ORIGINAL RESEARCH PAPER

Gynaecology

THE ROLE OF NIFEDIPINE IN HYPERTENSIVE DISORDER OF PREGNANCY

KEY WORDS: Nifedipine, Pregnancy, Hypertension

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ABSTRACT

Pregnancy may induce Hypertension in previously normotensive women or aggravate hypertension in women who are already hypertensive. The triad of complication of haemorrhage, hypertension and sepsis is responsible for majority of maternal deaths. Good prenatal supervision with detection of signs and symptoms of hypertension and incipient preeclampsia can avert maternal-infant mortality and morbitiy. Among the calcium antagonist, nifedipine has been used extensively in later pregnancy. **OBJECTIVE:** To study the efficacy and adverse effects of oral nifedipine in hypertensive disorders of pregnancy and to assess the maternal and perinatal outcome with use of oral nifedipine in hypertensive disorders of pregnancy. **MATERIALS AND METHOD:** About 75 patients with pregnancy hypertension were admitted in the hospital over a period of one year. In majority of the patients after detailed history, examination and investigation, oral nifedipine in the dose of 10 mgs orally and sublingually was given. The onset of action, peak effect, mean duration of action, side effects of the drug, maternal and perinatal outcome were noted. **RESULTS:** The onset of action was seen in 15 minutes in most of patient, peak effect was seen by 1 hr and mean duration of action was 6 hours. Drug was well tolerated with minimal side effects like headache, tachycardia and flushing. Majority patients delivered vaginally(63.7%) and 37.3% underwent caesarean section for other reasons like failure of induction, prolonged labour etc. Maternal complications were placental abruption (2.6%), convulsions (1.3%) and post-partum haemorrhage (PPH) (6.6%). No maternal death was seen. Perinatal mortality rate was 5.2%. **CONCLUSION:** Nifedipine is an effective drug to treat hypertension in pregnancy. Since it is given by oral route it is easier to use with minimal maternal and fetal side effects.

INTRODUCTION:

Pregnancy is a physiological state with many alterations in metabolic, biochemical, haematological and immunological processes. If there are no complications, all these changes are reversible following a few days to few months after delivery[1].

Hypertensive disorders of pregnancy complicate 5 to 10% all pregnancy and preeclampsia is identified in 3.9% of all pregnancy[2]. Mild preeclampsia occurs in 15% approximately and eclampsia complicates 1 in 2000 pregnancy[3], [4]. Placenta is implicated in the pathogenesis of disease. Other theories such as immunological intolerance between maternal and fetal tissue, genetic predisposition, nutritional imbalance and oxidative stress etc. are also postulated[5].

International guidelines define mild pregnancy hypertension as 140/90 and severe pregnancy hypertension as systolic blood pressure (SBP) ≥ 160-170 mmHg and/or diastolic BP (DBP) ≥ 110mm Hg[6]. Severe hypertension is the only modifiable end-organ complication of preeclampsia, the most dangerous of the hypertensive disorder of pregnancy.

Women with severe hypertension are at increased risk of stroke and in order to prevent complications anti hypertensive are to be given[7]. All International pregnancy hypertension guidelines recommend immediate treatment of severe pregnancy hypertension, a recommendation endorsed as 'strong' by WHO[8] while severe requires treatment, it is appropriate to lower BP over hours and this could be achieved with oral or parental hypertensive therapy. Traditionally severe hypertension has been treated with short acting anti-hypertensive agents like I/V hydralazine or labetalol[9].

These agents have been widely studied in RCT (Randomised controlled trials) although systematic reviews have failed to reveal clear differences between agents[10]. Parenteral require more monitoring and supervision because they have potential to lower BP within minutes and cause maternal hypotension and fetal compromises.
Oral therapy in the form of Nifedipine, a calcium channel blocker was used for the treatment of hypertensive disorder of pregnancy. They act by blocking the calcium influx into smooth muscle cells which interferes with excitation and contraction coupling. It is a potent vasodilator and has a rapid onset of action when given orally. It also produces preferential dilatation of cerebral arteries and arterioles which benefits in eclampsia patients.

MATERIAL AND METHOD:

The present study is based on the statistical analysis of patients of hypertensive disorders of pregnancy admitted in the third trimester of pregnancy over a period of one year in the Department of Obstetrics and Gynecology, SMGS Hospital, Jammu. A total of 75 patients were studied.

A detailed history, general examination and investigation like blood chemistry and necessary investigations related to hypertension were done.

The baseline pulse, blood pressure (BP) and fetal heart rates were measured after 15 minutes period of rest in the left lateral position. On the basis of diastolic blood pressure, the patients were divided into three groups:

- Mild - BP ≥ 140/90 mm of Hg & < 160/110 mm of Hg
-Severe - BP ≥ 160/110 mm of Hg.

