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Treatment of gestational hypertension with oral labetalol and methyldopa in Iraqi pregnant women

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SUMMARY

AUTHORS' CONTRIBUTION: (A) Study Design · **(B)** Data Collection . **(C)** Statistical Analysis · **(D)** Data Interpretation · **(E)** Manuscript Preparation · **(F)** Literature Search · **(G)** No Fund Collection

Background: NICE guidelines recommend labetalol as first-line antihypertensive therapy for gestational hypertension and pre-eclampsia, while methyldopa and nifedipine are also available. Pre-existing medications and adverse effect profiles should be considered when choosing an antihypertensive therapy during pregnancy. It investigated how well oral labetalol and oral methyldopa treated hypertension in expectant women. This study aims to determine whether labetalol can be administered as a monotherapy for hypertension and to lower the danger of adverse effects, monotherapy is crucial.

Methods: Observational prospective cohort research was undertaken by the Obstetrics and Gynecology Department of Baghdad Teaching Hospital at Medical City/Baghdad, as well as the Gynecology Clinic. As a single agent, using the maximal dosage of labetalol. A total of 60 pregnant women were separated into two groups (A, and B). Group A was given oral labetalol, whereas Group B was given oral methyldopa.

Results: A few people require the addition of additional treatment (13.3%). Methyldopa was required by almost 87% of patients, with a statistically significant (p-value of 0.02). Additionally, with a p-value of 0.13, most patients didn't require a dose modification. Methyldopa and labetalol had statistically significant side effects in patients, with 83.3% and 16.7% respectively. The mean difference in SBP and DBP post-treatment was not significant in either group. The association between type of side effect and drug is significant between using methyldopa and labetalol, with a p-value of 0.03 compared to labetalol. The time required to control BP was also significant in the labetalol group.

Conclusions: Treatment of pregnancy hypertensive disorders is correlated with decreased blood pressure levels and adverse effects.

Keywords: Labetalol; Gestational hypertension; Methyldopa; Antihypertensive therapy; National Institute for Health and Care Excellence (NICE)

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INTRODUCTION

Hypertension, whether chronic or due to pregnancy, is a common pregnancy concern. About 5–10% of pregnancies are complicated by hypertensive disorders of pregnancy, which result in maternal, fetal, and neonatal morbidity and death [1]. It can cause stroke and death if it is severe, but early detection and treatment can lower the risk of these problems [2]. Hypertension is defined as Systolic Blood Pressure (SBP) ≥ 140 mmHg and/or Diastolic Blood Pressure (DBP) ≥ 90 mmHg on two different occasions during pregnancy. The first trimester of a normal pregnancy sees a progressive fall in blood pressure due to a decrease in systemic vascular resistance. It reaches a low point at 22-24 weeks, and then rises from 28 weeks to preconception levels by 36 weeks [3].

There are four categories, according to the American College of Obstetricians and Gynecologists (ACOG) criteria [4]:

1. Hypertension that is chronic or pre-existing, preconception or before 20 weeks of pregnancy, with a postpartum period of more than 42 days.
2. Gestational Hypertension, after 20 weeks of pregnancy, appears and normally goes away within 42 days following delivery.
3. Preeclampsia/Eclampsia.

Gestational hypertension is accompanied by one of the following:

1. Proteinuria.
2. Uteroplacental dysfunction (fetal growth restriction, abnormal umbilical artery Doppler waveform analysis, or stillbirth).
3. Maternal organ dysfunction includes the following:
   - Acute kidney injury.
   - Liver involvement (transaminitis) with or without right upper quadrant or epigastric abdominal pain.
   - Neurological complications (eclampsia, altered mental status, blindness, stroke, clonus, severe headache, persistent visual scotomata).
   - Hematological complications (decreased platelet count <150,000/uL, disseminated intravascular coagulation, hemolysis).

Epidemiology

According to the National Health and Nutrition Examination Survey (NHANES), the prevalence of hypertension among reproductive age (20-44 years old) is around 7.7%, and that of chronic hypertension during pregnancy varies between 0.9 and 1.5% [5,6].

Pathophysiology

A chronically hypoxic, defective placenta releases harmful chemicals into the maternal blood due to insufficient Spiral Uterine Artery (SUA) remodeling by Extra-Villous Trophoblasts (EVTs). Antiangiogenic factors, microparticles (including pro-inflammatory mediators), cell-free nucleic acids, oxidized lipids, and free radicals have all been identified as placental factors capable of triggering ED and the syndrome. They can cause second-order mediators such as autoantigens bodies against Angiotensin receptor 1 (AA-AT1) or effectors like Endothelin-1 (ET-1) and superoxide to be produced in the maternal circulation [7].

