

Study of Methyl Dopa Versus Labetalol in Management of Preeclampsia and Gestational Hypertension

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Abstract

Objective: To assess the efficacy and safety of labetalol compared with methyl dopa in the management of mild and moderate cases of pregnancy-induced hypertension (PIH).

Methods: Eighty patients with PIH were randomly allocated to receive either labetalol (group A) or methyl dopa (group B). Administration of drugs with respect to Age, Gravid Status, Blood Pressure, Urine albumin Levels, Side Effects, Drug dosage, Additional Treatment, Prolongation of Pregnancy, New born Screening Test (NST), mode of termination, Indication of caesarean section, Perinatal safety and APGAR scores were studied. The statistical level of significance was taken at P<0.05.

Results: A labetalol has been very effective in control as well as earlier onset of action in patients with methyl dopa. With effective control of blood pressure, prevention of eclampsia and the pregnancy can be prolonged to achieve fetal maturity. Labetalol has lesser side effects when compared to methyl dopa. Labetalol is not associated with adverse fetal effects in the immediate and late neonatal period. The chances of spontaneous onset of labor were greater in the labetalol group when compared to methyl dopa group. Though there was no difference in the groups with regard to obstetric intervention. At clinically effective doses, both the drugs were found to be safe for the neonate.

Conclusions: Labetalol is safer, quicker in achieving adequate control of blood pressure with considerable prolongation of the duration of pregnancy with fewer side effects on the mother as well as the neonate when used in the management hypertensive disorders of pregnancy.

Keywords: Antihypertensive drugs; Pregnancy; Pre eclampsia; Hypertension; Management

Introduction

Hypertension is the most common medical problem encountered during pregnancy [1]. Hypertensive disorders seem to complicate approximately 10% of pregnancies and are important causes of maternal and fetal morbidity and mortality [2]. Validation studies of the reporting of hypertension in pregnancy have been conducted in Australia, Canada, Denmark, Norway, Sweden and the USA, with consistent findings about the reliability of each country's ascertainment methods [3,4]. In India the incidence of hypertension occurs in well over 6% to 8% of all pregnancies [5-7]. In addition to the risk they present to the pregnancy, hypertensive disorders of pregnancy have been linked to future high blood pressure and cardiovascular disease in women [8-11].

The population prevalence of factors associated with increased and decreased risk of pregnancy hypertension and pre-eclampsia has changed over time, but the impact of these changes is unknown. Hypertension complicates up to 10% of all pregnancies and is associated with increased risk of adverse fetal, neonatal and maternal outcomes, including preterm birth, intrauterine growth restriction, multiple births, diabetes, chronic hypertension, perinatal death, acute renal or hepatic failure, antepartum haemorrhage, postpartum haemorrhage and maternal death [12-17]. Decreased risk of pregnancy hypertension and pre-eclampsia has been associated with placenta praevia, smoking (although smoking may only be protective in the non-obese), summer births, low-dose aspirin and calcium supplementation in high-risk women, treatment of gestational diabetes and use of antihypertensive medications [14,15]. As the majority of cases of pregnancy hypertension and preeclampsia occur at term, increasing rates of early elective delivery may reduce their frequency [18,19]. Trends in pregnancy

hypertension and pre-eclampsia are the result of the effects of changes in all these factors.

Identification of this specific risk made the control of acutely raised blood pressure as central point for women with severe hypertension, particularly that of pre-eclampsia. During this period the maternal and foetal conditions are monitored along with control of hypertension by antihypertensive drugs. The risk of developing severe hypertension is reduced to half by using antihypertensive medications [20]. Severe hypertension is treated to prevent severe maternal complications [21].