Patients with mild hypertension were given nifedipine orally & in patients with severe, it was given sublingually in a dose of 10 mgs followed by 10 mgs 6-8 hourly or earlier if required. The maternal pulse, blood pressure & fetal heart rate was measured as follows:

- every 15 minutes for the first hour, - hourly for next 6 hours, - 6 hourly for next 24 hours.

Thereafter the above parameters were measured twice daily. Any side effects on the patients were noted and the patients were followed till delivery. The onset, duration and progress of labour were noted. Any complications during labour or after delivery were recorded. The fetal Apgar score, birth weight and admission to neo-natal intensive care unit (NICU) were recorded and the

indications for admission to NICU were also noted.

The results were subjected to statistical analysis and the maternal and perinatal outcome was assessed.

RESULTS AND OBSERVATION:

Total 75 patients admitted in third trimester of pregnancy over a period of 1 year were studied.

Majority of women were in the age group of 20-25 years (42.7%). Demographic characteristics of women are given in Table-1.

TABLE: 1 - DEMOGRAPHIC CHARACTERISTICS OF WOMEN IN PRESENT STUDY

	No of patients	Percentage
Age (in years)		
16-20	6	8%
21-25	32	42.7%
26-30	27	36%
31-35	10	13.3%
Parity		
P0	48	64%
P1	17	22.7%
P2 and above	10	13.3%
Region		
Rural	45	60%
Urban	30	40%
Socio-Economic Status		
Upper	2	64%
Upper Middle	14	18.7%
Lower Middle	30	40%
Lower	29	38.7%
Literacy		
>10th standard	11	14.6%
<10th standard	64	85.4%

The most common complaint was swelling feet (56%), headache (34.7%) and 5.3% complained of giddiness weight gain. 4% patients were admitted with eclampsia. 46.7% of patients were admitted between 34-37 weeks, 10.6% were less than 34 weeks and 42.7% patients were above 37 weeks.

Distribution of Patients according to various complaints is given to Table-2.

TABLE: 2- DISTRIBUTION OF PATIENTS ACCORDING TO VARIOUS COMPLAINTS

	No of patients	Percentage
BP		
Mild	10	13.3%
Severe	65	86.6%
Grade of Edema		
Nil	4	5.3%
Grade I	20	26.7%
Grade II	45	60%
Grade III	6	8%
Proteinuria		
Nil	4	5.3%
Traces	22	29.3%
1+	26	34.7%
2+	15	20.0%
Above 2+	8	10.7%
Fundoscopy findings		
Macular edema	1	
Pallor of disc	1	
Grade II retinopathy	2	
No finding	71	

Our results showed that nifedipine given in a dose of 10mg orally resulted in a significant fall of BP both systolic and diastolic and effect was evident within 15 minutes. Mild showed a pre-treatment BP of 140/90 mm Hg and post-treatment BP of 120/83 mm Hg and fall was statistically significant. The fall in BP was also noticed in severe disease. The overall mean fall was 21.4/18.1 mm Hg in both the groups. The mean period of administration was 6.73 days and range was 1-39 days. Overall drug was well tolerated with minimal side effects.

The main side effect was headache seen in 20 patients. 25.3% patients had tachycardia. Only one patient had no fall in BP and she was taken up for caesarean for impending eclampsia. One patient had rapid fall of BP from 170/130 mm Hg to 120/80 mm Hg over a period of 1 hour and developed severe headache, flushing, fetal and maternal tachycardia. No other side effect was noticed.

The majority of patients had vaginal delivery (62.7%) and the rest were delivered by caesarean section (37.3%) and indication of caesarean were CPD, malpresentations and failure of induction. One patient had abruption and convulsion at 34th week of gestation. Mild PPH was noticed in 2 and severe PPH and Haematoma in 2 patients. No maternal death was observed.

IUD was observed in 2 patients and perinatal death in 2 patients and admission in NICU were 6 because of prematurity and meconium aspiration syndrome. Perinatal mortality was 5.2%.

DISCUSSION:

PIH continues to take a heavy toll of maternal and fetal lives in the developing as well as developed countries. The only definitive treatment of the condition is to deliver the fetus. Thus the rationale for use of antihypertensive drugs is to reduce the maternal complications of hypertension and optimise neonatal outcome by prolonging pregnancy where required.

The present study was conducted with an aim to assess the efficacy of this drug in pregnancy hypertension. A total of 75 patients were studied. The maximum number of patients were in the age group of 21-25 years (42.7%) and 78.7% were in the age group of 21-30 years. Our observations are in consonance with SP Jaiswar (2011)[11] where maximum number of patients belonged to age group of 21-30 years.