Risk factors

Hypertension, obesity, diabetes mellitus, advanced age, hypercholesterolemia, dyslipidemia, microalbuminuria, antiphospholipid syndrome, vasculitis, and thrombophilia are only a few of the risk factors. A previous history of preeclampsia (PE), multiple pregnancy, twin birth, a family history of PE, and nulliparity are also clinical risk factors [8,9].

Diagnosis & monitoring blood pressure

BP should be measured in either a seated or left lateral recumbent posture (during labor) using an appropriately sized arm cuff at heart level and Korotkoff for Diastolic BP (DBP). Patient convenience, greater treatment adherence, confirmation of white coat hypertension, and aid with medication adjustments, when there is a question,are all advantages of out-of-office and self-monitoring. Furthermore, the majority of home blood pressure monitors are marketed without official certification of exact readings [10,11].

Prevention

The ESC has been recommended 100–150 mg of aspirin daily from week 12 to weeks 36–37 for both high- and moderate-risk women [12]. The ACOG recommends a low-dose aspirin daily beginning in the late first trimester for women with a history of early-onset preeclampsia and preterm delivery at less than 34 weeks of gestation or for women with more than one prior pregnancy complicated by preeclampsia [13]. The USPSTF recommends the use of low-dose aspirin (81 mg/day) as preventive medication after 12 weeks of gestation in women who are at high risk for preeclampsia [14].

Management

ACOG recommends antihypertensive medication when blood pressure is consistently increased to >160 mmHg systolic and/or >105 mmHg diastolic, while European guidelines recommend drug treatment in women with gestational hypertension [1]. Chronic Hypertension and Pregnancy (CHAP) project CHAP project randomly assigns pregnant women to either receive antihypertensive therapy or no antihypertensive or low-dose therapy to keep blood pressure below 160/105 mmHg [15].

Non-pharmacological management

The most prevalent key factor in the therapy of hypertension is lifestyle adjustment. Between (10-20) weeks of pregnancy, especially in women who are overweight (BMI 25 kg/m^2). Women with a BMI of less than 30 kg/m^2 are recommended not to acquire more than 6.8 kg during pregnancy [16].

Pharmacological treatment

When treating pregnant women, the efficacy of the antihypertensive medicine must be balanced against the risks to the fetus. For the treatment of a severe form of hypertension, the choice of antihypertensive drug and method of administration is dependent on the predicted delivery time. Because of the severity of poisoning sodium nitroprusside, should be used only as a last option for cyanide poisoning in a fetus, intravenous labetalol, oral methyldopa, or nifedipine should be administered initially [1,17].

Beta-blockers

Beta-Blockers (BBs) are the most prescribed medicine during pregnancy and breastfeeding. Asthma is a common contraindication, and using BBs might cause bronchospasm. One of the most prescribed medicines for Hypertension During Pregnancy (HDP) is labetalol. Labetalol inhibits both alpha and beta-adrenergic receptors. Early investigations in experimental models revealed that it may protect uteroplacental blood flow to a higher extent than standard beta-blockers, making it the favored medication in this class. In cases of a severe type of HTN, it can also be given intravenously. Because BB can induce fetal bradycardia or intrauterine growth retardation, the fetus must be closely monitored. When administered early in pregnancy, drugs that lack alpha-blocking qualities (such as atenolol) have been linked to decreased placental and fetal weight at birth, and are typically avoided if a more effective treatment with a better safety profile is available [1,18-20].

Calcium channel blockers

Most recommendations recommend Calcium Channel Blockers (CCBs), such as long-acting nifedipine, as a first-line treatment. In pregnancy, nifedipine is the most often used medication in this class. It comes in three different formulations: immediate-release rapid-acting, intermediate-acting, and extended-release. We prefer to utilize a recipe with an intermediate or prolonged-release time [1,21,22].

Methyldopa

Methyldopa is commonly used in pregnant women, and its long-term safety for the fetus has been shown. However, it is just a moderate antihypertensive with a long onset of effect (3 to 6 hours). Methyldopa has been used for decades, and its safety is more proven than that of other antihypertensive drugs, administered this drug with the belief that women who were given methyldopa had better results than those who were given labetalol, albeit the findings might be skewed by residual effects [23,24].

