European Journal of Molecular & Clinical Medicine
ISSN 2515-8260 Volume 07, Issue 07, 2020

Management of Hypertension during Pregnancy

Navneet Duggal

School of Pharmaceutical Sciences, Lovely Professional University, Jalandhar-Delhi G.T. Road, Phagwara (Punjab) 144411, INDIA.

Email: navneet.duggal@lpu.co.in

ABSTRACT: There are 5 to 10 percent females who develop hypertension during pregnancy which can adversely affect both mother and the fetus. The objective of treating the mother is that to prevent both cardiovascular and cerebrovascular complications in mother associated with high blood pressure without adversely affecting the health of the fetus. Depending upon the condition of the patient both pharmacological and non-pharmacological interventions play an important role in managing hypertension during pregnancy. The treatment of hypertension during pregnancy should be individualized depending upon the condition of the patient. While instituting pharmacological therapy due consideration should be given to the benefit to risk ratio. This present review focus on management of hypertension during pregnancy.

1. INTRODUCTION

Hypertension related problems are one of the most common complications during pregnancy. These problems affect around 5 to 10 percent of the total women who got pregnant[1]. These disorders can lead to maternal, fetal, and neonatal morbidity and mortality such as gestational hypertension, chronic hypertension, pre-eclampsia and chronic hypertension associated with pre-eclampsia[2]. Present data is not sufficient to justify the target blood pressure to be achieved in pregnant women and also there is lack of data regarding efficacy of the treatment of pregnancy related hypertensive disorders[3]. The treatment of blood pressure in pregnancy depends upon the gestational age, raised level of blood pressure and appearance of other mother or fetus risk factors. As per the current international guidelines, the safety profile of all the drugs recommended to treat hypertension during pregnancy is questionable[4,5], therefore risk benefit analysis is one of the essential key parameter before starting drug therapy. Another option that can also be useful while managing hypertension during pregnancy is non-pharmacological treatment. There are randomized controlled clinical trials that has proved their efficacy as well as safety[6]. Therefore non-pharmacological treatment can also play a key role in management of the patients depending upon the condition of the patient[7].Therefore the present review is going to pay attention to both the pharmacological and non-pharmacological treatment while management of the patients suffering from hypertension during pregnancy.

NON-PHARMACOLOGICAL THERAPEUTIC APPROACH

There is no current evidence to support that performing physical activity before pregnancy can prevent the risk of hypertension during pregnancy[8]. The females who are overweight or obese are at greater risk of developing hypertension during pregnancy as compared to females with normal weight before getting pregnant[9,10]. The pregnant mothers with normal

weight (BMI 18.5–24.9) before getting pregnant can gain weight 25–35 lbs whereas the females who are overweight before pregnancy (body-mass index (BMI) 25–29.9) can gain only 15–25 lbs weight. The pregnant females who fall under obese category with a BMI > 30, according to new guidelines must should gain only 11–20 lbs of weight[11].
Reduction in plasma level is common in preeclampsia, decrease in amount of salt in diet is not usually recommended. Bed rest is very important during pregnancy. The advantages of bed rest during pregnancy are: lower blood pressure, leads to diuresis, and decrease the chances of premature labor[12,13].

ROLE OF NUTRACEUTICALS

The health of the fetus is directly affected by the blood pressure level of the mother[14,15]. Control of the body weight also plays an important role while management of hyper tension during pregnancy. Body weight can be controlled through control on diet and adequate physical activity. Mild cases of hypertension in pregnancy should be managed if possible without pharmacological treatment because of adverse effects of the drugs on the health of the fetus. Therefore most of the cases the drug treatment should be prescribed only for patients that cannot be managed without non-pharmacological treatment[4–6]. Nutraceuticals can also be an option for management of hypertension during pregnancy but again due care is required while using nutraceuticals as they can also adversely affect the health of the fetus[16]. Nutraceuticals can be used for both prevention as well as treatment of hypertensive disorders during pregnancy. Nutraceuticals that are used for this purpose and supported by the evidence are vitamin D, calcium, resveratrol and sodium/potassium. These compounds have also additional benefit because of their ability to control blood glucose level[17]. Among all lack of sodium in diet along with vitamin D supplements is most crucial in management of hypertension during pregnancy. Calcium should only be prescribed to mothers in which deficiency of calcium is established. The safety profile of nutraceuticals like vitamin D and resveratrol is well established and they can be used alongwith traditional antihypertensive drugs to control blood pressure in pregnancy and to prevent relapse in pre-eclampsia. Other nutraceuticals that can also be used in prevention of hypertension include folic acid, zinc and melatonin. The above described nutraceuticals are able to well control blood pressure in general population but their safety profile in pregnancy still to be established. Therefore these agents should be used in pregnancy by properly assessing the risk benefit ratio[18].

