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Current issues on hypertensive disorders of pregnancy and puerperium

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ARTICLE INFORMATION

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Acronyms
APE: acute pulmonary edema
BP: blood pressure
CVD: cerebrovascular disease
HDP: hypertensive disorders of pregnancy
HT: hypertension
IUGR: intrauterine growth retardation
NHBPEP: National High Blood Pressure Education Program

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ABSTRACT
Hypertensive disorders of pregnancy complicate 5 to 7% of all pregnancies and are one of the leading causes of maternal morbidity and mortality worldwide. These disorders vary from mild hypertension to severe preeclampsia/eclampsia. Recently, there have been major advances in the study of these disorders; however, many aspects need to be resolved, mainly concerning pathogenesis, prevention and management. This review is based on the latest available evidence on hypertensive disorders of pregnancy. Aspects related with classification, diagnosis and management of hypertension in pregnancy and its main complications are discussed in this article.
Key words: Preeclampsia, Eclampsia, Blood pressure, Obstetrics, Hypertension

Consideraciones actuales acerca de la enfermedad hipertensiva del embarazo y el puerperio

RESUMEN
La enfermedad hipertensiva del embarazo afecta entre el 5-7 % de las gestaciones y figura entre las principales causas de morbilidad y mortalidad materna mundialmente. Esta enfermedad varía desde formas leves hasta preeclampsia grave/eclampsia. Aunque recientemente se ha observado un auge en las investigaciones, aún quedan muchos puntos por esclarecer, fundamentalmente en el campo de la patogenia, la profilaxis y el tratamiento. La presente revisión se basa en las más recientes evidencias disponibles sobre la enfermedad hipertensiva del embarazo. Aspectos relacionados con la clasificación, el diagnóstico y el tratamiento específico de la hipertensión arterial en el embarazo y sus principales complicaciones se analizan en el presente artículo.
Palabras clave: Preeclampsia, Eclampsia, Presión arterial, Obstetricia, Hipertensión arterial

INTRODUCTION

Hypertension (HT) is among the most common disorders of pregnancy and

puerperium and affects between 5 and 7 % of all pregnancies[1]. Although mortality from this cause has declined in recent years, the hypertensive disorders of pregnancy (HDP) remains a major cause of maternal and fetal morbidity and mortality worldwide[2]. According to the US National Center for Health Statistics, HDP was the second leading cause of hospitalization related to childbirth (7.37 %) between 1998 and 1999 (the first was preterm birth), and was the third leading cause of maternal death (17,6 %). Along with obstetric hemorrhage, hypertensive emergency accounts for 50 % of admissions in obstetric intensive care units[1,3].

Interventions to reduce the incidence of HDP, including preeclampsia/eclampsia, in the general population have been discouraging. The mainstay of treatment includes the monitoring of prenatal maternal and fetal health and opportune termination of pregnancy to mitigate the consequences of the disease. Although the incidence of HDP is progressively increasing, studies on antihypertensive drugs for use in pregnant women are scarce, and the same drugs are being used. Many of them are contraindicated in pregnancy, as they cross the placenta and may cause fetal abnormalities.

The arrival at the emergency department of a pregnant or puerperal woman with high blood pressure (BP) is a worrying situation for the patient, her family and physicians, as it may involve a fatal outcome. It is imperative to rate the intensity and type of HDP in each patient to take the most appropriate actions in each case.

PHYSIOLOGICAL CHANGES IN THE CARDIOVASCULAR SYSTEM OF THE PREGNANT WOMAN

Pregnancy entails an extension of circulation to meet placental-fetal and uterine growing needs; thus a series of changes that allow the growth and development of the fetus take place. A marked increase in cardiac output and in intravascular and extravascular volumes occurs rapidly during the first half of pregnancy and then become stabilized. BP follows a somewhat parabolic curve with a progressive decrease during the first three months of pregnancy and a marked decrease between the 22 and 24 weeks; then, it slightly increases near the end of pregnancy[4]. The evident increase in cardiac output does not cause a significant increase in BP due to a decrease in peripheral vascular resistance, which is largely caused by the effect of hormones. Peripheral vascular resistance increases in patients with preeclampsia/eclampsia[5].