Maximum number of patients in this study were nulliparous and the incidence decreased as parity increased as putative misalliance of fetal trophoblast with maternal tissues in uteroplacental bed as a fundamental factor in etiology of preeclampsia. A resulting aberrant reaction is initiated as the first response to foreign paternal and fetal antigens of placenta. Majority of patients in our study belonged to lower socioeconomic groups. Joshi (1990)[12] also observed that maximum patients were ignorant, illiterate, had failed to utilise antenatal services and had malnutrition. John and colleagues (2002)[1] showed that in general population a diet high in fruits and vegetables is associated with decreased BP. Aamer Imded (2011)[13] showed that calcium supplements in pregnancy is associated with a reduction in risk of hypertensive disorder of pregnancy, preeclampsia, neonatal motality and preterm birth.

On analysis of presenting symptoms, majority of patients (56%) had complaint of swelling feet with or without headache. 2nd most common complaint (34.7%) was headache. 60% of patients were with grade II edema and 8% were with grade III edema. The mechanism for pathological fluid retention is thought to be due to endothelial injury Linette C (2014)[14].

65.4% of patients in our study showed significant proteinuria (1+ and above) and 57% patients were with proteinuria of 2+ and above were in the severe hypertension group. Zwart (2008)[15] showed that maximum no. of patients had proteinuria but at the same time 17% of eclampsia women did not have proteinuria.

Blood urea and serum creatinine levels were within normal limits but evaluation of uric acid levels showed 28% have uric acid level > 5.5mgs % correlating with severity of disease and 87.5% of patients with uric acid levels > 5.5mgs % were in the severe hypertension group. Plasma uric acid level is elevated in preeclampsia and likely is also due to enhanced tubular

reabsorption. Powers (2006)[16] showed that one of the earlier laboratory manifestation of preeclampsia is hyperuricaemia. Most of the patients in the present study showed normal liver function test and fundoscopy revealed positive findings in four patients which included macular edema, pallor of disc and grade II retinopathy.

Tachycardia was seen in 25% of patients which settled during therapy. Mean pre-treatment and post-treatment showed no change in fetal heart rate pattern during treatment. Walter and Redman (1994)[17] also observed no changes in fetal heart rate pattern. The main side effects in our study were headache (26.5%) and transient tachycardia (25.3%). Others included vomiting and giddiness. Only one patient had marked fall in BP within 1 hour and developed significant headache and flushing.

Oral nifedipine caused a significant fall in mild hypertensive disorder of pregnancy (15.6/13.8 mm Hg) and in severe hypertension (29.8/24.1 mm Hg). The onset of action on an average was seen by 15 minutes, the peak effect was seen at 1 hour and mean duration of action lasted 6 hours and overall average mean fall was 21.4/18 mm Hg. This calcium blocking agent has become popular because of its efficiency for control of acute pregnancy related hypertension.

The NHBPEP (2000)[18] recommend 10mg oral dose to be repeated in 30 min.

Only one patient who did not show any fall in BP with dose upto 20mg four hourly and was taken up for LSCS.

Out of 75 patients 62.7% delivered vaginally and 37.3% delivered by caesarean section. The main indications of caesarean section were cephalopelvic disproportion, malpresentations (12%) and failure of induction (8%) and prolonged labour. Greer et al. (1989)[19] also observed high rates of caesarean section mainly for fetal interests.

Maternal complication during labour included placental abruption (2.6%), PPH (6.6%) and eclampsia in one patient and haematoma in one patient. No maternal death was observed in our series as in Sibai et al. (1994)[20]. Two intra uterine deaths were noticed in present study. One patient had history of previous 2 IUD at term with severe PIH and intrauterine growth retardation in present pregnancy. In postnatal period 2 deaths were seen and perinatal mortality rate was 5.3%. Sibai et al. (1996)[21] in a study of patients observed no IUD and complication were minimum in patients on nifedipine therapy.

Walter and Redman (1984)[17] stated that the ideal hypotensive in pregnancy should have the properties of effectiveness, ease of administration, rapid onset, long duration of action, lack of serious maternal and fetal side effects and maintenance of placental blood flow. All these criteria are fulfilled by nifedipine with the added advantage of being cheap and freely available.

CONCLUSION

Nifedipine appears to be a potent antihypertensive with a rapid onset, sustained duration of action and is easily administrable (orally, sublingually). It is well tolerated with minimal maternal side effects and no demonstrable adverse effects on the fetus, besides being cheap and freely available. The added beneficial effects like selective cerebral, coronary and renal vasodilatation together with inhibition of platelet aggregation and thromboxane synthesis could offset the vasospasm and micro-coagulopathy seen in pre-eclampsia and eclampsia.

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