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Comparison of Labetalol and Methyldopa's Effectiveness in Treating Hypertension in Pregnancy

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Abstract:

Background: A significant number of the population lacks access to healthcare in an Iraq-like country, despite the country's constant growth and development in the healthcare sector, the rate of fatal maternal deaths is still high.

The most common medical issue during pregnancy is high blood pressure. On a global scale, 6-8% of pregnancies are said to have been complicated by high blood pressure. Antihypertensive treatments are frequently utilized to lower the blood pressure in order to prevent the pressure from increasing to a level that would negatively affect the mother or baby. Using anti-hypertensive drugs reduces the likelihood of developing severe high blood pressure by half. Therefore, the goals of this study were to determine how well labetalol and methyldopa manage blood pressure in PIH patients and to look into the effects of pregnancy and the perinatal period.

Methods: 180 PIH patients were split into two groups at random. Following random assignment, group A was given 250 mg of methyldopa every other day, and group B was given 100 mg of labetalol. The formula employed to calculate the average pressure in the arteries (MAP) was 2 + 3.5 diastolic BP /6. Patients were monitored for signs of hypotension every six hours. Every day, the MAPs of the two groups were calculated to assess the effectiveness of a particular medicine. Observations regarding the drop in blood pressure with Labetalol/ Methyldopa were documented. the average amount of medication necessary to regulate blood pressure, the beginning of labor--induced or spontaneous--Bishop's initial score during the onset of labor's effects on drugs.

Results: The MAP of patients on labetalol decreased significantly. The average time required in group A to control B.P. was Group B had an average sleep duration of 36.97 hours, compared to group A's 42.22 hours. In the present study, group A's average Bishop score at induction was 8.27, but group B's was 9.33. The statistical analysis revealed a significant difference between the two groups, with $p<0.05$. In group B, 23 patients, or 48.94 percent of the patients, had spontaneous labor experience; in group A, 33.33 percent of the patients experienced spontaneous labor.

Final thoughts: Because of its effective hypotensive effect and lack of negative side effects on either the mother or the baby, labatalol is safe during childbirth.

Introduction

The mortality rate of mothers is still very high despite improvements in healthcare.

Precise estimates of the number of maternal deaths are still lacking. When you study the causes of fatalities during childbirth, you'll discover that the majority of fatalities are avoidable. Hypertensive disorders are one of the causes of this complexity, which accounts for 10% of pregnancies, and it is detrimental to both the mother and the baby[1]. One common medical condition that arises during pregnancy is high blood pressure. 2. Between 6% and 8% of people worldwide are thought to have hypertension. a pregnancy complicated by hypertension.[3] Pregnant women worldwide lose their lives to eclampsia and preeclampsia every three minutes.[2,4] Though doctors haven't done so yet, oral medicines are currently frequently utilized to treat pregnancy-induced hypertension. You have a lot on your plate. Antihypertensive drugs are used to reduce blood pressure in order to stop it from getting worse and from having an adverse effect on the fetus and mother. Antihypertensive drugs can lower the chance of developing high blood pressure..[5] Treating severe hypertension may prevent serious complications in mothersr.[6] 6 These are long-acting methyldopa, labetalol, and nifedipine.

Pregnant women who exhibit mild to moderate hypertension symptoms are to be closely monitored while taking oral antihypertensive medicines. In addition to comparing the side effects on the mother and the perinatal period, the purpose of this study was to assess how successfully labetalol and methyldopa controlled blood pressure in pregnant women with pregnancy-induced hypertension.[7].

Methods:

The study was carried out at the Department of Obstetrics and Gynecology at the Imam Sadiq Teaching Hospital and Al Shira General Teaching Hospital in Iraq over a two-year period, from February 2020 to December 2022..

Study population: women who develop hypertension after 20 weeks of pregnancy

180 PIH patients were included in the sample; 90 received labetalol treatment and 90 received methyldopa treatment. Patients who passed the subsequent tests were chosen: (i) Health history (ii) clinical assessment, including systemic and general examination.

Inclusion criteria: hypertensive pregnant ladies according to the following standards:

Six hours later, blood pressure was measured twice and found to be greater than 140/90 mmHg both times.

2-From 20 weeks of gestation to the due date, two midstream urine samples were used to obtain Albuminuria 1+ test strips at 4-hour intervals.

