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Review Article

Current Prescribing Pattern of Antihypertensive Drugs in Preeclampsia

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ABSTRACT

Introduction: Preeclampsia is a medical disorder encountered during pregnancy. It is a multisystem disorder characterized by new onset of hypertension presenting after 20 weeks of gestation with clinically relevant proteinuria. Failure to control blood pressure can affect both mother and fetus health.

Methods: The present study was evaluated and collected the data from Pubmed and Google Scholar databases since 2010 to 2014 and summarized current pattern of antihypertensive drugs used in preeclampsia.

Results: Among the antihypertensive drugs most commonly preferred drugs in mild to moderate hypertension by clinicians are alpha methyldopa, labetalol and nifedipine.

Conclusion: The pattern of antihypertensive drugs for treatment of preeclampsia remain same for many years due to limited clinical trials of alternative drugs.

KEY WORDS: Preeclampsia, Antihypertensive, Pregnancy, Prescribing pattern.

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INTRODUCTION

Hypertension in pregnancy remains a significant public health problem [1], which complicate 6–8% of pregnancies and cause significant maternal and fetal morbidity and mortality [2]. This rate will probably rise in the years to come due to the notable tendency among women to delay the decision to become pregnant, occurrence of arterial hypertension increase with age, as well as due to the growing problem of obesity resulting from inappropriate dietary habits and lack of regular everyday physical activity [3]. Pre-eclampsia is more common among women likely to have a large placenta (such as those with multiple pregnancy) and among women with medical conditions associaed with microvascular disease (such as diabetes, hypertension, and collagen vascular disease) and may result from deficient placental implantation during the first-half of pregnancy [4]. Preeclampsia was formerly defined as a multisystem disorder characterized by new onset of hypertension i.e. systolic blood pressure (SBP) $\geq$ 140 mmHg and/or diastolic blood pressure (DBP) $\geq$ 90 mmHg) and proteinuria (> 300 mg/24 h) arising after 20 weeks of gestation in a previously normotensive woman. Recently, the American College of Obstetricians and Gynecologists has stated that proteinuria is no longer required for the diagnosis of preeclampsia [5].

Gestational hypertension is a new hypertension presenting after 20 weeks gestation without clinically relevant proteinuria. Severe pre-eclampsia is the pre-eclampsia with severe hypertension or with symptoms, biochemical abnormalities, or hematological impairment (or any combination thereof). Chronic hypertension is a hypertension that present at booking visit or before 20 weeks gestation, or being treated at time of referral to maternity services; can be primary or secondary in etiology [6].

Few antihypertensive drugs are used for the treatment of preeclampsia to control blood pressure, as there is little to guide the choice of agent. The reason behind this is less amount of scientific research during pregnancy. Based on the above findings, the present study was to determine prevalence of antihypertensive drugs used in preeclampsia.

METHODOLOGY

For the present study, the information and data were collected from Pubmed and Google scholar databases, which has been published in English since 2010 to 2014 and identified the drugs used for preeclampsia.

RESULTS

Optimal timing and choice of therapy for antihypertensive drugs during preeclampsia is very important to improve maternal and fetal morbidity and mortality. The choice of which agent to use should be based on the clinician's experience with a particular agent, its cost, and its availability. There are many antihypertensive drugs but majority articles suggests centrally acting sympathoplegic, calcium channel blocker and β -adrenoceptor blocker. Angiotensin converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB) and direct renin inhibitors are contraindicated, β-adrenoceptor blocker (especially atenolol) is associated with fetal growth restriction, hydrochlorothiazide can cause volume contraction and electrolyte disorder [7]. We have studied all the available articles published on Pubmed database since 2010 to 2014. Almost all studies suggested about alpha methyldopa (centrally acting sympathoplegic), nifedipine (calcium channel blocker) and labetalol (α- adrenoceptor blocker). There is ongoing debate about whether antihypertensive therapy impairs intra-uterine fetal growth, and if so, whether this effect is restricted to β-adrenoceptor blocker therapy [8].

Table 1: Summary of recommended antihypertensive drugs for the treatment of preeclampsia.

