Publisher
MEDRESEARCH
www.medresearch.in

Obs Gyne Review - Journal of Obstetric and Gynecology

2024 Volume 10 Number 1 Jan-Dec

E-ISSN:2455-5444
P-ISSN:2581-4389
RNI:MPENG/2017/74037

Research Article

Tablet Labetalol

# Comparative Study Between Tablet Labetalol and Methyldopa In Treatment Of Pregnancy Induced Hypertension

**Sultana A[1*], Begum T[2], Siddique MAB[3], Akter A[4], Patuary S[5], Nasrin UT[6]**

DOI:10.17511/joog.2024.i01.04

[1*] Afroza Sultana, Medical Officer, Obstetrics and Gynae, Shaheed Ahsan Ullah Master General Hospital, Tongi, Gazipur, Bangladesh.
[2] Tashrin Begum, Senior Consultant, Obstetrics and Gynae, Shaheed Ahsan Ullah Master General Hospital, Tongi, Gagipur, Bangladesh.
[3] Md Abu Bakar Siddique, Assistant Professor, Department of Surgery, Shaheed Tajuddin Ahmad Medical College Hospital, Gazipur, Bangladesh.
[4] Ahsana Akter, Senior Consultant, Obstetrics and Gynae, Shaheed Ahsan Ullah Master General Hospital, Tongi, Gagipur, Bangladesh.
[5] Sakila Patuary, Junior Consultant, Obstetrics and Gynae, Shaheed Ahsan Ullah Master General Hospital, Tongi, Gagipur, Bangladesh.
[6] Ummae Tania Nasrin, Resident Surgeon, Obstetrics and Gynae, Shaheed Ahsan Ullah Master General Hospital, Tongi, Gagipur, Bangladesh.

**Background:** Pregnancy-induced hypertension is one of the most significant health problems in pregnancy. This is the 2nd most common obstetrics cause of maternal death in Bangladesh. It is the leading cause of infant morbidity and mortality.

**Methodology:** A randomized controlled trial was carried out among 100 pregnant women with pregnancy-induced hypertension (PIH) attending the Obstetrics & Gynaecology Department at Dhaka Medical College & Hospital from November 2010 to April 2011. 50 patients treated with tab. Labetalol (Group A) and 50 treated with tab. Methyldopa (Group B).

**Results:** Findings of the study showed mean age, gestational age and occupation did not differ significantly variation between Labetalol (group A) and Methyldopa (group B). Among 36% had gestational HTN, 62% had preeclampsia and 2% had eclampsia in group A. On the other hand in group B 32% had gestational HTN, 64% had preeclampsia and 4% had eclampsia. Among 23 patients in group A (46%) went in normal whereas (32%) went in normal vaginal delivery in group B. Maternal morbidity was more in Group B than in Group A. The most common morbidity was pulmonary oedema (6%) in group A and 14% had pulmonary oedema in group B. At the time of discharge, in the group, 85.41% of patients had normal blood pressure and 95.83% of patients had no proteinuria. Whereas in group B 80.43% had normal blood pressure and 91.30% had no proteinuria. The incidence of stillbirth was higher in the methyldopa group (group B). Low birth weight was lower in the labetalol group (group A).

**Conclusion:** It concluded that labetalol is more advantageous than methyldopa in terms of better and quicker control of blood pressure. The chances of normal vaginal delivery were greater in the labetalol group than in the methyldopa group.

**Keywords:** Pregnancy Induced Hypertension, Methyldopa, Labetalol

**Corresponding Author**

Afroza Sultana, Medical Officer, Obstetrics and Gynae, Shaheed Ahsan Ullah Master General Hospital, Tongi, Gazipur, Bangladesh.
Email: drafrozaruma@gmail.com

**How to Cite this Article**

Sultana A, Begum T, Siddique MAB, Akter A, Patuary S, Nasrin UT, Comparative Study Between Tablet Labetalol and Methyldopa In Treatment Of Pregnancy Induced Hypertension. Obs Gyne Review J Obstet Gynecol. 2024;10(1):25-31.
Available From
https://obstetrics.medresearch.in/index.php/joog/article/view/170

