COMPARATIVE STUDY OF FOETAL AND MATERNAL OUTCOME IN CONTROL OF GESTATIONAL HYPERTENSION BY ASSESSING THE MEAN ARTERIAL PRESSURE (> 105 - < 125) AND CONVENTIONALLY TREATING BLOOD PRESSURE

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ABSTRACT

BACKGROUND

Hypertensive disorders complicate 5% - 10% of all pregnancies and contribute greatly to maternal and foetal morbidity and mortality. There is a lack of consensus on the classification/ definition of hypertensive disorders of pregnancy, the Blood Pressure (BP) level at which anti-hypertensive therapy needs to be initiated, the appropriate anti-hypertensive agent and maternal and foetal risk-benefit ratio of treatment. It is generally agreed that severe hypertension (diastolic BP >= 110 mmHg) requires treatment due to risk of cardiovascular and/or target organ damage. However, in mild-to-moderate hypertension, there is no consensus regarding the blood pressure at which treatment needs to be initiated.

Aim- To compare maternal and foetal outcome of patients in whom anti-hypertensive treatment was started at Mean Arterial Pressure (MAP) of 106 – 109 mmHg and in whom anti-hypertensive treatment was started at MAP >= 110 mmHg.

MATERIALS AND METHODS

This is a randomised controlled trial study of patients from Department of Obstetrics and Gynaecology, Government Medical College, Kozhikode, from April 2014 to March 2015. Hundred patients were selected in each group on diagnosing hypertension with the above-mentioned mean arterial pressure and were initiated on anti-hypertensive treatment and managed as per protocol. Statistical analysis was done by SPSS 16. Data was analysed with Chi-square test and Fisher's exact test.

RESULTS

In our study, 70% of women in either group were in the age group of 21 - 30 years. Gestational hypertension was found more commonly in primigravidae. There was no significant difference between various drug usages in controlling blood pressure. At initial presentation, the incidence of pre-eclampsia was 37% in patients with MAP 106 – 109 mmHg and there was a lesser incidence of proteinuria when anti-hypertensives were initiated in mild hypertension. An improved renal function and an overall reduction in maternal complications were found on early initiation of anti-hypertensive therapy.

CONCLUSION

Gestational hypertension is more common in primigravidae during 3rd decade of life. Maternal and foetal complications were significantly reduced, and perinatal outcome was better when anti-hypertensives were started with the MAP of 106 – 109 mmHg at initial diagnosis. There was no difference between drugs used with regard to control of blood pressure and the need for an additional drug.

KEY WORDS

MAP, HELLP, IUGR, NICU, IUD, NND, BP.

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BACKGROUND

Hypertensive disorders complicate 5% - 10% of all pregnancies and contribute greatly to maternal and neonatal morbidity and mortality. It is a multisystem disease of unknown aetiology and there is a constant search for better prognostic factors to predict the progression and severity of the disease. By 19th century, it was recognised that eclampsia is preceded by a collection of circulatory disturbances now known as pre-eclampsia. Pre-eclampsia is best described as a pregnancy-specific syndrome that can affect virtually every organ system[1] and there is no cure for the disorder when it progresses, other than delivery of the foetus.[2] Things kept on changing regarding the understanding of this disorder and even the name has changed from toxaemia of pregnancy to pre-eclampsia.[3] Young and nulliparous women are particularly vulnerable, though race, ethnicity and genetic predisposition have roles. Obesity, multifoetal gestation and age older than 35 years are risk factors.[4] The aim of anti-hypertensive therapy is to prevent complications associated with hypertension while prolonging the course of pregnancy. It is generally agreed that severe hypertension (Diastolic BP >= 110 mmHg) requires treatment due to risks of cardiovascular and/or end-organ damage. However, in mild-to-moderate hypertension, there is no consensus regarding the blood pressure at which treatment needs to be initiated.