Renal blood flow is increased by vasodilation, leading to a rise in glomerular filtration rate and a marked stimulation of the renin-angiotensin-aldosterone axis. The increased filtration rate causes a decreased in creatinine levels in these patients[6]. Thus, a creatinine level > 80 mol/L (0.9 mg/dL) may be indicative of a nephropathy in pregnancy or the postpartum period. The intravascular volume is increased by about 2 liters due to water and sodium retention. The fall in BP during the second three months of pregnancy, when most of pregnancies are detected, may cause that a chronic HT goes undetected and later be misinterpreted as a preeclampsia/eclampsia. The general nature of physiological changes in pregnancy makes it difficult to find the probable cause of chronic HT in pregnant women.

TECHNIQUE FOR MEASURING BLOOD PRESSURE

According to the National High Blood Pressure Education Program (NHBPEP)[7], for the correct measurement of BP, the patient should remain seated, at 45 degrees, and quiet for a few minutes. The sphygmomanometer cuff should cover 2/3 of the right arm at the level of the heart and should be inflated slowly to 30 mmHg above the pressure at which radial pulse is blocked. Then the air is let out 2-3 mmHg/s until the first Korotkoff sound is heard (systolic BP). The cuff pressure is further released until no sound can be heard (fifth Korotkoff sound) (diastolic BP). HT is considered when systolic BP is ≥ 140 mmHg or diastolic BP is ≥ 90 mmHg, preferably measured at least on two occasions, and separated by 4-6 hours[7]. Previously, an increase of 30 mmHg over baseline systolic BP or 15 mmHg over baseline diastolic BP was considered HDP. However, the NHBPEP consensus does not recognize these values as HDP, since they has taken into account some studies showing that the result is similar in pregnant women with a 30/15 mmHg increase and in those whose BP pressure does not exceed 140/90 mmHg. However, these patients should be considered at risk. Electronic BP measuring devices may underrate their measurement.

CLASSIFICATION OF THE HDP

Several classifications have been proposed[8]. The classification accepted by NHBPEP divides HDP into four groups or categories[7]:

1. Preeclampsia-eclampsia: HT ≥ 140/90 mmHg accompanied by damage to one or more organ systems (central nervous, cardiopulmonary, gastrointestinal, hematologic, renal, uterus-placental/fetal circulation), which disappears in a period of three months postpartum.
2. Chronic HT: HT that is diagnosed before 20 weeks of pregnancy.
3. Chronic HT with superimposed preeclampsia: pregnant women with chronic HT and damage to organs or systems of organs not previously affected by chronic HT.
4. Gestational HP: hypertension that appears after 20 weeks of pregnancy without damage to the organ systems.

Preeclampsia-eclampsia

Preeclampsia is a multisystem disease, only present in humans, characterized by HT and damage to organ systems, with varying intensity. Most deaths from preeclampsia/eclampsia are due to peripartum bleeding, cerebrovascular disease (CVD), pulmonary edema with acute respiratory failure, liver failure and bleeding disorders, among others. Women with preeclampsia have higher risk of HT, CVD or ischemic heart disease in later stages of life[9]. Although uric acid is frequently increased, it has not been shown that this metabolite is a predictor of a negative outcome for the mother. Some rare situations can cause preeclampsia before 20 weeks. They include hydatidiform mole, multiple gestation, antiphospholipid syndrome, fetal or placental abnormalities, or severe renal disease[10,11].

Severe preeclampsia shows markedly elevated BP levels (≥ 150/110 mmHg), accompanied by a significant deterioration of organ function (Table 1)[10,12-16]. The HELLP syndrome is considered a form of severe preeclampsia characterized by hemolysis, elevated liver enzymes (SGPT and LDH) and thrombocytopenia (<100 x 10^9/L)[17]. Mild initial forms may go unnoticed. Patients suspected of having this syndrome should be admitted to hospital with a strict monitoring; and termination of pregnancy should be considered if alterations increase. Changes may persist up to one week after delivery. In these patients, alterations in placentation often cause fetuses with intrauterine growth retardation (IUGR), preterm delivery or intrauterine death.