**To Browse**

| Manuscript Received | Review Round 1 | Review Round 2 | Review Round 3 | Accepted |
|---|---|---|---|---|
| 2024-09-20 | 2024-09-27 | 2024-10-04 | 2024-10-11 | 2024-10-18 |

| Conflict of Interest | Funding | Ethical Approval | Plagiarism X-checker | Note |
|---|---|---|---|---|
| None | Nil | Yes | 12.26 | |

# Introduction

Hypertension is a common medical disorder that affects 20-30% of adults in the United States and complicates as many as 5-8% of all pregnancies [1]. Pregnancy-induced hypertension remains a major cause of maternal and perinatal morbidity and mortality, especially in developing countries. [2], [3],[4]. Hypertension is defined as a sustained blood pressure higher than 140/90mm of Hg. [1] Pregnancy-induced hypertension (PIH), includes gestational hypertension. Preeclampsia, eclampsia [5]. Gestational hypertension, which develops after 20 weeks of gestation & complicates 5-10% of pregnancies [6].

Hypertension associated with proteinuria, greater than 0.3g/L in a 24-hour urine collection or 1+ by qualitative urine examination, after 20 weeks of gestation called preeclampsia. Convulsions occurring in a patient with preeclampsia are known as eclampsia [7]. Diagnosis of pregnancy-induced hypertension (PIH) depends on the presence of hypertension after 20wks of gestation and was normotensive before 20wks of gestation, oedema, headache, blurring of vision, epigastric pain, disturbed sleep, proteinuria etc.5 Management of pregnancy-induced hypertension (PIH) involves control of convulsion (if occurs), control of blood pressure, anticipation & treatment of complications and termination of pregnancy (depends on gestationalage) [6].

Maternal complications include eclampsia, pulmonary oedema, renal failure, abruptio placenta, post-partum circulatory collapse and even maternal death. Foetal complications include prematurity, intrauterine growth restriction, foetal death etc. [8] It is evident that PIH is very dangerous for both the mother and her baby, but most important of all is that it is preventable and treatable if proper and timely efforts are taken. [9],[10] Antenatal care is the key point in the selection of patients who are most likely to develop severe PIH are to be hospitalised, monitored carefully and pregnancy continued, if possible, up to a favourable state of foetus and termination of pregnancy is done with an expectation of good maternal & foetal outcome. But when due to the absence of or irregular antenatal checkup or failure of proper intention, a patient develops the fatal condition, her as well as foetal outcome worsens. So, a vital point in the management of PIH is to control blood pressure.

Various drugs have been used for these purposes such as methyldopa, labetalol, nifedipine, diazepam, phenobarbitone etc. The aim and objective of our study are to compare the efficacy of the two drugs, used in our country, labetalol and methyldopa.

# Methodology

**Study design:** It was a randomized controlled trial.

**Place of study:** Department of Obstetrics & Gynecology of Dhaka Medical College Hospital, Dhaka, Bangladesh.

**Duration of study:** November 2010 to April 2011.

**Study population:** This study was carried out among 100 pregnant women suffering from PIH attending Obstetrics & Gynaecology, Dhaka Medical College & Hospital, Dhaka, Bangladesh.

**Sample size:** To determine the sample size, the formula is n-z²pq/d² Where, n=desired sample size z=the standard normal deviation, usually set at 1.96 at a 5% level which corresponds to a 95% confidencelevel. Total duration of the study was 6 months & population size was roughly estimated at 130 (N), if N is <10,000 the required sample size will be smaller. In this case, the final sample estimated (nf) by using the following formula

$$\text{Nf}+\frac{n}{1+n/N}+\frac{384}{1+384/130}=97.1=100(target\ sample\ size)$$

**Grouping of the sample**

Group A 50 patients who were treated with tab. Labetalol.

Group B 50 patients who were treated with tab. Methyldopa.

**Inclusion criteria**

Patients who were diagnosed as a case of PIH 2.8.