Exclusion criteria:

1. Multiple pregnancy.
2. Eclampsia.
3. Pregnant women who have comorbidities or pre-existing medical disorders, such as diabetes, thyrotoxicosis, renal illness, heart disease, hemophilia, or chronic hypertension, may experience pregnancy-related hypertension.

Following randomization, the patients were split into two groups at random: Group B was given labetalol 100 mg three times a day, while Group A was given methyldopa 250 mg three times a day. Systolic + 2 (diastolic)/3 is the formula used to calculate mean arterial pressure (MAP)..[8]

Monitor the patient's blood pressure every 6 hours. Comparisons between the two drugs were based on mathematical comparisons of daily MAP in both groups. Adjust the dosage of these drugs according to changes in blood pressure. If blood pressure does not fall after 48 hours of treatment, double the dose. The blood pressure lowering response was assessed over a period of one week. A reduction in blood pressure has been observed. labetalol/methyldopa, the amount of time needed to get blood pressure under control, and the typical dosage of medication needed to accomplish so. Bishop has achieved results in initiating contractions and pharmaceutical adverse effects in both

natural and induced labor. Outcomes The chi-square test was used to statistically examine and analyze the results that were acquired in this manner. It was determined that a p value of less than 0.05 was statistically significant..

Result:

The distribution of ages and the total number of patients are displayed in Figure 1. There are 180 patients in all. Ninety-two cases, or 48 cases (53.33%) in group A and 44 cases (4889%) in group B, were between the ages of fifteen and twenty-four. Patients in groups A and B were 24.41 and 24.85 years old on average. The two groups' mean ages did not differ statistically. There were 102 primiparous patients in this trial, 53 (58.89%) in the methyldopa group and 49 (54.44%) in the labetalol group, as Figure 2 illustrates. Between the two groups, there is no statistically significant difference.

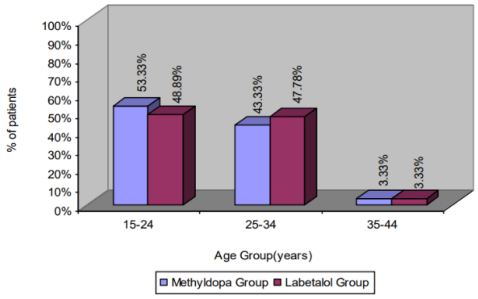

Figure 1: Patient age distribution in the two groups.

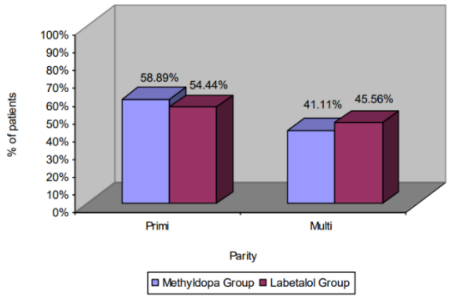

Figure 2. compares the two groups' MAP values on days one and seven.

Patients receiving methyldopa had their mean arterial blood pressure evaluated in this study. After seven days, the blood pressure reduced to 98.15 mmHg with a statistically significant p value < 0.05, from 109.86 mmHg upon admission. The mean arterial pressure for labetalol was roughly 109.48 mmHg on day 1 and dropped to 96.90 mmHg on day 7. There was a statistically significant decrease in MAP. When MAP was compared between the two medications at admission, it was shown that individuals receiving the second medication had a significantly lower MAP on day 7.

Table 1: Comparison of the two groups' MAPs on days 1 and 7.

Day	Group N	Mean [mmHg]	Std. Deviation	Mean Difference	p-value
Day 1	Methyldopa 90	109.86	2.91	0.37±0.42	0.37
Day 1	Labetalol 90	109.49	2.78	0.37±0.42	0.37
Day 7	Methyldopa 90	98.15	3.44	1.24±0.46	0.008
Day 7	Labetalol 90	96.90	2.70	1.24±0.46	0.008

Table 2 compares the time required to regulate blood pressure between the two groups. In this study, the average time spent controlling blood pressure was 42.22 hours in group A and 36.97 hours in group B. The difference between the two: labetalol has statistical significance in early lowering blood pressure in both groups of patients.

Table 2: Comparison of the two groups' blood pressure control times.