MEDICATIONS

α-adrenergic agonists

The most important drug of this class and the most widely used to control blood pressure is methyldopa. No physical or mental health problems were found in children born to mothers who were prescribed methyldopa during pregnancy. The safety profile of methyldopa makes it the first choice drug for management of hypertension during pregnancy. Methyldopa is drug that acts on central nervous system and it decrease the sympathetic outflow which is responsible for control of blood pressure. The problems associated with use of methyldopa are sedation and disturbance in sleep. Other side effect encountered with the use of methyldopa is mild elevation of liver enzymes. As discussed methyldopa is a relatively safe drug but it is not a potent drug to control blood pressure. Thereforeit can be combined with other blood pressure lowering medications to control blood pressure[19].
Clonidine another drug belongs to the same class with same mechanism of action but is more potent drug to control blood pressure as compared to methyldopa. Clonidine can adversely affect the growth of fetus if after starting the therapy, there is decline in heart rate of

mother. Clonidine also leads to rebound hypertension, therefore lesser safety profile as compared to methyldopa. Therefore clonidine should only be prescribed to the mothers who are not able to tolerate methyldopa[20].

Beta-blockers

Beta-blockers are another category of drugs which are having good safety profile during pregnancy and are very well tolerated. The most appropriate drug of the class is Labetalol. Labetalol is blocker of beta receptors as well as alpha-1 receptors. The side effects of Labetalol include lethargy, decreased exercise tolerance and bronchospasm. The safety profile of Labetalol is similar with methyldopa and both the drugs did not negatively affect both the maternal and fetus health. The formulations available in market are both intravenous and oral forms. Therefore it can be used for management of both inpatients as well as outpatients[21].

It has been observed in clinical studies that Atenolol does not have much effects on systolic BP and is also responsible for intrauterine growth retardation. As there are more effective medicines available to control blood pressure in pregnancy, therefore both Labetalol and atenolol should be avoided during pregnancy[22].

Calcium channel blockers

Calcium channel blockers as the name suggests block the entry of calcium ions into vascular smooth muscles and therefore cause arterial vasodilation. The most impotant drugs of this class are oral nifedipine and verapamil. These are the second class drugs for treatment of hypertension during pregnancy. They do not cause the fetal health issues[23]. The primary action of nifedipine is on blood vessels whereas verapamil is the drug that acts on heart calcium channels. The side effects of calcium channel blockers in mother are increase in heart rate, palpitations, headaches, facial flushing and peripheral edema. Nifedipine and verapamil are usually safe when prescribed to lactating mothers[24].

Direct vasodilators

Hydralazine is the drug reserved for severe hypertension in pregnancy and is administered through intravenous route. It can also be prescribed to lactating mothers. Hydralazine is the dug that selectively relaxes smooth muscles of arteries. Adverse effects associated with hydralazine are nausea, headache, palpitations and flushing. No abnormalities in fetus were found on administration of hydralazine in pregnancy. There are cases thrombocytopenia in new born on long term use of hydralazine and also very few reports of pyridoxine-responsive polyneuropathy[25].

Intravenous hydralazine is the option which is reserved only for patients suffering from severe hypertension. There are certain reports establishing that intravenous labetalol or oral nifedipine may be preferred in severe hypertension. Sodium nitroprusside is administerd only for pregnant females with life-threatening severe hypertension. The side effects associated with sodium nitroprusside include thiocyanate and cyanide toxicity and also there is risk of cardio-neurogenic syncope[26].

Diuretics

The is always a challenge to use of diuretics to manage hypertension during pregnancy as diuretics cause reduction in plasma volume. There was a clinical study that demonstrates that there was reduction in plasma volume on diuretic therapy during pregnancy but it has not resulted into and adverse effects on pregnancy[27,28]. If the mother is already on maintenance therapy on diuretics before pregnancy, it should be continued until there are signs of proteinuria. If there are signs of proteinuria, the diuretic therapy should be stopped otherwise this may worsen condition of hypertension. Diuretics may interfere with milk production in lactating mothers. Spironolactone should not be used as it has the potential to cause fetal antiandrogen effects [29].