Hydralazine

Intravenous hydralazine has been widely used for the treatment of acute severe hypertension in pregnancy for many years and has a good antihypertensive effect. Although hydralazine may be given orally, it might produce reflex tachycardia and fluid retention, limiting its usage during pregnancy. Blood pressure lowering is less predictable with oral labetalol than with IV labetalol [25].

Thiazide diuretics

Except for the treatment of pulmonary edema, diuretics are rarely used during pregnancy. For decades, the function of thiazide diuretics has been a topic of debate; however, some recommendations imply that these medications can be continued in women with persistent hypertension who were on them before pregnancy [6].

Drugs to avoid in pregnancy ACE inhibitors, ARBs, and direct renin inhibitors

When women are exposed to Renin-Angiotensin-Aldosterone System (RAAS) inhibitors during the second or third trimester of pregnancy, they have been linked to oligohydramnios, intrauterine growth restriction, and a variety of renal and other congenital disorders [4].

Mineralocorticoid receptor antagonists

Mineralocorticoid Receptor Antagonists (MRA, e.g., spironolactone, eplerenone) are typically not indicated for the treatment of hypertension in pregnancy. They're also diuretics, and they're very good for salt-sensitive hypertension and hyperaldosteronism patients. Spironolactone has never been demonstrated to be safe during pregnancy since it crosses the placenta. One case report of ambiguous genitalia in a human infant delivered to a woman who had been treated with spironolactone, as well as a few examples of healthy newborns following spironolactone exposure, were recorded in a review [26]. While it is uncertain if eplerenone, an MRA without anti-androgenic properties that were released around 20 years ago, is safe for a human pregnancy because experience is limited to a few case studies that did not reveal severe fetal consequences [27-29].

Nitroprusside

Nitroprusside would be the last medication for the treatment of refractory severe HTN. As a result, in an emergency, it should only be used for a brief time [30].

Choice of drug & dosing acute therapy for severe hypertension

A comprehensive evaluation of medications for the treatment of very high blood pressure in pregnancy found that the antihypertensive drug of choice is determined by the physician's experience and comfort with the drug, as well as side effects and patient preferences [31].

First-line drugs Intravenous use of labetalol or hydralazine as a first-line treatment for severe hypertension. During acute treatment of severe hypertension, the heart rate of a fetus should be regularly monitored.

Labetalol

Intravenous labetalol is recommended as a first-line treatment because it is efficacious, has a fast start of action, and has a favorable safety profile. If blood pressure stays above aim, start with 20 mg intravenously over 2 minutes, followed by doses of 20 to 80 mg at 10-minute intervals, up to a maximum total cumulative dose of 300 mg if blood pressure remains above target [21,32].

Hydralazine

Intravenous hydralazine has an acceptable antihypertensive effect and is used to treat acute severe hypertension in pregnant women. The hypotensive reaction to IV hydralazine is not as dramatic as it is with labetalol. Even though hydralazine may be given orally, it produces reflex tachycardia and fluid retention, limiting its usage during pregnancy. Its dosage is to start with a 5 mg IV bolus over 1 to 2 minutes; if the blood pressure goal is not met within 20 minutes, deliver a 5 to 10 mg bolus, depending on the first response. If hydralazine fails to work, ACOG recommends shifting to labetalol [30,32,33].

Nifedipine

When a patient has severe HTN (160/110 mmHg) and symptomatic hypertension, nifedipine is utilized as the first-line treatment for acute blood pressure lowering, and it is recommended to use the immediate-release rapid-acting formulation of nifedipine. Because of concerns regarding the consequences of immediate-release quick-acting nifedipine's rapid and significant blood pressure lowering. In the absence of intravenous access, the ACOG committee opinion approved immediate-release rapid-acting nifedipine as a first-line alternative for emergency treatment of acute, severe hypertension in pregnancy or postpartum [30,34].

Target blood pressure

When treatment is recommended, we focus on reducing mean arterial pressure by no more than 25% over 2 hours to achieve goal blood pressures of (130-150) mmHg systolic and (80-100) mmHg diastolic. As soon as feasible, BP should be lowered to safe levels.

Prolonged antihypertensive treatment might cause cerebral or myocardial ischemia or infarction if blood pressure falls below the range where tissue perfusion can be maintained by autoregulation [35].