**Exclusion criteria**

- Patients who did not give consent.
- Subjects who have diabetes, heart disease or any contraindication of beta-adrenoceptor blocker and unconscious [19]

**Study procedure**

100 patients with pregnancy-induced hypertension will be studied. All patients in study were less than 40 weeks pregnant and were normotensive before 20 weeks allocated to either of treatment groups who satisfied eligibility criteria were recruited.

Patients were given either labetalol 200-400mg twice daily or methyldopa 750-2000mg/day according to the patient's response to maintain a mean arterial pressure ≤130 mmHg. Venous blood was taken for biochemical analysis. Urine R/M/E were done to detect albumin.

**Procedure of data analysis of interpretation:** All data were entered, checked, rechecked & scrutinized by the principal investigator following standard procedure & were analyzed by the SPSS program. Chi-square tests were done at a significance level.

# Results

**Table 1:** Age distribution of the patients

| Age in years | Group A(n=50) | | | Group B(n=50) | | | P value |
|---|---|---|---|---|---|---|---|
| | NO | % | Mean±SD | NO | % | Mean±SD | |
| <20 | 2 | 4 | | 4 | 8 | 25.42±3.92 | 0.225 |
| 20-25 | 22 | 44 | | 23 | 46 | | |
| 26-30 | 20 | 40 | 26.50±4.87 | 21 | 42 | | |
| 31-35 | 6 | 12 | | 2 | 4 | | |
| Total | 50 | 100 | | 50 | 100 | | |

The table-1 shows a maximum of 44% were aged between 20-25 years followed by 40% were 26-30 years and 12% were 31-35 years in group A. On the other hand in group B maximum of 46% were aged between 20-25 years followed by 42% 26- 30 years age group and 4% were age group 31-35 years.

The average age was 26.50 years in group A and 25.42 years in group B. The difference was statistically not significant between the two groups(P>0.05).

**Table 2:** Distribution of gravidity

| Gravida | Group A(n=50) | | Group B(n=50) | | P value |
|---|---|---|---|---|---|
| | No | % | No | % | |
| Primi | 31 | 62 | 33 | 66 | 0.677 |
| Multi | 19 | 38 | 17 | 34 | |
| Total | 50 | 100 | 50 | 100 | |

Table-2 shows multigravida were more in group A than group B which was 38% vs 34% respectively. On the other hand, primigravida were more in group B than group A which was 66% vs 62% respectively. The difference was statistically not significant between the two groups(P>0.05). Table shows maximum patients were 34-37 weeks of gestational age between two groups group A (54%) and group B (46 %).

The difference was statistically not significant between the two groups(P>0.05).

**Table 3:** Distribution of pregnancy-induced hypertension between two groups

| PIH | Group A(n=50) | | Group B(n=50) | | P value |
|---|---|---|---|---|---|
| | No | % | No | % | |
| Gestational HTN | 18 | 36 | 16 | 32 | 0.792 |
| Preeclampsia | 31 | 62 | 32 | 64 | |
| Eclampsia | 1 | 2 | 2 | 4 | |
| Total | 50 | 100 | 50 | 100 | |

The table-3 shows that 36% had gestational HTN, 62% had preeclampsia and 2% had eclampsia in group A. On the other hand in group B 32% had gestational HTN, 64% had preeclampsia and 4% hadeclampsia.

**Table 4:** Blood pressure status of the study subjects

| Blood pressure(mmHg) | Group A(n=50) | | Group B(n=50) | | P value |
|---|---|---|---|---|---|
| | No | % | No | % | |
| SBP | | | | | |
| <160 | 32 | 64 | 34 | 68 | 0.673 |
| <160 | 18 | 36 | 16 | 32 | |
| DBP | | | | | |
| <110 | 29 | 58 | 31 | 62 | 0.683 |
| <110 | 21 | 42 | 19 | 38 | |

In systolic blood pressure maximum 64% were <160 mmHg and 36% were >160 mmHg in group A and groups group B 68% were <160 mmHg and 32% were >160mmHg In diastolic blood pressure maximum of 58% were <110 mmHg in group A and 62% were <110 mmHg and 38% were >110 mmHgingroupB.