Alterations in liver function without hemolysis should be differentiated from HELLP syndrome. These include the acute fatty liver of pregnancy (which is not usually associated with HT) and the thrombotic thrombocytopenic purpura/hemolytic uremic syndrome, which is characterized by five findings: 1) thrombocytopenia, 2) microangiopathic hemolytic anemia, 3) neurological signs and symptoms, 4) renal impairment and 5) fever. Differentiation is important because treatment varies depending on the disease.

Table 1. Diagnosis of severe preeclampsia.

Systolic HT (≥ 140 mmHg), Severe (≥ 160 mmHg) and hypertensive crisis (≥ 180 mmHg). Diastolic HT (≥ 90 mmHg) and hypertensive crisis (≥ 110 mmHg). With one or more of the following conditions	
Organs and organ systems	**Disorders**
Cardiovascular system	Pulmonary edema
Central nervous system	Seizures (eclampsia) Headache Visual disturbances Papilledema Hyperreflexia /clonus
Gastrointestinal system	Elevated liver enzymes: transaminases (SGOT, SGPT ≥ 70 IU) Pain and liver disorders Nausea and vomiting Epigastralgia
Hematologic system	Hemolysis Thrombocytopenia < 100 x 10^9/L Disseminated intravascular coagulation
Renal system	Proteinuria > 0.3 g/24 hours or more than one qualitative + in urine strips * Protein/creatinine ratio > 0.5 g/mmol Urine output < 500 ml/24 hours kidney failure
Utero-placental-fetal circulation	Placental abruption Presence of IUGR Abnormalities of flow in the uterine or umbilical artery or reversed telediastolic flow or absent flow.

* Some authors accept a proteinuria greater than 0.5 g/24 hours and more than 3 +++ in test strips as pathological in preeclampsia.
SGOT: serum glutamic oxaloacetic transaminase, SGPT: serum glutamic-pyruvic transaminase.

Chronic HT

It is a relatively common disease among pregnant (3%) and postpartum women, but may not be recognized. The progressive increase in maternal age and obesity levels, especially in developed countries, increases the frequency of chronic HT[18]. The risk of superimposed preeclampsia/eclampsia is 17-25% *vs.* 3-5% in normotensive pregnant women[19]. As in the rest of the patients, a well-defined cause usually cannot be identified. The secondary causes include renal artery stenosis, pheochromocytoma, endocrine tumors, Cushing's syndrome, and collagen diseases, among others[20].

Table 2. Classification of hypertension in pregnancy, according to Davey, *et al*[22].

New-onset hypertension and/or proteinuria in pregnancy
• Gestational hypertension (without proteinuria)
• Gestational proteinuria (without hypertension)
• Preeclampsia (hypertension + proteinuria)
Chronic hypertension and renal disease
• Chronic hypertension without proteinuria
• Chronic kidney disease (proteinuria with/without hypertension)
• Chronic hypertension with superimposed preeclampsia (e.g. with new onset proteinuria in pregnancy)
Not classified
• Hypertension and/or proteinuria detected after 20 weeks
• It is detected for the first time during pregnancy, delivery or postpartum period, but there is insufficient data for diagnosis in the above categories

Gestational HT

It is characterized by a mild to moderate increase in BP after 20 weeks of pregnancy, but without proteinuria or alteration of other organ systems. It often appears in the final stages of pregnancy. Special care must be taken with these patients as a number of them actually suffer from preeclampsia although the other symptoms appear later. Improper evaluation and monitoring of these cases may result in a fatal outcome. Some of these patients will suffer from diabetes mellitus, HT in subsequent pregnancies and in later stages of life[21].