Beta-blockers (including labetalol) are considered fourth-line antihypertensive therapies by NICE and are not recommended as first-line drugs for the treatment of hypertension outside of pregnancy. Women should be offered treatment based on their current prescription, adverse effect profiles, and potential teratogenicity. Hypertension is estimated to complicate around 8% of pregnancies and encompasses pre-existing (chronic) hypertension, gestational hypertension (de novo hypertension >140/90 mm Hg after 20 weeks gestation), and pre-eclampsia (worsening pre-existing or de novo hypertension with proteinuria) [36].

There is enough evidence to recommend labetalol as the first-line therapy for hypertension in pregnancy. Labetalol is a racemate that inhibits alpha and non-selective beta-adrenoceptors. Once blood pressure exceeds 150/100 mm Hg, the NICE recommends labetalol as a first-line antihypertensive medication for non-severe (160/110 mm Hg) pregnant hypertension and pre-eclampsia [37].

NICE recommends labetalol as a first-line antihypertensive agent for gestational hypertension and preeclampsia since it has been proven to be "as effective and safe as other antihypertensive agents" in the treatment of these disorders and has a pregnancy license. Beta blockade is three to seven times more powerful than alpha blockade with labetalol. Beta adrenoceptor blockage prevents reflex sympathetic stimulation of heart rate and cardiac output while also reducing renal renin production, while alpha blockade causes reduced peripheral vascular resistance and hence vasodilation, lowering blood pressure. When taken with meals, labetalol undergoes substantial first-pass hepatic metabolism and has higher bioavailability. Peak plasma concentrations normally occur 2 hours after oral intake, with the greatest blood pressure-lowering impact occurring 1 to 2 hours afterward [20,38].

Lethargy, weakness, and somnolence are all possible side effects, and it's not recommended for women with asthma since it might induce bronchospasm. The only antihypertensive medication with a Medicines and Healthcare Regulatory Agency license for use during pregnancy is labetalol, however, this is mostly due to the challenges and indifference surrounding drug licensing for use during pregnancy. Despite this, the manufacturers of labetalol recommend that it be avoided during the first trimester because it can cause hypertension or pre-eclampsia, and it may not be feasible for women with chronic hypertension who would benefit from other agents anyway; however, the fetal risks of labetalol appear to be low [36].

Labetalol may be used to treat chronic hypertension in pregnant women, but the evidence for treating persistent hypertension in the first trimester is limited. A recent meta-analysis found that antihypertensive treatment reduced severe hypertension incidence compared to non-active treatment, with no difference in adverse perinatal outcomes [39].

Methyldopa's antihypertensive effects stem from methylated catecholamine analogs in the central nervous system, affecting noradrenaline synthesis. Randomized controlled studies show no harmful effects in offspring [40,41]. NICE, on the other hand, advises against cessation in the postnatal period due to the risk of depression. Methyldopa is the medicine of choice for hypertensive conditions in pregnancy in several countries. Despite this, there is little proof of its safety in early pregnancy. So far, most methyldopa safety studies have focused on therapy during the second and third trimesters [36,42,43].

PATIENTS AND METHODS

Study design

Observational prospective cohort research was undertaken by the Obstetrics and Gynecology Department of Baghdad Teaching Hospital at Medical City / Baghdad, as well as the Gynecology Clinic. Study duration from February 1, 2021, until November 1, 2021.

Patients

- The usefulness of oral labetalol combined with oral methyldopa in the treatment of hypertension in pregnant women was explored in this study. As a single agent, using the maximal dosage of labetalol. A total of 60 pregnant women. In each group (30) women. Group A was given oral labetalol, whereas Group B was given oral methyldopa. From each patient, the following data had been collected upon admission.
- Initial assessment: complete full history taking, including age, address, phone number, and occupation. History of diabetes and history of other comorbid conditions such as cardiac disorder.
- The clinical examination focuses on general examinations, essential symptoms (BP, Temp., Respiratory, and Heart rates), weight, height, and BMI.
- **Laboratory study:**

- **Complete Blood Picture (CBC):** hemoglobin concentration (Hb%), Red Blood Cells (RBCs), White Blood Cells (WBCs), and platelet count.
- **Renal function testing:** blood urea, serum creatinine, and urine analysis.
- **Liver test profile:** Serum aspartate and alanine aminotransferases (AST and ALT), serum albumin, serum bilirubin, serum Gamma-Glutamyl Transferase (GGT), prothrombin time and International Normalized Ratio (INR).

