

Updates in Management of Hypertensive Disorders of Pregnancy

Abanoub Gabra^{1*} and Mariam Gabra²

¹Department of Obstetrics and Gynecology, Assuit University, Egypt

²Registered Nurse program, Hillsborough Community College, Florida, USA

*Corresponding author: Abanoub Gabra, Department of Obstetrics and Gynecology, Assuit University, Egypt, E-mail: abanoub.gabra@med.au.edu.eg

Received date: January 07, 2019; Accepted date: January 18, 2019; Published date: January 28, 2019

Citation: Gabra A, Gabra M (2019) Updates in Management of Hypertensive Disorders of Pregnancy. J Cardiovasc Med Ther Vol.2 No. 1:1.

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Abstract

Hypertensive disorders of pregnancy (HDP) were discovered a long time ago but our knowledge about their etiopathogenesis are still limited. These disorders can affect many pregnant women all over the world putting them, their families and their countries under significant health burden. The main goal of all research efforts regarding treatment of HDP is how to prevent highly morbid complications and mortality of HDP that may affect both mother and fetus. Delivery is the main line of treatment for severe cases but we have to put in our mind risk of prematurity as a possible outcome in case of termination besides the possibility of incidence of complications like eclampsia and hypertensive emergency postnatally. Researchers believed that studies working on prevention would result in major improvement of overall women care worldwide, and screening will definitely allow prompt starting therapy for those patients and prevent further sequences. Recently many guidelines support and recommend Aspirin 81 mg for the prevention of preeclampsia in high-risk patients using evidence-based data about the time and indications of its intake. Great efforts have been contributed to developing evidence-based guidelines to enhance our strategies to deal with these disorders. Reviewing, pooling and comparing these guidelines would help us to refine our questions that may need to be answered by further studies. Trials confirmed that application of standardized strategies for treating HDP significantly improves both maternal and fetal outcomes. In this article, we are going to review recent updates and guidelines about the treatment of HDP and provide references for your further readings.

putting them, their families and their countries under significant health burden. For instance in USA, 240,000 pregnant suffer HDP which equal to 6-12% of all pregnancies and this accounts for 10% of maternal mortality being the second common cause of maternal death after postpartum hemorrhage [2,3]. Moreover, HDP may cause intrauterine fetal death, intrauterine growth restriction and prematurity [4]. Higher prevalence of HDP was found in African Americans, obese, patients with renal disease, chronic hypertensive patients, patients with autoimmune diseases, multiple pregnancy, diabetics and in pregnant women >35 years old or less than twenty [5,6]. Moreover, when we imagine the size of that problem in developing countries, we realize that it is a real disaster affecting families worldwide [7].

Many societies try to classify HDP in spite of presence of an overlap between these classes and subgroups under each category [1]. According to The American College of Obstetricians and Gynecologists (ACOG) and the National High Blood Pressure Education program working group on High blood pressure in pregnancy, HDP is classified into chronic hypertension, gestational hypertension, preeclampsia-eclampsia, and preeclampsia-eclampsia superimposed on chronic hypertension [7]. The main goal of all research efforts in treating HDP is how to prevent highly morbid complications and mortality of HDP that may affect both mother and fetus [8]. Mothers with HDP are at risk of renal and liver failure as part of multisystem nature of the disease that is not understood completely. Besides that, coagulopathies increase her risk of postpartum hemorrhage which is the leading cause of maternal mortality worldwide [9]. Indeed, HDP increase risk of cardiovascular and cerebrovascular event in the lifetime and its mortality through their systematic metabolic and vascular abnormal changes [10]. With the growing concept of the 4th-trimester care, HDP remain a cornerstone in the postnatal care which includes measuring BP and patient's awareness of symptoms of that disease till 4-6 weeks to anticipate any complications that may threaten women health [1].

Because of all those complications, researchers believed that studies working on prevention would result in major improvement of overall women care worldwide, and screening will definitely allow prompt starting therapy for those patients [10,11]. In this article, we are going to review recent updates

Keywords: Hypertension; Pregnancy; Management; Guideline

Introduction

Interestingly, Hypertensive disorders of pregnancy (HDP) were discovered two thousand years ago but our knowledge and data about their nature and pathogenesis are still limited [1]. These disorders can affect many pregnant women all over the world

and guidelines about the treatment of HDP and provide references for your further readings.

