DOI: https://doi.org/10.53350/pjmhs211551061

ORIGINAL ARTICLE

Role of Labetalol in Control of Hypertension during Pregnancy

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ABSTRACT

Aim: To valuate the effectiveness of labetalol in controlling hypertension during pregnancy.
Study design: Descriptive case series
Place and duration of study: Department of Obstetrics & Gynaecology, Allama Iqbal Medical College/Jinnah Hospital Lahore from 1st September 2018 to 31st March 2019.
Methodology: Sixty four patients were enrolled. All the patients were started with lowest effective dose of100mg orally three times daily and if required after 72 hours, the escalation dose up to 200mg every 8hours. When adequate reduction in blood pressure was obtained it was labelled as achievement of primary end point.
Results: The age range between 18-35 years with mean age 25.8±5.0 years. There were 12 primigravida (18.8%) and multigravida 52(81.2%). Reduction in blood pressure was observed in56 cases (87.5%).
Conclusion: The labetalol appears to be an effective agent in controlling hypertension during pregnancy with possible advantages and no apparent disadvantage during its use.
Keywords: Pregnancy-induced hypertension; Labetalol, Control of hypertension

INTRODUCTION

Pregnancy alters the normal physiology of woman and put them under many risks of developing pregnancy induced maternal and fetal complications like pregnancy induced hypertension, gestational diabetes mellitus, eclampsia, still birth etc. 10% of the pregnancies are complicated by pregnancy induced hypertension putting maternal and fetal wellbeing under risk resulting in increased perinatal morbidity and mortality.[1] Controlling hypertension during pregnancy leads to favorable results in terms of decrease perinatal mortality, and the recent data has proved it in terms of better survival. Despite of these favorable outcome, clinicians have concerns in their choices of treatment regarding efficacy of oral treatments and their side effects because these side effects and poor hypertension control made many antihypertensive drugs of no use in controlling hypertension in pregnancy.[2] Labetalol (trandate),non-selectively antagonizes beta-adrenergic, and selectively antagonizes alpha-1-adrenergic, has been proved as a safe drug of choice by many researchers in controlling severe hypertension resulting decrease perinatal mortality and increases fetal survival. However, its role in controlling mild to moderate cases of hypertension complicating pregnancies has yet to be established.[3-7]

Antihypertensive drugs may lead to poor placental perfusion; care should be taken to avoid side effects of these drugs in both mother and fetus; making them undesirable for use in pregnancy.[4] Reserpine may affect mothers in various ways like maternal depression, lethargy, tendency to develop hypothermia, and also causing increase in volume of respiratory tract secretions. Methyldopa, however, may affect both fetus and mother adversely. It effects on developing neural mechanisms of the fetus while the mother may have a positive Coomb's titer and also results in decrease cardiac output and increase sodium retention.[3] Maternal postural hypotension and diarrhoea are the known side effects of bethanidine and guanethidine.[4] Recent trails of using propranolol has reported fetal bradycardia and hypotension. These conditions may then ultimately potentiate fetal distress and can hide the diagnostic clinical features of fetal hypoxia. This drug may also be responsible for unique perinatal complications of increase neonatal hypoglycemia as well.

In a study conducted in Western Australia on role of labetalol in controlling severe hypertension during pregnancy. The study results show that effective reduction in blood pressure (BP) was achieved in 88% of the patients treated.[5] Another study conducted in India also evaluated the effectiveness of labetalol and shows that labetalol is effective in controlling hypertension in pregnancy.[6]

Received on 13-12-2020
Accepted on 17-04-2021

PATIENTS AND METHODS

This descriptive case series was carried out at Department of Obstetrics & Gynaecology of Allama Iqbal Medical College/Jinnah Hospital Lahore from 1st September 2018 to 31st March 2019 and 64 women with hypertension during pregnancy were entered. All patients age between 18-35 years of age, primi or multipara, blood pressure of 150/100 mmHg or more during pregnancy and with and without proteinuria were included. All pregnant women with hypertension with ischemic heart disease determined on echocardiography, hypertension with congenital heart disease determined on echocardiography and women taking corticosteroid or cough and cold preparations containing epinephrine were excluded. Informed consent was taken from all the patients and an initial oral dose of 100mg three times a day was considered in subjects. Blood pressure was recorded in every 8 hours (6am, 2pm and 10pm) for 72 hours starting from first dose. It was always

measured in dominant hand of the patient in supine position using a standard mercury sphygmomanometer. Later, blood pressure was recorded daily in evening at 10pm for the next 7 days. The end point of effective treatment was considered as SBP of 140mmHg or less and DBP of 90 mmHg or less on 7th day. All the patients were started with 100mg orally three times daily dose which is the lowest effective dose to control hypertension and if required after 72 hours, the escalation of dose upto 200mg every 8 hours when adequate reduction in BP was obtained and it was labelled as achievement of primary end point. The data was entered and analyzed through SPSS-21.

