**MINISTRY OF EDUCATION AND SCIENCE OF UKRAINE**

**State Higher Educational Institution**

**“UZHGOROD NATIONAL UNIVERSITY”**

**MEDICAL FACULTY**

**DEPARTMENT OF OBSTETRICS AND GYNECOLOGY**

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**Hypertension of pregnancy. Preeclampsia. Eclampsia.**

**Tutorial for practical lessons of obstetrics**

**for students of the 5th course of medical**

**faculty**

**Uzhhorod – 2021**

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**Approved by the Academic Council of the medical faculty, protocol № \_**

**from « \_\_\_» 2021 year.**

**LATE GESTOSES**

**HYPERTENSIVE DISORDERS IN PREGNANCY**

**Defenition** Arterial hypertension is the increase of systolic blood pressure to 140 mm Hg or higher and/or diastolic blood pressure to 90 mm Hg or above in two measurements at rest with interval of not less than 4 hours or one-time increase of blood pressure to160/110 mm Hg.

Hypertension is one of the serious complications of pregnancy which may be couse of maternal and perinatal morbidity and mortality.

**Effects of pregnancy on the hypertonic disease**

1) There may be a mid-pregnancy fall of blood pressure in about 50%. The blood pressure tends to rise in the last trimester which may or may not reach its previous level

2) In 50%, the blood pressure tends to rise progressively as pregnancy advances.

3) In about 20%, it is superimposed by pre-eclampsia evidenced by rise of blood pressure to the extent of 30 mm Hg systolic and 15mm Hg diastolic associated with edema and/or proteinuria.

4) Rarely, malignant hypertension supervenes.

5) In 30%, there is permanent deterioration of the hypertension following delivery.

**Effects of the hypertonic disease on the pregnancy**

**Maternal risk:** In the milder form, the maternal risk remains unaltered but in the severe form or when superimposed by pre-eclampsia, the maternal risk is much increased.

**Fetal risk:** Due to chronic placental insufficiency, the babies are likely to be growth retarded. Preterm birth is high. In the milder form, with the blood pressure less than 160/100 mm Hg, the perinatal loss is about 10%. When the blood pressure exceeds 160/100 mm Hg, the perinatal loss doubles and when complicated by pre-eclampsia, it trebles. Risk of placental abruption is high (0.5–10%).

**Classification of hypertension in pregnancy**

**Hypertension**( BP≥140/90 mm Hg measured 2 times with at least a 6-hour interval)

**Proteinuria** (urinary excretion of ≥ 0,3 gm protein/24 hours specimen or 0,1gm/L)

**Chronic hypertension** (hypertension before pregnancy or hypertension diagnosed first time before 20 weeks of pregnancy)

**Gestational hypertension** (BP ≥ 140/90 mm Hg for the first time in pregnancy after 20 weeks, without proteinuria)

**Transient gestational hypertension** is the normalization of blood pressure in women who experienced gestational hypertension within 12 weeks after childbirth (a retrospective diagnosis).

**Pre-eclampsia** (gestational hypertension with proteinuria

**Eclampsia:** Women with pre-eclampsia complicated with convulsions and/or coma

**Hypertension is superimposed pre-eclampsia or eclampsia** (occurrence of new onset of proteinuria in women with chronic hypertension).

**Unspecified hypertension** is hypertension, diagnosed after 20 weeks of pregnancy in the absence of information about blood pressure prior to 20 weeks of pregnancy.

*Pregnancy-induced hypertension is diagnosed and estimated according the degree of severity on the basis of* ***diastolic pressure*** *which demonstrate the peripheral vascular resistance and, depending on the emotional state of the woman, is less variable than systolic one.* ***Diastolic pressure*** *is also assumed in determining the amount of treatment and antihypertensive therapy (BP target level).*

**The requirements for the measurement of diastolic BP**

The patient should be on rest for at least 10 min, hand freely lying on a hard surface, the cuff is at the level of the heart and wrapped around the shoulder of not less than three quarters. Measurement of the BP is repeated twice, and in case of disagreement of results – three times or more. To determine a diastolic pressure the fifth Korotkoff sound is used, considering the point of complete disappearance of arterial noise.

**Protein urine rapid test**

The average single dose of urine is brought to boil in a glass tube adding 2% acetic acid. The occurrence of sustainable sediment indicates the presence of protein in urine, and the quantity of sediment correlates with impressiveness of proteinuria.

**CHRONIC HYPERTENSION IN PREGNANCY**

**1. Chronic hypertension**

Chronic hypertensive disease (CHD) is defined as the presence of hypertension of any cause antedating or before the 20th week of pregnancy and its presence beyond the 12 weeks after delivery. The condition poses a difficult problem as regards the diagnosis and management when seen for the first time, beyond the 20th week of pregnancy.

Overall incidence is 2–4% of which 90% are due to essential hypertension.

The high risk factors for CHD are:

 age (> 40 years)

 duration of hypertension (>15 years)

 level of BP (>160/110 mm Hg)

 presence of any medical disorder (renovascular)

 presence of thrombophilias. Severity of CHD is shouded by table №2.

Table 2.

**Levels of blood pressure (WHO-ISH\*, 1999)**

|  |  |  |
| --- | --- | --- |
| Arterial hypertension | Systolic BP, mm Hg | Diastolic BP, mm Hg |
| Stage 1 (mild) | 140–159 | 90–99 |
| Stage 2 (moderate) | 160–179 | 100–109 |
| Stage 3 (severe) | ≥180 | ≥110 |
| Isolated systolic | ≥140 | <90 |

\* ISH –International Society of Hypertension

**Diagnostics**

**The diagnosis** of chronic hypertension during pregnancy is made on the basis of:

– history of elevated BP ≥140/90 mm Hg preceding pregnancy and/or

– measurement of BP ≥140/90 mm Hg on rest twice with the interval of not less than 4 hours, or ≥ 160/110 mm Hg one-time at 20 weeks of pregnancy.

Pregnant women with chronic hypertension constitute a risk group for the development of preeclampsia, premature detachment of placenta, delayed fetal growth restriction and complications of pregnancy.

**Contraindications to carrying of pregnancy (before 12 weeks):**

 severe arterial hypertension (hypertension of the 3 stage according to the WHO) – BP >≥ 180/110 mm Hg

 hypertension-induced severe lesions of end-organs: heart (old myocardial infarction, heart failure), brain (old stroke, transient ischemic attacks, hypertensive encephalopathy), retina (hemorrhages and exudates, of optic nerve disc edema), kidneys (renal failure), vessels (dissecting aortiс aneurysm)

 malignant clinical course of hypertension (diastolic BP>130 mm Hg, neuroretinopathia-like alterations of eyeground).

The principles of management are:

1) To stabilize the blood pressure to below 160/100 mm Hg,

2) To prevent superimposition of pre-eclampsia,

3) To monitor the maternal and fetal well-being,

4) To terminate the pregnancy at the optimal time. Preconceptional evaluation and counseling is essential to assess the etiology, severity of hypertension and possible outcome of pregnancy.

**Prevention of the development of preeclampsia:**

 it is recommended not to reduce the intake of cooking salt and liquid;

 acetylsalicylic acid at 60–100 mg/day, starting from 20 weeks of pregnancy;

 calcium 2 g/day (in term of elementary calcium) starting from 16 weeks of pregnancy;

 sea food with high content of polyunsaturated fatty acids supplementation of dietary regimen;

 regular antihypertensive therapy does not prevent the development of superimposed preeclampsia but can reduce the manifestation of the latter, as well as the incidence of maternal complications.

The mainstay of treatment is early (timely) detection of the development of preeclampsia is thorough supervision of pregnancy.

**Signs of the development of preeclampsia:**

 proteinuria ≥0,3 g/24 hours after 20 weeks of gestation;

 progression of hypertension and lowering of the efficiency of previous antihypertensive therapy;

 occurrence of generalized edemas;

 occurrence of threatening symptoms (strong persistent headache, blurred vision, epigastric or right-upperquadrant pain, hyperreflexia, oliguria).

**Surveillance for the pregnant.**

 Checkup in the maternity welfare center with measurement of BP before 20 weeks of gestation once every 3 weeks; from 20 to 28 weeks once every 2 weeks and after 28 weeks every week.

 A 24-hour urine collection for protein at the first visit to maternity welfare center, from 20 to 28 weeks once every 2 weeks, after 28 weeks every week.

 A daily self-control of BP at home. Checkup by ophthalmologist at the first antenatal visit, at 28 and 36 weeks of gestation.

 ECG at the first antenatal visit, at 26-30 weeks and after 36 weeks of gestation.

 Biochemical blood test on the first antenatal visit and after 36 weeks of gestation. Surveillance for the fetus.

 Records of movements of fetus) is made daily after 28 weeks of gestation.

 Cardiotocography (after 30 weeks), Doppler ultrasonography of uteroplacental and fetal blood flow.

 Ultrasonography of the fetus (embryo) and placenta (chorion) at 9–11 weeks, 18–22 weeks, 30–32 weeks.

**Indications for hospitalization**

– development of preeclampsia;

– uncontrolled severe hypertension, hypertensive crisis;

– occurrence or progression of eye-ground alterations;

– stroke;

– coronary pathology;

– heart failure;

– renal dysfunctions;

– fetal growth restriction;

– premature birth threat.