- Each participant had undergone the following measures related to this research:

- Measuring baseline BP using a standard mercury sphygmomanometer, Seat the case for 5 to 10 mins before BP measurements.

Participant selection

Inclusion criteria:

Pregnant who match the following inclusion criteria and have a systolic blood pressure of 150 mm Hg or higher or diastolic blood pressure of 100 mm Hg or higher on repeat blood pressure measurement after 15 minutes of rest will be included:

- At any clinical or hospital visit, any pregnant woman who requires antihypertensive medicines for hypertension.
- Patients who are expecting a singleton or multiple.
- Patients of all ages are accepted.

Exclusion criteria:

- Asthmatic patients.
- Patients with heart block and cardiac failure.
- Patients who have pacemakers or are experiencing any form of cardiac arrhythmia.
- Severe hypertension.
- Preeclampsia complications.

Study objectives:

Primary outcome measures:

Controlling blood pressure with an appropriate agent with avoiding adverse effects is possible as compared to another agent.

Secondary outcome measures:

1. Adverse effects of both agents.
2. Hypotension is a symptom of the mother.

Ethical consideration

Approved by the Ethical Committee at Iraqi Board for Medical Specializations, Baghdad/Iraq.

Data analysis

All the patients' data was input into computerized statistical software (Statistical Package for Social Sciences, version 21) (SPSS). Frequencies are represented as percentages, and descriptive statistics are expressed as (mean + std dev). An independent sample t-test was used when comparing two means. In all statistical analyses, the degree of significance (p less than 0.005) is calculated.

RESULTS

The study examined hypertensive pregnant women of all ages, with 3.3% under 20, 61.7% between 21 and 30, 33.3% between 31 and 40, and 1.7% above 40. Patients had gravida, parity, and abortion histories, and 96.6% had no comorbidities. In terms of the requirement for additional therapy, 86.7% did not require it, whereas 13.3% did. 87.5% of those who needed it were on methyldopa, whereas 12.5% were on labetalol. There was a statistically significant link between the requirement for extra anti-HT and being on methyldopa, with a p-value of 0.02.

Regarding the change in the dose, 93.3% didn't need a change in dose, one patient on labetalol, her dose being decreased, and 3 patients on methyldopa, whose dose is decreased. No statistically significant association between changing the dose and type of treatment, with a p-value of 0.13.

The majority of the patient didn't develop side effects (80%), in those who develop side effects, 83.3% were on methyldopa and 16.7% were on labetalol, a statistically significant association between the development of side effects and being treated with methyldopa, p-value 0.01, as presented in **Tab. 1.** & **Tab. 2**.

Tab. 1. Demographic data of included patients.

Characteristic		N	%
Age group	Less than 20 yrs.	2	3.30%
	21-30 yrs.	37	61.70%
	31-40 yrs.	20	33.30%
	More than 40 yrs.	1	1.70%
Type of treatment	Methyldopa	30	50.00%
	Labetalol	30	50.00%
Gravida	Gravida less than 3	39	65%
	Gravida 3-5	12	20%
	Gravida more than 5	9	15%
Parity	Parity of less than 3	47	78.30%
	Parity 3-5	10	16.70%
	Parity of more than 5	3	5.00%
Abortion	No History of abortion	38	63.30%
	HX of 1 or 2 abortion	21	35%
	Abortion of >2 pregnancy	1	1.70%
Comorbidities	CHD (VSD)	1	1.70%
	DM	1	1.70%
	No comorbidities	58	96.60%

HX= History, CHD (VSD)= Congenital Heart Diseases (Ventricular Septal Defect), DM= Diabetes Mellitus

The change in BP at the beginning of the study and after was assessed using paired t-tests by comparing systolic and diastolic blood pressure before and after in each group.

Regarding the users of the methyldopa group of patients, SBP pre-treatment was 149.50 ± 9.03 and DBP pre-treatment was 99.66 ± 7.30, a statistically significant decrease in the mean of SBP post-treatment (137.83 ± 6.11) and DBP post-treatment (88.83 ± 6.52), p-value 0.00 and 0.00, respectively.