Delayed postpartum HT refers to a HT that occurs in women whose pregnancies and early postpartum weeks (up to six months) have passed without HT, then they begin to develop a HT that may last up to one year after delivery. Perhaps this situation predicts a chronic HT and is a phenomenon not well understood[20].

Another classification of HDP is proposed by Davey *et al*[22] (**Table 2**). It is very useful though less used in our environment.

CLINICAL SYMPTOMS

The HDP shows a wide spectrum of symptoms, in intensity and manifestations, ranging from oligosymptomatic forms to coma and death. Chronic HT may occur without major impact to the mother and fetus, as long as it is kept balanced and within acceptable levels (mild to moderate). Conversely, preeclampsia tends to appear with serious complications, so its identification and early treatment is a must. Even with proper treatment, the disease may progress and endanger the lives of the mother and fetus. Given that gestational HT is often a hidden preeclampsia and that chronic HT and preeclampsia may overlap, it is always preferable to treat the mother as if it was the diagnosis.

This disease may present with a rapid weight gain and be associated with bleeding disorders and impaired liver function. It is more common in nulliparous women and almost always appears in the second half of pregnancy, near its term. Some authors prefer to classify it as mild and severe, although this classification may be misleading as an initially mild disease can progress rapidly and become a severe form (Table 3)[23,24]. Other symptoms and signs may be found, these include headache, hyperreflexia, and laboratory abnormalities such as thrombocytopenia (<100 x 10^9/L), hemolysis, elevated liver enzymes, hyperbilirubinemia, and proteinuria. The early-onset preeclampsia (< 34 weeks) is often associated with increased morbidity. The main risk factors are age (≥ 40 years in primiparous or multiparous women), a family history of the disease, nulliparity, multiple pregnancy, diabetes mellitus, body mass index ≥ 35 kg/m^2, previous preeclampsia, assisted pregnancy, chronic renal disease, collagen diseases (such as systemic lupus erythema-

tosus) and antiphospholipid syndrome[1].

The seizures or coma associated with preeclampsia is what is known as eclampsia, which is a potentially fatal complication if goes untreated. These patients often complain of headache, visual disturbances, epigastric pain, chest tightness, apprehension and hyperreflexia before seizures. However, seizures may appear suddenly without premonitory signs and in a patient without severe HT. Although most of eclampsia occur in the peripartum period, late seizures may occur (48 hours after delivery), which is called late postpartum eclampsia[25]. It is important to rule out other potentially lethal diagnoses in all patients with a suspected eclampsia that does not improve with the usual treatment. CVD, epilepsy, head injuries, poisoning and infections of the central nervous system are among the main diseases that may be mistaken for this serious condition.

Table 3. Signs of seriousness of preeclampsia [23,24].

Variables	Menos grave	Más grave
Time of occurrence	Gestational time ≥ 34 weeks	Gestational time < 34 weeks
Diastolic BP	< 100 mm Hg	≥ 110 mm Hg
Headache	Absent	Present
Visual disturbances	Absent	Present
Abdominal pain	Absent	Present
Oliguria	Absent	Present
Glomerular filtration	Normal	High
LDH, SGPT	Normal	High
Proteinuria	Mild to moderate	Nephrotic range (> 3g/24h)
Blood disorders (e.g. hemolysis, thrombocytopenia)	Absent	Present
Stabilization of fetal tests	Absent	Present

LDH: lactate dehydrogenase, SGPT: serum glutamic-pyruvic transaminase.

COMPREHENSIVE DIAGNOSTIC AND THERAPEUTIC ACTIONS

Maternal assessment

In all pregnant women, signs of HT and proteinuria should be sought, once a month until 30 weeks, and once every two weeks until the end of pregnancy. In patients at risk or with symptoms that are suggestive of preeclampsia/eclampsia, it is necessary to conduct a 24-hour proteinuria test, coagulation test, including platelet count, peripheral smear, uric acid and liver function tests (SGPT and LDH).