Management

Great efforts have been contributed to developing evidence-based guidelines to enhance our strategies to deal with these disorders. Reviewing, pooling and comparing these guidelines would help us to refine our questions that may need to be answered by further studies. Trials confirmed that application of standardized strategy for treating HDP improves so much both maternal and fetal outcome [12,13].

Chronic hypertension

Chronic hypertension affects about 5% of pregnancies and increases the risk of both fetal and maternal morbidity [14]. It is defined as systolic BP of 140 or more or diastolic BP of 90 or more or both on 2 separate occasions at least 4 h apart [15]. This condition is diagnosed at or before 20 gestational weeks or already documented before pregnancy [16], however, ACOG suggest that gestational hypertension or early onset preeclampsia should be considered if 1st trimester BP measures are within normal range [17]. Mostly clinicians attribute this condition to essential hypertension but they should consider secondary causes in case of young aged onset and refractoriness to therapy [14].

Regarding management, chronic hypertension should be managed because of its lifelong end-organ damaging effects but pregnancy is a short time event and data suggest fetal risk with excessive low BP and placental hypo perfusion so pharmacological treatment is recommended when BP equal or is greater than 150/100 mmHg [15,18]. But other researchers recommend the goal of below 140/90 when patient has multiple risk factors that increase risk of maternal mortality and morbidity [14].

Complete metabolic panel should be done, and patient should be counseled about daily BP monitoring with log and how to use automated devices, we can use video materials like the educational video of American Medical Association (AMA) and American Heart Association (AHA). She should be also counseled in both antepartum and postpartum care visits about symptoms of severe preeclampsia and imminent eclampsia [14]. Moderate exercise is encouraged but weight loss and extreme low salt diet are not recommended [18]. First lines drugs are alpha-methyldopa, nifedipine and labetalol and drugs affecting the renin-angiotensin system should be avoided because of their well know teratogenic effect [18]. Diuretics are also not recommended because it aggravates hem concentration of preeclampsia which may predispose to clots [19].

According to ACOG, Fetal wellbeing should be assessed by ultrasound and umbilical artery Doppler should be done to assess placental perfusion in case of abnormal US findings like IUGR and oligohydramnios [18]. NICE recommends fetal assessment by US and umbilical artery Doppler at 28-30 weeks and at 32-34 weeks. If results are normal, clinicians should not repeat them unless clinically indicated [19].

In uncomplicated patients of chronic hypertension, delivery is not recommended before 38 weeks but progression of the disease to preeclampsia and eclampsia affect decision making regarding time of delivery [18].

Gestational hypertension and preeclampsia without severe features

Gestational hypertension is defined as elevated BP above 140/90 mmHg after 20 weeks at two separate occasions 6 h apart in absence of features of severe preeclampsia [20]. Severe gestational hypertension is defined by sustained elevated BP at more than or equal 160/110 mmHg [21]. It is the most common cause of high BP in pregnancy [1,21]. Some authors recommend the term "pregnancy-induced hypertension" to describe this condition that may include preeclampsia as well [2]. This condition should be distinguished from chronic hypertension and transient gestational hypertension [21]. The return of BP to normal after 42 days postpartum means that it is gestational hypertension; this indicates the importance of postpartum care for those patients and the relative accuracy of diagnosis till that time [5]. Presence of proteinuria indicates its progression to preeclampsia [18]. Those cases may develop severe preeclampsia or eclampsia with progression of pregnancy especially with elevated uric acid and with onset at less than 34 weeks [22]. Some cases with mild disease and its onset at or beyond 37 weeks have a similar outcome to normotensive cases [21].

