Blood pressure should be measured daily at home in patients being managed expectantly with preeclampsia without severe features and at least twice weekly in the office.
- A sustained elevation of systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg or both for ≥15 minutes should prompt immediate hospitalization for further evaluation and management. Antihypertensive therapy should be initiated as soon as reasonably possible, ideally within 30 to 60 minutes.

The use of antihypertensive drugs to control mild hypertension (defined as systolic blood pressure <160 mmHg and diastolic blood pressure <110 mmHg) in the setting of preeclampsia does not alter the course of the disease or diminish perinatal morbidity or mortality, and should be avoided in most patients.'

-

- **Assessment of fetal growth — Early fetal growth restriction may be the first manifestation of preeclampsia and is a sign of severe uteroplacental insufficiency. At the time of diagnosis of preeclampsia, we perform sonography to estimate fetal weight and assess amniotic fluid volume for evaluation of fetal growth restriction and oligohydramnios. If the initial examination is normal, we repeat the ultrasound examination for fetal growth every three weeks.**
- **Assessment of fetal well-being** .
- We suggest at minimum daily fetal movement counts and twice weekly nonstress testing plus assessment of amniotic fluid volume, or twice weekly biophysical profiles, beginning at the time of diagnosis of preeclampsia.

- **Antenatal corticosteroids — Although preeclampsia may accelerate fetal lung maturation, neonatal respiratory distress remains common in premature neonates of pregnancies with preeclampsia .**

Antenatal corticosteroids (betamethasone) to promote fetal lung maturity should be administered to women <34 weeks of gestation since

. However, delivery should not be delayed solely for administration of a full course of steroids.

course of steroids is administered when the clinician believes delivery within the next seven days is likely and neonatal resuscitation is planned. Use of steroids after 34 weeks is more complicated and discussed separately.

✓ ACUTE THERAPY OF SEVERE HYPERTENSION

Choice of therapy — We suggest **labetalol** or **hydralazine** administered intravenously as a first-line agent for acute therapy of severe hypertension. The author prefers to limit use of oral immediate-release rapid-acting nifedipine as a first-line option to patients in whom intravenous access is not readily available because a rapid large reduction in blood pressure may occur

- (ACOG) considers labetalol, hydralazine, or immediate-release rapid-acting nifedipine similarly safe and efective as first-line options for urgent treatment of acute, severe hypertension

LABETALOL DOSING

- — We suggest intravenous labetalol for first-line therapy because it is efective, has a rapid onset of action , and has a good safety prole . Asthma or maternal heart rate <50 beats/minute is a contraindication to use, whereas labetalol is preferred to other classes of antihypertensive drugs if the maternal heart rate >110 beats/minute.

Begin with 20 mg intravenously over 2 minutes followed at 10-minute intervals by doses of 20 to 80 mg up to a maximum total cumulative dose of 300 mg if blood pressure remains above target level. As an example, give 20 mg, then 40 mg, then 80 mg, then 80 mg, then 80 mg. A constant infusion of 1 to 2 mg/minute can be used instead of intermittent therapy.

- The fall in blood pressure begins within 5 to 10 minutes and lasts from three to six hours.

HYDRALAZINE

- **Begin with 5 mg intravenously over 1 to 2 minutes; if the blood pressure goal is not achieved within 20 minutes, give a 5 to 10 mg bolus depending on the initial response.**
- **The fall in blood pressure begins within 10 to 30 minutes and lasts from two to four hours**
- **● If a total cumulative dose of 20 to 30 mg per treatment event does not achieve optimal blood pressure control or heart rate exceeds 100 beats/minute, another agent should be used.**
- **● If hydralazine is inefective, we suggest switching to labetalol**

CANDIDATES FOR SEIZURE PROPHYLAXIS

- Magnesium sulfate should be used for the prevention of seizures in patients with preeclampsia with severe features. magnesium sulfate treatment reduced the risk of eclampsia
- We do not administer seizure prophylaxis to women with only gestational hypertension , as the seizure risk in these patients is less than 0.1 percent

✓ (ACOG) has opined that the "clinical decision of whether to use magnesium sulfate for seizure prophylaxis in patients with preeclampsia without severe features should be determined by the physician or institution, considering patient values or preferences, and the unique risk-benfit trade-off of each strategy".

CONTRAINDICATIONS MG SULFATE

- **Magnesium sulfate is contraindicated in women with myasthenia gravis since it can precipitate a severe myasthenic crisis. Alternative anticonvulsant drugs should be used**
- **Although at least one guideline considers pulmonary edema a contraindication to use of magnesium sulfate , the authors administer the drug cautiously to patients with pulmonary edema, with attention to fluid restriction, diuresis, and oxygen supplementation.**

Timing – MAGNESIUM sulfate for seizure prophylaxis is usually **initiated at the onset of labor or induction**, or prior to and throughout the duration of a cesarean delivery. It is usually not administered to stable antepartum patients, but is sometimes given to women with preeclampsia with severe features while they are being considered for expectant management. **Prolonged antepartum therapy (more than five to seven days)** should be avoided as it has been associated with **adverse effects on fetal bones**

Dosing – **The most common magnesium sulfate regimen in patients with normal renal function** is: a loading dose 4- 6 g of a 10 percent solution intravenously over 15 to 20 minutes followed by 2 g/hour as a continuous infusion .