The issues on the possibility of pregnancy termination are decided by the board of doctors, including cardiologist, ophthalmologist, neurologist, obstetrician-gynecologist and other specialists.

**Indications for pregnancy termination at late term:**

– malignant clinical course of hypertension;

– dissecting aortiс aneurysm;

– acute stroke (only after patient’s rehabilitation);

– early development of preeclampsia, which is not subject to intensive care.

**According to the abovementioned indication the way of late-term pregnancy termination is the abdominal caesarean section.**

**Management of arterial hypertension**

Medical treatment after the final diagnosis of pregnancy is discontinued in pregnant women with mild or moderate essential arterial hypertension (AH) who received regular antihypertensive therapy before pregnancy. Diastolic pressure ≥ 100 mm Hg is the indication for prescription of regular antihypertensive therapy to a patient with chronic AH during pregnancy. If chronic AH is characterized by elevated predominately systolic blood pressure, antihypertensive therapy is indicated when its level is ≥150 mm Hg.

*During pregnancy antihypertensive therapy is aimed at sustainable maintenance of diastolic blood pressure at 80 – 90 mm Hg.*

In pregnant women with hypertension, which is characterized by a predominant increase of systolic blood pressure the treatment is aimed at stabilization of the latter at the level of 120-140 mm Hg (not lower than 110!).

**Nonmedical treatment of pregnant women with chronic AH include:**

- relaxed regimen;

- proper nutrition;

- psychotherapy;

- physical therapy.

**It is not recommended to:**

 limit the consumption of cooking salt and liquid,

 loose excessive weight before childbirth, physical activities.

**Medical treatment of arterial hypertension during pregnancy:**

**Central ἀ2-adrenoagonists:** Methyldopa per os 250–500 mg 3–4 times; Clonidine sublingual 0,075–0,2 mg 2–4 times or 0,5–1 ml 0,01% sol. i/m or i/v, 3–4 times, Labetalol per os 100–400 mg 2–3 times;

**Channal blockers**: Nifedipine sublingual or oral 10–20 mg 3-4 times;

**LOOP diuretics:** Furosemide 40–100 mg i/v bolus (only in the case of pulmonary edema or acute renal failure);

**Sedatives:** Magnesium sulphate 4 g i/v bolus with subsequent continuous 1–3 g/h infusion (facilitates BP lowering , but is applied only to prevent or treat seizures in case of superimposed preeclampsia/eclampsia).

**Glucocorticosteroid**s are used to prepare surfactant system of fetus lungs in case of delivery at the term up to 34 weeks of pregnancy. In the case of spontaneous onset of labor activity to complete 34 weeks the decision on labor management is made by the board of doctors considering the state of the parturient woman, the state of the fetus and obstetric circumstances. The third period of labor is led actively. **Use of Ergometrine and its derivatives in hypertensive patients is contraindicated.**

**Delivery**

In case if no preeclampsia occurs and hypertension is under control, the pregnancy is continued to the term of physiological birth.

In most cases, the delivery is vaginal. During the childbirth strict monitoring of BP and cardiac function of a parturient woman, as well as monitoring of fetus state is to be ensured. Drug antihypertensive therapy is to be initiated if BP is ≥ 160/110 mm Hg, and it is recommended no to low the BP below 130/90 mm Hg. Labor pain relief is appropriate in the І and ІІ periods of childbirth (the effective prevention of the progression of hypertension). The method of pain relief selecting is epidural anesthesia.

**Scheduled cesarean section is indicated in case of:**

–uncontrolled severe hypertension;

– destruction of the end-organs;

– severe fetal growth restriction.

**Postpartum period**

In the postpartum period the thorough supervision of physician (cardiologist), checkup by an ophthalmologist, daily BP control, proteinuria detection, creatinine blood tests is provided. Preliminary antihypertensive treatment is continued. Lactation is not to be excluded. **Contraindications** to lactation and breastfeeding could be: malignant hypertension, severe damage of end-organs.

Drug antihypertensive therapy provided for a mother is not interfered with breastfeeding. It is worth remembering that diuretics reduce breast milk

**After discharge** from the midwifery hospital the follow up period of a patient with chronic hypertension is under the supervision of the local physician (a cardiologist) or family doctor.

**PREECLAMPSIA**

Preeclampsia (sometimes called toxemia of pregnancy) is a multisystem disorder that is thought to arise as a consequence of inadequate cytotrophoblastic invasion of the spiral uterine arteries and failure to establish the normal low resistance uteroplacental circulation. **The criteria for diagnosis of superimposed pre-eclampsia.** Hypertension arising after 20 weeks gestation confirmed ***on 2 or more*** occasions and accompanied by one or more of the organ/systems features identified in table 3.

Diagnosis of preeclampsia.

• Raised BP is common but not always the first manifestation

•Pre-existing hypertension is a strong risk factor for the development of preeclampsia1 and requires close clinical surveillance

•Proteinuria is common but should not be considered mandatory to make the clinical diagnosis

Table 3.

**Diagnosis of preeclampsia**

|  |  |
| --- | --- |
| Organ/System | Feature |
| Proteinuria | • Random urine protein to creatinine ratio greater than or equal to 30 mg/mmol  Presence of total protein in 24 h urine of more than 0,3 gm /L on at least two random clean-catch urine samples tested > 4 h apart in the absence of urinary tract infection is considered significant. |
| Edema | • Serum or plasma creatinine greater than or equal to 90 micromol/L or  • Oliguria |
| Haematological | • Thrombocytopenia (platelets less than 100 x 109/L)  • Haemolysis: schistocytes or red cell fragments on blood film, raised bilirubin, raised lactate dehydrogenase (LDH), decreased haptoglobin  • Disseminated intravascular coagulation (DIC) |
| Liver | • Raised transaminases  • Severe epigastric or right upper quadrant  pain |
| Neurological | • Severe headache  • Persistent visual disturbances (photopsia, scotomata, cortical blindness, retinal vasospasm)  • Hyperreflexia with sustained clonus  • Convulsions (eclampsia)  • Stroke |
| Pulmonary | • Pulmonary oedema |
| Uteroplacental | • Fetal growth restriction (FGR) |

**Risk factors of preeclampsia**

 Primigravida or woman’s age is greater than to 40 years or new paternity

 Previous history of preeclampsia

 Placental abnormalities (hyperplacentosis, twin, placental ischemia)

 Obesity (insulin resistance, raised BMI).

 Pre-existing vascular disease (diabeis)

 Thrombophilias (antiphospholipid syndrome, protein C deficiency).

**Etiopatologial factors for preeclampsia**

 Failure of trophoblast invasion (abnormal placentation)

 Vascular endothelial damage

 Inflammatory mediators (cytokines)

 Immunological intolerance between maternal and fetal tissues

 Coagulation abnormalities

 Genetic predisposition (polygenic disorder)

Etiopathogenesis of preeclampsia is showed by figure-scheme 1.

The underlying basic pathology is endothelial dysfunction and intense vasospasm, affecting almost all the vessels, particularly those of uterus, kidney, placental bed and brain. The basic underlying pathology remains as endothelial dysfunction and vasospasm. The responsible agent for endothelial dysfunction and vasospasm, still has not been isolated precisely, but it seems certain to be humoral in origin. The following are the considerations: increased circulating pressor substances. Increased sensitivity of the vascular system to normally circulating pressure substances.

**Trophoblast Invasion and Uterine Vascular Changes:** Normally, there is invasion of the endovascular trophoblasts into the walls of the the spiral arterioles of the uteroplacental bed. In the first trimester (10–12 weeks) endovascular trophoblasts invades up to decidual segments and in the second trimester (16–18 weeks) another wave of trophoblasts invades upto the myometrial segments. This process replaces the endothelial lining and the muscular arterial wall by fibrinoid formation. The spiral arterioles thereby become distended, tortuous, and funnel-shaped. This physiological change transforms the spiral arterioles into a low resistance, low pressure, high flow system

**PATHOPHYSIOLOGY**

While the question as to why the syndrome occurs still remains unsolved, the pathological changes are well documented, specially in severe pre-eclampsia or in eclampsia.

Uteroplacental bed: There is increased evidences of premature aging of the placenta. Areas of occasional acute red infarcts and white infarcts are visible on the maternal surface of the placenta.

Villi: Syncitial degeneration, increased syncitial knots, marked proliferation of cytotrophoblast, thickening of the basementlayer, and proliferative endarteritis are evident in varying degrees.

In pre-eclampsia, the normal endovascular invasion of cytotrophoblast into the spiral arteries fails to occur beyond decidua-myometrial junction. As a result, the musculoelastic media in the myometrial segment remains responsive to vasoconstrictor stimuli resulting in decreased blood flow. There is acute atherosis of spiral arteries with obliteration of lumen.

Intervillous circulation: The blood flow is impaired to the extent of about onethird, secondary to the changes in the maternal blood vessels. This results in placental changes, anatomical and functional, which are responsible for fetal jeopardy.

