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Pregnancy-induced hypertension: a review about management

Doença hipertensiva específica da gestação: uma revisão sobre tratamento

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ABSTRACT: *Background*: It is estimated that hypertensive disorders in pregnancy affect 6-8% of pregnant women in the United States, and they are considered one of the main factors of maternal mortality. In Brazil, according to DATASUS, if consider the categories of O13 to O16 ICD-10, hypertensive disorders accounted for about 20.22% of maternal deaths in the period of 2004 to 2014. *Objectives*: This review aims to present the most current treatments for the management of hypertensive disorders during pregnancy. *Methodology*: The Medline/Pubmed, LILACS/SciELO, Cochrane library and Scopus databases were consulted, looking for national and international articles published between 2006 and 2016, in English and Portuguese, as well as consensuses set by the World Health Organization and DATASUS government statistics. *Results*: The recommended managements to prevent preeclampsia (PE) were calcium supplementation for pregnants with low dietetic ingestion and the administration of low doses of aspirin. In front of PE, if it happens on term, the procedure is to induce the delivery, but if it occurs pre-term, is to monitore, administrate magnesium sulfate (MS), antihypertensive and corticoid. In case of eclampsia, the MS is very effective to reduce eclamptic seizures. The drugs used in treatment of severe chronic hypertension (HY) is methyldopa in association or not, with nifedipine or hydralazine. The acute HY is treated with first line drugs, nifedipine and hydralazine, and alternatively with sodium nitroprusside. *Conclusion*: The main worldwide protocols basically follow the same orientation, only changing specific details of conduct according to each country's health system resources. The control of maternal blood pressure shows satisfactory results for both, the mother and the fetus, since it reduces the risk of PE and eclampsia. The definitive treatment for PE and eclampsia is the induction of delivery, because they have no cure, only therapeutic measures to control.

Keywords: Eclampsia; Preeclampsia; Pregnancy-induced hypertension/therapy; Pregnancy; Therapeutics.

RESUMO: *Introdução*: Estima-se que os distúrbios hipertensivos na gravidez afetam 6-8% das gestantes nos Estados Unidos e são considerados um dos principais fatores de mortalidade materna. No Brasil, de acordo com o DATASUS, se considerarmos as categorias O13 a O16 do CID-10, os distúrbios hipertensivos representaram cerca de 20,22% das mortes maternas no período de 2004 a 2014. *Objetivos*: O objetivo da revisão é demonstrar os tratamentos mais atuais para o tratamento de distúrbios hipertensivos durante a gravidez. *Métodos*: Foram consultadas as bases de dados Medline/Pubmed, LILACS/SciELO, Cochrane e Scopus, procurando artigos nacionais e internacionais publicados entre 2006 e 2016, em inglês e português, bem como os consensos estabelecidos pela Organização Mundial da Saúde e as estatísticas do DATASUS. *Resultados*: As medidas recomendadas para prevenir a pré-eclâmpsia (PE) foram a suplementação de cálcio para gestantes com baixa ingestão dietética e a administração de baixas doses de aspirina. Na PE, se acontecer no termo, o tratamento é induzir o parto, mas se ocorrer pré-termo, é monitorar, administrar sulfato de magnésio (SM), anti-hipertensivos e corticóide. Em caso de eclâmpsia, a SM é muito eficaz para reduzir as convulsões eclâmpticas. Os fármacos utilizados no tratamento da hipertensão crônica grave são metildopa em associação ou não, com nifedipina ou hidralazina. A crise hipertensiva aguda é tratada com fármacos de primeira linha, como nifedipina e hidralazina, e alternativamente com nitroprussiato de sódio. *Conclusão*: Os principais protocolos mundiais seguem basicamente a mesma orientação, mudando apenas detalhes específicos de conduta de acordo com os recursos do sistema de saúde de cada país. O controle da pressão arterial materna apresenta resultados satisfatórios para o binômio materno-fetal, pois reduz o risco de PE e eclâmpsia. O tratamento definitivo para PE e eclâmpsia é a indução de parto, sendo utilizado apenas medidas terapêuticas para controle, já que não têm cura.

Descritores: Eclâmpsia; Preeclâmpsia; Hipertensão induzida pela gravidez/terapia; Gravidez; Terapêutica.