Gestational hypertension and preeclampsia without severe features are managed by the same strategy, control of hypertension and expectant management are the main concepts in this strategy [15]. Prenatal care should include BP measurement and proteinuria once weekly at office besides assessment of platelet count and liver enzymes are suggested weekly in order to detect progression to severe preeclampsia [18,21]. As well, patients should be counseled about symptoms of severe preeclampsia and seeking ER as rapid as they can [21]. Bed rest is no longer recommended especially with raising concerns of thromboembolism [18,21]. Because of risk of fetoplacental insufficiency, fetal monitoring should be done twice weekly in case of preeclampsia or once weekly in case of gestational hypertension by US (include Amniotic Fluid Index) and Non Stress Test besides daily count of fetal movements [18,23]. Fetal monitoring in form of Non Stress Test and Biophysical Profile should be done till 34 weeks and it should not be repeated after except if clinically indicated [19,21]. Pharmacological therapies are reserved to patients with BP more than 160/110 and the same drugs as chronic hypertension with well documented fetal safety [7,18]. This concept is applied till 37-39 weeks or more in presence adequate resources in a nearby maternal-fetal unit [17,19,22]. Magnesium sulfate is not recommended for seizure prophylaxis because of its low incidence in gestational hypertension [1]. In presence of rupture of membranes, abnormal fetal monitoring or ultra-sonographic findings of fetal growth restriction confirmed by Doppler, delivery is indicated at 34 weeks [15,18,19]. But in presence of any maternal or fetal instability, delivery is recommended as soon as possible after stabilization of general condition [18].

Preeclampsia with severe features/eclampsia

SOMANZ defines preeclampsia with severe features as a unique condition of pregnancy with multisystem effects involving liver, kidney and other hematological parameters [16]. ACOG criteria for diagnosis include new onset hypertension after 20 weeks associated with new onset proteinuria (>300 mg/24 h urine collection) [18]. In absence of proteinuria can be made upon presence of gestational hypertension plus any of the following: low platelet count less than 100,000/cc, creatinine level more than 1.1 (double the baseline creatinine level in absence of other renal problem), raised liver enzymes (double baseline), pulmonary edema, visual or cerebral symptoms [17]. ACOG recommends that decision of delivery should be made based neither on the severity of proteinuria nor on the change in the amount of proteinuria [17]. As a result of our limited knowledge about etiopathogenesis of preeclampsia, we should expand our management to involve preconception care of high-risk women or patients with positive personal history until 4th-trimester care postnatally [24].

The rationale of management of those patients focused on risk-benefit balance of termination of pregnancy to avoid maternal or fetal complications or cautious expectant management to avoid neonatal risks of prematurity [25]. The decision should be made based on severity of the disease and gestational age because initial presentation is not a reliable tool to predict the course of progression of the disease [10]. When expectant management is considered till 34 weeks, ACOG recommends steroid administration to enhance fetal lung maturity and close monitoring for signs and symptoms of severity on both mother and fetus should be considered [17]. Reviewers of Cochrane trials conclude that there is a lack of sufficient evidence in order to make a clinical guidance for bed rest and it should not be routinely recommended [26]. Most guidelines agree that termination should be done at or beyond 37 weeks, it could be also done at or beyond 34 weeks in presence of IUGR, oligohydramnios, rupture of membranes, progressive labor and biophysical profile of 6/10 or less [16,17,22,25]. But in presence of any fetal or maternal instability, delivery is indicated regardless of gestational age because delivery has a very beneficial effect on preventing serious maternal complications [18,26]. As control of BP alone does not prevent seizures, Magnesium sulfate is a cornerstone in the prevention of eclampsia [25]. It should be administered prenatally, at labor and at least 24 h postnatally [10]. Researchers suggest that it may contribute to slowing neuromuscular conduction and increase seizure threshold [26]. Special protocols are used for patients with renal insufficiency in addition to regular monitoring of serum Mg level and watchful observation of signs of Mg toxicity [10]. Pharmacological treatment of cases with BP above 160/100 has been shown to decrease the incidence of a cerebral vascular incident on those patients [10]. NICE guidelines support labetalol as combined alpha and beta blocker as the first line of treatment [19]. ACOG and SOGC recommend labetalol, hydralazine, and nifedipine as first-line agents [27]. ACOG recommends that mode of delivery should be individualized based on fetal presentation, gestational age, cervical status, and maternal-fetal stability and it does not need to be generalized as cesarean section [17]. Combined

oxytocin and ergometrine use should be avoided in managing the third stage of labor as ergots cause more elevation of BP in those patients [26].