Aim of the Study

To compare maternal and foetal outcome of patients in whom anti-hypertensive treatment is started at mean arterial pressure (MAP) 106 - 109 mmHg and in whom anti-

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hypertensive treatment is started at mean arterial pressure >= 110 mmHg.

MATERIALS AND METHODS

This is a randomised controlled trial study of 200 cases of hypertension from the Outpatient and Inpatient Department of Obstetrics and Gynaecology, Government Medical College, Kozhikode from April 2014 to March 2015. The sample size was taken for convenience. Hundred patients were selected in each group with diagnosed hypertension during routine antenatal check-up or on admission. Patients were randomly allocated into two groups with 100 patients in each group by sealed sequential number enveloped before the study. Hypertension is defined as a systolic blood pressure > 140 mmHg and diastolic blood pressure > 90 mmHg on at least two occasions, measured at least 6 hours apart and the MAP is found. Diastolic blood pressure is defined by Korotkoff phase V.

Study Group

Group-1: 100 patients.
Group-2: 100 patients.

We recruited 100 patients in each arm and this sample size was taken for convenience. Permission from Institutional Ethics Committee had been taken prior to initiation of the study.

Inclusion Criteria- Antenatal patients with hypertension who are initiated on anti-hypertensive treatment with above-mentioned MAP are included.

Exclusion Criteria- Those patients of severe pre-eclampsia already on treatment were excluded. Patients of chronic hypertension and those with co-existing diseases like gestational diabetes mellitus, heart disease, renal disease, auto-immune disorders, multiple pregnancy etc. too were excluded.

Patients were divided into two groups, each comprising of 100 patients. Group 1 contained 100 patients in whom treatment was started at MAP of 106 – 109 mmHg and Group 2 patients were started on treatment at a MAP of >= 110 mmHg. Treatment was started at the time of diagnosis in both the groups either with nifedipine, methyldopa or labetalol and were followed up with blood pressure check-up, clinical and symptomatic assessment with routine tests including complete blood count, urine analysis, renal and liver function tests, random blood sugar, serum electrolytes and 24-hour urine protein. Ultrasound and Doppler studies were performed as and when required and both groups were followed up till delivery.

Maternal morbidity was assessed in terms of development of pre-eclampsia, eclampsia, HELLP syndrome, abruptio placentae, end-organ damage, caesarean section, gestational age at delivery, pre-term labour and postpartum haemorrhage. Foetal outcome was assessed by Apgar score, birth weight, IUGR, intrauterine foetal demise, neonatal death, NICU admission and Respiratory Distress Syndrome (RDS).

Statistical Analysis-

It was done using SPSS version 16.0 for windows. Qualitative data was presented as frequency and percentage and quantitative data as Mean and Standard Deviation (SD) if normal or as median and Interquartile Range (IQR). Comparison between the groups was done by Chi-square or Fisher's exact test for qualitative data and by student's t-test and Mann-Whitney U test for quantitative data. A two-sided p-value of < 0.05 was considered as statistically significant.

RESULTS

In our study, 70% of women in either group were in the age group of 21 - 30 years. Gestational hypertension is found more commonly in primigravidae. In the present study, at initial presentation, the incidence of pre-eclampsia was 37% in patients with MAP >=110 mmHg and 7% in those with MAP 106 - 109 mmHg. There was no significant difference between various drug usages in controlling blood pressure. There was a lesser incidence of proteinuria when anti-hypertensives were initiated in mild hypertension. An improved renal function and an overall reduction in maternal complications were found on early initiation of anti-hypertensive therapy. Risk was calculated in terms of relative risk and 95% confidence interval for the same was estimated. A two-sided p-value < 0.05 was considered as statistically significant. The two groups were comparable with respect to age and parity.

	Age (Years)				**Total**
	< = 20	21 - 30	31 - 35	35	
Group 1	10	70	14	6	100
Group 2	13	69	17	1	100
Total	**23**	**139**	**31**	**7**	**200**

Table 1. Age

The two groups were comparable with respect to age, p=0.235.