Prevention

Several researchers have tried to find a substance with prophylactic properties for preeclampsia. To date, only low-dose aspirin has achieved a reduction of only 10% in patients with preeclampsia, although results are controversial[26-30]. The 2013 guidelines for management[31] have taken into account the discrepancies between the different studies and recommend aspirin treatment only in those patients at high risk of preeclampsia (HT in previous pregnancies, chronic renal disease, autoimmune diseases such as systemic lupus erythematosus, antiphospholipid syndrome, and diabetes mellitus or chronic HT), or in patients with more than one risk factor for moderate preeclampsia (first pregnancy, age ≥ 40, birth interval of more than 10 years, BMI ≥ 35 kg/m^2 at detection, a family history of preeclampsia and multiple pregnancy), for which a dose of 75 mg/day of aspirin is recommended starting at week-12 until delivery. According to one study[32], it was considered the possibility that calcium might be useful in patients with a low income of this mineral in their diet (< 600 mg/day) which could reduce the adverse effects of the disease, such as fetal deaths, however, preeclampsia could not avoided[32]. The other drugs, such as vitamins and mineral supplements have shown no beneficial effect to prevent this disease, and in some studies they proved to be harmful in certain risk populations[33-35]. Thromboprophylaxis should be performed with caution in patients with preeclampsia, and take into account the time of action of the drugs used, and the likely need for spinal anesthesia or emergency surgical procedures.

Specific treatment

The HDP treatment, including preeclampsia/eclampsia, is complex. First, it is important to decide when and how to treat patients, and secondly, the proper selection of the drug, given its deleterious effects on the fetus. According to recent studies[36], the care of pregnant women by multidisciplinary teams seems to be more efficient.

The ideal BP may vary from patient to patient. Although standardized reference levels are used to guide treatment, these cutoffs may be arbitrary. At the mere suspicion of preeclampsia/eclampsia the pregnant women should be admitted to hospital under close surveillance. In term or near-term pregnancy, termination of pregnancy should be seriously considered. Pregnancies with moderate preeclampsia in the early stages of fetal development may go on with close monitoring, allowing the end of pregnancy, unless any signs of deterioration are present (**Table 3**). If BP rises to unacceptable levels, the antihypertensive drugs routinely used during pregnancy should be tried (**Table 4**); and if the condition does not improve within 24-48 hours, despite adequate treatment, then, termination of pregnancy is necessary. Current recommendations state that levels of diastolic BP > 105 mmHg require treatment[23]. Some patients and adolescents with baseline diastolic BP ≤ 70 mmHg, or other patients with cardiac decompensation or neurological symptoms (headache, confusion, or drowsiness), should be treated even if they have lower BP levels. Steroids have been tested for the treatment of HELLP syndrome, but no sufficient evidence has been found to support its use[37-39].

Eclampsia

The seizures of eclampsia have been associated with increased maternal mortality due to intracranial hemorrhage and cardiac arrest. Magnesium sulfate is the recommended treatment, both prophylactic and abortive treatment, for seizure, as it has proven to be superior to other anticonvulsants, and reduces the risk of recurrence[40]. The Collaborative Eclampsia Trial Group recommends the administration of 4-6 g intravenously over 5 minutes, followed by an infusion of 1 g/h for 24 hours. If, despite the initial dose, seizures persist, an additional intravenous dose of 2 g may be added[41]. This treatment should be reserved for severe forms of preeclampsia or eclampsia, and be on the watch for signs of poisoning and blood magnesium levels. Motor paralysis, hyporeflexia or areflexia, respiratory depression and cardiac arrhythmias indicate magnesium poisoning; therefore, it is necessary to stop it and administer intravenous calcium gluconate (10 %), 1-2 g in 10 minutes, until improvement of symptoms is achieved. Serum magnesium levels > 3.5 mmol/L indicate poisoning. Patients with renal impairment or oliguria (urine output < 30 ml/h) are at increased risk of poisoning. It is important to remember that magnesium is not an antihypertensive drug. If coma or seizures do not stop, or if they recur, other anticonvulsants may be tried, such as diazepam or lorazepam, and other causes, different from eclampsia, should be considered.