**Table 5:** Mode of delivery

| Mode of delivery | Group A(n=50) | | Group B(n=50) | | P value |
|---|---|---|---|---|---|
| | No | % | No | % | |
| Normal vaginal | 23 | 46 | 16 | 32 | |
| delivery | | | | | 0151 |
| LSCS | 27 | 54 | 34 | 68 | |
| Total | 50 | 100 | 50 | 100 | |

The table-5 shows that 46% were normal vaginal delivery and 54% were LSCS. On the other hand in group B 32% were normal vaginal delivery and 68% were LSCS The difference was statistically not significant between the two groups(P>0.05).

Choup A= Labetol

Group B-=Methyldopa

**Table 6:** Time taken to control blood pressure

| Time taken | Group A(n-50) | | Group A(n-50) | | P value |
|---|---|---|---|---|---|
| | No | % | No | % | |
| Within 24 hours | 18 | 36 | 10 | 20 | |
| 2-3 days | 22 | 44 | 18 | 36 | |
| 4-7 days | 8 | 16 | 12 | 24 | 0.032 |
| >7 days | 2 | 4 | 10 | 20 | |
| Total | 50 | 100 | 50 | 100 | |

Table-6 shows that 36% in group A and 20% in group B had their blood pressure controlled within 24 hours. After 7 days of treatment, 4% of Group A and 20% of Group B patients remained hypertensive. The difference was statistically significant betweenthe twogroups.

**Table 7:** Maternal morbidity

| Complication | Group A(n=50) | | Group B(n=50) | |
|---|---|---|---|---|
| | No | % | No | % |
| Aspiration pneumonia | 2 | 4 | 5 | 10 |
| Pulmonary oedema | 3 | 6 | 7 | 14 |
| Cerebrovascular accident (CVA) | 0 | 00 | 2 | 4 |
| Disseminated Intravascular | 0 | 00 | 2 | 4 |
| coagulation (DIC) | | | | |
| Cardiac arrest | 2 | 4 | 0 | 0 |
| Postpartal shock | 2 | 4 | 1 | 2 |
| Postpartum haemorrahge | 0 | 00 | 1 | 2 |
| Psychosis | 0 | 00 | 1 | 2 |

Table-7 shows 4% had aspiration pneumonia, 6% had pulmonary oedema, 4% had cardiac arrest, 4% had postpartum shock and had no cerebrovascular accident (CVA), disseminated intravascular, postpartum haemorrhage and psychosis in group A.

**Table 8:** Fetal outcome

| Outcome | Group A(n=50) | | Group B(n=50) | | P value |
|---|---|---|---|---|---|
| | No | % | No | % | |
| Fetal outcome | | | | | 0.298 |
| Alive | 43 | 86 | 39 | 78 | |
| Stillbirth | 7 | 14 | 11 | 22 | |
| Birth weight: n= | 43 | | 39 | | 0.939 |
| ≤2.5 kg | 25 | 58.1 | 23 | 59.0 | |
| >2.5kg | 18 | 41.9 | 16 | 41.0 | |
| APGAR score: n= | 43 | | 39 | | 0.015 |
| <7 at 1 minute | 29 | 67.4 | 31 | 89.7 | 0.016 |
| <7 at 5 minutes | 15 | 34.9 | 24 | 61.5 | |
| Admission to neonatal ward:n= | 43 | | 39 | | 0.009 |
| Yes | 14 | 32.6 | 24 | 61.5 | |
| No | 29 | 67.4 | 15 | 38.5 | |

On the other hand in group B 10% had aspiration pneumonia, 14% had pulmonary oedema, 2% had a postpartum shock, 4% had a cerebrovascular accident (CVA), 4% disseminated intravascular coagulation, 2% had a postpartum haemorrhage and 2% psychosis. So it was observed that maternal morbidity was more in Group B thanin GroupA.

Majority were alive babies between the two groups which were 86% in group A and 78% in group B. 58.1% were birth weight ≤2.5 kg and 41.9% were birth weight >2.5 kg in group A. On the other hand in group B 59% were birth weight ≤2.5 kg and 41% were birth weight >2.5 kg. In APGAR scores <7 at 5 minutes were more in group B than group A which was 61.5% vs 34.9% respectively. Need admission to the neonatal ward was 32.6% in group A and 61.5%ingroupB.