Gravida					
	1	**2**	**3**	**> 3**	**Total**
Group 1	57	23	9	11	100
Group 2	62	16	17	5	100
Total	**119**	**39**	**26**	**16**	**200**

Table 2. Parity

Majority of the patients in Group 1 and 2 were primigravidae and comparable with p-value of 0.184.

Gestational Age (Weeks)						
Group 1	**< 24**	**24 - 28**	**29-32**	**33-36**	**> 37**	**Total**
	1	0	13	50	36	100
Group 2	5	5	18	37	35	100
Total	**6**	**5**	**31**	**87**	**71**	**200**

Table 3. Gestational Age at Diagnosis

In Group 1 and Group 2, 86% and 72% respectively were diagnosed after 32 weeks of gestation.

	Drug			**MAP**		**Total**
	Methyl-dopa	**Nifedipine**	**Labetalol**	**>105**	**<105**	
Group 1	41	55	4	41	59	100
Group 2	26	65	9	64	36	100
Total	**67**	**120**	**13**	**105**	**95**	**200**

Table 4. Drugs used and MAP Maintained

Complications	Group 1	Group 2	Total
Nil	80	46	126
Severe PET	7	37	44
Renal dysfunction	1	1	2
Impending eclampsia	2	1	3
Preterm labour	2	0	2
Mild PET	3	3	6
Uncontrolled hypertension	4	5	9
HELLP syndrome	0	5	5
Liver dysfunction	1	2	3
Total	**100**	**100**	**200**
Table 5. Maternal Complications			

P-value significant = 0.003, relative risk - 2.7, Confidence interval 1.75 - 4.16

	Nil	IUGR	Abnormal Doppler	IUGR + Abnormal Doppler	IUGR + Abnormal Doppler + Oligoamnios	Foetal Distress	Total
Group 1	78	12	5	4	1	0	100
Group 2	57	30	8	1	3	1	100
Total	**135**	**42**	**13**	**5**	**4**	**1**	**200**
Table 6. Foetal Complications							

Foetal complications were higher in group 2, which was statistically significant; p= 0.016.

Abnormal Investigations	Group 1	Group 2	Total
0	86	72	158
Urine albumin	7	12	19
Urine albumin + abnormal LFT	0	1	1
Urine albumin + abnormal RFT	1	1	2
Urine albumin + low platelet	1	0	1
Urine albumin + > 1 abnormal result	0	1	1
Abnormal LFT	1	3	4
Abnormal LFT + low platelet	0	2	2
Abnormal RFT	4	7	11
Low platelet	0	1	1
Total	**100**	**100**	**200**
Table 7. Investigations			

Weeks	Group 1	Group 2	Total
0	1	0	1
< 32	4	6	10
32-34	1	8	9
35-36	17	24	41
> = 37	75	56	131
5	2	6	8
Total	**100**	**100**	**200**
Table 8. Gestational Age at Termination (Weeks)			

In group 2, more patients needed termination by 36 weeks of gestation and this is statistically significant. P value < 0.025.

Indication	Group 1	Group 2	Total
0	12	13	19
Severe PE	15	35	50
Severe PE + foetal cause	0	3	3
Foetal distress	1	1	2
Renal dysfunction	0	2	2
HELLP	0	7	7
Liver dysfunction	5	0	5
Term	5	0	5
Foetal cause	9	12	21
Gestational HT	53	27	80
Total	**100**	**100**	**200**
Table 9. Indications for Termination			

Mode	Group 1	Group 2	Total
Spontaneous	14	11	25
Induced	53	55	108
LSCS	33	34	67
Total	**100**	**100**	**200**
Table 10. Mode of Delivery			

Spontaneous labour occurred more commonly in Group 1.

