

## Effect of methyldopa and labetolol on fetal outcomes in hypertensive disorders of pregnancy

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### ABSTRACT

**Background:** Hypertensive disorders represent the most common medical complication of pregnancy, with a reported incidence of 6-10% and accounts for 15% of maternal mortality. Effective management of pregnancy induced hypertension is vital to improve maternal and foetal outcomes. As data are scarce on comparison of labetolol and methyldopa this study was undertaken. The objectives of the study were to evaluate effect of both drugs on fetal outcomes.

**Methods:** A comparative observational Study is designed. 30 patients who received Methyldopa and 30 patients who received Labetolol were included in the study. Methyldopa was started at a dose of 250-500mg thrice daily while Labetolol was started at a dose of 100-400mg twice daily. Patients were followed up during antenatal, intrapartum and postpartum period for perinatal outcomes.

**Results:** Intra Uterine Growth Retarded (IUGR) babies were 10% in Methyldopa group and 6.66% in Labetolol group. 20% of new borns in Methyldopa group and 10% of new borns in Labetolol group got admitted in Neonatal Intensive Care Unit (NICU) because of distress. 13.3% of new borns in Methyldopa group are small for gestational age (SGA), whereas only 3.33% in Labetolol group are small for gestational age.

**Conclusions:** Chances of development of IUGR, NICU admissions of neonates with respiratory distress syndrome and small for gestational age babies were more with methyldopa compared to Labetolol, but there was no statistically significant difference between two drugs.

**Keywords:** Fetal side effects, Labetolol, Methyldopa, PIH

### INTRODUCTION

Hypertensive disorders are the most common medical complications of pregnancy (6-10%) and a major cause of fetal morbidity and mortality (22%).<sup>1</sup>

Women with gestational hypertension are at risk for progression to Pre-Eclampsia, Eclampsia, and abruption. The risks are decreased if patients are diagnosed at lower gestational age.<sup>1</sup> Though hypertensive disorders in

pregnancy cannot be prevented, early diagnosis and treatment helps in favourable maternal and fetal outcomes.

Antihypertensive drugs are often used to lower blood pressure with the aim of preventing this progression to adverse outcomes for the mother and the fetus. The benefits of antihypertensive therapy for mild to moderately increased blood pressure in pregnancy ( $\geq 140/90$  and  $\leq 160/110$  mmHg), either chronic or de novo, have not been shown in clinical trials.

Methyldopa is the most commonly used drug for Pregnancy induced hypertension, but it takes longer time to act.<sup>2,3</sup> In cases where monotherapy is inadequate to control blood pressure in patients with PIH other drugs have been used.

Advantage of Labetolol is that it is available in both oral and injectable formulations and onset of action is fast compared to Methyldopa.

Since the literature, effect of methyldopa and Labetolol on fetal outcomes is scarce, this study was undertaken to assess effect of above drugs on fetal outcomes in the treatment of mild to moderate pregnancy induced hypertension.

## METHODS

This comparative, prospective, observational study was conducted in Gynaecology and Obstetrics Department of MediCiti Institute of Medical Sciences, over a period of one and half year (November 2012 to June 2014).

Size of the sample was 60 patients (30 patients in each group).

### Inclusion criteria

- All pregnant women with mild to moderate hypertension (systolic BP 140-160mm of Hg and diastolic BP 90-110mm of Hg)
- Age of the patient between 18-35 years
- Primigravida or multigravida
- Vertex presentation
- Singleton pregnancy

### Exclusion criteria

- Patient's age more than 35 years
- Severe pregnancy induced Hypertension (systolic BP  $\geq 160$ mm HG; diastolic BP  $\geq 110$ mm HG)
- Severe Pre-eclampsia (severe hypertension with proteinuria 2+ or more or 2g or more / 24 hrs, headaches, visual disturbances, epigastric pain)
- Chronic hypertension
- Multiple pregnancy
- Bad Obstetric History

30 patients received methyldopa and 30 patients received Labetolol. Patients received treatment as per the assessment of the treating obstetrician.

Informed consent was obtained from all the patients before enrolment. Medical and obstetric history was taken, and physical examination was conducted at the time of initial recruitment.

Outcomes measured were Birth Weight of the babies, Apgar score at one minute and 5 minutes, all other perinatal outcomes like Intra Uterine Growth Retardation,

Small for gestational age babies and admissions into NICU due to distress were also considered.

## Statistical analysis

Data were entered in MS excel 2007, same were exported into STATA (version 10). For normally distributed continuous data, comparison for significance of difference were done by using;

- Student's unpaired t test was used for comparison of normally distributed continuous data between the two treatment groups.
- Categorical data were analyzed for associations using chi square test.

P value  $< 0.05$  was considered statistically significant.

## RESULTS

This comparative study was carried out in obstetrics and gynaecology department in MediCiti institute of medical sciences, ghanpur, medchal. 30 patients receiving Methyldopa and 30 patients receiving Labetolol were included in this study.

Table 1 shows the comparison of birth weight (kg) between two groups of patients studied. The Mean birth weight was similar between two groups (P value= 0.409). Majority of newborns, 40% in Methyldopa group and 56.66% in Labetolol group weighed between 2.6-3kg.

