Original Article

Study on Prescribing Pattern of Antihypertensives in Pregnancy at a Tertiary Care Teaching Hospital, India

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Abstract

Objective: To assess Prescribing Pattern of Antihypertensives In Pregnancy at A Tertiary Care Teaching Hospital, India. **Methodology:** The study was carried out for duration of 6 months enrolling 100 patients. Pregnant women of any age admitted in the gynecology department and willing to participate in the study were included. The prescriptions were assessed on the basis of patient details including age, category of hypertension during pregnancy and drugs prescribed. Neonatal outcome was assessed with the category of hypertension during pregnancy. **Result:** During the study period, data of 100 pregnant women were analyzed, out of which 22 patients were diagnosed with hypertension. The mean age of the patients was 25.2years; with a minimum age of 18 years and maximum 38 years. Among 22 hypertensive pregnant women, 53%were primigravida whereas 5% multigravida. Among the Pregnant women associated with hypertension, 13 were diagnosed as pregnancy induced hypertension, 5 were preeclampsia and 2 patients were severe eclampsia. The prescribing pattern of antihypertensives which includes both monotherapy as well as combination therapy. Severe hypertension in pregnancy is a threat to the mother and child affecting their wellbeing. We observed various hypertensive disorders, among which prevalence of pre-eclampsia was high. In the current research, prescribing pattern of antihypertensives was based on the efficacy and safety profile in pregnancy. Accordingly, labetalol and nifedipine were frequently administered to patients as monotherapy and combination therapy. Labetalol has a status of first line therapy in the treatment of hypertensive urgency. The current study has reported a major drug interaction between labetalol and diltiazem. Concurrent use of these drugs may increase the risk of bradycardia, hypotension, and AV conduction disturbances. Therefore, monitoring the cardiac function and blood pressure is essential. Drug interaction between nifedipine and fosphenytoin was observed in the current study with major severity. Co-administration of these drugs may decrease the efficacy of nifedipine. Hence these combinations must be avoided and alternate hypertensive management should be recommended. **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 frequency of maternal and fetal side-effects along with the brilliant perinatal result in a condition typically joined by a high maternal and fetal mortality and morbidity affirms its appropriateness for use during pregnancy.

Keywords: Prescription Pattern, Antihypertension, Pregnancy, drugs interaction

Introduction

Hypertensive disorders are the most common medical complications of pregnancy with an incidence of 2 to 8%. [1, 2] It is one of the major causes of maternal and perinatal morbidity and mortality worldwide. There are a few significant classes of hypertensive issues in pregnancy extending from mellow to direct ascent in circulatory strain without proteinuria generally called pregnancy incited hypertension (PIH), toxemia (hypertension with proteinuria), serious toxemia and eclampsia. Maternal hypertension, even of the gentle to direct class, can prompt unfriendly perinatal results like low birth weight, rashness, stillbirth and intrauterine development impediment. [3] Though hypertension occurs in 2 to8% of pregnancies, yet information on the safety of antihypertensive medication use during pregnancy is limited. For severe hypertension, anti-hypertensive medication is used to prevent serious maternal and foetal complications; however, there is no consensus on when to treat mild-to-moderate hypertension. According to ACOG (American college of gynecology) technical bulletin recommends that drugs not to be administered in pregnancy associated with hypertension, if systolic BP is less than 160 and diastolic BP less than 110. [4]

PIH is defined as high blood pressure more than 140/90 mmHg with or without proteinuria more than 300mg per 24

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hrs. after 20th week of pregnancy and may last up to 12 weeks after delivery. Based on the national high blood pressure education program working group on high blood pressure in pregnancy, hypertensive disorders are classified into following type: chronic hypertension, preeclampsia-eclampsia, pre-eclampsia superimposed on chronic hypertension and gestational hypertension. WHO states that every seven minutes, at least one pregnant woman dies due to hypertension problem. The maternal and foetal complications of hypertension during pregnancy can be avoided by appropriate use of antihypertensive agents. [5, 6] Eclampsia is a mortal pregnancy disease which accounts as important cause of death during pregnancy around the world. According to world health organization, 16% of deaths during pregnancy are due to hypertensive disorders, which emphasize more on eclampsia. Women with pre-eclampsia are more likely to develop eclampsia. There is lack of studies on eclampsia in low income countries but available literatures states that factors such as low educational level, lack of health awareness, lack of proper access to antenatal care during pregnancy are significant reasons for the development of eclampsia [7]. Eclampsia is a serious health problem causing more than 50,000 deaths per year among pregnant population [8]. Various factors such as personal history of pre-eclampsia, diabetes, multiple babies, primigravida, family history of pre-eclampsia, obesity, age above 40 years are the main risk factors for preeclampsia [9]. As the morbidity and mortality rate increases in patients with PIH, the management of hypertension in pregnant women is essential. Women with history of hypertension in their pregnancies may have an increased risk of future cardiovascular complications and may benefit from early monitoring and management in order to reduce the risk of maternal morbidity [10]. The aim of current study was to analyze the management of pregnancy induced hypertension, to compare the pregnancy category of drugs prescribed with FDA (food and drug administration) and TGA (therapeutic good administration) guidelines, identification of drug interaction and their severity and to educate the patients on lifestyle modifications.