RESULTS

The range between 18-35 years with mean age was 25.8±5.0 years. The mean values of gestational age 36.3±4.5 week, BMI 25.2±2.3Kg/m2, gravidity 2.6±1.7, parity 1.4±0.6, SBP before treatment 156.5±4.1, DBP before treatment 103.2±2.6, SBP 134.7±10.7 on 7th day after treatment and DBP 80.0±10.2 on 7th day after treatment. There were 12 primigravida (18.8%) and multigravida 52(81.2%). Reduction in blood pressure was observed in 56 cases (87.5%) [Table 1]. Stratification with regard to age, gestational age, parity and BMI was also carried out (Table 2).

Table1: Demographic information of the patients (n=64)

Variable	No.	%
Age (years)		
18-25	36	56.2
26-35	28	43.8
Gestational age (weeks)		
≤ 37	30	46.9
> 37	34	53.1
BMI (Kg/m^2)		
≤ 25	33	51.6
> 25	31	48.4
Parity		
Primigravida	12	18.8
Multigravida	52	81.2
Reduction in BP		
Yes	56	87.5
No	8	12.5

Table 2: Comparison of age, gestational age, parity and body mass index according to reduction in blood pressure

Variable	Reduction in BP		P value
	Yes	No	
Age (years)			
18-25	33	3	0.253
26-35	23	5	
Gestational age (weeks)			
≤ 37	26	4	0.850
> 37	30	4	
Parity			
Primigravida	8	4	0.015
Multigravida	48	4	
Body mass index (Kg/m^2)			
≤ 25	29	4	0.925
> 25	27	4	

DISCUSSION

Under physiologic conditions, mother's body undergoes physiological changes for wellbeing of fetus and herself which includes the blood pressure of pregnant women to start lowering than normal. As a result, cardiac output started increasing which affects peripheral vascular resistance to decrease significantly. These changes results in increase in renal blood flow which ultimately increases the estimated glomerular filtration rate as well. All of these physiological changes peak at 12 weeks of gestational age. During second trimester, peripheral vascular resistance starts rising and so do the blood pressure as well until third trimester, and returns to the pre-pregnancy level after 36 weeks of gestational age[8].

Pregnancy-induced hypertension (PIH) threatens the maternal and fetal health. These patients with PIH tends to deliver small for gestational age babies and early placental abruption while at the same time putting mothers at the risk of developing brain edema, acute heart failure, stroke, and acute renal failure[9]. A large meta-analysis published recently has shown that risk of developing long term (5-15 years) complications like ischemic heart disease, stroke and venous thromboembolic events were approximately double in those females who had history of pre-eclampsia during pregnancy with an additional risk of developing hypertension is almost four-fold[10,11].

Ultimate goal of controlling hypertension is not only to reduce its prevalence but mainly is to reduce the risk of maternal and fetal complications[12,13]. Undesirable and unsafe side effects of oral antihypertensive agents leave clinicians in avoidance of using these drugs with fear of reducing placental blood perfusion. This compromised blood flow may effect fetal wellbeing and is an important issue. Our study has proved that majority (87%) patients were benefited of using labetalol in controlling maternal blood pressure with no potentially threatening effect on fetus. Michael et al has shown the same benefits to maternal and fetal health with use of labetalol for pregnancy induced hypertension[5].

Labetalol has non-selective antagonizing beta-adrenergic receptors effect, and selective antagonizing alpha-1-adrenergic receptors effect which is a unique feature of this drug making it favorable to maintain placental perfusion, in the presence of vasoactive substances, by blocking the response of adrenergically innervated radial and arcuate branches of uterine artery[14]. Additionally, its partial intrinsic sympathomimetic effect helps in controlling pregnancy induced hypertension without compromising cardiac output. This special feature of labetalol maintains fetal blood supply by maintaining placental perfusion and ultimately fetal oxygenation which is required for lung maturation. Various studies have shown its widespread use in controlling pregnancy induced hypertension[15,16].

Long term use of labetalol has favorable results in controlling blood pressure, heart rate and also the peripheral vascular resistance while keeping normal cardiac output at the same time.[17] Uncontrolled trails of using it has shown beneficial results without any harm.[5,18] While the controlled trails has proven it even safer, effective and hence superior than methyldopa with an additional benefit of fetal lung maturations[18,19].

CONCLUSION

The labetalol may be considered as safe and an effective drug in controlling hypertension during pregnancy with

proven benefits and potentially minimal side effects of using it.

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