# Discussion

Pregnancy-induced hypertension is a disease with worldwide significance to mothers and infants. Its greatest impact is in developing countries where it accounts for 20-40% of the strikingly increased maternal mortality. However, even in developed countries, there is a major effect, primarily on the fetus. In developed countries, perinatal mortality of infants of preeclamptic mothers is 5-fold greater than for non-preeclamptic women and indicated preterm deliveries for preeclampsia account for 15% of preterm births.[11]

In this study statistically, there was no significant age difference between group A and group B. The mean age of patients was 26.50±4.87 years in the control group and 25.42±3.92 years in the case group ranging from 18-40 years. Thedifference was statistically not significant (P>0.05). A maximum of 46% of patients were age group 20-25 years in group A. This finding is consistent with the study of Duckitt and Harrington in which they found young maternal age did not seem to affect the risk of developing pregnancy-induced hypertension. [12]

About the gravidity, the study revealed primigravida were more in group B than that of group A which was 66% vs 62% respectively but multigravida were more in group A than group B which was 38% vs 34% respectively. The difference was statistically significant between the two groups (P<0.05). So primgravida more significantly higher in group B than in group A women.

This finding is consistent with the findings of Dutta [13] which he has found the incidence of PIH in primigravida is about 10% and in multigravida 5%. The gestational age from 20 weeks to 40 weeks of both labetalol (Group A) and methyldopa (Group B). It showed the maximum patients were from 54 weeks to 37 weeks of gestational age between two groups, group A 54% and group 42%. The difference was statistically not significant between the two groups (P905) This study shows 30% had gestational HTN, 62% had preeclampsia and 2% had eclampsia in group A. On the other hand in group B 32% had gestational HTN, 64% had preeclampsia and 4% had eclampsia. This study shows systolic blood pressure maximum 64% were 160 mmHg and 36% were 160 mmHg in labetalol (Group A) and methyldopa (Group B) 68% were <160 mmHg and 32% were 160 mmHg in diastolic blood pressure maximum 58% were <110 mmHg in group A and 42% were 110 mmg in group B 62% were <110 mmHg and 38% were 110 mmHg. This is consistent with the findings of Roberts and Redman [14]. In the present study, 23 patients in group A (46%) went in normal vaginal delivery while 27 patients (66.67%) were LSCS. In group B, 16 patients (32%) went in normal vaginal delivery and 34 patients (68%) were LSCS. These values were found to be statistically not significant with ($p>0.05$). Thus the rate of normal vaginal delivery was more in patients treated with labetalol (group A). These findings are consistent with Subhedar et al [15]. The observation made by Garmalawi et al suggests a higher incidence of spontaneous onset of labour in thelabetalol group [16]. Lamming et al too reported a higher incidence of spontaneous labour in the labetalol group. [17]. This study shows that at the time of discharge, in group A 85.41% of patients had normal blood pressure and 95.83% of patients had no proteinuria. Whereas in group B 80.43% had normal blood pressure and 91.30% had no proteinuria. This is consistent with the finding of Michael [18] in which they have identified a relatively specific relation of proteinuria with preeclampsia. This study shows maternal morbidity was more in group B (methyldopa-treated group) than in group A (labetalol-treated group). The most common morbidity was pulmonary oedema (6%) in group A and 14% had pulmonary oedemaingroup B.The study conducted by Verma et al. [19] states that adverse events observed were lower in the labetalol-treated group compared to the methyldopa group. [19]

This study found that 36% of Group A and 20% of Group B had their blood pressure controlled within 24 hours. After 7 days of treatment, 4% of group A and 20% of group B patients remained hypertensive. The difference was statistically significant between the two groups. These findings consisted of D.J. Cruickshank, et al [20] who found 35% labetalol-treated women (88%) within 24 hrs. Interestingly, several other workers have found similar response rates. [21], [22] Incidence of stillbirth was more in the methyldopa group (group B). Low birth weight was lower in the labetalol group (group A). In APGAR scores <7 at 5 minutes were more in group B than group A which was 61.5% vs 34.9% respectively. Both methyldopa and labetalol are efficacious and safe for use in hypertensive disorders of pregnancy [23]. Parenterally, labetalol is used to treat severe hypertension whereas methyldopa is not among the recommended drugs for use in severe hypertension. [24] El-Qarmalawi, et al and Mahmoud, et al had earlier found better fetal and neonatal outcomes with labetalol. [25], [26]. This is also supported by a more recent meta-analysis. [27]