Methodology

This was a prospective observational study conducted in the department of obstetrics and gynecology. The study was carried out for duration of 6 months enrolling 100 patients. Pregnant women of any age admitted in the gynecology department and willing to participate in the study were included. The outpatients, intensive care patients and patients not willing to participate in the study and patient with insufficient data in their record were excluded from the study. This was a retrospective study which included analysis of all the prescriptions from case records of hypertensive pregnant women in a tertiary care hospital for a period of one year. Hypertension is defined and staged according to the guidelines of the seventh report of the Joint National committee on prevention, detection, evaluation, and treatment of high blood pressure. This study was undertaken after taking clearance from institutional ethics committee of hospital. Inclusion criteria for our study were pregnant woman with hypertension aged more than 18 years. The prescriptions were assessed on the basis of patient details including age, category of hypertension during pregnancy and drugs prescribed. Neonatal outcome was assessed with the category of hypertension during pregnancy.

Result and Discusion

During the study period, data of 100 pregnant women were analyzed, out of which 22 patients were diagnosed with hypertension. The mean age of the patients was 25.2years; with a minimum age of 18 years and maximum 38 years. Among 22 hypertensive pregnant women, 53%were primigravida whereas 5% multigravida. Among the Pregnant women associated with hypertension, 13 were diagnosed as pregnancy induced hypertension, 5 were preeclampsia and 2 patients were severe eclampsia (Table 1). When timing of diagnosis of hypertension was analyzed, 95% of the patients were belong to gravida more than 28 weeks.

Table 1: Diagnosis of hypertensive pregnant women.

Diagnosis	No of patient	percentage
Pregnancy induced hypertension	13	59.1
Preeclampsia	5	21.3
Severe Preeclampsia	2	10.7
Eclampsia	1	4.5
Chronic hypertensive	1	4.5
total	22	100

The prescribing pattern of antihypertensives is presented in table 1 which includes both monotherapy as well as combination therapy. Severe hypertension in pregnancy is a threat to the mother and child affecting their wellbeing. We observed various hypertensive disorders, among which prevalence of pre-eclampsia was high and this result was comparable with the study conducted by Thais et al [11]. In the current research, prescribing pattern of antihypertensives was based on the efficacy and safety profile in pregnancy. Accordingly, labetalol and nifedipine were frequently administered to patients as monotherapy and combination therapy. Labetalol has a status of first line therapy in the treatment of hypertensive urgency. According to U.S FDA and ADEC (Australian drug evaluation committee) the drug falls under the pregnancy category C in all trimesters. Labetalol acts as an adrenergic receptor blocker by inhibiting both beta-adrenergic receptors and alpha-1 adrenergic receptors. It is administered at a dose of 100 to 400 mg orally with or without thiazide diuretics.

Table 2: Prescribing Pattern of Antihypertensives

Antihypertensives	GH	PE	PE with CH	GE	Total (n=22)	Percentage
Labetalol + Nifedipine	1	8	3	--	12	54.54%
Labetalol	1	4	--	3	8	36.36%
Telmisartan + Amlodipine	--	1	--	--	1	4.54%
Labetalol + Nifedipine + Diltiazem + Spironolacton Telmisartan	1	--	--	--	1	4.54%

GH: Gestational hypertension, PE: Pre-eclampsia, PE with CH: Pre-eclampsia superimposed with chronic hypertension, GE: Gestational eclampsia.

Table 3: Category of Antihypertensives

Drug name	FDA Categories	TGU category	Frequency	Percentage (%)
Labetalol	C	C	21	95.45%
Nifedipine	C	C	13	59.9%
Diltiazem	C	C	1	4.54%
Spironolactone	Fetal risk can't be ruled out	B3	1	4.54%
Telmisartan	Fetal risk can't be ruled out	D	2	9.09%
Amlodipine	Fetal risk can't be ruled out	C	2	9.09%

FDA - C: No controlled studies are conducted in women and animals.
TGA - C: May cause harmful effects on fetus or neonate without malformation.
TGA - B3: Harmful effects on the fetus have been observed.
TGA - D: Higher incidences of human fetal malformations are observed.