Group N	Mean [hours]	Std. Deviation	Std. Error	Mean	p-value
Methyldopa	90	42.22	3.04	0.32	0.000
Labetalol	90	36.97	2.94	0.31	

The mean dose needed to manage blood pressure in Group A is depicted in Figure 3. It is 1111.11 mg per dose. Forty patients (44.4%) were in Group A. In 20 of the 40 patients who remained, or 22.2%, the ideal blood pressure management was attained with a daily dose of 750 mg. It takes 1000 mg per day to have the best blood pressure control. A daily dosage of 1500 mg was necessary for the remaining 20 patients (22.2%) in order to attain satisfactory blood pressure management. For the best blood pressure management, 10 people need 2000 mg daily.

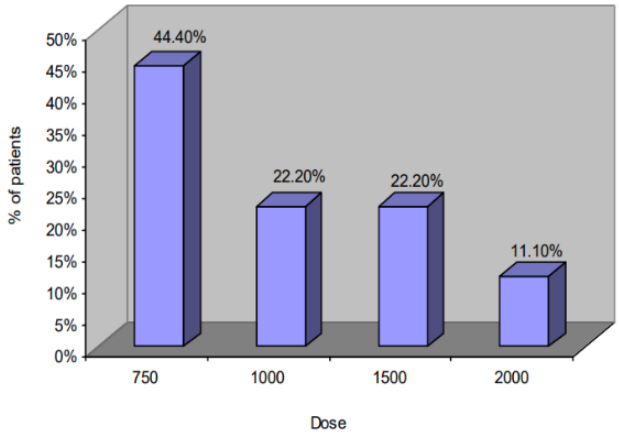

Figure 3: Patients in the methyldopa group are distributed according to dosage

According to Figure 4, the average required dose in Group B was 382.22 mg. Using 300 mg/day, 50 patients (55.6%) maintained blood pressure within the control range. Twenty subjects (22.2%) required a dose of 400 mg/day. Of the remaining 20 patients, 10 (11.1%) required 500 mg/day and 10 (11.1%) required 600 mg/day.

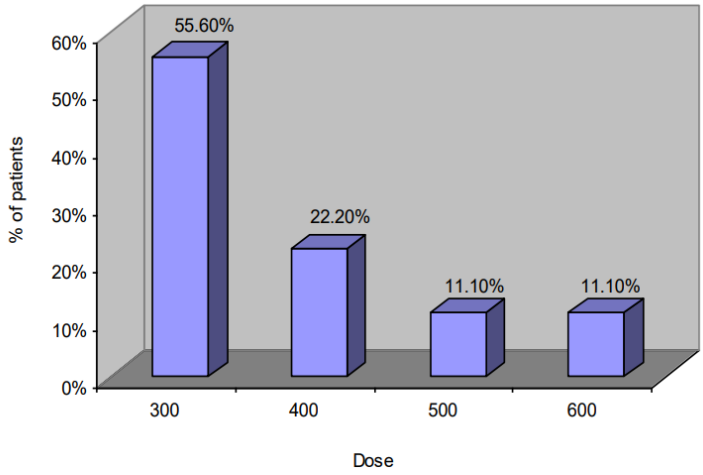

Figure 4: Distribution of patients in the labetalol group by dose.

Nine patients in the first group in the current study went into spontaneous labor, whereas the remaining eighteen patients experienced labor that was induced. Twenty-three spontaneous labors and twenty-four induced labors were recorded in group B; these figures were deemed statistically significant ($p < 0.05$). Consequently, spontaneous deliveries occur more frequently in patients on labetalol treatment. The effects of labetalol on cervical ripening may help to explain this.

These findings are displayed in Figure 5, and a comparison of the two sets of Bishop scores is shown in Figure 6. The average Bishop score at induction in this study was 9.33 for group B and 8.27 for group A, with a statistical significance of $p < 0.05$.

Figure 7 displays the patient distribution based on side effects. In the current investigation, headaches were the most often reported adverse impact. Ten trial participants in arm A and eight patients in arm B both experienced the symptoms. Additional adverse effects include somnolence (which is more common in individuals receiving methyldopa treatment) and weakness (which is more common in people receiving labetalol). Myalgia, vomiting, and nausea were among the side effects that both groups experienced equally frequently.