**Table 1: Comparison of birth weight between two groups.**

Weight	Methyldopa	Labetolol
<2.5kg	12	9
2.6-3.5kg	18	21
total	30	30
Mean birth wt	2.649 $\pm$ 0.433	2.731 $\pm$ 0.318
P value	0.409	

Apgar score at 1 minute was 6 in 5 new borns in Methyldopa group and 1 new born in Labetolol group. There was no difference between two groups (P value= 0.062) statistically (Table 2).

**Table 2: Comparison of Apgar score at 1 minute in both groups.**

Apgar Score	Methyldopa	Labetolol
6	5	1
7	13	12
8	12	16
9	0	1
P Value	0.062, Non Significant	

Table 3 shows Apgar score at 5 minutes. 9 new borns in Methyldopa group and 4 new borns in Labetolol group has

Apgarscore of 8 after 5 minutes. Majority of new borns 14 (46.66%) in Methyldopa group and 18(60%) in Labetolol group had Apgar score of 10. There was no statistically significant difference between two groups (P value 0.155).

**Table 3: Comparison of Apgar score at 5 minutes in both groups.**

Apgar score at 5 mins	Methyldopa	Labetolol
8	9	4
9	7	8
10	14	18
P Value	0.155, Non Significant	

Table 4 shows the comparison of perinatal outcome between two groups of patients studied. IUGR were 10% in Methyldopa group and 6.66% in Labetolol group. 20% of new borns in Methyldopa group and 10% of new borns in Labetolol group got admitted in NICU because of distress. 13.3% of new borns in Methyldopa group are small for gestational age, whereas only 3.33% in Labetolol group are small for gestational age. There was no difference between two groups statistically. (P value 0.054).

**Table 4: Comparison of peri-natal outcomes between two groups.**

	Methyldopa	Labetolol
Normal	19	25
IUGR	3	2
NICU Admissions	6	3
SGA	4	1
P Value	0.054	

## DISCUSSION

Hypertensive disorders seem to complicate approximately 10% of pregnancies and are important causes of maternal and fetal morbidity and mortality.<sup>1</sup> The major goal of antihypertensive medication was to prevent adverse outcomes for the mother and fetus.

**Table 5: Comparison of mean birth weight with previous studies.**

Drugs	Present study	Verma, et al	Qarmalawi, et al
Methyldopa	2.649±0.433	2.6±0.36	2.77±0.15
Labetolol	2.731±0.318	2.5±4.3	3.00±0.15

Table 5 shows that mean birth weight of newborns did not differ in two groups. In the present study the mean birth weight was 2.649kg in Methyldopa group and 2.731 in Labetolol group, there was no statistically significant difference between two groups (P value=0.693). Present study findings were comparable with the study of Qarmalawi et al, where the Mean birth weight in Labetolol group was 3kg and 2.77kg in Methyldopa group.<sup>4</sup>

In Verma et al, study Mean birth weight of Methyldopa group was more than Labetolol group.<sup>5</sup> The Mean birth weight of the present study was also comparable with the studies of Plouin et al, Lamming et al.<sup>6,7</sup>

## Apgar score

There was no statistically significant difference between the two groups regarding Apgar Score at 1 minute (P value = 0.062, Non significant).

There was no statistically significant difference between the two groups regarding Apgar Score at 5 minutes (P value = 0.155, Non significant).

These findings were similar to Lamming et al, and Qarmalawi et al, where there was no statistically significant difference between two groups.

Table 6 shows that 3 patients among the Methyldopa group and 2 among the Labetolol group developed IUGR (P value = 1, Non significant). There was no significant difference between the two groups in the development of IUGR.

**Table 6: Comparison of peri-natal outcomes with previous studies.**

Drugs	Present study		Molvi S, et al	
	Methyldopa	Labetolol	Methyldopa	Labetolol
N, % of IUGR	3 (10%)	2 (6.66%)	18%	28%

Findings in the present study were comparable with the studies of Molvi et al, Plouin et al, Qarmalawi et al Lamming et al.<sup>8</sup> 4 patients in the Methyldopa group delivered SGA babies while only 1 patient in the Labetolol group delivered SGA baby (P value = 0.35, Non significant). There was no statistically significant difference between the two groups in having babies with SGA.

6 new borns, in the Methyldopa group were admitted in the NICU with RDS and 3 newborns in the Labetolol group were admitted in the NICU with RDS. There was no difference between the 2 groups statistically, as regards to NICU admissions (P value = 0.47, Non significant).

These findings were supported by previous studies by pickles et al, plouin et al, and walker et al, who have found no difference between two groups statistically.<sup>9,10</sup>

Limitations of the study was smaller sample size and single centre study.

## Recommendations

The results of this study need to be confirmed in multicentre studies with large sample size.

## CONCLUSION

There was no significant difference in the Mean birth weight of the babies and Apgar Score at 1 minute and 5 minutes.

Chances of development of IUGR, NICU admissions of neonates with respiratory distress syndrome and small for gestational age babies were more with methyldopa compared to Labetolol, but there was no statistically significant difference between two drugs.

The low incidence of maternal and fetal side effects together with excellent perinatal outcome confirms Labetolol suitability for use during pregnancy.

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