Chronic HT

Although chronic HT is usually less dangerous for the mother and fetus than preeclampsia, pregnant women with many years suffering from the illness, target organ damage and obesity are at increased risk of complications. Treatment of pregnant women with chronic HT is controversial. A systematic review showed that treatment of mild forms does not prevent maternal and fetal adverse events and, conversely, could cause smaller fetuses, although it seems to decrease the number of hospitalizations for decompensation of HT[42,43]. The NHBPEP and the American College of Obstetricians and Gynecologists recommend treating chronic HT patients with diastolic BP > 100 mmHg, unless there is evidence of target organ damage, or risk factors such as renal disease. However, there is no consensus on what levels are the cutoffs for initiating treatment in these cases. Systolic BP levels higher than 150-160 mmHg have been associated with an increase in the occurrence of CVD, and should always be treated. Some recommendations suggest that mild to moderate HDP (140-179/90-109 mmHg) could be treated without drugs, as drugs have not been shown to improve neonatal outcome[44]. This may cause anxiety in patients and physicians, and it appears that BP control decreases the risk of severe HT and cerebrovascular complications, although does not reduce the risk of preeclampsia, neonatal death, preterm delivery or IUGR. The European Society of Hypertension recommends pharmacological treatment of HDP in pregnant women with BP levels ≥ 140/90 mmHg[31,45] and with:

a) Gestational HT (with or without proteinuria)
b) Previous HT with superimposed gestational HT, and

Table 4. Commonly used drugs for the treatment of hypertensive disease associated with pregnancy.

Drug	Type or action mechanism	Habitual dose	Observations/adverse reactions
Methyldopa	Agonist of central action	0.5-3.0 g/day (in two sub-doses)	Increased safety tested for the fetus. Hepatotoxic , hemolytic anemia, nervous system depression
Labetalol	Combined alpha and beta-adrenergic blocker	Oral: 0.2-1.2 g/day (in two or three doses). Parenteral: 20 mg/IV and then 20-80 mg/ every 20-30 min up to 300 mg; or continuous infusion at the rate of 1-2 mg/min	Currently considered the first line drug[11]. Contraindicated in asthma. Do not exceed 160 mg/h. Bradycardia, bronchospasm, hepatotoxic.
Metoprolol	Beta-blocker	Oral: 25-200 mg 2 times a day	Can cause fetal growth retardation, the same as atenolol. Others such as pindolol and propranolol have been used safely.
Nifedipine	Calcium channel blocker	Oral: 30-60 mg/day (up to 120 mg in extended-release tablets). Repeat in 45 minutes if necessary.	It can inhibit delivery. Avoid use in conjunction with magnesium because the effect is enhanced. Inform the anesthesiologist about its use. Extended-release tablets are preferred to avoid hypotension. Other calcium channel blockers have been used safely (e.g. amlodipine)
Hydralazine	Peripheral vasodilator	Oral: 50-300 mg/day (2-4 subdoses) Parenteral: 5 mg/IV or IM, then 5-10 mg/every 20-40 min, or continuous infusion at a rate of 0.5-10 mg/h	Few adverse events reported. May cause fetal thrombocytopenia. Useful in combination with sympatholytics. Widely used and recommended after labetalol. Great experience on safety and efficacy.
Hydrochloro -thiazide	Thiazide diuretic	12.5-50 mg/day	May cause volume depletion, electrolyte disturbances. It may be useful in fluid retention. Use with caution.
Sodium nitroprusside	Peripheral vasodilator	Infusion at a rate of 0.5-10 µg/kg/min	Use with caution. Risk of severe hypotension. Possible thiocyanate intoxication with prolonged use. Drug of choice when other drugs fail.
Nitroglycerin	Peripheral vasodilator	Infusion at a rate of 0.25-5 µg/kg/min	Second-line drug the same as nitroprusside. Of choice in acute pulmonary edema. Use cautiously due to risk of severe hypotension.

c) HT with asymptomatic or symptomatic target organ damage at any time during pregnancy.