**Kidney:** The changes are conspicuous in the glomerulus which becomes enlarged (glomerular endotheliosis). Endothelial cells swell up and fibrin like deposits occur in the basement membrane. The lumen may be occluded. Interstitial cells in between the capillaries proliferate. There is associated spasm of the afferent glomerular arterioles. Patchy areas of damage of the tubular epithelium due to anoxia are evident. The net effects are reduced renal blood flow and glomerular filtration rate (25%) and impaired tubular reabsorption or secretory function. Recovery is likely to be complete, following delivery. In severe cases, intense anoxia may produce extensive arterial thrombosis leading to bilateral renal cortical necrosis.

**Blood vessels:** There is intense vasospasm. Circulation in the vasa vasorum is impaired leading to damage of the vascular walls, including the endothelial integrity.

**Liver:** Periportal hemorrhagic necrosis of the liver occurs due to thrombosis of the arterioles. The necrosis starts at the periphery of the lobule. There may be subcapsular hemorrhage. Hepatic insufficiency seldom occurs because of the reserve capacity and regenerative ability of liver cells. Liver function tests are specially abnormal in women with HELLP syndrome.

**Clinical types of preeclampsia**

The clinical classification of pre-eclampsia is arbitrary and is principally dependent on the level of blood pressure for management purpose. But proteinuria is more significant than blood pressure to predict fetal outcome.

• Mild. This includes cases of sustained rise of blood pressure of more than 140/90 mm Hg but less than 160 mm Hg systolic or 110 mm Hg diastolic without significant proteinuria. Edema on the face and hands, sporadic headaches are present.

• Severe.

 A persistent systolic blood pressure of >160 mm Hg or diastolic pressure of >110 mm Hg.

 Generalized significant edemas

 Protein excretion of >5 gm/24 hr.

 Oliguria (<400 ml/24 hr).

 Platelet count < 100,000/mm3.

 HELLP syndrome.

 Cerebral or visual disturbances, headache.

 Persistent severe epigastric pain.

 Retinal hemorrhages, exudates or papilledema.

 Intrauterine growth restriction of the fetus.

 Pulmonary edema.

From the prognostic point of view, a diastolic rise of blood pressure is more important than the systolic rise. Moreover, convulsions may occur even with moderate rise of blood pressure; conversely, even with alarming high rise of pressure, the pregnancy may have an uneventful outcome. This calls for a strict vigilance whenever the blood pressure is raised to the pre-eclamptic level or even before that.

**Symptoms.** Pre-eclampsia is principally a syndrome of signs and when symptoms appear, it is usually late.

**Mild symptoms.** Slight swelling over the ankles which persists on rising from the bed in the morning or tightness of the ring on the finger is the early manifestation of pre-eclampsia edema. Gradually, the swellingmay extend to the face, abdominal wall, vulva and even the whole body (fig.)



**Alarming symptoms:**

 headache — either located over the occipital or frontal region;

 disturbed sleep;

 diminished urinary output—Urinary output of less than 400 ml in 24 hours is very ominous;

 epigastric pain—acute pain in the epigastric region associated with vomiting, at times coffee color, is due to hemorrhagic gastritis or due to subcapsular hemorrhage in the liver;

 eye symptoms—there may be blurring, scotomata, dimness of vision or at times complete blindness. Vision is usually regained within 4–6 weeks following delivery. The eye symptoms are due to spasm of retinal vessels (retinal infarction), occipital lobe damage (vasogenic edema) or retinal detachment. Reattachment of the retina occurs following subsidence of edema and normalization of blood pressure after delivery.

**Signs**

1. **Abnormal weight gain.** Abnormal weight gain within a short span of time probably appears even before the visible edema. A rapid gain in weight of more than 2,3kg a month or more than 0,5 kg a week in later months of pregnancy is significant.

2. **Rise of BP**: The diastolic pressure usually tends to rise first followed by the systolic pressure.

3. **Edema.** Visible edema from the bed in the morning is pathological. Sudden and generalized edema may indicate imminent eclampsia.

4. **Pulmonary edema** due to leaky capillaries and low oncotic pressure.

5. **Obstetric examination** may reveal evidences of chronic placental insufficiency, such as scanty liquor or growth retardation of the fetus.

Thus, the manifestations of pre-eclampsia usually appear in the following order—rapid gain in weight → visible edema and/or hypertension → proteinuria.

**INVESTIGATIONS**

Initial investigations for new onset hypertension after 20 weeks are reflected in the table 4 from Queensland Clinical Guideline: Hypertensive disorders of pregnancy, 2015 (see table 4).

Table 4.

**Initial investigations of pations with Hypertensive disorders of pregnancy**

|  |  |
| --- | --- |
| Investigation | Considerations |
| BP measurement | • Correct measurement techniques are critical to the correct diagnosis of HDP18   • Confirm non-severe hypertension by measuring BP over several hours  Up to 70% of women with an office BP of 140/90 mmHg have normal BP on subsequent measurements on the same visit17  • Refer to Appendix A: Measurement of blood pressure |
| Proteinuria | • Screen women for proteinuria with urinary dipstick at each visit17 1  • Quantify by laboratory methods if:  o Greater than or equal to 2+ proteinuria or  o There is repeated 1+ proteinuria or  o Preeclampsia is suspected  • Spot urine protein to creatinine ratio greater than 30 mg/mmol is diagnostic of proteinuria in pregnancy1,13,17  • 24 hour urine collection is not necessary in routine clinical management  • Proteinuria testing does not need to be repeated once significant proteinuria in the setting of confirmed preeclampsia has been detected |
| Blood tests | • Tests may be abnormal even when BP elevation is minimal:  o Full blood count (FBC)  o Urea, creatinine, electrolytes1 and urate  o Liver function tests (LFT)1 including LDH |
| Preeclampsia investigations | • Urinalysis and microscopy on a carefully collected mid-stream urine sample  • If there is thrombocytopenia or a falling haemoglobin, investigations for DIC and/or haemolysis including:  o Coagulation studies  o Blood film  o LDH  o Fibrinogen  o Haemolytic studies  • If severe or early onset preeclampsia consider investigation for associated conditions (e.g. systemic lupus erythematosus (SLE), APLS, chronic renal disease)  Ophthalmoscopic examination: In severe cases there may be retinal edema, constriction of the arterioles, alteration of normal ratio of vein. There may be hemorrhage. |
| Fetal assessment | • Cardiotocograph (CTG) if greater than 24 weeks gestation  • Ultrasound scan (USS) assessment of:  o Fetal growth  o Amniotic fluid volume (AFV) or deepest vertical pocket (DVP)  o Umbilical artery flow (Doppler)  o And follow-up to assess fetal growth velocity |

**Complications of preeclampsia**

**Maternal**

 Eclampsia (2%) — more in acute than in subacute cases

 Accidental obstetrical hemorrhage

 Oliguria and anuria

 Dimness of vision and even blindness

 Preterm labor

 HELLP syndrome

 Cerebral hemorrhage

 Acute respiratory distress syndrome

 Shock (puerperal vasomotor collapse)

 Sepsis (incidence of induction, operative interference).

**Fetal**

 Intrauterine death—due to spasm of uteroplacental circulation leading to accidental hemorrhage or acute red infarction,

 Intrauterine growth restriction—due to chronic placental insufficiency,

 Asphyxia,

 Prematurit.

**Remote**

• Residual hypertension may persist even after 6 months following delivery in about 50% cases..

• Recurrent pre-eclampsia: There is 25% chance of pre-eclampsia to recur in subsequent pregnancies.

• Chronic renal disease. There is high incidence of glomerulonephritis in women with pre-eclampsia remote from term.

• Risk of placental abruption for those women with pre-eclampsia ranges from 5%–20% and women with HELLP syndrome.

**MANAGEMENT OF PRE-ECLAMPSIA**

**HOSPITAL MANAGEMENT**

**Rest.** Admission in hospital and rest is helpful for continued evaluation and treatment of the patient.

**Diet:** The diet should contain adequate amount of daily protein (about 100 gm). Usual salt intake is permitted. Fluids need not be restricted. Total calorie approximate 1600 cal/day.

**Diuretics:** The diuretics should not be used injudiciously, as they cause harm to the baby by diminishing placental perfusion and by electrolyte imbalance.

**Indications for using diuretics:**

 Cardiac failure,

 Pulmonary edema,

 Along with selective antihypertensive drug therapy (diazoxide group) where blood pressure reduction is associated with fluid retention,

 Massive edema, not relieved by rest and producing discomfort to the patient.

 The most potent diuretic commonly used is frusemide (Lasix) 40 mg, given orally after breakfast for 5 days in a week. In acute condition, intravenous route is preferred.

**Antihypertensives are used only when the indications present**. Angiotensin Converting Enzyme (ACE) inhibitors and angiotensin receptor blockers are contraindicated in pregnancy.

**The indications are:**

 Persistent rise of blood pressure specially where the diastolic pressure is over 110 mm Hg. The use is more urgent if associated with proteinuria.