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INTRODUCTION

It is estimated that hypertensive disorders in pregnancy affect 6-8% of pregnant women in the United States[9]. In Brazil, according to DATASUS, hypertensive disorders account for about 20.22% of maternal deaths in the period of 2004 to 2014.

The hypertensive disorders of pregnancy (HDP) have a dichotomous frequency: young women in their first pregnancy and in older multiparous women.

Morphological and functional changes in the body of pregnant women with HDP are caused by a large increase in peripheral vascular resistance, hyperreactivity to vasoconstrictor, endothelial dysfunction, vasospasm, and activation of coagulation mechanisms help in raising the pressure[3,9]. Placenta, kidney, liver and brain have their functions depressed by up to 60%, which proves that the HDP are severe, therefore intensify the risks of placental abruption, prematurity, low weight at birth, and maternal and fetal death[9].

HPD is defined as systolic blood pressure (SBP) >140 mmHg and diastolic blood pressure (DBP) >90 mmHg[5]**.** Pre-eclampsia is defined as hypertension associated with proteinuria. Proteinuria is defined as the excretion of 300 mg or more of proteins in 24 h or proteinuria with a concentration of 300 mg / L or more of proteins (≥ 1 + dipstick) in two different urine samples with a range of at least 4 to 6 h[3]. PE can manifest like a presence the swellings in face, hands, lower limbs or generalized swelling. The diagnosis is usually made after the 20th week of gestation, although early cases may occur in the hydatidiform mole or fetal hydrops.

Severe preeclampsia is defined as systolic blood pressure ≥ 160 mmHg and/or diastolic ≥ 110 mmHg associated with proteinuria; hypertension associated with severe proteinuria (above 2.0 g in 24 h); hypertension associated with multiple organ involvement (pulmonary edema and oliguria - <500 mL / day); And hypertension associated with persistent symptoms (visual, cerebral and persistent epigastric or right upper quadrant pain) or altered laboratory tests (platelet count - <100,000 per μL and hepatic enzymes)[3].

Eclampsia is defined by expression of one or more seizures or coma in pregnant women with gestational hypertension or preeclampsia, in the absence of neurological diseases and HELLP syndrome, which consists in the presence of thrombocytopenia, microangiopathichemolysis and liver dysfunction in pregnancy toxemia. It can occur during pregnancy, labor and immediately after delivery.

In view of the risks exposed and risk factors for HDP, was determined as objective to present the main and most current treatments in clinical practice for the management of hypertensive disorders during pregnancy; in alerting health professionals for early diagnosis of different clinical forms and thus reduce damage to mothers and concepts.

Table 1. **Diagnostic Criteria for Pregnancy-Associated Hypertension**

Diagnostic Criteria for Pregnancy-Associated Hypertension
Gestational Hypertension - Blood Pressure (BP) ≥ 140/90 mmHg for first time during pregnancy - No proteinuria - BP returns to normal < 12 weeks postpartum - Final diagnosis made only postpartum
Preeclampsia *Minimum Criteria* - BP ≥ 140/90 mmHg after 20 weeks gestation - Proteinuria ≥ 300mg/24hours or ≥ 1+ dipstick *Increased certainty of preeclampsia* - BP ≥ 160/110 mmHg - Proteinuria 2g/24hours or ≥ 2+ dipsticks - Serum creatinine > 1,2mg/dL unless known to be previously elevated - Platelets < 100,000/mm - Microangiopathic hemolysis (Increased LDH) - Elevated ALT or AST - Persistente headache or other cerebral or visual disturbance - Persistent epigastric pain
Eclampsia - Preeclampsia + convulsion - Seizures (generalized and may appear before, during or after labor) that cannot be attributed to other causes on woman with preeclampsia
Preeclampsia Superimposed on Chronic Hypertension - New-onset proteinuria ≥ 300mg/24hrs in hypertensive women but no proteinuria before 20 weeks gestation - A sudden increase in proteinuria or BP or platelet count <100,000mm in women with hypertension and proteinuria before 20 weeks gestation
Chronic Hypertension - BP ≥ 140/90 mmHg before pregnancy or diagnosed before 20 weeks gestation (not attributable to gestational trophoblastic disease) or - Hypertension first diagnosed after 20 weeks gestation and persistent after 12 weeks postpartum

METHODS

This is a review of the bibliography, where the following databases were consulted: Medline/Pubmed, LILACS/SciELO, Cochrane library and Scopus. Searching for national and international articles published between 2006 and 2016, in English, Portuguese and Spanish (languages understood by the review authors) as well as consensuses set by the World Health Organization (WHO) and DATASUS government statistics. Were selected 8 papers to make this review.The articles that were selected covered the topics of: definition, diagnosis, treatment and management. The descriptors used were "eclampsia", "preeclampsia" "pregnancy-induced hypertension", "treatment" and "pregnancy".