A wide spectrum of antihypertensive agents represents the key of successful pregnancy hypertension treatment and opportunity of choice, in accordance with indications and availability of drugs provided by drug tendering [22-24]. Methyl dopa was most commonly used for treatment of hypertension during pregnancy based on its effectiveness and safety for both mother and foetus as an anti-hypertensive drug but it takes longer time to act and also less efficacious as hypotensive drug. It is still the most commonly used drug for long term control of blood pressure in pregnancy. Methyl dopa is a centrally-

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acting adrenergic antagonist that acts by stimulation of the central alpha 2 receptors, leading to a decrease in sympathetic nerve activity with resultant arterial dilatation and reduction in BP. Long term follow up data of 7 years shows no detrimental effects to the off springs in the Methyl dopa treated group. At high doses the sedative and depressant effects of methyl dopa are marked. Methyl dopa should not be used if there is a substantial risk of maternal depression when a beta-blocking agent or calcium antagonist may be more suitable.

Labetalol gives better control of blood pressure compared to other anti-hypertensive agents [25]. Labetalol is a combined alpha- and beta-blocker and has the advantage over other beta blockers due to its additional arteriolar vasodilator action that helps to lower peripheral vascular resistance with little or no decrease in cardiac output. Advantage of labetalol is that, it is available as both injectable and oral and time of onset of action is earlier than methyl dopa [25]. However now, it is known that b-blockers cross the placental barrier and may cause foetal bradycardia. Experimental evidence also suggests that b-blocking agents reduce foetal tolerance to hypoxic stress. Out of the 80 patients in our study, 1 patient's NST at admission was non-reactive hence it was not included however the rest 79 patients non-stress tests taken after 48 hours of drug administration for both the groups were reactive depicting that either one of the drugs do not have any adverse effect on the foetus.

Materials and Methods

Subject recruitment

A prospective randomized study was carried out in 80 pregnant women from 2011-2013 in the Department of Obstetrics and Gynaecology, Yenepoya Medical College and Hospital, Mangalore. All pregnant women attending the antenatal clinic were screened for and hypertensive pregnant women were included in the study after obtaining informed consent. The study was approved by the institutional ethics committee of the hospital. The criteria for diagnosis and classification of the hypertensive disorder of pregnancy will be obtained according to the National High Blood Pressure Education Program Working Group (NHBPEPWG). Medical and obstetric history taking and physical examination were performed at the time of initial recruitment. Serial BP recordings were measured twice in a day 12 hours apart from the time of administration of the drugs to patients who are divided into two groups based on the drug they receive. The duration required for the drug to act was then calculated along with assessment of other parameters such as side effects, prolongation of the duration of the pregnancy and number of additional drugs required. Neonatal morbidity in terms of birth weight, 5 minute APGAR scores, NICU stay and indication of the stay were all taken into account.

The pregnant women with BP of more than or equal to 140/90 with or without proteinuria were included irrespective of their gravid status, gestational age and maternal age were included in our study. Selection of patients was restricted to those who, Non-consenting patients, patient coming for the first time during labour, patient with eclampsia, platelet count <100000/mm³, HELLP syndrome, pulmonary edema, recurrent pregnancy loss and also known case of diabetes mellitus, renal disease, cardiac disease, haematological disorders hydatidiform mole, multiple gestations.

A total number of 80 patients attending the ante-natal clinic were included after diagnosing them with hypertension or pre-eclampsia ward. Among them 40 of subjects with preeclampsia and the others 40 with gestational hypertension. These patients were randomly assigned with either Labetalol (Group A) or Methyl dopa (Group B) in groups of

20 cases each. A detailed history, examination and investigated in detail. BP was recorded using mercury sphygmomanometer with patient in left lateral recumbent position after 20 min rest. Conventional mercury sphygmomanometer was used for BP measurement and phases I and V Korotok off sounds were respectively used to define systolic and diastolic BP.

Patients close to term were followed up in the hospital whereas others were discharged after 7-10 days provided they had good control of BP, and did not show significant proteinuria or gross intra uterine growth retardation. On discharge, patients were advised to take the dose titrated for them based on their assessment during their hospital stay and were advised to come for weekly follow up and get re-admitted if BP control was unsatisfactory.

Patients whose BP remained uncontrolled in spite of therapy in both the groups were closely monitored in the hospital and attempt was made to continue the pregnancy with additional drugs such as nifedipine in varying doses or phenobarbital or magnesium sulphate were given. Prophylactic corticosteroids were given in patients who were less than 36 weeks period of gestation to better the neonatal outcome especially in those patients in whom the pregnancy had to be terminated early by induction of labour, and/or caesarean section done. The efficacy was measured in terms of the fall in both systolic and diastolic BP by 48 hours as well as 5th day of the drug administration and the results were tabulated.