 In severe preeclampsia to bring down the blood pressure during continued pregnancy and during the period of induction of labor, the common oral drugs used are in table 5

Table 5

**Oral antihypertensive drug therapy**

|  |  |  |
| --- | --- | --- |
| Oral antihypertensive drug therapy | Oral dose | Adjust frequency and dose as clinically indicated |
| \*Methyldopa  central and peripheral antiadrenergic action | 250–500 mg | Initially: 125–250 mg BD Up to: 500 mg QID  Maximum: 2 g |
| \*Labetalol adrenoceptor antagonist (α and β blockers) | 100–400 mg | Initially: 100 mg BD Up to: 200– 400 mg QID  Maximum: 2.4 g |
| \*Oxprenolol | 25–50 mg | Initially:25 mg BD Up to: 50–100 mg BD  Maximum: 200 mg |
| "Nifedipine (SR)  Calcium channel blocker | 20 mg | Initially: 20–30 mg daily Up to: 60-120 mg daily  Maximum: 120 mg |
| Nifedipine (immediate release) | 10–20 mg | Initially:10–20 mg BD Up to: 40 mg BD  Maximum: 80 mg |
| "Prazosin | 0.5–5 mg | Initially:0.5 mg BD Up to: 1 mg TDS  Maximum: 20 mg |
| "Clonidine | 75–300 mcg | Initially:50–150 mcg BD Up to: 150–300 mcg BD  Maximum: 600 mcg |

**NOTE:\*** First line drugs: " Second line drugs: ^Not on QH LAM:

**To avoid labetalol in women having asthma or cardiac failure.**

**Magnesium therapy.**

Magnesium therapy is the bolus administration of 4 g magnesium sulphate dry matter with subsequent intravenous infusion with the rate determined by the state of the patient. Magnesium therapy is initiated from the moment of hospitalization if diastolic BP > 130 mm Hg. Magnesium therapy aims at support of the concentration of magnesium ions in the blood of the pregnant at the level required to prevent seizures.

**The initial dose** of 4 g of dry matter (16 ml 25% of magnesium sulphate solution) is administered with a syringe very slowly over 15 minutes (over 5 minutes in case of eclampsia). Considering the fact that the concentrated solution of magnesium sulphate can cause significant irritation of the wall of the vein, where the infusion is made (up to necrosis), the initial dose of magnesium sulphate is dissolved in 0,9% sodium chloride solution or Ringer-Locke solution. For this purpose in sterile small bottle 4 g magnesium sulphate is injected out of 34 ml of the solution (16 ml of 25% solution).

**Montoring of the state of pregnant** during the magnesium sulphate therapy involves:

- BP measuring every 20 minutes;

- heart rate count;

- observation of the rate and mode of breath (respiratory rate should be not less 14 per min);

- determination of O2 saturation (not less 95%);

- cardiomonitoring control;

- ЕCG;

- check up of tendon reflexes every 2 hours;

- control of hourly diuresis (should be not less 50 ml/h).

**Additionally the following is to be controlled:**

- the symptoms of augmenting severe preeclampsia: headache, blurred vision, scotoma (seeing spots or ―snow‖), epigastric pain;

- symptoms of possible pulmonary edema: heaviness in the chest, coughing with sputum or without it, choke, increasing of CVT, occurrence of crepitation or moist rales in lung auscultation, increased heart rate and augmenting signs of hypoxia, decreased level of consciousness;

- state of the fetus (hourly auscultation of heartbeats, fetal monitoring).

Magnesium therapy is conducted during 24-48 hours after childbirth along with symptomatic treatment. Importantly, the use of magnesium sulphate during the childbirth and at early postpartum period reduces the contractive activity of the uterus. If magnesium sulphate is not available diazepam can be used; however it is a high risk for neonatal respiratory distress (diazepam freely penetrates through placental barrier).

**DURATION OF TREATMENT**

The definitive treatment of pre-eclampsia is termination of pregnancy (delivery). As such, the aim of the above treatment is to continue the pregnancy, if possible, without affecting the maternal prognosis until the fetus becomes mature enough to survive in extrauterine environment (>37 weeks). Thus, the duration of treatment depends on —

 severity of pre-eclampsia

 duration of pregnancy

 response to treatment

 condition of the cervix

**Mild Preeclampsia.**

At pregnancy term up to 37 weeks the supervision in conditions of day patient facility is possible.

The pregnancy term is defined.

The patients are provided with study of the self-monitoring of major indicators for the development of preeclampsia: BP measuring, liquid balance and edema control, fetal movements’ records.

**Laboratory tests:** urinalysis, daily proteinuria, creatinine and urea in blood plasma, hemoglobin, haematocrit, the platelets count, coagulogram, ALT and АSТ, identification of the state of the fetus (nonstress test, if possible). **No medication therapy is indicated. It is recommended not to reduce the intake of cooking salt and liquid.**

**Indications for hospitalization:**

–pregnancy term over 37 weeks;

–occurrence of at least one of the manifestations of moderate preeclampsia;

– fetus state impairment.

In case of the stable status of women within the criteria for mild preeclampsia – the management of pregnancy is expectant.

The delivery is vaginal.

**Severe Preeclampsia**

**Hospitalization.**

The patient is hospitalized to Intensive Therapy Unit to assess the degree of risk for pregnancy for the mother and the fetus, and the choice of the method of delivery during 24 hours. Individual ward is provided with intensive 24-hour supervision by the medical personnel. Immediate medical advises of a general practitioner, neurologist and ophthalmologist.

**Catheterization** of the peripheral vein, the central vein and urinary bladder is made for prolonged infusion therapy, the control of the central venous pressure (CVP) and hourly diuresis, respectively. Transnasal gastric catheterization is made on indications.

**Initial laboratory tests:** complete blood count, haematocrit, the platelets count, coagulogram, ALT and АSТ; blood group and rhesus factor (if not available); urinalysis, determination of proteinuria, creatinine, urea, whole protein, total bilirubin and its fractions, electrolytes.

**Thorough dynamic examination:**

– hourly BP control;

– auscultation of fetal heart tones every 15 minutes;

– urinalysis – every 4 hours;

– hourly diuresis control (urinary bladder catheterization by the Foley’s catheter);

– daily hemoglobin, haematocrit, the platelets count, liver function test, plasma creatinine;

– monitoring of the fetus state: the number of movements during 1 hour period, daily heart rate, if possible, Doppler control of the blood flow in the umbilical cord vessels, fetal brain vessels, placenta vessels and fetoplacental complex;

– the evaluation of the volume of the amniotic fluid and biophysical profile of the fetus is made on indications;

– test for the absence of fetal stress is made in worsening of indicators of daily monitoring of the fetus and compulsorily before delivery (evaluation of the fetal cardiac status using the fetal monitor).

**Management.**

Safe regimen (strict bed rest).

Vitamin complex for pregnant.

In the pregnancy term before 34 weeks of gestation corticosteroids for RDSsyndrome prophylaxis (6 mg dexamethasone after 12 hours four times a day during 2 days) are indicated. **Management mode** is active with the delivery in the nearest 24 hours from the moment of the diagnosis was made. Expectant management is not recommended in all cases of the severe preeclampsia.

**Antihypertensive therapy**

Treatment of arterial hypertension is not pathogenic, but necessary for the mother and the fetus. Lowering of BP aims at prevention of hypertensive encephalopathy and brain hemorrhages. The BP should be brought to the safe level (150/90 – 160/100 mm Hg, not below!), which ensures the preservation of adequate cerebral and placental blood flow.

**Rapid and sharp reduction of BP may cause deterioration of the condition of the mother and the fetus.**

Antihypertensive therapy is conducted in elevated diastolic pressure > 110 mm Hg along with magnesium therapy. The volume of blood circulation should be restored in advance.

Labetalol is used first 10 mg intravenously. BP is monitored every 10 min and if the diastolic pressure remains above 110 mm Hg 40 mg Labetalol with subsequent 80 mg is administered (max to 300 mg).

In case if Labetalol is not available the use of 5-10 mg Nifedipine sublingually is possible. In case of no effect is observed then after 10 minutes 5 mg more is administered sublingually.

**IMPORTANT!** Nifedipine can lead to rapid development of hypotension along with administration of magnesium sulphate.

In severe preeclampsia Hydralazinum is also used to low the BP: 20 mg (1 ml) Hydralazinum is dissolved in 20 ml of 0,9% sodium chloride solution and introduced slowly intravenously per 5 ml (5 mg Hydralazinum) every 10 minutes until the diastolic BP low to a safe level (90 – 100 mm Hg).

Methyldopa is used less often to treat the severe preeclampsia since the drug has a delayed action (the effect comes in 4 hours). Generally, the doses of 1,0–3,0 g per day are used as a monotherapy or in combination with 0,5 mg/kg/day Nifedipine.

In the case of incomplete pregnancy the daily dose of Methyldopa should not exceed 2,0 g, because this can lead to the development of meconium obstruction in preterm infants.

**Even the regular doses of sodium thiopental can lead to collapse along with administration of Methyldopa.**

As the antihypertensive medication Clonidine can be used in patients with severe preeclampsia: 0,5–1 ml 0,01% solution intravenously or intramuscularly or 0,15–0,2 mg sublingually 4-6 times a day.

In the case of hyperkinetic type, it is advisable to use a combination of Labetalol with Nifedipine, and in hypokinetic type Clonidine + Nifedipine in restoration of the volume of blood circulation is recommended, and in eukinetic type – Methyldopa + Nifedipine.

Magnesium sulphate can be prescribed as anticonvulsant with simultaneous antihypertensive effect and is the drug of choice for the prevention and treatment of the seizures.