Regarding the users of the labetalol group of patients, a statistically significant decrease in the mean of SBP post-treatment and DBP post-treatment (138.66 ± 3.69, 88.33 ± 5.77) in comparison to pre-treatment (149.00 ± 4.43, 97.33 ± 6.66), p-value 0.000 and 0.003, respectively, as presented in **Tab. 3.**

Both drugs decrease BP; independent t-test was used to assess the mean difference in SBP and DBP post-treatment in both groups of drugs. No statistically significant difference in the mean of SBP post-treatment, mean in methyldopa (137.83 ± 6.1) and labetalol (138.66 ± 3.69), p-value 0.52. No statistically significant difference in the mean of DBP post-treatment, mean in methyldopa (88.83 ± 6.52) and labetalol (88.33 ± 5.77), p-value 0.75, as presented in **Tab. 4.**

The association between type of side effect and anti-hypertensive drug, the result revealed that 12 of all included patients have a side effect. Two of them use labetalol and ten use methyldopa, a statistically significant association between using methyldopa and the development of headache, leg edema, palpitation, and weight gain, with a p-value of 0.03. All had a headache, leg edema palpitation, and weight gain were used methyldopa, as presented in **Tab. 5.**

The time required or needed **Tab. 6.** for BP controlling in the labetalol group was significantly lower in comparison to the methyldopa group. With methyldopa 6.33 ± 3.94 and labetalol 4.38 ± 2.85, with a significant p-value of 0.04.

DISCUSSION

National Institute for Health and Care Excellence [NICE] (2019) has recommended labetalol as a first-line antihypertensive for gestational hypertension and preeclampsia. This is based on limited data from randomized controlled studies, but it is equally effective and safe as other drugs for treating these disorders.

In the current study, most of the patients obtain efficacy with monotherapy (labetalol) without the addition of another agent in treatment (p-value=0.02). While in the methyldopa group, most patients needed an increased dose or addition of another agent for obtaining a response to treatment (p-value=0.13). Non-significant value shows labetalol can be taken as a stand-alone medication.

In comparison to our findings, Roychoudhary, et al. showed a highly significant labetalol in reducing blood

Tab. 2. The need to use additional anti-HT agents, changing the dose either increased or decreased side effects development in both treated groups.

Outcome		Methyldopa	Labetalol	Total	P-value
Needed to Additional Agent	No added therapy	23 (44.2%)	29 (55.8%)	52 (86.7%)	0.02*
	Needed additional anti-HTN**	7 (87.5%)	1 (12.5%)	8 (13.3%)	
Change in the Dose	No change	27 (48.2%)	29 (51.8%)	56 (93.3%)	0.13
	Increased x1	0 (0.0%)	1 (100.0%)	1 (1.7%)	
	Increased x2	3 (100%)	0 (0.0%)	3 (5.0%)	
Side Effect Development	No side effects developed	20 (41.7%)	28 (58.3%)	48 (80%)	0.01*
	Developed side effect	10 (83.3%)	2 (16.7%)	12 (20%)	
Total		30 (50.0%)	30 (50.0%)	60 (100.0%)	

*p-value ≤ 0.05, ** anti-HTN= antihypertensive

Tab. 3. Pair test results of SBP and DBP of the two drugs in pre and post-treatment.

Type of anti-HT agent		Mean ± SD	P-value
Methyldopa	SBP pre-treatment	149.50 ± 9.03	0.00*
	SBP post-treatment	137.83 ± 6.11	
	DBP pre-treatment	99.66 ± 7.30	0.00*
	DBP post-treatment	88.83 ± 6.52	
Labetalol	SBP pre-treatment	149.00 ± 4.43	0.00*
	SBP post-treatment	138.66 ± 3.69	
	DBP pre-treatment	97.33 ±6.66	0.003*
	DBP post-treatment	88.33 ± 5.77	

*p-value ≤ 0.05

Tab. 4. Mean difference in SBP and DBP post treatment in both groups of drugs.

	Type of anti-HT agent	Mean ± SD	P-value
SBP post-treatment	Methyldopa	137.83 ± 6.1	0.52
	Labetalol	138.66 ± 3.69	
DBP post-treatment	Methyldopa	88.83 ± 6.52	0.75
	Labetalol	88.33 ± 5.77	

*p-value ≤ 0.05, anti-HTN= antihypertensive

Tab. 5. The association between type of side effect and anti-hypertensive drug.