Indications	Group 1	Group 2	Total
0	68	65	133
Failed induction	10	23	33
Uncontrolled BP	1	0	1
Eclampsia	3	3	6
HELLP	0	1	1
Foetal cause	3	2	5
Obstetric cause	13	4	17
Unfavourable cervix	0	1	1
Abruptio placentae	1	0	1
MSAF®	1	1	2
Total	**100**	**100**	**200**
Table 11. Indications for Caesarean Section			

®Meconium stained amniotic fluid.

Outcome	Group 1	Group 2	Total
Live	98	82	180
IUD	2	11	13
NND	0	7	7
Total	**100**	**100**	**200**
Table 12. Perinatal Outcome			

Perinatal outcome was significantly better in Group 1, statistically significant with p-value 0.001.

Weight (Kg)	Group 1	Group 2	Total
< 1	6	11	17
1 – 1.5	2	9	11
1.6 - 2	9	13	22
2.1 – 2.5	19	25	44
> 2.5	64	42	106
Total	**100**	**100**	**200**
Table 13. Birth Weight			

Apgar	Group 1	Group 2	Total
Normal	85	82	167
Low	15	18	33
Total	**100**	**100**	**200**
Table 14. Apgar			

RDS	Group 1	Group 2	Total
Yes	15	17	32
No	85	83	168
Total	**100**	**100**	**200**
Table 15. RDS			

NICU	Group 1	Group 2	Total
Yes	23	35	58
No	77	65	142
Total	**100**	**100**	**200**

Table 16. NICU Admission

Perinatal outcome was better in Group 1, statistically significant with p-value of 0.001.

DISCUSSION

In our study 70% of women in either group were in the age group of 21 - 30 years, which is similar to the study by Romy Gilliard et al,[5] who also found an increased incidence of gestational hypertension in the third decade of life. The present study showed that gestational hypertension is more common in primigravidae and were 57% and 62% in Group 1 and Group 2 respectively, comparable to the results obtained by Caritis S,[6] Eras JL[7] and Trupin LS[8] et al. In all established studies, hypertensive disorders are more common in primigravidae and is dubbed as a disease of primiparity. Majority of the patients with Mean Arterial Pressure (MAP) between 106 – 109 mmHg at initial presentation were diagnosed near term in both the groups. Saudan P et al[9] in a similar study found that mild gestational hypertension presented at term or near term. Nifedipine was started at diagnosis in 55% and 65% of patients in Group 1 and 2. In 41% and 26% of patients in Group 1 and 2, methyldopa was used. There was no significant difference between various drug usages in controlling blood pressure. Magee LA et al[10] in a similar study showed no differences between drugs or drug class in control of gestational hypertension.

In the present study, at initial presentation the incidence of pre-eclampsia was 37% in patients with MAP>= 110 mmHg and 7% in those with MAP 106 – 109 mmHg. This is statistically significant with p-value < 0.003. Rubin P et al[11] have reported a lesser incidence of proteinuria when anti-hypertensives were initiated in mild hypertension. In a Cochrane Database review by Abalos E et al,[12] there is no overall difference in the risk of developing pre-eclampsia with early use of anti-hypertensives. There were no cases of HELLP syndrome in patients of Group 1. With MAP >= 110 mmHg, 7% of the patients developed HELLP syndrome which is statistically significant with a p-value of 0.003, whereas Sibai BM et al[13] got p= 0.4. No statistically significant difference was noted in the incidence of mild pre-eclampsia between the groups, which is similar to the various established studies. Renal dysfunction was slightly higher in patients with MAP >= 110 mmHg at initial diagnosis. Though not statistically significant, this is similar study by Ellenbogen A et al,[14] where an improvement in renal function was observed in patients with early treatment. Overall maternal complications were reduced in patients in whom anti-hypertensive therapy was initiated with MAP 106–109 mmHg at initial presentation. Cochrane database review by Abalos et al[12] concluded that anti-hypertensive agent halves the risk of developing severe hypertension and there is a lesser need of an additional anti-hypertensive. In Group 2, eight percent of the patients had deranged renal function parameters and 12% developed proteinuria, which is statistically significant. This correlates with similar studies by Rubin P et al,[11] Ellenbogen et al[14] which show improved renal functions with early use of anti-hypertensive therapy.