Studies	Centrally acting sympathoplegic	Calcium Channel blocker	β-adrenoceptor blocker	Combinations/Others
Abalos E et al.,2014 [9]	Alpha Methyldopa			Combination of Calcium channel blocker and β-adrenoceptor blocker
Firoz T et al., 2014 [12]	Alpha Methyldopa	Nifedipine	Labetalol	Hydralazine
Kumar S et al., 2014 [10]	Alpha Methyldopa	Nifedipine, Amlodipine	Labetalol, Atenolol	
Arulkumaran N, Lightstone L, 2013 [20]	Alpha Methyldopa	Nifedipine	Labetalol	
Kattah AG, Garovic VD, 2013 [2]	Alpha Methyldopa	Nifedipine	Labetalol	Thiazide, Hydralazine
Lalani S, Firoz T, Magee LA et al., 2013 [11]	Alpha Methyldopa	Nifedipine	Propranolol, Atenolol	
Xie RH, Guo Y, Krewski D et al.,2013 [21]	Alpha Methyldopa		Labetalol	
Carles G, Helou J, Dallah F et al., 2012 [14]				Urapidil
Liu QQ, Yu YH, Gong SP, et al., 2012 [22]		Nifedipine		
Szczepaniak-Chicheł L, Tykarski A, 2012 [3]	Alpha Methyldopa	Nifedipine, Verapamil	Labetalol, Metoprolol	
Vest AR, Cho LS, 2012 [13]	Alpha Methyldopa	Nifedipine	Labetalol	Hydralazine
Brown CM, Garovic VD, 2011 [7]	Alpha Methyldopa	Nifedipine	Labetalol	Oxprenolol, Clonidine, Hydralazine
Magee LA, Abalos E, von Dadelszen P et al., 2011 [8]	Alpha Methyldopa	Nifedipine	Labetalol	Hydralazine
Podymow T, August P, 2011 [23]	Alpha Methyldopa	Nifedipine	Labetalol	
Solomon CG, Seely EW, 2011 [24]	Alpha Methyldopa		Labetalol	
Buch J, 2010 [15]				Urapidil
Fabry IG, Richart T, Chengz X et al., 2010 [25]	Alpha Methyldopa	Nifedipine		

Abalos E et al.,2014 [9] suggested combination of calcium channel blocker and β-adrenoceptor blocker along with alpha methyldopa. Among calcium channel blocker all studies suggested nifedipine, Kumar S et al., 2014 [10] suggested nifedipine and amlodipine and Szczepaniak-Chiche L, Tykarski A, 2012 [3] suggested nifedipine and verapamil. Regarding β-adrenoceptor blocker all studies suggested labetalol, Kumar S et al., 2014 [10] suggested labetalol and atenolol, Lalani S, Firoz T, Magee LA et al., 2013 [11] suggested propranolol and atenolol and Szczepaniak-Chiche L, Tykarski A, 2012 [3] suggested labetalol and metoprolol. Other than these, hydralazine (vasodilator) is suggested by Firoz T et al., 2014 [12], Kattah AG, Garovic VD, 2013 [2], Vest AR, Cho LS, 2012 [13], Brown CM, Garovic VD, 2011 [7] & Magee LA, Abalos E, von Dadelszen P et al., 2011 [8], urapidil (α-adrenoceptor antagonist) is suggested by Carles G, Helou J, 2012 [14] & Buch J, 2010 [15]. Table 1 summarizes the recommended antihypertensive drugs for the treatment of preeclampsia that are most widely accepted and practiced.

DISCUSSION

Pre-eclampsia is a major cause of maternal mortality and morbidity, preterm birth, perinatal death, and intrauterine growth restriction. Unfortunately, the pathophysiology of this multisystem disorder, characterized by abnormal vascular response to placentation, is still unclear [16]

Antihypertensive medications used to control hypertension in early pregnancy can alter placental and circulating cytokines. The interaction between trophoblasts and maternal endothelium is important for placental vascular modeling. Methyldopa, labetalol, hydralazine, and clonidine increased trophoblast integration into TNF-α-preincubated endothelial cellular networks. Methyldopa increases vascular endothelial growth factor (VEGF) and decreases placental growth factor [17]. There is also a reduction in the overall risk of developing proteinuria/pre-eclampsia when beta blockers and calcium channel blockers considered together are compared with methyldopa [9].

Up regulation of inducible nitric oxide synthase (iNOS) has been reported in both experimental and clinical hypertension. Inducible nitric oxide synthase inhibitors (iNOS) could be clinically useful in the therapy of preeclampsia, especially in particular groups of patients genetically more prone to express higher levels of iNOS [18]. Aminopeptidase A (APA) acts as an antihypertensive agent in the pregnant spontaneously hypertensive rat by degrading vasoactive peptides and as a result returns the animal to a normotensive state [19].

It is important to note that mild to moderate hypertension requires therapy in pregnancy, although somewhat different among various groups and professional societies. One important reason behind this difference is that, there are few well-designed clinical trials establishing the benefit of treating mild to moderate hypertension during pregnancy. The antihypertensive choice for preeclampsia has been limited to those that have relatively less adverse effects and have a long history of clinical use by obstetricians and gynecologists.

CONCLUSION

Current antihypertensive recommendations for the treatment of preeclampsia remained same for many years. It is due to lack of studies in a critical period of life which can affect both mother and fetus health. Further studies are required for effective control blood pressure during pregnancy.

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