If intravenous access is not available :An alternative regimen is 5 g of a 50 percent solution intramuscularly into each buttock (total of 10 g) followed by 5 g intramuscularly every four hours (may be mixed with 1 mL of xylocaine 2% solution to reduce pain). These regimens generally result in similar magnesium levels; however, intramuscular administration results in more fluctuation and is associated with more side effects, particularly pain at the injection site .

- **Management of thrombocytopenia** — The risk of bleeding due to thrombocytopenia is generally considered to increase only when the platelet count is below 100,000/microL, and the risk increases substantially only with platelet counts below 50,000/microL. Platelet transfusion should not be used to normalize the platelet count in nonbleeding patients, as long as the platelet count is above 10,000 to 20,000/microL.

- Although a platelet count >50,000/microL is generally considered safe for delivery (vaginal or cesarean)

- For severely thrombocytopenic patients (platelet count <20,000/microL), the author notifies the blood bank and has platelets readily available in the delivery room for transfusion in case excessive bleeding develops at vaginal delivery or excessive oozing is observed at the time of the skin incision at cesarean. Excessively bleeding patients are transfused

- **Route delivery**— Cesarean delivery is reserved for standard obstetric indications . --
  *Cervical ripening
- but if we fail to see significant cervical change in response to cervical ripening agents within 12 hours, we consider moving to cesarean. Obviously, we would move to cesarean sooner if the patient's condition worsens.

PREECLAMPSIA: PREVENTION

- . In women at high risk of developing preeclampsia, low-dose aspirin prophylaxis has preventive effects,.

Evidence of efficacy:

Reduction in proteinuric preeclampsia: Risk ratio (RR) 0.82, 95% CI 0.77-0.88

- Reduction in fetal or neonatal death: RR 0.85, 95% CI 0.76-0.95
- Reduction in overall preterm birth <37 weeks: RR 0.91, 95% CI 0.87-0.95
- Reduction in small for gestational age infants: RR 0.84, 95% CI 0.76-0.92
- Reduction in composite serious adverse maternal and neonatal outcomes: RR 0.90, 95% CI 0.85-0.96

The intervention may have slightly increased the risk of postpartum hemorrhage >500 mL (RR 1.06, 95% CI 1.00-1.12) but did not have a significant effect on risk of abruption (RR 1.21, 95% CI 0.95-1.54).

CANDIDATESPREGNANT WOMEN WITH ANY ONE OF THESE HIGH RISK FACTORS:

- Previous pregnancy with preeclampsia, especially early onset and with an adverse outcome
- Multifetal gestation
- Chronic hypertension
- Type 1 or 2 diabetes mellitus
- Chronic kidney disease
- Autoimmune disease with potential vascular complications (APS/SLE)

- ✓ **Low-dose aspirin (60 to 150 mg daily) is the only drug for which there is proven evidence of benet in reducing the risk of preeclampsia when administered throughout the second and third trimesters in patients at high risk.**
- ✓ **For women at low risk for development of preeclampsia, available evidence does not support use of low-dose aspirin for prevention of preeclampsia, but a modest (approximately 10 percent) reduction in the risk of preeclampsia and its sequelae (growth restriction, preterm birth)**

LOW-DOSE ASPIRIN FOR PREECLAMPSIA PREVENTION WITH TWO OR MORE OF THE FOLLOWING (**MODERATE RISK FACTORS**)DEVELOPMENT OF PREECLAMPSIA

- **Nulliparity**
- **Obesity (body mass index >30 kg/m^2)**
- **Family history of preeclampsia in mother or sister**
- **Age ≥35 years**
- **Sociodemographic characteristics (African American race, low socioeconomic level)**
- **Personal risk factors (eg, previous pregnancy with LBW or SGA or previous adverse pregnancy outcome [eg, stillbirth], interval >10 years between pregnancies)**

Even though nulliparous women are the group comprising the largest proportion of preeclampsia cases, nulliparity alone is not an indication for prophylaxis

Timing of initiation — We initiate low-dose aspirin for preeclampsia prevention at ≥12 weeks of gestation, and ideally prior to 16 weeks

Dose — The optimal dose of aspirin for preeclampsia prevention is controversial. We use 81 mg daily.

Safety — The short-term safety of low-dose aspirin use in the second and third trimesters is well established, but questions linger regarding use in the first trimester (eg, possible increase in minor vaginal bleeding (but not pregnancy loss) or gastroschisis

POSSIBLY EFFECTIVE INTERVENTIONS

- ✓ **Low-dose aspirin prophylaxis is the generally accepted therapy for prevention of preeclampsia.**
- ✓ **Calcium supplementation — Low dietary calcium intake is associated with hypertension in the general population**
- ✓ **(WHO) recommends 1500 to 2000 mg elemental calcium supplementation per day for pregnant women to reduce the risk of preeclampsia, particularly among those at higher risk of developing hypertension.**
- ✓ **Weight loss — In overweight and obese women, prepregnancy weight loss is recommended as it has a variety of reproductive,**

- The use of prophylactic anticoagulation in selected high-risk women, particularly those with known thrombophilic genetic variants (eg, factor V Leiden) plus a history of adverse pregnancy outcomes such as previous early severe preeclampsia, has been suggested to prevent recurrent pregnancy complications

PROBABLY INEFFECTIVE INTERVENTIONS

- Vitamin C and E supplements
- Vitamin D supplements
- Folic acid supplementation
- Fish oil supplements

با آرزوی موفقیت و سلامت