Patients with refractory HT often require more than one drug for BP control[46]. The choice of the antihypertensive drug depends on comorbidities and the experience of the clinician. Labetalol is the first-line drug treatment for pregnant women with HDP and no contraindications for its use. Its combined effect, blocking alpha and beta adrenergic receptors, improves its antihypertensive effect while avoiding the alpha compensatory sympathomimetic effect observed in treatment with "pure" beta blockers. Atenolol is not recommended because it causes fetal

growth restriction, but may be used in the postpartum period. Other beta blockers (except labetalol) appear to be less effective than calcium channel blockers and are contraindicated in patients with bronchial asthma.

Nifedipine is the most common calcium channel blocker used in the treatment HDP, because of its safety; however, it may cause headache, which may be intense sometimes. Extended-release tablets improve treatment acceptance. As it is a potent antihypertensive, it should not be administered sublingually, because may cause severe hypotension and fetal distress. The calcium channel blockers are not prescribed together with magnesium as they have a synergistic effect which results in hypotension.

Years of experience in the use of methyldopa in HDP have shown it is quite safe with respect to the fetus. After labetalol, methyldopa is the drug of choice in pregnancy but has been associated with postnatal depression and drowsiness.

Hydralazine is another mainstay of HDP treatment. It is not recommended as first-line drug because it has more perinatal adverse effects than other drugs, but remains in the therapeutic arsenal around the world. Maternal tachycardia may occur after its use and may be corrected with an infusion of crystalloid solution, reducing the possibility of sudden hypotension after administration.

Sodium nitroprusside is reserved for the treatment of hypertensive crisis. Its main side effects include hypotension, paradoxical bradycardia in women with preeclampsia, and fetal thiocyanate poisoning, when used for a long time[31,45].

Other drugs, such as high-dose diazoxide, ketanserin and nimodipine should be avoided[47]. As in all hypertensive emergencies, it is important to avoid sudden drops in BP, as it may cause serious maternal and fetal complications. The drop in BP should not be sharp and should never be below 140-150/80-100 mmHg (or 25 % of baseline BP), at an average rate of 10 to 20 mmHg every 10-20 min.

Table 4 shows a summary of the main drugs used to control HDP[24].

About 70 % of acute pulmonary edema (APE) occurs in the postpartum period. Treatment is similar to the treatment in non-pregnant population. Furosemide is administered in 20-40 mg bolus, followed by doses of 40-60 mg, not to exceed 120 mg/h. Intravenous morphine (2-5 mg) may also be used until the condition is resolved; and it is important to be on the watch for BP and signs of respiratory depression that might occur. Control of the fluids administered to the pregnant women is important to decrease the risk of APE, as it is recognized that a positive balance of more than 5 L has been associated with this complication[48]. The drug of choice for its treatment during preeclampsia is nitroglycerin at a rate of 0.5-5 µg/kg/min or a rate of 5 µg /min, with an increase in dose up to 100 µg, according to response. The oxygenation should be monitored to maintain a SpO_2 > 92 % and use mechanical ventilation, endotracheal or not, if necessary. Other causes of APE must be ruled out, such as mitral stenosis or peripartum cardiomyopathy.

Thrombocytopenia < 50 x 10^9/L in pregnant women with active bleeding, or in those that will undergo some type of surgical treatment, should be corrected quickly. Levels above these are generally well tolerated[46].

CONCLUSIONS

Recently, there has been a revival in HDP research. Preeclampsia/eclampsia is a potentially serious illness and is frequent during pregnancy and puerperium. Early diagnosis and proper treatment may save the life of the mother and fetus. Severe HT should always be treated (> 150/110 mmHg) to prevent maternal and fetal complications. The risk/benefit of antihypertensive treatment in patients with mild to moderate HT needs further well-designed research, as there is great controversy about it. Drugs such as labetalol, methyldopa and calcium channel blockers are the most commonly used drugs. Although new drugs for the treatment of HT have appeared on the market, few have been tested in pregnant women, so they are not currently used. Termination of pregnancy is the only definitive treatment for preeclampsia.

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