**Infusion therapy**

**The condition** for the adequate infusion therapy is a strict control for the volume of the introduced and consumed liquid and diuresis. Diuresis should be not less 60 ml/h.

**The total volume** of the introduced liquid should correspond the daily physiological need of a woman (average of 30–35 ml/kg), considering the volume of non-physiological loss (hemorrhage, etc.).

**The rate of administration** of liquid should not exceed 85 ml/h or hourly diuresis + 30 ml/h.

The drugs of choice for infusion therapy before the delivery moment are isotonic saline solutions (Ringer’s solution, 0,9% NaCl).

In case of circulating blood volume (СBV) restoration the optimal medications are 6% or 10% Amylum hydroxyaethylicum solutions.

It is advisable to include donor fresh frozen plasma to infusion-transfusion therapy to eliminate hypoproteinemia (plasma protein indicators < 55 g/l), normalization of anticoagulants/procoagulants ratio, which is the prevention of bleeding in childbirth and the postpartum period.

**Dextrans** can be the components of the infusion therapy of the severe preeclmpsia, which effectively elevate СBV and enhance microcirculation. Their dose should not be greater 10 ml/kg/day, since it can lead to hypocoagulation.

**Methylergometrine is contraindicated!**

**METHODS OF DELIVERY**

**Inductions of labor**

 Aggravation of the preeclamptic features in spite of medical treatment and/or appearance of newer symptoms such as epigastric pain.

 Hypertension persists in spite of medical treatment with pregnancy

 reaching 37 weeks or more.

 Acute fulminating pre-eclampsia irrespective of the period of gestation.

 Tendency of pregnancy to overrun the expected date.

**Methods of delivered**

If the cervix is ripe, surgical induction by low rupture of the membranes is the method of choice. Oxytocin infusion may be added. If the cervix is unripe, prostaglandin (PGE2) gel 500 μg intracervical or 1–2 mg in the posterior fornix is inserted to make the cervix ripe when low rupture of the membranes can be performed. In severe pre-eclampsia, antihypertensive drugs should be used during induction.

**Cesarean section**

Indications:

 When an urgent termination is indicated and the cervix is unripe

 Severe pre-eclampsia with a tendency to prolong the induction.

 Associated complicating factors, such as elderly primigravidae, contracted pelvis, malpresentation, etc.

The operation should be done by an experienced surgeon with the help of an expert anesthetist. Epidural anesthesia is preferred, unless there is coagulopathy.

**Management during labor.** Blood pressure tends to rise during labor and convulsions may occur (intrapartum eclampsia). The patient should be in bed. Antihypertensive drugs are given if the blood pressurebecomes high. Blood pressure and urinary output are to be noted frequently so as to detect imminent eclampsia. Prophylactic MgSO4 is started when systolic BP >160 diastolic >110, MAP >125 mm Hg. Careful monitoring of the fetal well-being is mandatory. Labor duration is curtailed by low rupture of the membranes in the first stage; and forceps or ventouse in second stage. Intravenous ergometrine following the delivery of the anterior shoulder is withheld as it may cause further rise of blood pressure. However, there is no contraindication of syntocinon IM or slow IV and to keep the patient under close observation for several hours.

**Postpartum preeclampsia.**

The patient is to be watched closely for at least 48 hours, the period during which convulsions usually occur. Antihypertensive drug treatment should be continued if the BP is high (systolic >150 mm Hg ordiastolic >100 mm Hg). Oral nifedipine 10 mg at every 6 hours is given until BP remains below the hypertensive levels for at least 48 hours. Oral frusemide 20 mg a day for 5 days is also found to improve recovery and toreduce the need of antihypertensive drugs in severe preeclampsia. Magnesium sulfate (for at least 24 hours) and antihypertensive drugs may be needed in women with severe hypertension and symptoms of acute fulminant preeclampsia during the postpartum period. The patient is to be kept in the hospital, till the blood pressure is brought down to a safe level and proteinuria disappears.

**Prevention of preeclamsia**

- Regular antenatal check up for early detection of rapid gain in weight or a tendency of rising blood pressure specially the diastolic one.

- Antithrombotic agents: Low dose aspirin 60 mg daily beginning early in pregnancy in potentially high risk patients is given. It selectively reduces platelet thromboxane production. Aspirin in low doses is known to inhibit cyclo-oxygenase in platelets thereby preventing the formation of thromboxane A2 without interfering with prostacyclin generation.

- Heparin or low molecular weight heparin is useful in women with thrombophilia and with high risk pregnancy.

- Calcium supplementation (2 gm per day) reduces the risk of gestational hypertension.

- Antioxidants, vitamins E and C and nutritional supplementation with magnesium, zinc, fish oil and low salt diet have been tried but are of limited benefit.

- Balanced diet rich in protein may reduce the risk.

**ECLAMPSIA**

The term eclampsia is derived from a Greek word, meaning ―like a flash of lightening‖. It may occur quite abruptly, without any warning manifestations. In majority (over 80%); however, the disease is preceded by features of severe preeclampsia.

**Eclampsia is characterized by the development of the preeclampsiainduced generalized tonic-clonic seizures during the pregnancy, delivery or the postpartum period.** Eclampsia is the clinical manifestation of the apparent syndrome of multiple organs failure with primary affection of the CNS. It occurs in 0,2-0,5% of all pregnancies and threatens by the high perinatal (30-40%) and the maternal (3-4%) mortality.

The following variants of the clinical course of eclampsia are defined according to the prominence of seizure syndrome:

 individual seizure;

 eclamptic status – series of seizures that follow one after another over the short intervals;

 eclamptic coma – loss of consciousness after seizures;

 ―eclampsia without eclampsia‖– unexpected loss of consciousness without seizures.

Pre-eclampsia when complicated with generalized tonic–clonic convulsions and/or coma is called eclampsia. Thus, it may occur in patients with pre eclampsia or in patients who have pre-eclampsia superimposed on essential hypertension or chronic nephritis.

**CAUSE OF CONVULSION:** The cause of cerebral irritation leading to convulsion is not clear. The irritation may be provoked by:

1) Anoxia — spasm of the cerebral vessels → increased cerebral vascular resistance → fall in cerebral oxygen consumption → anoxia.

2) Cerebral edema — may contribute to irritation.

3) Cerebral dysrhythmia — increases following anoxia or edema. There is excessive release of excitatory neurotransmitters (glutamate).

**ONSET OF FITS:** Fits occur more commonly in the third trimester (more than 50%). On rare occasions, convulsion may occur in early months as in hydatidiform mole.

— Antepartum (50%): Fits occur before the onset of labor. More often, labor starts soon after and at times, it is impossible to differentiate it from intrapartum ones.

— Intrapartum (30%): Fits occur for the first time during labor.

— Postpartum (20%): Fits occur for the first time in puerperium, usually within 48 hours of delivery. Fits occurring beyond 48 hours but less than 4 weeks after delivery is accepted as late postpartum eclampsia.

— Intercurrent (antenatal): When the patient becomes conscious after recovery from convulsions and the pregnancy continues beyond 48 hours. The time limit is arbitrary as a period of 7–10 days has also been mentioned.

Cerebral pathology includes cortical or subcortical edema, infarction and hemorrhage. The neurological abnormalities areoften due to hypoxia, ischemia or edema. Several neurodiagnostic tests e.g. EEG, CAT, cerebral Doppler Velocimetry, MRI, MRI angiography reveal presence of edema and infarction. Findings are similar

to those as seen in hypertensive encephalopathy. Cerebral imaging is indicated when there is focal neurologic deficits, prolonged coma, or atypical presentation for eclampsia.

**CLINICAL FEATURES OF ECLAMPSIA**

Except on rare occasions, an eclamptic patient always shows previous manifestations of acute fulminating pre-eclampsia — called premonitory symptoms (mentioned earlier).

**Prodromal symptoms**, indicating that eclamptic seizure is about to happen:

- headache (often localized in the temporal and occipital areas);

- visual impairment: blurred vision or scotoma;

- retrosternal, epigastric and/or right-upperquadrant pain;

- rapid elevation of the BP;

- hypersalivation, nausea and vomiting;

- alternating pupillary constriction and dilation (due to the fluctuations of intracranial pressure);

- agitation or retardation;

- minor facial spasms.

Seizures last on the average of 1 to 3 minutes and several alternating stages are differentiated:

**The fits are epileptiform and consist of four stages.**

I stage. Premonitory stage: The patient becomes unconscious. There is twitching of the muscles of the face, tongue, and limbs. Eyeballs roll or are turned to one side and become fixed. This stage lasts for about 30 seconds.

II stage. Tonic stage: The whole body goes into a tonic spasm — the trunkopisthotonus, limbs are flexed and hands clenched. Respiration ceases and the tongue protrudes between the teeth. Cyanosis appears. Eyeballs become fixed. This stage lasts for about 30 seconds.

III stage. Clonic stage: All the voluntary muscles undergo alternate contraction and relaxation. The twitchings start in the face then involve one side of the extremities and ultimately the whole body is involved in the convulsion.

Biting of the tongue occurs. Breathing is stertorous and blood stained frothy secretions fill the mouth; cyanosis gradually disappears. This stage lasts for 1–4 minutes.