Renin-Angiotensin-Aldosterone System Blockade

The two categories of drugs that work by this mechanism are angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs). Both categories of drugs are contraindicated in pregnancy because of the concerns regarding their use to control blood pressure during pregnancy [30]. There is an evidence that eplerenone was able to control blood pressure control in a mother during pregnancy who was suffering from primary hyperaldosteronism[31].

SUMMARY

Hypertension is one of the problems that adversely affect both the mother as well as fetal health during pregnancy. Therefore it is important to control blood pressure during pregnancy. Non-pharmacological treatment as well as nutraceuticals can also play an important role while management of hypertension during pregnancy. For management of severe hypertension during pregnancy, the first line agents are intravenous hydralazine, intravenous labetalol and immediate release nifedipine. For cases of non-severe hypertension the drugs of choice are oral labetalol, oral extended release nifedipine, and methyldopa. Beta-blockers and diuretics can also be used to control blood pressure during pregnancy considering their benefit to risk ratio, while ACE inhibitors and ARBs are contraindicated during pregnancy.

REFERENCES

[1] J. Villar, G. Carroli, D. Wojdyla, E. Abalos et al., "Preeclampsia, gestational hypertension and intrauterine growth restriction, related or independent conditions?" Am. J. Obstet. Gynecol., 94, 921–931, 2006.

[2] J. A. Hutcheon, S. Lisonkova and K. S. Joseph, "Epidemiology of pre-eclampsia and the other hypertensive disorders of pregnancy" Best Pract. Res. Clin. Obstet. Gynaecol., 25, 391–403, 2011.

[3] N. LeFevre and E. Krumm, "Antihypertensive Drug Therapy for Mild to Moderate Hypertension During Pregnancy" Am. Fam. Physician, 100, 403–405, 2019.

[4] V. Regitz-Zagrosek, J. W. Roos-Hesselink, J. Bauersachs, C. Blomström-Lundqvist et al., "2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy" Eur. Heart J., 239, 3165–3241, 2018.

[5] "ACOG. Practice Bulletin No. 202: Gestational Hypertension and Preeclampsia" Obstet. Gynecol., 133, e1–e25, 2019.

[6] L. C. Poon, A. Shennan, J. A. Hyett, A. Kapur et al., "The International Federation of Gynecology and Obstetrics (FIGO) initiative on pre-eclampsia: A pragmatic guide for first-trimester screening and prevention" Int. J. Gynaecol. Obstet., 145 (Suppl. S1), 1–33, 2019.

[7] J. Ding, Y. Kang, Y. Fan and Q. Chen, "Efficacy of resveratrol to supplement oral nifedipine treatment in pregnancy-induced preeclampsia" Endocr. Connect., 6, 595–600, 2017.

[8] R. Artal R and M. O'Toole, "Guidelines of the American College of Obstetricians and Gynecologists for exercise during pregnancy and the postpartum period" Br J Sports Med., 37(1), 6–12, 2003.

[9] S. Falcao, S. Bisotto, C. Michel et al., "Exercise training can attenuate preeclampsia-like features in an animal model" J Hypertens., 28(12), 2446–2453, 2010.