Result

A total of 80 patients were included in this study by a prospective randomized trial 40 of them with pre eclampsia and 40 of them with gestational hypertension. Pre-eclamptic 40 were divided into two groups of 20 each and given labetalol & methyl dopa, similarly 40 patients of gestational hypertension were divided in two groups of 20 each and labetalol and methyl dopa were administered.

The mean birth weight in the labetalol group with gestational hypertension and pre-eclampsia were 2.6 and 2.56 while the mean birth weight in the methyl dopa group hypertension and pre-eclampsia was 2.5 and 2.635 respectively showing that there wasn't a significant difference in either drug groups. The mean 5 minute APGAR scores for labetalol group with hypertension 8 and pre-eclampsia 7.55. The methyl dopa group for hypertension and pre-eclampsia were 7.6 and 7.85 respectively. In the labetalol group there were 13 neonates with hyperbilirubinemia, 4 with Respiratory Distress Syndrome (RDS) and 2 suffered from Meconium Aspiration Syndrome (MAS). In the methyl dopa group similar numbers were seen 10 hyperbilirubinemia, 5 RDS and 2 with MAS. There was no statistically significant in the neonatal morbidity between the two drug groups.

The mean difference in the fall with labetalol of the systolic/diastolic BP by 48 hours was 9/6.7 mmHg and by the 5th day it was 11.9/8.7 mmHg as compared to methyl dopa being 3.5/3.6 mmHg in the first 48 hours followed by 8.3/5.9 in the hypertension patients. Similar numbers were seen in the pre-eclampsia patients, 48 hour fall 8.7/7.2 and 5th day fall of 16.8/13.2 with labetalol as compared 48 hour fall of 1.5/2.2 mmHg and 5th fall of 8.3/6.6 mmHg of methyl dopa patients clearly stating that labetalol is a better drug in effectively reducing the BP of the patients and then maintain optimal BP levels.

In the present study the mean age of patients who are in Preeclampsia receiving the drugs under study shows that there is no statistically significant difference in the age distribution of the patients (p=0.567) and patients with Gestational hypertension had statistically significant difference between the drugs when it comes to the age

parameter (p=0.211) (Table 1). There is no statistically significant difference between both the drug groups with respect to the gravid status of the patients with Pre-eclampsia and gestational hypertension (Table 2). No statistically significant differences were found between both the drug groups (Booked or Unbooked (B/U)) (Table 3). Table 4 depicts the following two graphs unequivocally depict that labetalol has a better effect on control of BP added by quick onset of action which is not the case with methyl dopa. Further-more the maintenance of optimal BP levels were seen through-out the course of therapy. Table 5 Describes the total dose required per day was more with methyl dopa and labetalol required comparatively lesser dosage as evidenced by the p-value in both the groups. Labetalol shows a statistically significant p-value of 0.005 in gestational hypertension patients with respect to prolongation of pregnancy how-ever it is not reflected in the patients with pre-eclampsia (Table 6). There was no significant difference in birth weight of the neonates in either drug groups (Table 7). The APGAR scores of the neonates at 5 min were in the same range in both labetalol and methyl dopa with no significant statistical difference (Table 8). There is a small but statistically insignificant increase in the NICU stay

with methyl dopa (Table 9). Table 10 shows the neonatal morbidity of pregnancy, the various causes of morbidity were hyperbilirubinemia, respiratory distress syndrome, meconium aspiration syndrome IUGR and Pre-maturity however when compared in either drug groups there was no statistical significance.