A statistically significant number of patients (30%) in Group 2 had Intrauterine Growth Restriction (IUGR), even after excluding those with severe pre-eclampsia at initial presentation. Oligoamnios and abnormal Doppler findings were slightly higher in Group 2. Overall, foetal complications were significantly reduced in the first group. This is in contrast to a similar study by Xiong X et al,[15] where there was no difference in foetal outcome with early treatment.

In Group 1 and 2, labour was induced in 53% and 55% respectively. Majority in Group 1 had gestational hypertension as the main indication, whereas in Group 2 patients had induced labour mainly for the associated complications. This correlates with the study by Gofton EN et al[16] stating that obstetric intervention rates are much higher in women with hypertensive disorders of pregnancy. In Group 2 patients 34% had caesarean section, of which 23% cases were for failed induction, whereas in a majority of cases in Group 1 caesarean section was done for obstetric indications like failed progress of labour and cephalopelvic disproportion. This is similar to a study by Alanis MC et al,[17] which states that early use of anti-hypertensive drugs may reduce the caesarean section rates for failed induction (17 vs 36%). In Group 1 delivery at term was in 75%, whereas with Group 2 it was only 56%. The difference is statistically significant with p-value < 0.001. This is consistent with the study by Buchbinder A et al[18] that women with severe hypertension had higher rates of preterm delivery.

In Group 2 birth weight above 2.5 kg was found in 42%, whereas in Group 1 it was 64% which is statistically significant after excluding preterm babies. According to Hjertberg R et al,[19] in a similar study, birth weight were significantly lower when treatment was not started early. In the present study, 11% of patients in Group 2 and 2% in Group 1 had Intrauterine Foetal Demise (IUD) and neonatal death of 7% was observed in Group 2 which is significant. Jabeen M et al[20] observed a difference in neonatal death with early treatment. In Group 2, low Apgar score were noted in 18% of the babies and 35% of them needed admission in NICU, which is comparable to the studies by Olusanya BO et al[21] and Habli M et al.[22] Incidence of Respiratory Distress Syndrome (RDS) was not significantly different in both the groups in contrast to a study by Bowen JR et al,[23] where a reduced incidence was noted with anti-hypertensive treatment. Overall neonatal complications were reduced in Group 1, which is statistically significant. This is in contrast with similar studies in which no significant difference in adverse perinatal outcome is seen between early and late treated groups. Magee LA et al[24] in their study "The control of hypertension in pregnancy study pilot trial" could not find a significant difference in perinatal outcome in less tight versus tight control of blood pressure.

CONCLUSION

In the present study, gestational hypertension is more common in primigravidae during 3rd decade of life. Maternal and foetal complications were significantly reduced, and perinatal outcome was better when anti-hypertensives were started with MAP of 106 - 109 mmHg at initial diagnosis as compared to initiation of treatment at MAP >= 110 mmHg. There was no difference between drugs used with regard to

control of blood pressure and the need for an additional drug. Though the caesarean section rates were almost comparable between the groups, failed induction as an indication was more in Group 2. The increased rates of complications in Group 2 may be partially due to the inherent probability of developing pre-eclampsia. Limitation of the study was in Group 1 as initiation of anti-hypertensives could have been withheld, but may require intense monitoring which is difficult in our scenario. In a confidential review, it is reported that maternal morbidity in severe pre-eclampsia is mostly due to cerebral haemorrhage. The complications which occurred postpartum were not statistically different between the groups. Close clinical monitoring and more frequent laboratory investigations may go a long way in improving maternal and perinatal outcome in hypertensive disorders of pregnancy.

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