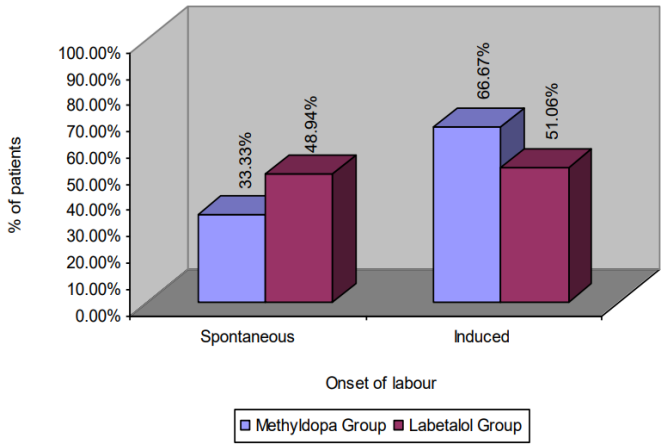

Figure 5: Patients divided into groups for vaginal birth following the start of labor.

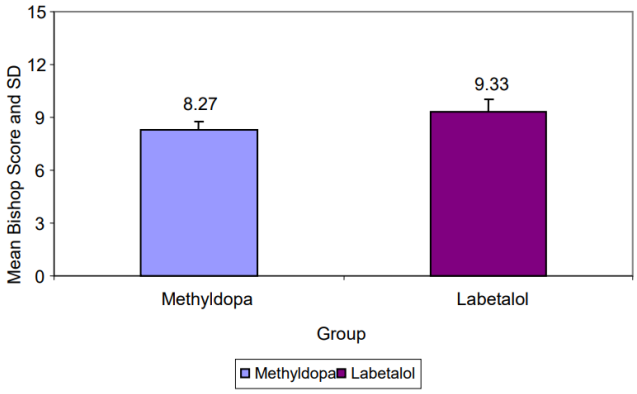

Figure 6: Bishop scores were compared between the two groups.

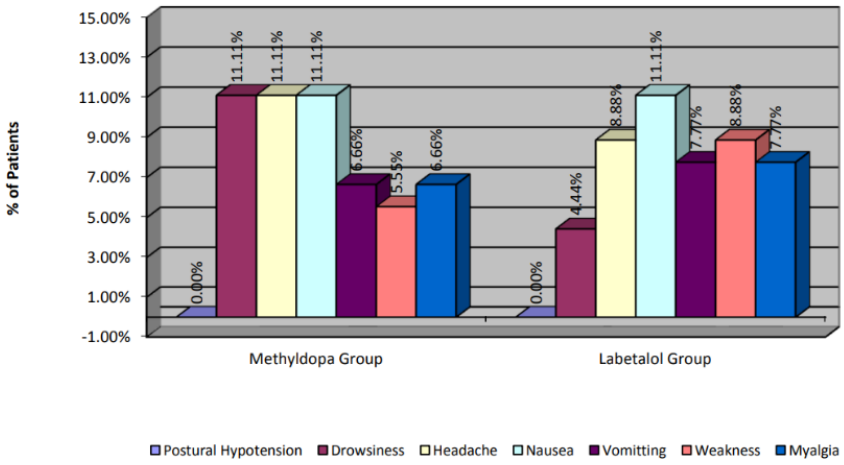

Figure 7: Patients are grouped based on side effects.

Discussion:

In the said study that involved 180 patients, most of those who belonged to Arms A and B, which corresponded to the methyldopa and labetalol groups, respectively, were aged between 15 and 24 years. As for pregnancy distribution, all gestational hypertension cases were observed among primigravida patients, regardless of group assignment. On admission, the patients who received methyldopa had a mean arterial pressure of 109.86 mmHg, but this value dwindled significantly to 98.15 mmHg by day 7, with a noteworthy p-value <0.05. Similarly, after initiation of treatment using labetalol, the mean arterial pressure of patients decreased from 109.48 mmHg during admission to 96.90 mmHg on day 7. On day 7, those taking labetalol experienced a statistically significant decrease in MAP. Interestingly, the comparison of MAP on admission for both drugs was not significantly different. Lamming et al.'s research notes that the mean MAP of both groups was similar before treatment.

MAP dropped dramatically in the group treated with labetalol ($p<0.001$), but not in the group treated with methyldopa ($p>0.05$).[8].

In a comparable trial, 81.4% of patients receiving labetalol experienced a statistically significant drop in MAP, while 68.5% of patients receiving methyldopa experienced the same decrease (El Qarmalawi et al.).[9].