RESULTS

Prevention

After all, it was obtained that the first step is prevention, since it is able to reach a larger number of pregnant women andit is more cost-effective. It basically consists in: Family history assessment, prior health assessment of the pregnant woman (Knowledge of basal levels in the pre conception to better pregnancy monitoring), identify pregnant women's risk group (chronic hypertension, diabetes, obesity, nephropathy, neurological disorders, previous case report of preeclampsia and eclampsia), attentive evaluation in prenatal risk groups. Recommendations for risk groups to reduce vigorous activities, low sodium and low protein diet, awareness and guidance pregnant women to watch for signs installation of hypertensive disorders of pregnancy are essential either for prevent HDP. In developed countries there are already prevention campaigns to this problem. For now consider that the efficient and valuable way to pre-eclampsia and prevent eclampsia[9].

The pioneer drug in the prevention and PE installation reversal is the Calcium Supplementation for pregnant women. It appears to be effective that was observed as an inverse ratio between calcium intake and hypertensive disorders in pregnancy. In a study of recent research, daily supplementation with 2000 mg calcium for pregnant woman produces a reduction in the risk of developing preeclampsia about 66.70% and 40.90% of the risk of a premature birth. The Dietary Intake references indicate appropriate recommendations for calcium for pregnant women: Between 14 -18 years 1300mg Ca^2 / day and between 19-50 years old 1000mg Ca^2 / day (Table 2).

Table 2. Calcium intake in pregnancy women to prevent hypertensive disorders of pregnancy

Age	Dietary Intake
14 -18 years	1300mg Ca^2 / day
19-50 years	1000mg Ca^2 / day

Treatment of Preeclampsia

Regarding the treatment of preeclampsia, there are two possibilities: expectant management with rigorous monitoring of disease evolution according gestation age, fetal vitality and severity of the disease or resolution of pregnancy to cure the disease[3].

Expectant management may be the first conduct in pregnant women with gestational age of less than 34 weeks, always evaluating the risk of prolonged gestation[11]. It consists of high-risk prenatal counseling with laboratory evaluation of proteinuria, relative rest, weight control, follow-up with hemogram, liver and renal function, as well as assessment of fetal vitality[5]. The use of hypotensive drugs such as Pindolol and Methyldopa must be individualized for each case according to the evolution of the disease, since its use is not mandatory[12]. If there is no complication, theseactions should be taken until the 34th week when the resolution of gestations can be performed, but they should be delivered at term[6]. For those who gestational age is greater than 34 weeks, the delivery should be indicated, but the best way acting depends on fetal vitality. If there is no sign of fetal compromise, the gestations can usually go through to the end.

Treatment of Severe Preeclampsia

Two different paths could be adopted, which are based on gestational age. Thus, before 23 or after 34 weeks, delivery is the treatment of choice[11]. After 34 weeks if uncontrolled maternal hypertension, increasing maternal organ dysfunction or fetal distress are absent and can be monitored, between 34 and 37 weeks of gestation, a policy of expectant management may be recommended[2].

When the concept is between 23 and 34 weeks, the initial procedure to be performed is to administrate Hydralazine 5mg EV every 15 minutes until the control of the condition or until reaching 20mg. If the goal is not achieved, a second drug may be used, nifedipine 10mg, which can be repeated after 30 minutes. If still the clinical condition remains, consider the use of sodium nitroprusside 0.2 - 5 mcg /kg /min (Figure 1), which should only be used in these refractory cases, since its degradation in cyanide is toxic to the fetus.

In association of BP control procedure, magnesium sulfate should be used to prevent evolution to eclampsia. Reminding that corticoid use is essential for fetus's lung development when the delivery is before 34 weeks. If the symptoms remain unchanged or the patient develops eclampsia or HELLP syndrome, C-section is recommended. During all patient management, clinical and laboratorial monitoring of mother and fetal well-being is essential.