[10] A. Saftlas, W. Wang, H. Risch, R. Woolson et al., "M. Prepregnancy body mass index and gestational weight gain as risk factors for preeclampsia and transient hypertension" Ann Epidemiol., 10(7), 475, 2000.
[11] A. M. Siega-Riz, M. Viswanathan, M. K. et al., "A systematic review of outcomes of maternal weight gain according to the Institute of Medicine recommendations: birthweight, fetal growth, and postpartum weight retention" Am J Obstet Gynecol., 201(4), 339 e331–314, 2009.
[12] E. Papiernik and M. Kaminski, "Multifactorial study of the risk of prematurity at 32 weeks of gestation. I. A study of the frequency of 30 predictive characteristics" J Perinat Med., 2(1), 30–36, 1974.
[13] H. A. Abenhaim, E. Bujold, A. Benjamin and R. A. Kinch, "Evaluating the role of bedrest on the prevention of hypertensive diseases of pregnancy and growth restriction" Hypertens Pregnancy, 27(2), 197–205, 2008.
[14] C. Borghi, A. F. Cicero, D. Degli Esposti, V. Immordino et al., "Hemodynamic and neurohumoral profile in patients with different types of hypertension in pregnancy" Intern. Emerg. Med., 6, 227–234, 2011.
[15] A. F. Cicero, D. Degli Esposti, V. Immordino, M. Morbini et al., "Independent Determinants of Maternal and Fetal Outcomes in a Sample of Pregnant Outpatients With Normal Blood Pressure, Chronic Hypertension, Gestational Hypertension, and Preeclampsia" J. Clin. Hypertens., 17, 777–782, 2015.
[16] A. De Boer, A. Bast and R. Godschalk, "Dietary supplement intake during pregnancy; better safe than sorry?" Regul. Toxicol. Pharm., 95, 442–447, 2018.
[17] A. M. Patti, R. V. Giglio, K. Pafili, M. Rizzo et al., "Pharmacotherapy for gestational dabetes" Expert Opin. Pharm., 19, 1407–1414, 2018.
[18] F. Fogacci, G. Tocci, V. Presta, A. Fratter et al., "Effect of resveratrol on blood pressure: A systematic review and meta-analysis of randomized, controlled, clinical trials" Crit. Rev. Food Sci. Nutr., 59, 1605–1618, 2019.
[19] J. Cockburn, V. A. Moar, M. Ounsted and C. W. Redman, "Final report of study on hypertension during pregnancy: the effects of specific treatment on the growth and development of the children" Lancet, 1(8273), 647–649, 1982.
[20] S. Rothberger, D. Carr, D. Brateng, M. Hebert, "Pharmacodynamics of clonidine therapy in pregnancy: a heterogeneous maternal response impacts fetal growth" Am J Hypertens., 3(11), 1234–1240, 2010.
[21] B. M. Sibai, W. C. Mabie, F. Shamsa, M. A. Villar et al., "A comparison of no medication versus methyldopa or labetalol in chronic hypertension during pregnancy" Am J Obstet Gynecol., 162(4), 960–966, 1990.
[22] L. Butters, S. Kennedy and P. C. Rubin, "Atenolol in essential hypertension during pregnancy" Bmj., 301(6752), 587–589, 1990.
[23] L. A. Magee, B. Schick, A. E. Donnenfeld, S. R. Sage et al., "The safety of calcium channel blockers in human pregnancy: a prospective, multicenter cohort study" American journal of obstetrics and gynecology, 174(3), 823–828, 1996.
[24] D. N. Papatsonis, C. A. Lok, J. M. Bos, H. P. Geijn et al., "Calcium channel blockers in the management of preterm labor and hypertension in pregnancy" European journal of obstetrics, gynecology, and reproductive biology, 97(2), 122–140, 2001.
[25] E. Widerlov, I. Karlman and J. Storsater, "Hydralazine-induced neonatal thrombocytopenia" The New England journal of medicine, 303(21), 1235, 1980.
[26] C. T. Shoemaker and M. Meyers, "Sodium nitroprusside for control of severe hypertensive disease of pregnancy: a case report and discussion of potential toxicity" American journal of obstetrics and gynecology, 149(2), 171–173, 1984.

[27] B. M. Sibai, R. A. Grossman and H. G. Grossman, "Effects of diuretics on plasma volume in pregnancies with long-term hypertension" American journal of obstetrics and gynecology, 150(7), 831–835, 1984.
[28] A. Singh, Y. Lin, W. Liu, S. Yu, J. Pan, C. Ren, D. Kuanhai, "Plant derived cationic dye as an effective corrosion inhibitor for 7075 aluminum alloy in 3.5% NaCl solution" Journal of Industrial and Engineering Chemistry, *20*(6), 4276-4285, 2014.
[29] B. Jim, S. Sharma, T. Kebede and A. Acharya, "Hypertension in pregnancy: a comprehensive update" Cardiology in review, 18(4), 178–189, 2010.
[30] W. O. Cooper, S. Hernandez-Diaz, P. G. Arbogast, J. A. Dudley et al., "Major congenital malformations after first-trimester exposure to ACE inhibitors" The New England journal of medicine, 354(23), 2443–2451, 2006.
[31] A. Cabassi, R. Rocco, R. Berretta, G. Regolisti et al., "Eplerenone use in primary aldosteronism during pregnancy" Hypertension, 59(2), e18–19, 2012.