In the current study, blood pressure control took an average of 42.22 hours for Group A and 36.97 hours for Group B. The two groups differed statistically significantly, with labetalol reaching blood pressure management earlier than methyldopa.

The mean duration required by both cohorts to attain ideal blood pressure levels. Comparable is a research by Sanders et al. on management.

.[10].

According to D.J., Labetalol has Cruickshank et al..[11], Forty-five of 51 treated women (88%) experienced a reduction in blood pressure in less than 24 hours. A clear advantage is the rapid control of blood pressure with oral labetalol, with 88% (45/51) of cases achieving an acceptable response within 24 hours. Notably, many other researchers found similar response rates (82% by Lardoux's group and 92% by CA Michael).[11, 13]

Significant drops in both systolic and diastolic blood pressure were noted by S. F. Hans; these drops typically happened 24 to 48 hours after starting methyldopa medication..[14].

Achieving the desired blood pressure level of group A required an average dose of 1111.11 mg. Approximately 44.4% of patients in Group A reached their target blood pressure when taking a daily dosage of 750 mg. The remaining 55.6% required a higher dose - 22.2% required a daily dose of 1000 mg, and another 22.2% needed 1500 mg. To accomplish target blood pressure regulation, 10 patients had to consume 2000 mg each day.

Taking 300 mg daily to regulate blood pressure was done by fifty individuals in Group B, which accounts for 55.6%. Whereas, a daily dosage of 400 mg was required by twenty patients, roughly 22.2%. The mean dose needed by the group was 382.22 mg.

The labetalol study found that 10 of the final 20 subjects needed either a daily 500 mg dose or a daily 600 mg dose to control their blood pressure, accounting for roughly 11.1% each. Meanwhile, the mean daily maintenance dose for methyldopa recorded by Sanders et al. was 1183 mg, with labetalol coming in at 810 mg. Surprisingly, despite similar doses, the study showed that labetalol required significantly less medication compared to Sanders et al.'s study. Conversely, the labetalol research team discovered that an average of 600 mg was the sweet spot for controlling blood pressure, as opposed to the 810 mg recorded by Sanders et al. Overall, twelve participants received the optimal dose.

A remarkable observation came to light during the study where labetalol was administered to patients. In Group A, a total of 9 patients (33.33%) had the privilege of experiencing spontaneous labor, while 18 patients (66.67%) had to undergo induction of labor. However, in Group B, 23 cases

(48.94%) had natural childbirth and 24 cases (51.06%) underwent induction of labor. A statistically significant difference was noted in these values at $p<0.05$. This suggests that labetalol tends to increase the probability of spontaneous labor, which could be explained by its cervical ripening effects.

According to the observations of Qarmalawi et al. Natural labor occurred more frequently in the labetalol group[9]. According to Laming et al. Spontaneous contractions also occurred more frequently in the labetalol group[8]. During the induction phase, Group A boasted an average Bishop score of 8.27 while Group B had 9.33; $p<0.05$ showed statistical significance. Research by Laming et al. concludes that labetalol-treated individuals, on average, possess a 10 Bishop score, while the corresponding score for methyldopa-treated patients is 7.1.8. Headache, one of the most frequently cited side effects, affected 10 members of Group A and eight from Group B. Incidences of asthenia and somnolence were noted in patients who had been administered methyldopa and labetalol, respectively. The group that experienced similar occurrences of nausea, vomiting, and myalgia consisted of both subjects..

According to a study by Verma et al. The labetalol group had fewer side effects than the methyldopa group[15]. A study by Qarmalawi et al reported on patients taking methyldopa. Adverse symptoms such as drowsiness (22.2%), headache (14.8%), nasal congestion (7.4%), and orthostatic hypotension (5.6%) were reported[9]. Six patients in the labetalol group reported only dyspnea; no other side effects were reported.

Conclusion:

In comparison to methyldopa, labetalol was shown to be a superior blood pressure regulator in this investigation, with faster and more effective results. Additionally, those in the labetalol group had a greater likelihood of delivering spontaneously than those in the methyldopa group. Patients who were taking labetalol and needed labor induction at the time had higher Bishop scores. It's important to note that labetalol is a safe antihypertensive drug to use during pregnancy without any adverse effects on the mother or fetus. Furthermore, it can decrease perinatal mortality rates that usually result in higher instances of fetal miscarriage.

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