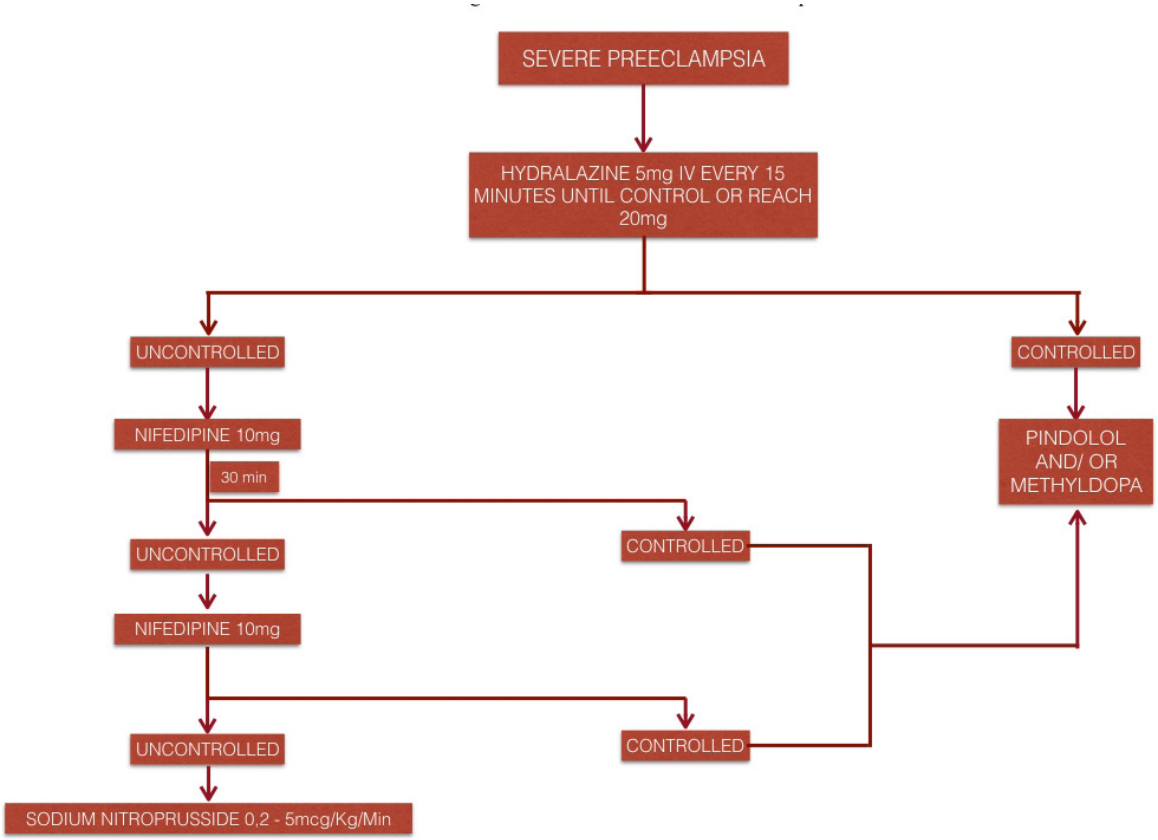

Figure 1. Treatment of severe preeclampsia

Treatment of Eclampsia

The eclampsia's management is administration of magnesium sulfate, ventilatory and hemodynamic support. After stabilization, immediate resolution of pregnancy is indicated. Zuspan's scheme is preferred, despite a higher risk of intoxication, which consistsin a loading dose of magnesium sulfate 200mg /ml EV for 10-20min followed by a maintenance dosing of magnesium sulfate 10mg / ml EV in an infusion pump at a rate of 100ml/h.

CONCLUSION

Several studies look for an efficient method to reduce the incidence and severity of HDP, however, this methodology has not been found yet.In this way, we have the conclusion to our results that appropriate interventions in the prenatal collaborate to reduce complications and maternal deaths from hypertension.

So, it is essential greater investments in prevention and early diagnosis.

And the care of hypertensive pregnant patient should be done with rest and diet, being recommended drug treatment only when necessary.

As a future perspectives of study, in view of statistical relevance and complications that HDP can cause to the mother and the fetus,were suggested the initiative of a project to conduct a Systematic Review to assist in developing an effective prevention protocol and improved clinical management and also assess the impact on public management.

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