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SPECIAL ARTICLE

Challenges associated with hypertensive disease during pregnancy in low-income countries

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ABSTRACT

Objective: To assess the challenges associated with the diagnosis, management, and prevention of hypertensive disease during pregnancy in low-income countries, following the success of the Magpie Trial. *Methods:* Descriptive review of the literature from 1990 to 2009 on the diagnosis, management, and prevention of hypertensive disease in pregnancy. *Results:* In the absence of credible measures to predict and prevent hypertension in pregnancy, diagnosis and treatment remain the only viable options, although they are still associated with important challenges in low-income countries. Despite the presence of high-quality evidence that magnesium sulfate is safe and effective at preventing and treating eclampsia, its use is extremely limited in many low-income countries. *Conclusion:* There is a need for cheap and reliable tools with which to address the diagnostic, preventive, and management challenges associated with hypertensive disease during pregnancy in low-income countries. It is recommended that such countries incorporate magnesium sulfate protocols into their national health and/or practice policies.

1. Introduction

Hypertensive disease in pregnancy comprises a spectrum of conditions associated with adverse fetomaternal outcome [1,2] (Fig. 1). The number of maternal deaths from hypertensive disease during pregnancy has decreased in high-income countries, but it remains high in low-resource areas—second only to the number of deaths due to hemorrhage [3–7].

The present study assessed some of the main challenges regarding the diagnosis, management, and prevention of hypertensive disease in pregnancy.

2. Diagnosis of hypertensive disease in pregnancy

Blood pressure measurement and urinalysis are the mainstay of the diagnosis and monitoring of hypertensive disease during pregnancy; therefore, appropriate and reliable tools are essential. Where resources are available, biochemical and hematologic indices are used for further diagnosis and assessment. The mercury sphygmomanometer is used extensively in low-income countries for the measurement of blood pressure; although it can be cumbersome to handle—especially because mercury spillage and breaking of the glass column are common—it is more accurate than the aneroid type [8], which may produce errors in readings unless regularly calibrated. Automated devices remove inter- and intra-observer errors—and facilitate measurement and even self-measurement [7]—but they are expensive and require regular battery replacement. Because automated devices are becoming more popular than mercury devices, owing to mercury being bio-accumulable and toxic to the environment, the costs of procurement and maintenance have to be noted because the sphygmomanometer remains the main diagnostic tool for hypertensive disease. Low-income countries need instruments that give accurate results and which are easy to use, robust, and cheap.

The association between significant proteinuria and hypertension after 20 weeks of pregnancy is the main clinical criterion for diagnosing pre-eclampsia. Reagent strips are widely used to estimate proteinuria because accurate quantification via 24-hour urine collection is expensive and occurs only in well-equipped hospitals. Effective urinalysis technology that provides quantitative values of albumin and detects significant proteinuria at a high sensitivity and a specificity of 94% [9] is an essential tool in low-income countries for obviating the need for 24-hour urine collection.

Five of 6 observational studies in low-resource settings reported a positive association between chronic hypertension and pre-eclampsia [10]. In low-income countries, the contribution of chronic hypertension to hypertensive disease during pregnancy remains speculative because pre-pregnant blood pressure is not widely available. The burden of hypertensive disease in pregnancy remains mainly among women who are nulliparous, younger than 35 years of age, non-hypertensive, without renal or connective tissue disease, and who develop high blood pressure and proteinuria after 20 weeks—both of which worsen as the pregnancy advances.

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Gestational hypertension

- Hypertension detected for the first time after 20 weeks of pregnancy; no proteinuria
- Hypertension defined as systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg
- Blood pressure resolves within 3 months post partum

Pre-eclampsia and eclampsia

- Hypertension and proteinuria detected for the first time after 20 weeks of pregnancy
- Proteinuria defined as ≥1+ on urine dipstick, ≥300 mg/d, or ≥30 mg/dL
- Eclampsia defined as the occurrence of seizures in pre-eclampsia

Chronic hypertension

- Hypertension present before the onset of pregnancy or noticed before 20 weeks of pregnancy
- Called "essential hypertension" if there is no underlying cause; called "secondary hypertension" if there is an underlying cause

Pre-eclampsia superimposed on chronic hypertension

- Emergence of new features of pre-eclampsia, in addition to existing chronic hypertension, after 20 weeks

Fig. 1. Classification of hypertensive disease in pregnancy.

3. Screening

Although eclampsia can be prevented by terminating a pre-eclamptic pregnancy, the primary prevention of this condition is difficult. The several clinical, biochemical, and biophysical tests for identifying women who may develop pre-eclampsia in any pregnancy have been largely unsuccessful. The 2004 WHO systematic review of screening tests for pre-eclampsia concluded that there was no clinically useful test to predict the development of this condition [11]. The main challenge is that, even if the screening tests receiving further evaluation in prospective longitudinal studies proved to have a high predictive value, their unsuitability for large-scale use and the expensive or resource-intensive technology involved in their application would exclude their use in most low-income countries.

4. Management of hypertensive disease in pregnancy

The 3 main principles of the management of hypertensive disease in pregnancy are: management of hypertension; management and prevention of complications, including seizures; and safe delivery, with good outcome for mother and infant.

4.1. Management of hypertension

There is a lack of credible large randomized trials investigating antihypertensives for the treatment of hypertensive disease during pregnancy in low-resource countries, with existing information coming mainly from observational studies [12]. The majority of randomized trials and meta-analyses on this subject from high-resource countries have involved the treatment of pregnant women with chronic hypertension. Although chronic hypertensive patients who received antihypertensive treatment showed less progression to severe hypertension and needed fewer additional antihypertensives, it has not been shown conclusively whether treatment improves other outcomes such as perinatal death, abruption, or fetal growth restriction [13]. Antihypertensives should be used in pregnancy only if they do not reduce uterine blood flow or adversely affect fetal growth [14]. Methyldopa—a centrally acting antihypertensive—is widely used for the long-term control of hypertension in pregnancy because there is no evidence of major fetal adverse effects; it is unclear whether the 1–10/100 000 risk of developing hepatitis with this medication is modified by pregnancy [13]. It will, therefore, continue to be useful in low-income countries.

The calcium-channel blocker nifedipine, which can be used on its own or in combination with methyldopa, is also widely used in low-resource countries for both short- and long-term control of hypertension in pregnancy. Sublingual nifedipine has been used to treat severe pre-eclampsia and eclampsia, with its rapid onset of action enabling a fast reduction in blood pressure [12]. There is no evidence of major adverse fetomaternal events with this medication; however, it can cause severe headache, which may mimic worsening disease, although the addition of methyldopa tends to ameliorate this effect.

The potent vasodilator hydralazine rapidly lowers blood pressure and can be used intravenously in the initial treatment of severe hypertension during pregnancy. Labetalol—an α- and β-blocker with a good safety record [13,15]—can be administered both orally and intravenously; it is not widely used in low-resource countries, but is becoming more prevalent in the USA.

Atenolol is associated with fetal growth restriction [13,14], and ketanserin—which is a selective serotonin receptor blocker with α-blocking activity—is not popular in low-income countries, despite being described as beneficial [13]. Angiotensin-converting enzyme inhibitors are not recommended because they are associated with unacceptable fetal adverse effects [13,15].

4.2. Management and prevention of complications, including seizures

Hypertensive diseases of pregnancy are characterized by multisystem involvement, with complications commonly occurring in the renal, hepatic, cardiovascular, hematologic, and central nervous systems. Prevention or management of organ-specific complications requires early detection and prompt multidisciplinary treatment, together with obstetric intervention, and must balance maternal and fetal risks such