IV stage. Stage of coma: Following the fit, the patient passes on to the stage of coma. It may last for a brief period or in others deep coma persists till another convulsion. On occasion, the patient appears to be in a confused state following the fit and fails to remember the happenings. Rarely, the coma occurs without prior convulsion. The fits are usually multiple, recurring at varying intervals. When it occurs in quick succession, it is called status eclampticus. Following the convulsions, the temperature usually rises; pulse and respiration rates are increased and so also the blood pressure. The urinary output is markedly diminished; proteinuria is pronounced, and the blood uric acid is raised.

**DIFFERENTIAL DIAGNOSIS:** The diseases, which are associated with convulsions and/or coma are to be borne in mind while arriving at the diagnosis of eclampsia. Such diseases are: epilepsy, hysteria, encephalitis, meningitis, puerperal cerebral thrombosis, poisoning, cerebral malaria in tropics, and intracranial tumors. Absence of previous history of convulsion with presence of edema, hypertension and proteinuria along with fits or coma during pregnancy or soon after, points to the diagnosis of eclampsia. In doubtful cases, it is desirable to place the patient in the obstetric unit for observation until the final diagnosis is made.

**MATERNAL COMPLICATIONS OF ECLAMPSIA**

• Injuries:

Tongue bite, injuries due to fall from bed, bed sore.

• Pulmonary complications:

– Edema—due to leaky blood capillaries

– Pneumonia—due to aspiration, hypostatic or infective

– Adult respiratory distress syndrome

– Embolism

**• Hyperpyrexia • Cardiac—Acute left ventricular failure**

**• Renal failure**

**• Hepatic—necrosis, Subcapsular hematoma**

**• Cerebral: Edema (vasogenic) hemorrhage**

**• Neurological deficits**

**• Disturbed vision: Due to retinal detachment or occipital lobe ischemia.**

**• Hematological:**

– Thrombocytopenia

– Disseminated intravascular Coagulopathy

• Postpartum:

– Shock

– Sepsis

– Psychosis

**PROGNOSIS**

Once the convulsion occurs, the prognosis becomes uncertain. Prognosis depends on many factors and the ominous features are:

 Long interval between the onset of fit and commencement of treatment (late referral).

 Antepartum eclampsia specially with long delivery interval.

 Number of fits more than 10.

 Coma in between fits.

 Temperature over 102°F with pulse rate above 120/minute.

 Blood pressure over 200 mm Hg systolic.

 Oliguria (<400 mL/24 h) with proteinuria>5 gm/24 h.

 Nonresponse to treatment. (9) Jaundice.

If treated early and adequately, the mortality should be even less than 2%.

**Causes of maternal deaths:**

 Cardiac failure.

 Pulmonary edema.

 Aspiration and/or septic pneumonia.

 Cerebral hemorrhage.

 Acute renal failure.

 Cardiopulmonary arrest.

 Adult respiratory distress syndrome (ARDS).

 Pulmonary embolism.

 Postpartum shock.

 Puerperal sepsis.

Maternal complications are higher in antepartum eclampsia.

**Remote:** If the patient recovers from acute illness, she is likely to recover rapidly within 2–3 weeks. Recurrence of eclampsia in subsequent pregnancies is uncommon, although chance of pre-eclampsia is about 30%.

The perinatal mortality is very high to the extent of about 30–50%.

**The causes of the perinatal mortality are:**

 Prematurity — spontaneous or induced,

 Intrauterine asphyxia due to placental insufficiency arising out of infarction, retroplacental hemorrhage and spasm of uteroplacental vasculature,

 Effects of the drugs used to control convulsions,

 Trauma during operative delivery.

**MANAGEMENT**

**FIRST AID TREATMENT OUTSIDE THE HOSPITAL:** The patient, either at home or in the peripheral health centers should be shifted urgently to the tertiary referral care hospitals. There is no place of continuing the treatment in such places. Transport of an eclamptic patient to a tertiary care center is important. Such a patient needs neonatal and obstetric intensive care management. Important steps in transport are: • All maternal records and a detailed summary should be sent with the patient • BP should be stabilized and convulsions should be arrested • Magnesium sulfate (4 gm IV loading dose with 10 gm IM) is given. Labetalol 20 mg is given to control hypertension. Diuretic is given if there is pulmonary edema. Diazepam if used should be given 5 mg slowly over one minute period to avoid apnea or cardiac arrest • One medical personnel or a trained midwife should accompany the patient in the ambulance equipped to prevent injury, recurrent fits and to clear air passage.

**HOSPITAL—THE PRINCIPLES OF MANAGEMENT ARE:**

• Maintain: airway, breathing and circulation

• Hemodynamic stabilization (control BP)

• Oxygen administration 8–10 L/min

• Organize investigations

• Arrest convulsions

• Deliver by 6-8 hours

• Ventilatory support (if needed)

• Prevention of complications

• Prevention of injury

• Postpartum care (intensive)

**GENERAL MANAGEMENT (MEDICAL AND NURSING)**

- Supportive care:

 to prevent serious maternal injury from fall,

 prevent aspiration,

 to maintain airway and

 to ensure oxygenation.

Patient is kept in a railed cot and a tongue blade is inserted between the teeth. She is kept in the lateral decubitus position to avoid aspiration. Vomitus and oral secretions are removed by frequent suctioning, oxygenation is maintained through a face mask (8–10 L/min) to prevent respiratory acidosis. Oxygenation is monitored using a transcutaneous pulse oximeter. Arterial blood gas analysis is needed when O2 saturationfalls below 92 percent. Sodium bicarbonate is given when the pH is below 7,1. The patient should have a doctor or at least a trained midwife for constant supervision.

- Detailed history is to be taken from the relatives, relevant to the diagnosis of eclampsia, duration of pregnancy, number of fits and nature of medication administered outside.

- Examination: Once the patient is stabilized, a thorough but quick general, abdominal and vaginal examinations are made. A self retaining catheter is introduced and the urine is tested for protein. The continuousdrainage facilitates measurement of the urinary output and periodic urine analysis.

- Monitoring: Half hourly pulse, respiration rates and blood pressure are recorded. Hourly urinary output is to be noted. If undelivered, the uterus should be palpated at regular intervals to detect the progress of labour and the fetal heart rate is to be monitored. Immediately after a convulsion, fetal bradycardia is common.

- Fluid balance: Crystalloid solution (Ringer’s solution) is started as a first choice. Total fluids should not exceed the previous 24 hours urinary output plus 1000 ml (insensible loss through lungs and skin). Normally, it should not exceed 2 litres in 24 hours. Infusion of balanced salt solution should be at the rate of 1 ml/kg per hour. In pre-eclampsia–eclampsia although there is hypovolemia, the tissues are over loaded. An excess of dextrose or crystalline solutions should not be used as it will aggravate the tissue overload leading to pulmonary edema and adult respiratory distress syndrome. Colloids (albumin or hemaccel) remain in the vascular tree and they withdraw fluids from the interstitial space. Unless used carefully, they can lead to circulatory overload. CVP monitoring is needed for a patient with severe hypertension and reduced urine output. In pre-eclampsia, eclampsia, both the PCWP and CVP appear to be in the low to normal range. Invasive hemodynamic monitoring is rarely indicated.

- Antibiotic: To prevent infection, Ceftriaxone 1 gm IV twice daily is given.

**SPECIFIC MANAGEMENT:**

- Anticonvulsant and sedative regime: The aim is to control the fits and to prevent its recurrence. In areas where eclampsia is frequently encountered, it is obvious that the obstetric care isinadequate. In such circumstances any complicated regime is unlikely to give good result.

- Magnesium sulfate is the drug of choice. It acts as a membrane stabilizer and neuroprotector. It reduces motor endplate sensitivity to acetylcholine. Magnesium blocks neuronal calcium influx also. It induces cerebral vasodilatation, dilates uterine arteries, increases production of endothelial prostacyclin and inhibits platelet activation. It has no detrimental effects on the neonate within therapeutic level. It has got excellent result with maternal mortality of 3%. It does not control hypertension. Regimens of MgSO4 for the management of severe pre-eclampsia and eclampsia Regimen Loading dose Maintenance dose Intramuscular (Pritchard) 4 gm IV over 3– 5 min followed by 10gm deep IM (5 gm in each buttock) 5 gm IM 4 hourly in alternate buttock

- Intravenous (Zuspan or Sibai) 4–6 gm IV over 15–20 min 1–2 gm/hr IV infusion Repeat injections are given only if the knee jerks are present, urine output exceeds 30 mL/hour and the respiration rate is more than 12 per minute. The therapeutic level of serum magnesium is 4–7 mEQ/L.

- Antihypertensives and diuretics: Inspite of anticonvulsant and sedative regime, if the blood pressure remains more than 160/110 mm Hg, antihypertensive drugs should be administered. Drugs commonly used are parenteral, hydralazine, labetalol, calcium channel blockers or nitroglycerin. Presence of pulmonary edema requires diuretics. In such cases, the potent one (frusemide) should be administered in doses of 20–40 mg intravenously and to be repeated at intervals.

**Management during fit:**

 In the premonitory stage, a mouth gag is placed in between the teeth to prevent tongue bite and should be removed after the clonic phase is over.