Characteristics		Methyldopa	Labetalol	Total	P-Value
Type of SE	Headache	2 (66.7%)	1 (33.3%)	3 (25%)	0.03*
	Headache, Leg Edema	0 (0.0%)	1 (100%)	1 (8.3%)	
	Headache, Leg Edema, Palpitation,	1 (100%)	0 (0.0%)	1 (8.3%)	
	Headache, Leg Edema, Palpitation, Drowsiness	7 (100%)	0 (0.0%)	7 (58.4%)	
Total		10 (100.0%)	2 (100.0%)	12 (100.0%)	

*p-value ≤ 0.05, SE= Side Effect

Tab. 6. The time required for BP controlling.

	Methyldopa	Labetalol	P-value
Time (day)	6.33 ± 3.94	4.38 ± 2.85	0.04*

*p-value ≤ 0.05

pressure than methyldopa with quick and more efficacious control of BP mothers with gestational hypertension. This was found to be statistically significant with a P-value of <0.001. Also, Subhedar, et al. had been found a p-value = 0.008, a significant blood pressure control and efficiency more in labetalol than methyldopa [44].

In a current study, systolic BP (pre-and post-) and diastolic (pre-and post-) of both labetalol (0.00*, 0.003*), and methyldopa (0.00*, 0.00*), a statistically significant decrease in the mean of SBP post-treatment and DBP post-treatment *p-value ≤ 0.05.

In comparison with findings in El-Sadek, et al. they found there was a nonsignificant change among study groups (labetalol and methyldopa) regarding BP before management p values (0.629, 0.656). A significant change was found among the studied group concerning the mean drop in SBP and DBP after treatment with a p-value (0.00, 0.00) [45].

Pentareddy, et al. concluded that methyldopa decreased BP from mean diastolic BP, there was a significant reduction in BP before and after treatment (p-value <0.001), and labetalol reduced mean diastolic BP, also a significant decrease of BP before and afterward management (p value<0.001). In comparison between methyldopa and labetalol groups, the change in a drop in mean DBP was nonsignificant (p-value >0.005) [46].

In the current finding, there is no statistically significant difference in the mean of SBP post-treatment, the mean in methyldopa and labetalol [p-value 0.52]. Also, no statistically significant difference in the mean of DBP post-treatment, mean in methyldopa and labetalol (p-value 0.75).

In comparison between methyldopa and labetalol groups, Pentareddy, et al. showed the change in a drop in mean DBP was nonsignificant (p-value >0.005) [46].

In the current study, we found a relationship between the type of side effect and anti-hypertensive drug, which resulted mostly from the methyldopa group. Though, patients with labetalol also complain of side effects but with minimal effect. A statistically significant association between using methyldopa and the development of headache, leg edema, palpitation, and drowsiness, with a p-value of 0.03.

In comparison to our findings, a study conducted by Verma, et al. stated that adverse events observed were lower in the labetalol-treated group compared to the methyldopa group. Also, in a study by Qarmalawi, et al. patients have received methyldopa complained of side effects such as drowsiness, headache, nasal congestion, and postural hypotension. Patients in the labetalol group complained of dyspnea, but no other side effects were noticed. With labetalol, only a few patients (6) complain of dyspnea [47,48].

Of all the side effects, methyldopa regularly causes drowsiness, and its tendency to cause it is significantly more than labetalol with P = 0.023 as mentioned in Rudra Patel, et al. [49].

Subhedar, et al. showed adverse effects seen with both drugs are of known types and labetalol caused fewer adverse effects compared to methyldopa and the side effects were minor and did not necessitate stoppage of any drugs or change of medications [44].

Furthermore, in the current study, we found that period needed for BP control in labetalol cases was significantly lower compared to the methyldopa group, a significant p-value of 0.04.

A study by Subhedar, et al. concluded that the mean period needed for BP control was different. The variance among the studied groups was significant with labetalol displaying former control of BP in comparison to methyldopa [44].

Also, Alalfy, et al. revealed a decrease in the mean BP starting from a baseline that was the BP before receiving the anti-hypertensive therapy and the records afterward 2-days, 1, 3, 5, 7, 9-wks afterward medication receiving and at a born time in the methyldopa and labetalol cases, a significant change in BP controlling with levels of systolic, diastolic and mean arterial BP records are lesser in labetalol cases in comparison to methyldopa with p-value < 0.001, showing more good BP control [50].

CONCLUSION

This study found labetalol could be used as a single agent in treatment compared with the use of methyldopa. Therefore, minimal, or fewer adverse effects were observed with monotherapy (labetalol).

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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