Discussion

Most countries saw a decline in the rates of pregnancy hypertension and/or pre-eclampsia over time. This was an unexpected result, since factors thought to be positively associated with pregnancy hypertension such as pre-pregnancy overweight and obesity, diabetes, multiple births, and maternal age are generally recognised and associated with reduced rates of pregnancy hypertension [26]. Hypertensive disorders of pregnancy are one of the major causes of maternal and foetal mortality and morbidity and as long as its exact cause is unknown, its prophylaxis will be uncertain. Many drugs have been used in the management of hypertensive disorders in pregnancy. Variability in the age, parity, chronic disease, smoking and multiple

	Particulars	N	Mean ± SD	t	df	p-Value
AGE	Preeclampsia	Labetalol in Pre-Eclampsia	20	26.65 ± 3.731	0.577	38
		Methyl-dopa in pre-eclampsia	20	25.95 ± 3.94		
	Gestational Hypertension	Labetalol in GHTN	20	29.9 ± 3.81	1.271	38
		Methyl-Dopa In Ghtn	20	28.05 ± 5.276		

Table 1: Depicts the mean age of patients receiving the drugs.

			Group		Total	Group		Total
			Labetalol in gestational hypertension	Methyl-dopa in gestational hypertension		Labetalol in pre-eclampsia	Methyl-Dopa in Pre-Eclampsia	
Obstetric Score/ Gravid Status	G2P1L1	Count	8	6	14	0	6	6
		% within OS	57.1%	42.9%	100.0%	0.0%	100.0%	100.0%
		% within GROUP	40.0%	30.0%	35.0%	0.0%	30.0%	15.0%
	G2P1P1	Count	NA	NA	NA	2	0	2
		% within OS	NA	NA	NA	100.0%	0.0%	100.0%
		% within GROUP	NA	NA	NA	10.0%	0.0%	5.0%
	G5P4L3	Count	NA	NA	NA	0	1	1
		% within OS	NA	NA	NA	0.0%	100.0%	100.0%
		% within GROUP	NA	NA	NA	0.0%	5.0%	2.5%
	G3P2L2	Count	5	6	11	4	3	7
		% within OS	45.5%	54.5%	100.0%	57.1%	42.9%	100.0%
		% within GROUP	25.0%	30.0%	27.5%	20.0%	15.0%	17.5%
	G4P3L3	Count	1	2	3	2	1	3
		% within OS	33.3%	66.7%	100.0%	66.7%	33.3%	100.0%
		% within GROUP	5.0%	10.0%	7.5%	10.0%	5.0%	7.5%
	G5P4L4	Count	2	1	3	NA	NA	NA
		% within OS	66.7%	33.3%	100.0%	NA	NA	NA
		% within GROUP	10.0%	5.0%	7.5%	NA	NA	NA
	G6P5L4	Count	1	0	1	NA	NA	NA
		% within OS	100.0%	0.0%	100.0%	NA	NA	NA
		% within GROUP	5.0%	0.0%	2.5%	NA	NA	NA
	G6P5L5	Count	0	1	1	NA	NA	NA
		% within OS	0.0%	100.0%	100.0%	NA	NA	NA
		% within GROUP	0.0%	5.0%	2.5%	NA	NA	NA
Primi	Count	3	4	7	12	9	21	
	% within OS	42.9%	57.1%	100.0%	57.1%	42.9%	100.0%	
	% within GROUP	15.0%	20.0%	17.5%	60.0%	45.0%	52.5%	
Total	Count	20	20	40	20	20	40	
	% within OS	50.0%	50.0%	100.0%	50.0%	50.0%	100.0%	
	% within GROUP	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	

Table 2: Showed the difference between both the drug groups with respect to the gravid status of the patients.

			Group		Total	Group		Total
			Labetalol in Pre-Eclampsia	Methyl-Dopa in Pre-Eclampsia		Labetalol in gestational hypertension	Methyl-dopa in gestational hypertension	
B/U	B	Count	16	15	31	15	15	30
		% within B/U	51.6%	48.4%	100.0%	50.0%	50.0%	100.0%
		% within GROUP	80.0%	75.0%	77.5%	75.0%	75.0%	75.0%
	U	Count	4	5	9	5	5	10
		% within B/U	44.4%	55.6%	100.0%	50.0%	50.0%	100.0%
		% within GROUP	20.0%	25.0%	22.5%	25.0%	25.0%	25.0%
Total	Count	20	20	40	20	20	40	
	% within B/U	50.0%	50.0%	100.0%	50.0%	50.0%	100.0%	
	% within GROUP	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	

Table 3: Shows that the percentage of Booked OR Unbooked (B/U) value of both drug groups.