 The air passage is to be cleared off the mucus with a mucus sucker. The patient’s head is to be turned to one side and the pillow is taken off. Raising the footend of the bed, facilitates postural drainage of the upper respiratory tract.

 Oxygen is given until cyanosis disappears.

Status eclampticus: Thiopentone sodium 0.5 gm dissolved in 20 mL of 5% dextrose is given intravenously very slowly. The procedure should be supervised by an expert anesthetist. If the procedure fails, use of complete anesthesia, muscle relaxant and assisted ventilation can be employed. In unresponsive cases, cesarean section in ideal surroundings may be a lifesaving attempt.

Treatment of complications:

 Prophylactic use of antibiotics markedly reduces the complications like pulmonary and puerperal infection.

 Pulmonary edema: Frusemide 40 mg IV followed by 20 g. of mannitol IV reduces pulmonary edema and also prevents adult respiratory distress syndrome.

 Pulse oximeter is very useful to monitor such a patient. Aspiration of the mucus from the tracheobronchial tree by a suction apparatus is done.

 Heart failure: Oxygen inhalation, parenteral lasix and digitalis are used. For details.

 Anuria: The treatment should be in the line as formulated in anuria. Dopamine infusion (1 μg/kg) is given with oliguria when CVP is >8 mm Hg. It is often surprising that urine output returns to normal following delivery.

 Hyperpyrexia: It is difficult to bring down the temperature as it is central in origin. However, cold sponging and antipyretics may be tried.

 Psychosis: Chlorpromazine or Eskazine (trifluoperazine) is quite effective.

**Intensive care monitoring:** Patient with multiple medical problems needs to be admitted in an intensive care unit where she is looked after by a team consisting of an obstetrician, a physician and an expert anesthetist. Cardiac, renal or pulmonary complications are managed effectively. Use of blood gas analyzer (to detect hypoxia and acidosis), pulse oximeter and central venous pressure monitor should be done depending on individual case. A deeply unconscious patient with raised intracranial pressure needs steroid and or diuretic therapy. CT scan or MRI may be needed for the diagnosis.

**OBSTETRIC MANAGEMENT**

**• Fits controlled:**

— Baby mature: Delivery should be done.

 If the cervix is favorable and there is no contraindication of vaginal delivery, surgical induction by low rupture of the membranes is done. Oxytocin drip may be added, if needed.

 When the cervix is unfavorable, cervical ripening with PGE2 gel or pessary could be achieved before ARM.

 If the cervix is unfavorable and/or there is obstetric contraindication of vaginal delivery, cesarean section is done.

— Baby premature (<37 weeks): Delivery is recommended in a set up with neonatal intensive care unit (NICU). The underlying disease process of pre-eclampsia eclampsia persists until the woman delivers. At times the disease process may flare up. Moreover, there lies the risk of recurrent convulsions and IUFD. Steroid therapy is given when pregnancy is less than 34 weeks. Conservative management at very early pregnancy may improve perinatal outcome but this must be carefully balanced with maternal well being.

— Baby dead: The preeclamptic process gradually subsides and eventually expulsion of the baby occurs. Otherwise medical method of induction is started.

**• Fits not controlled:**

If the fits are not controlled with anticonvulsant within a reasonable period (6– 8 hours), termination of pregnancy should be done. If vaginal examination indicates a quick response to induction, low rupture of the membranes is done. Oxytocin infusion may be added. The uterus responds well to oxytocin in such cases. In presence of unfavorable factors, cesarean section gives a quick response.

During labor: In the absence of any contraindication to vaginal delivery, as soon as the labor is well established, low rupture of the membranes is to be done to accelerate the labor. The dose schedule of antihypertensive and anticonvulsant drugs may be increased to quieten the patient. Second stage should be curtailed by forceps, ventouse or craniotomy, if the baby is dead. Prophylactic intravenous ergometrine or syntometrine following the delivery of the anterior shoulder should not be given as it may produce further rise of blood pressure. Instead, 10 units of oxytocin IM or IV slowly should be given. One should remain vigilant about postpartum hemorrhage and shock.

Indications of cesarean section:

 Uncontrolled fits in spite of therapy.

 Unconscious patient and poor prospect of vaginal delivery.

 Obstetric indications (malpresentation).

Follow up and prognosis: Patient should be followed up in the postnatal clinic by 6 weeks time. Persistence of hypertension, proteinuria and abnormal blood biochemistry necessitates further investigation and consultation with a physician. Further pregnancy should be deferred till they are controlled. Management of eclampsia is according to Queensland Clinical Guideline: Hypertensive disorders of pregnancy, 2015 (see table 6)

Table 6

**Management of eclampsia**

|  |  |
| --- | --- |
| Aspect | Considerations |
| Goals of treatment1 | • Terminate the seizure  • Prevent recurrence  • Control hypertension  • Prevent maternal and fetal hypoxia |
| Context | • There are no reliable clinical markers that predict eclampsia  • Hypertension and proteinuria may be absent prior to the seizure1  • Seizures may occur antepartum, intrapartum or postpartum usually within 24 hours of birth1  • Reported incidence of eclampsia varies |
| Imminent eclampsia | o Frontal headache  o Visual disturbance  o Altered level of consciousness  o Hyperreflexia  o Epigastric tenderness |
| Treatment | • Follow the basic principles of resuscitation1  • Magnesium Sulfate is the anticonvulsant drug of choice for the prevention and treatment of eclampsia  Eclampsia  HELLP syndrome  HELLP syndrome is one of the most serious forms of preeclampsia. The syndrome was first described by Vainshtein in 1985, abbreviated from the first letters in English: H-hemolysis, EL- elevated liver enzymes, LP – low platelets count. The incidence of pre-eclampsia in hospital practice varies widely from 5 to 15%. The incidence in primigravidae is about 10% and in multigravidae 5%. Imperfect  o • If the seizure is ongoing or prolonged1 while initiating Magnesium Sulfate infusion or reoccurs during administration of Magnesium Sulfate give :  o Diazepam 5–10 mg IV at a rate of 2–5 mg/minute (maximum dose of 10 mg) or  o Midazalam 5–10 mg IV over 2–5 minutes or IM  o Clonazepam 1–2 mg IV over 2–5 minutes  • Do not use Phenytoin for eclampsia prophylaxis or treatment unless there is a contraindication to Magnesium Sulfate or it is ineffective  • Aim for BP below 160/100 mmHg |
| Post seizure care | • If birth has not occurred, plan as soon as feasible and when the woman’s condition is stable  • Close clinical surveillance is required in an appropriately staffed area |

**Eclampsia**

**HELLP syndrome**

HELLP syndrome is one of the most serious forms of preeclampsia. The syndrome was first described by Vainshtein in 1985, abbreviated from the first letters in English: H-hemolysis, EL- elevated liver enzymes, LP – low platelets count. The incidence of pre-eclampsia in hospital practice varies widely from 5 to 15%. The incidence in primigravidae is about 10% and in multigravidae 5%. Imperfect documentation and lack of uniformity in the diagnostic criteria are the responsible factors in variation of its frequency.

In HELLP syndrome the main pathophysiological changes occur predominantly in the liver. The main link in the development of the syndrome is disturbances in hemostasis due to damage of the endothelium and intravascular activation of the coagulation system. Fibrin deposits in the sinusoidal capillaries of the liver leads to the central necroses with stasis and tension of the Glisson’s capsule. Further progression of the process can lead to rupture of the liver. If this false circle fails to be discontinued, then in a few hours the DIC syndrome will develop deadly bleeding.

All symptoms of HELLP syndrome can be divided into specific, non-specific and distinctive (table 7)

**Table 7.**

**Symptoms of HELLP syndrome**

**(Haemolysis, Elevated Liver enzymes and Low Platelet count).**

|  |  |
| --- | --- |
| Symptoms | Manifestations |
| Specific | Hemolysis  Elevated liver enzymes  Thrombocytopenia |
| Non-specific | Malaise  Headache, fatigue  Nausea, vomiting  Abdominal pain, right-upperquadrant  pain |
| Distinctive | Blood stained vomiting  Jaundice. Seizures  Hemorrhage on the places of injections  Progressive hepatic failure |

**The major symptoms of the HELLP syndrome:**

– elevated bilirubin due to enhanced hemolysis of red blood cells; jaundice, lowering of hemoglobin up to 90 g/l and below, lowering of hematocrit to 0,25-0,3;

– elevated liver enzymes (AST, ALT, LDH), elevated plasma uric acid, nitrogen substances; hypoglycemia, associated with hepatic failure;

– disturbances in hemostasis (low level of antithrombin III, increase in prothrombin time and partial thromboplastin time, low level of fibrinogen), that are causes for the development of DIC syndrome.

**Critical care of HELLP-syndrome:**

Sequence of therapeutic actions.