Table 3 indicates the comparison of currently prescribed antihypertensives with FDA and TGA guidelines. The co-morbid conditions observed in the present study include hypothyroidism, diabetes mellitus, convulsion, gastric acidity, urinary tract infection and asthma. Various categories of drugs prescribed to treat these co- morbid conditions were thyroid supplements, antiepileptics, gastro protective agents, hormones, steroids, antihistamines, analgesics, antiplatelets and antibiotics. The hematological profile of fifty percentages of the patients indicates low hemoglobin levels and they were treated with iron supplements. In case of severe hypertension, I.V labetalol 20 mg can be given by slow infusion over two minutes. The current study has reported a major drug interaction between labetalol and diltiazem. Concurrent use of these drugs may increase the risk of bradycardia, hypotension, and AV conduction disturbances. Therefore, monitoring the cardiac function and blood pressure is essential. Nifedipine is a calcium channel blocker used extensively in the management of pregnancy induced hypertension in the present research work. The drug was prescribed in combination with labetalol to decrease the blood pressure. As per U.S FDA Anda DEC nifedipine is classified under pregnancy category C. The drug acts by reducing the intracellular calcium levels in cardiac smooth muscle cells of the coronary and peripheral vasculature, which results in dilation of coronary and peripheral arteries. Extended release nifedipine can be given orally to treat chronic hypertension. In this study, 17 drug-drug interactions were identified. Among the interactions, 3 falls into the category of major, 13 moderate and 1 minor severities. The mechanism and management of major drug interactions are given in table 4.

Table 4: Drug interactions in patient

Drugs	No observed (n=22)	percentage	Severity
Fosphenytoin+ Nifedipine	1	-4.54%	Major
Labetalol + Diltiazem	1	-4.54%	Major
Promethazine + Metoclopramide	1	-4.54%	Major

The contraindications observed in the prescription were olanzapine + metoclopramide and diclofenac + ketorolac. The mechanism and the management are discussed in the table 5

Drug interaction between nifedipine and fosphenytoin was observed in the current study with major severity. Co-administration of these drugs may decrease the efficacy of nifedipine. Hence these combinations must be avoided and alternate hypertensive management should be recommended.

Table 5: contraindications observed in the prescription

Drugs	No observed (n=22)	Interaction & Management
Olanzapine +Metoclopramide	1(4.54%)	Concurrent use of olanzapine and metoclopramide may result in an increased risk of extrapyramidal reactions & neuroleptic malignant syndrome. Monitor for extrapyramidal and neuroleptic symptoms

Diclofenac +ketorolac	1(4.54%)	Co- administration of diclofenac and ketorolac may result in gastrointestinal adverse effects. Concurrent use is not recommended.

The educational and employment statuses of the patients were analyzed. The results prove that the patients were aware about the disease, but had inadequate knowledge about the life style modification. Hence the patients were counselled about the disease, complications and life style modifications by providing the patient information leaflets.

According to the Canadian guidelines the first line drugs for the management of PIH are oral labetalol, methyldopa and long acting oral nifedipine [12]. Dharwadkar, M et al also concluded the labetalol was an effective agent for decreasing and maintaining the blood pressure in PIH patients [13]. Similar reports were observed in the present study. In contrast to these reports, Sajith, M et al proved that methyldopa was widely used as monotherapy and combination therapy, but methyl dopa was not prescribed for none of the patients in our study [14]. On comparison of the currently prescribed antihypertensives with FDA and TGA prescribing guidelines, labetalol, nifedipine and diltiazem can be safely prescribed in pregnancy. As per the FDA category, fetal risk cannot be ruled out when drugs such as spironolactone, telmisartan and amlodipine were prescribed. According to TGA category, the currently prescribed medications were safe except telmisartan, which may cause fetal risk. Here monitoring the prescriptions and follow up is essential by the pharmacist, in order to avoid adverse outcomes during pregnancy. Our study concluded that the prevalence of preeclampsia was high. Labetalol was widely used for its better efficacy, tolerability and immediate onset of action. The drugs selected for management of PIH (Pregnancy induced hypertension) were safe during pregnancy. It is essential for the pharmacist to have an updated knowledge on the pregnancy category of drugs and all the prescriptions should be monitored by the pharmacist, in order to prevent the adverse outcomes. Patients counseling is one of the significant roles of pharmacist, which assist the patients to sustain a better quality of life during pregnancy.

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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 frequency of maternal and fetal symptoms along with the brilliant perinatal result in a condition typically joined by a high maternal and fetal mortality and bleakness affirms its appropriateness for use during pregnancy. Relationship between preeclampsia and GDM is already well established. Hence, routine monitoring of blood glucose levels is essential during their regular check-up. Some patients were prescribed with the drugs from pregnancy category N, where interventions by the clinical pharmacist helped in avoiding the use of such drugs. It was found in our study that antihypertensive prescribed was rational. Most of the prescriptions contain monotherapy with alpha methyl dopa, which is considered to be safest antihypertensive in pregnancy since several decades. Neonatal outcome can be improvised if the hypertension is identified at early weeks of pregnancy; and managed with fewer medication and life style modification.

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