# Conclusion

This study showed that labetalol is more advantageous than methyldopa in terms of better and quicker control of blood pressure. The chances of normal vaginal delivery were greater in the labetalol group than in the methyldopa group. So, labetalol is comparable to methyldopa in treating and preventing adverse maternal, fetal and neonatal outcomes in pregnancy-induced hypertension during pregnancy. The development of pregnancy-induced hypertension is high in developing countries like Bangladesh where antenatal care is inadequate. Since this complication may be preventable in a large number of cases if detected and treated at an early stage, it is essential to detect the condition at an early stage and to provide adequate antenatal care induetime.

**Limitation**

- This study was undertaken in a tertiary-level hospital and a small number of patients. So, it does not reflect us actual scenariointhe country.

**Recommendation**

- In the context of the results of the present study, it is recommended to undertake further studies with large sample sizes.

- Large community-level studies should be done to support our results and should look for the ability of labetalol for pregnancy-induced hypertension.
- Patients should be instructed on proper BP measurement techniques if they are to perform home BP monitoring.
- All pregnant women should be assessed forproteinuria.

**Permission from Institutional research board:** Yes

**Funding:** Nil

**Conflict of interest:** None Initiated

# References

1. David A, Miller MD. Hypertension in pregnancy. In: Alam H eds. Current diagnosis and Treatment, obstetrics and Gynaecology 10th ed. *Lange Medical Publication 2007:318-26 [Crossref][PubMed] [Google Scholar]*

2. Walker JJ. Preeclampsia. Lancet 2000;356: 1260-5. . *[Crossref][PubMed][Google Scholar]*

3. World Health Organization. WHO International collaborate study of hypertensive disorders of pregnancy, geographic variation in the incidence of hypertension in pregnancy. Am J Obstet Gynecol 2008;158:80-3. . *[Crossref][PubMed][Google Scholar]*

4. Lopez-Jaramillo P. Garcia RG Lopez M. Preventing pregnancy induced hypertension: are there regional differences for this global problem? J Hypertens 2005;23:1121-9. . *[Crossref][PubMed][Google Scholar]*

5. Dutta DC. Hypertensive disorder in pregnancy. In: Koner H ed. Textbook of obstetrics including perinatology and contraception 5th ed. *New Central Book Agency (p) Ltd. 2001;233-56 [Crossref] [PubMed][Google Scholar]*

6. Magee LA, Ornstein MP, Dadelszen P. Management of hypertension in pregnancy. BMJ 1999;318:1332. . *[Crossref][PubMed][Google Scholar]*

7. Aris F. Hypertensive disorder in pregnancy. Practical guide to High Risk Pregnancy and Delivery 3rd ed. 2008;397-439. *[Crossref][PubMed][Google Scholar]*

8. Gibson P, Carson MD. Hypertension and pregnancy. Emedecine. Medscape. *com/article/261435 [Crossref][PubMed][Google Scholar]*

9. Sabour A. High blood pressure in pregnancy & coronary calcification. Hypertension 2007:2:75-80. . *[Crossref][PubMed][Google Scholar]*

10. Kincaid-Smith P, Bullen M, Mills J. Prolonged use of methyldopa in severe hypertension in pregnancy. BMJ 2006; 274-76. . *[Crossref][PubMed][Google Scholar]*

11. Sowers JR, Zemel MB, Bronsteen RA, Zemel PC, Walash MF, Standly PR. Sokol RJ. Erythrocyte cation metabolism in preeclampsia. Am J Obstet Gynecol 1989;161(2):441-445. *[Crossref][PubMed][Google Scholar]*