 Expedited delivery: vaginal delivery in case of ―ripe‖ cervix and cesarean section if the cervix is unfavorable

 Intensive therapy of severe preeclampsia, respiratory support (ALV on indications, oxygenotherapy)

 Treatment of DIC syndrome: transfusion of fresh frozen plasma, packed platelet (in thrombocytopenia <30-50·109), inhibitors of proteases, cryoprecipitate

 Infusion therapy: crystalloids, amylum hydroxyaethylicum (6% or 10%), albumin (10 and 20%)

 In hemoglobin less than 70 g/l: transfusion of packed red blood cells when expiration date does not exceed 3 days

 Dipyridamolum (curantyl), aspirin, prednisolone (300 to1000 mg/kg/day), cytostatics (after delivery)

 Hepatoprotectors, antioxidants, membrane stabilizers

 Antibacterial therapy

 Antithrombin III (prophylactic dose is 1000-1500 IU/day; the initial treatment dose is 1000-2000 IU/day, followed by 2000-3000 IU/day)

*Indications for expedited delivery:*

 progressing thrombocytopenia;

 dramatic worsening of preeclampsia clinical course;

 impaired consciousness and severe neurological symptoms;

 progressing worsening of liver and kidneys function;

 fetal distress.

Subcapsular hematomas and liver raptures occur more frequently in the antepartum manifestations of the HELLP syndrome. Spontaneous liver ruptures are characterized by the high maternal mortality (over 50%). Methods for treatment of the liver ruptures include evacuation of the hematoma and its drainage, stitching of the damaged part of the liver, application of local hemostatics, hepatic artery ligation, removal of the part of the liver and hepatic artery embolization. Survival after suturing with tamponage and drainage accounts for 82%, and after removal of the part of the liver constitutes only 25%. The improvement in survival could be achieved only through early recognition and intensive multi-component treatment of HELLP syndrome.

**CONCLUDING PROVISIONS**

1. Hypertensive disorders in pregnant women occur in 6-10% of cases and are one of the leading causes of perinatal loss and maternal mortality.

2. Preeclampsia increases the risk of premature detachment of placenta, preterm delivery, fetal growth restriction, as well as maternal brain damages.

3. Only diastolic BP is used to determine the severity of hypertension in pregnant as well as indication to start antihypertensive treatment and its effectiveness.

4. The term of the final retrospective confirmation or refutation of the diagnosis of gestational hypertension is 12 weeks postpartum period.

5. It is proved that drug antihypertension therapy should not be initiated unless the BP < 150/100 mm Hg. Lowering of BP due to drug therapy can improve the outcomes of pregnancy for the mother, but not for the fetus.

6. The following antihypertensive medications are used during pregnancy: methyldopa (the drug of choice), nifedipine, labetalol (the drugs of the second-line choice), β-blockers, clonidine, verapamil, hydralazine. Diuretics should be avoided especially in cases of preeclampsia (except pulmonary edema or renal failure). Angiotensin converting enzyme inhibitors and angiotensin II receptor blockers are strictly contraindicated.

7. Limitation of salt and fluid both to prevent and treat preeclampsia is proved to be irrational.

8. It is established that acetylsalicylic acid (60-100 mg/day) reduces the incidence of preeclampsia development in pregnant women at risk. Calcium (2 g/day) effectively reduces the risk of hypertension and, to a lesser extent, preeclampsia. Antioxidants (1 g/day Ascorbic acid, 400 mg/day E vitamin) reduce the risk of preeclampsia, but this fact has not been confirmed in controlled trials.

9. It has been proved by evidence that magnesium sulphate prevents the development of eclampsia and is the drug of choice for its treatment. All women with eclampsia should be given magnesium sulphate during labor and the following the 24 hours after delivery.

10. Delivery is the only care for preeclampsia/eclampsia. For the fetus wellbeing pregnancy prolongation is possible is hypertension is controlled by medications and no alarming signs of CHS, liver and kidneys injury are noted. The preferable

method of delivery is vaginal delivery after 35 weeks of gestation, if the cervix is favorable.

11. The large-scale perspective studies have demonstrated that women who experienced gestational hypertension or preeclampsia are at higher risk for:

– follow up development of arterial hypertension;

– death from the stroke;

– death from all cardiovascular causes.

Therefore, such obstetric patients should undergo thorough surveillance by the general practitioner and regular medical checkup measuring of the BP, cholesterin and glucose tests yearly).

**International Society for the Study of Hypertension in Pregnancy (ISSHP) has made the emphasis on the following key issues:**

1. Women with initially diagnosed preeclampsia should be admitted to the hospital in all cases.

2. Clinical evaluation of women with preeclampsia should include heart rate oximetry, if possible.

3. It has been proved by evidence that magnesium sulphate prevents the eclampsia, twice reducing its incidence. Magnesium sulphate is also effective in severe preeclampsia. ISSHP recommends prescription of magnesium sulphate to all women with preeclampsia.

4. ISSHP does not recommend distinguishing any clinical differences between the mild and severe preeclampsia in common clinical practice.

5. Indications for delivery according to ISSHP regulations:

- women with preeclampsia at 37 weeks of gestation must be delivered;

- expectant management can be provided for women with preeclampsia within 34 and 37 weeks of gestation;

- conservative treatment should be provided for women with preeclampsia at 34 weeks of gestation (expectant management).

*Delivery is required if one or more of the following sings occur:*

1) the inability to control the BP of the mother, despite the prescription of antihypertensive medications;

2) heart rate oximetry of the mother < 90% or presence of pulmonary edema;

3) progressive worsening of liver function, glomerular filtration rate, hemolysis or low platelets count;

4) occurrence of neurological symptoms or eclampsia;

5) placental abruption;

6) impairment of umbilical cord blood circulation according to Doppler ultrasonography and cardiotocography and stillbirth.

**Control Questions:**

1. What are the symptoms of late gestoses?

2. What are gestoses and what does abbreviation stand for?

3. Describe the mechanism of the occurrence of EPH- gestoses.

4. Mechanism of the occurrence of hypoproteinemia.

5. What are the manifestations of edemas of pregnant?

6. What is the mode of gaining weight in normal pregnancy?

7. Major principles of management of pregnant with edemas.

8. What is the ground for preeclampcia diagnosis in pregnant?

9. Classification of the preeclampsia according to its severity.

10.Management of pregnant with preeclampsia.

11.What is the effect of magnesium sulphate in treatment of

preeclampsia?

12.What are the signs of preeclampsia?

13.Emergency care in preeclampsia.

14. Signs of eclampsia.

15.Sequential development of eclamptic fit.

16.In what case do the eclamptic fits occur postpartum?

17.Current approach to treatment of eclampsia of pregnant.

18.Emergency care in eclampsia

19.Obstetric management of late gestosis.

20.Methods of delivery management in late gestosis.

21. Prevention of late gestosis.

TESTS.

1.Which of the following is true of blindness in conjunction of pregnancy

induced hypertension?

**A. occur in severe preeclampsia**

B. occur in moderate preeclampsia

C. occur in mild preeclampsia

D. is not present in pregnancy induced hypertension

E. there is no correct answer

2.Which of the following is NOT a sign of severe pregnancy-induced

hypertension?

**A. polyuria**

B. upper abdominal pain

C. oliguria

D. fetal growth retardation

E. visual disturbances

3.Which sign suggest about magnesium toxicity?

**A. decreasing of patellar reflex**

B. depression

C. increasing of breathing

D. polyuria

E. there is no correct answer

4.Which sign suggest about magnesium toxicity?

**A. oliguria**

B. increasing of breathing

C. polyuria

D. insomnia

E. there is no correct answer

5.All drugs should be prescribed in Hyperemesis gravidarum EXEPT?

**A. intravenous prostaglandyns**

B. infusion therapy

C. antiemetic

D. intravenous droperidol-diphenhydramine

E. metoclopramide parenterally

6.What index in the general blood analysis indicate the severity of pregnancy

induced hypertetnsion ?

**A. thrombocytes**

B. leukocytes

C. hemoglobin

D. basophiles

E. neutrophiles

7.In regard to preeclampsia, proteinuria is defined as how much urinary

excretion?

**A. 300 mg/24 hr**

B. 100 mg/24 hr

C. 200 mg/24 hr

D. 500 mg/24 hr

E. 600 mg/24 hr

8.Which of the following is NOT diagnostic of moderate preeclampsia?

**A. diastolic blood pressure 110 mm. Hg**

B. serum creatinine from 75 – 120 mkmol/L

C. <0,3 – 5 g proteinuria in 24 hour collection

D. 39 - 42 hematocrit

E. 180-150.000 thrombocytes

9.What is the significance of maternal thrombocytopenia in a patient with

preeclampsia?

**A. indicates severity of disease**

B. is a fetal indication for cesarean section

C. requires therapy with platelets

D. is a contraindication to scalp pH determination

E. there is no correct answer

10.Chronic hypertension defined as:

**A. hypertension present before the 12 week of gestation or beyond 6**

**weeks' postpartum.**

B. hypertension present before the 22 week of gestation or beyond 6

weeks' postpartum

C. hypertension present before the 24 week of gestation or beyond 8

weeks' postpartum

D. hypertension present before the 34 week of gestation or beyond 10

weeks' postpartum

E. hypertension present before the 4 week of gestation or beyond 12

weeks' postpartum

**SITUATIONAL TASKS**

1.Hypertension in pregnancy defined as:

2. The level of proteinuria in 24 hour collection is 0.2 g. For which degree

of pregnancy induced hypertension does it characterized?

3.What is the scheme of methyldopha prescription in the treatment of

moderate preeclampsia?

4.To which group does atenolol belong to?

5.What is the initial dose of magnesium sulfate in the treatment of moderate

preeclampsia?