		Group	N	Mean ± SD	t	df	P VALUE
Hypertension	systolic fall in 48 hrs	LABETELOL	20	9 ± 2.714	6.119	38	<0.001
		METHYL-DOPA	20	3.5 ± 2.965			
	diastolic fall in 48 hrs	LABETELOL	20	6.7 ± 2.849	3.976	38	<0.001
		METHYL-DOPA	20	3.6 ± 2.01			
	fall by 5 th day systolic	LABETELOL	20	16.2 ± 3.548	6.119	38	<0.001
		METHYL-DOPA	20	8.3 ± 4.555			
fall by 5 th day diastolic	LABETELOL	20	11.9 ± 3.463	5.851	38	<0.001	
	METHYL-DOPA	20	5.9 ± 3.007				
Pre-Eclampsia	systolic fall in 48 hrs	LABETELOL	20	8.7 ± 4.414	6.743	25.285	<0.001
		METHYL-DOPA	20	1.5 ± 1.821			
	diastolic fall in 48 hrs	LABETELOL	20	7.2 ± 4.561	4.366	28.29	<0.001
		METHYL-DOPA	20	2.2 ± 2.331			
	fall by 5 th day systolic	LABETELOL	20	16.8 ± 5.288	5.81	38	<0.001
		METHYL-DOPA	20	8.3 ± 3.854			
fall by 5 th day diastolic	LABETELOL	20	13.2 ± 4.607	5.167	38	<0.001	
	METHYL-DOPA	20	6.6 ± 3.378				

Table 4: Comparison of Blood Pressure control among the two groups.

Category	Group	N	Mean ± SD	t	df	Sig. (2-tailed)
Hypertension	LABETELOL	20	500 ± 189.181	-3.853	28.046	0.001
	METHYL-DOPA	20	862.5 ± 375.876			
Pre-eclampsia	LABETELOL	20	480 ± 188.065	-3.742	25.922	0.001
	METHYL-DOPA	20	875 ± 433.013			

Table 5: Depicts the mean Drug Dosage (TDPD-total dose per day) of patients receiving the drugs.

birth distributions will also influence the baseline rates of pregnancy hypertension and preeclampsia. Study conducted by Verma et al. [26] states that adverse events observed were lower in the labetalol treated group compared to the methyl dopa group. In a study by El-Qarmalawi et al. [23] patients receiving methyl dopa complained of side-effects such as drowsiness (22.2%), headache (14.8%), nasal congestion (7.4%), postural hypotension (5.6%). 96 patients in labetalol group complained of dyspnoea, no other side-effects were noticed. Trends in these factors have been proposed as possible explanations for the increase in pregnancy hypertension and pre-eclampsia rates reported for the entire USA from 1987 to 1998 (although the rates plateaued from 1999 to 2004) [27]. While advanced maternal age and obesity are more common, the magnitude of risk is lower (less than double) [28].

The mean drug dosage required by labetalol was (500 ± 189.181) in hypertensive women and 480 ± 188.065 for pre-eclamptic women in comparison methyl dopa was required in higher doses, 862.5 ± 375.876 for hypertensive women and 875 ± 433.013 for pre-eclamptic women illustrating that methyl dopa requires higher doses to achieve clinical efficacy (Table 5). Out of the 40 women on labetalol 8 (20%) underwent

caesarean section and the rest 32 (80%) underwent vaginal delivery. In the methyl dopa group 12 (30%) underwent caesarean section the rest 28 (70%) underwent vaginal delivery effectively proving that either of these drugs are not directly related to the mode of delivery however the number of inductions was very high 50% and 47.5% in labetalol and methyl dopa respectively. The indications for termination of pregnancy by caesarean section in either drug groups were varied, obstetric indications such as occipito posterior, cervical dystocia or foetal indications such as foetal distress, severe IUGR with altered Doppler parameters, severe oligohydramnios, PROM, meconium staining of the liquor sometimes existing simultaneously. However these indications did not directly attribute to the usage of either drug rendering the above graphical values statistically non-significant.