12. Jaramillo PL. Casas JP, Serrano N. Preeclampsia from epidemiological observation to molecular mechanism. Bart J Med Biol 2001;95. *[Crossref] [PubMed][Google Scholar]*

13. Ganong WF. Hormonal control of calcium metabolism and the physiology of bone, In: Review of Medical Physiology, 12th ed. New York; Mcgraw Hill Companies, Buston 2001;369-382. 26. *[Crossref][PubMed][Google Scholar]*

14. Roberts JM, Redman CW. Pre-eclampsia: more than pregnancy-induced hypertension. Lancet. 1993 Jun 5,341(8858):1447-51. *[Crossref][PubMed] [Google Scholar]*

15. Subhedar V, Inamdar S, Hariharan C, Subhedar S. Comparison of efficacy of labetalol and methyldopa in patients with pregnancy-induced hypertension. International Journal of Reproduction, Contraception. Int J Reprod Contracept Obstet Gynecol. *2013;2(1):27-34 28 [Crossref][PubMed] [Google Scholar]*

16. El-Qarmalawi AM, Morsy AH, al-Fadly A, Obeid A, Hashem M. Labetalol vs. methyldopa in the treatment of pregnancy-induced hypertension. Int J Gynaecol Obstet 1995; 49:125-30. *[Crossref] [PubMed][Google Scholar]*

17. Lamming GD & Symonds EM. Use of Labetalol and Methyldopa in Pregnancy-Induced Hypertension. Br J Clin Pharmacol. 2009;8:2178-228. *[Crossref][PubMed][Google Scholar]*

18. Michael CA. Use of labetalol in the treatment of severe hypertension during pregnancy. Br J Clin Pharmacol 2009; 8:2118-58. . *[Crossref][PubMed][Google Scholar]*

19. Verma R, Lahon K, Tonpay SD, Kale VJ, Jain DK. A comparative randomised controlled parallel group study of efficacy and tolerability of labetalol versus methyldopa in the treatment of new onset hypertension during pregnancy. Int J Life Sci Pharma Res 2012; 2:L23-31. . *[Crossref][PubMed][Google Scholar]*

20. Cruickshank DJ, Robertson AA, Campbell DM, MacGillivray 1. Does labetalol influence the development of proteinuria in pregnancy hypertension? A randomised controlled study. Eur J Obstet Gynecol Reprod Biol 1992;45:47-51. . *[Crossref][PubMed][Google Scholar]*

21. Lardoux H, Gerard J, Blazquez G, Chouty F, Flouvat B. Hypertension in pregnancy: evaluation of the two B-blockers atenalol and labetalol. Eur Heart J 2003;4(Suppl G):35-40. . *[Crossref][PubMed][Google Scholar]*

22. Michael CA. Use of labetalol in the treatment of severe hypertension during pregnancy. Br J Clin Pharmacol 2009; 8:211S-5S. . *[Crossref][PubMed][Google Scholar]*

23. Rosenthal T. Oparil S. The effect of antihypertensive drugs on the fetus. J Hum Hypertens 2002; 16:293-298. *[Crossref][PubMed][Google Scholar]*

24. Podymow T, August P. Update on the use of antihypertensive drugs in pregnancy. Hypertension 2008; 51:960-969. . *[Crossref][PubMed][Google Scholar]*

25. El-Qarmalawi AM, Morsy AH, Al-Fadly A, Obeid A, Hashem M. , Labetalol vs. methyldopa in the treatment of pregnancy-induced hypertension. Int J Gynecol Obstet 1995;49(2):125-130. *[Crossref][PubMed][Google Scholar]*

26. Mahmoud TZ, Bjornsson S, Calder AA. , Labetalol therapy in pregnancy induced hypertension: the effects on fetoplacental circulation and fetal outcome. Eur J Obstet Gynecol Reprod Biol 1993; 50(2):109-113. 39. *[Crossref][PubMed][Google Scholar]*

27. Abalos E, Duley L, Steyn DW, Henderson-Smart DJ. , Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Cochrane Database Syst Rev 2007 ;(1):CD002252, CD002252. . *[Crossref][PubMed][Google Scholar]*