Emergency Therapy

Acute onset of severe hypertension is defined as BP higher than 170/110 and it is considered persistent if remains the same 5-15 min later [28]. It is associated with a higher incidence of cerebrovascular stroke and eclampsia in preeclamptic patients so proper antihypertensive should be administered within 15-30 min of confirmed severe hypertension [13]. This condition requires urgent antihypertensive medications and close observation of both mother and her fetus [13]. ACOG and the National heart, lung and blood institute recommend that immediate release oral Nifedipine, intravenous labetalol, and hydralazine are the first lines of treatment for hypertensive emergency either during pregnancy or postnatally [13,29]. In a randomized double-blinded clinical trial of both oral nifedipine and IV labetalol, both found to be effective in this condition but oral nifedipine was found to be rapidly effective, has a longer duration of action and associated with improved urine output and less side effect [30-32]. Dropping of BP with Oral nifedipine is associated with no change in fetal heart rate nor in fetal and uteroplacental Doppler indices, although it is associated with a drop of mean blood pressure and systemic vascular resistance in addition to enhancement of cardiac index which is an accurate parameter of cardiac output [33-35]. Co-administration of nifedipine and magnesium sulfate do not increase incidence of toxicity and side effects of Mg sulfate [36]. Limited evidence suggests the effectiveness of nicardipine in this condition with safe maternal and fetal profile [37,38]. In refractory case, clinicians should seek consultation of fetomaternal or intensive care subspecialists for lines to control this condition [13].

Role of Preventive Medicine

Strong evidence of the role of low dose aspirin (<81 mg) causes many societies concerned about women health to admit its benefits in preeclampsia prevention in high risk pregnant women. ACOG, USPSTF, WHO, NICE and AAFP recommend its intake after 1st trimester at 12-16 weeks [4]. USPSTF recommends it in presence of one or more of high-risk factors like history of preeclampsia, multiple gestation, kidney disease, autoimmune disease like antiphospholipid syndrome, type 1 or type 2 diabetes, and chronic hypertension or more than one of several moderate-risk factors like prim gravidity, maternal age of 35 years or older, a body mass index greater than 30, family history of preeclampsia, sociodemographic characteristics, and personal history factors [6]. In absence of high-risk factors for preeclampsia, current evidence-based data does not support its use for the prevention of preeclampsia, IUGR, IUFD, or prematurity [6].

Evidence-based guidelines support Calcium supplements as a preventive tool against preeclampsia in societies with low calcium intake [17]. High dose Methylprednisolone was not found to be effective to prevent drop of platelets count in preeclamptic patient with count 150,000 unit/cc or keep it

above 100.000 unit/cc [39]. 5-day postpartum course of Toremide was not found to be effective in prevention of persistent postpartum preeclampsia [40]. Effective prenatal care and frequent antenatal visits are associated with improved outcomes of HDP regarding both maternal and fetal health [41]. USPSTF recommends screening for preeclampsia by frequent measurement of blood pressure through antenatal care [42]. ACOG recommends BP measure and detailed medical history to evaluate risk factors [17]. NICE and SOGC still recommend urinalysis for proteinuria in addition to BP measurement [42,43].

Conclusion

Hypertensive disorders of pregnancy (HDP) were diseases of a long time ago but our knowledge about their etiopathogenesis are still in need of more researches. These disorders can affect many pregnant women all over the world putting them, their families and their countries under significant health burden. The main goal of research efforts is how to prevent highly morbid complications and mortality of HDP that may affect both mother and fetus. Delivery remains the main line of treatment for severe cases indicating the role of fetoplacental unit in the disease, but we have to consider the risk of prematurity as a possible outcome in case of termination besides the possibility of incidence of complications like eclampsia and hypertensive emergency postnatally. Researchers believed that studies working on prevention would result in impressive improvement of overall women care worldwide, and screening will definitely allow prompt starting of treatment for those patients and prevent further sequences. Recently many guidelines support and recommend Aspirin 81 mg for the prevention of preeclampsia in high-risk patients using evidence-based data about the time and indications of its intake. Great efforts have been contributed to developing evidence-based guidelines to enhance our strategies to deal with these disorders. Reviewing, pooling and comparing these guidelines would help us to refine our questions that may need to be answered by further studies. Trials confirmed that application of standardized strategies improves both maternal and fetal outcomes.

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