In our study, the mean age of methyl dopa group was 25.95 ± 3.94 years and 26.65 ± 3.73 years in Labetalol group. Similarly, Verma et al. [26] conducted the study and mentioned the age distribution showed maximum patients between 19-24 years in both groups (64.44% in methyl dopa group and 57.77% in labetalol group) and there was no significant difference in age distribution in both groups. Most common

Category		Group	N	Mean	SD	t	df	Sig. (2-tailed)
Hypertension	prolongation of pregnancy	LABETELOL	20	14.4 days	4.489	2.977	38	0.005
		METHYL-DOPA	20	10.3 days	4.219			
Pre-Eclampsia	prolongation of pregnancy	LABETELOL	20	13.3 days	3.511	0.798	38	0.43
		METHYL-DOPA	20	12.25 days	4.723			

Table 6: Showed the Prolongation of Pregnancy (in days) in both drug groups.

Category		Group	N	Mean ± SD	t	df	Sig. (2-tailed)
Pre-Eclampsia	Birth Weight	LABETELOL	20	2.56 ± 0.213739	0.516	23.549	0.61
		METHYL-DOPA	20	2.635 ± 0.613253			
Hypertension	Birth Weight	LABETELOL	20	2.606 ± 0.2523	0.445	26.704	0.66
		METHYL-DOPA	20	2.545 ± 0.5482			

Table 7: Showed the Birth Weight of child by the patient in both drug groups.

Category		Group	N	Mean ± SD	t	df	Sig. (2-tailed)
Pre-Eclampsia	APGAR 5 min	LABETELOL	20	7.55 ± 1.538	-0.673	38	0.505
		METHYL-DOPA	20	7.85 ± 1.268			
Hypertension	APGAR 5 min	LABETELOL	20	8 ± 1.451	0.751	38	0.66
		METHYL-DOPA	20	7.65 ± 1.496			

Table 8: Describes the 5 Minute APGAR Scores in two groups.

Group Statistics					
	Group	N	Mean	Std. Deviation	Std. Error Mean
NICU	Labetelol	40	0.80	1.884	0.298
	Methyl-dopa	40	1.50	3.581	0.566

Table 9: Showed the statistical values of NICU Stay in both groups.

Particulars		Group		Total	Group		Total	
		Labetalol in pre-eclampsia	Methyl-dopa in pre-eclampsia		labetalol in gestational hypertension	methyl-dopa in gestational hypertension		
Neonatal morbidity	Hyperbilirubinemia	Count	5	4	9	4	3	7
		% within neonatal morbidity	55.6%	44.4%	100.0%	57.1%	42.9%	100.0%
		% within GROUP	25.0%	20.0%	22.5%	20.0%	15.0%	17.5%
	Meconium aspiration syndrome	Count	1	1	2	1	0	1
		% within neonatal morbidity	50.0%	50.0%	100.0%	100.0%	0.0%	100.0%
		% within GROUP	5.0%	5.0%	5.0%	5.0%	0.0%	2.5%
	Nil	Count	12	12	24	13	14	27
		% within neonatal morbidity	50.0%	50.0%	100.0%	48.1%	51.9%	100.0%
		% within GROUP	60.0%	60.0%	60.0%	65.0%	70.0%	67.5%
	RDS	Count	0	1	1	1	0	1
		% within neonatal morbidity	0.0%	100.0%	100.0%	100.0%	0.0%	100.0%
		% within GROUP	0.0%	5.0%	2.5%	5.0%	0.0%	2.5%
RDS+prematurity+hyperbilirubinaemia	Count	2	2	4	1	3	4	
	% within neonatal morbidity	50.0%	50.0%	100.0%	25.0%	75.0%	100.0%	
	% within GROUP	10.0%	10.0%	10.0%	5.0%	15.0%	10.0%	
Total	Count	20	20	40	20	20	40	
	% within neonatal morbidity	50.0%	50.0%	100.0%	50.0%	50.0%	100.0%	
	% within GROUP	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	

Table 10: Depicts the Neonatal Morbidity of two drug groups.

age group is in contrast to the findings of a large database study wherein there was a linear relationship between age and incidence of pregnancy induced hypertension [29]. In the present study, about 32.5% of the pregnant women in Methyl-dopa group and 37.5% in Labetalol group were primigravidae. The rest of the patients were multigravidae. However the percentage of primigravidae is greater in most other studies where the prevalence of primigravidae was 50% or above [30,31].

There was a fall of 40% after 48 hours in patients with urine albumin of 2+ and 15% fall of urine albumin 3+ recorded on the day

of admission with labetalol group in comparison with fall of 5% in patients with 2+ urine albumin and no fall in 3+ urine albumin levels from the day of admission to 48 hours of methyl dopa therapy. This demonstrates that labetalol improves the renal function better however other essential aspects of renal function such as blood urea and serum creatinine were not included in this study rendering the evaluation of these drugs on renal function incomplete.

Labetalol is an effective antihypertensive which decreases both systolic and diastolic BP in pregnancy induced hypertension was proved earlier. About 55% of the methyl-dopa group received

nifedepine and phenobarbitone where as only 22.5% of labetalol group received inj labetalol and phenobarbitone showing that methyl dopa requires additional drugs BP management than labetalol. In our study clearly exhibit that labetalol is a better drug in effectively reducing the BP of the patients and then maintain optimal BP levels (Table 4). Similarly, Cruickshank et al. [32] observed that Labetalol did control the blood pressure in 45 of the 51 treated women (88%) within 24 hrs. It is interesting that several other workers have found similar response rates - Lardoux's group 82%, CA Michael 92% [33,34]. Marked fall of both systolic and diastolic pressure generally between 24 and 48 hours from the start of using methyldopa was noticed by Hans and Kopelman [35]. The only limiting factor in use of labetalol is economic constraints among rural population of India. According to Brunton et al. [36] stated that labetalol provides more efficient control of BP than methyldopa in the treatment of mild hypertension in pregnancy which was also corroborated in our present study and the present study concluded that labetalol is more advantageous than methyldopa in terms of better and quicker control of blood pressure.

There were a total of 3 neonatal deaths, 2 (5%) in methyldopa group and 1 (2.5%) in labetalol group; controversially, Plouin et al. [31] made a findings and our report were not in corroboration with his report. He also demonstrated that four still births in methyldopa group. In a study by Redman et al. [30] he found that two babies born to women assigned to labetalol died but no deaths were reported in methyldopa group. Methyldopa had side effects such as drowsiness, depression and dry mouth whereas labetalol had only nausea however on comparison between the two, the numbers were statistically insignificant. The chances of spontaneous onset of labour were greater in the labetalol group than in the methyldopa group. Those patients on labetalol, who required induction of labour, were noted to have a better Bishop score at the time of induction. The freedom from maternal and fetal side-effects, the efficient hypotensive action and consequent improved perinatal mortality in a condition usually accompanied by high fetal loss, indicate that labetalol is suitable for use during pregnancy. The observation made by El-Qarmalawi et al. [23] suggest higher incidence of spontaneous onset of labour in the labetalol group and Lamming and Symonds [25] reported a higher incidence of spontaneous labour in the labetalol group.

Conclusion

The present study confirms the previous findings that labetalol is an effective and safe drug for use quicker in achieving adequate in the control of blood pressure in pregnancy-induced hypertension. The low incidence of maternal and foetal side-effects together with the excellent perinatal outcome in a condition usually accompanied by a high maternal and foetal mortality and morbidity confirms its suitability for use during pregnancy. Unlike other antihypertensive drugs labetalol reduces peripheral resistance without significantly reducing maternal cardiac output and pulse rate. This may be an additional factor in maintaining adequate placental perfusion and therefore foetal oxygenation in the treatment of pregnancy hypertension with labetalol. The only regulating factor in use of labetalol is economic constraints among rural population of India.

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