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RESEARCH ARTICLE

CONTROLLING BLOOD PRESSURE IN SEVER HYPERTENSION DURING LABOUR: A COMPARATIVE STUDY.

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Abstract

Background: Pregnancy induced hypertension with proteinuria occur in 5% of primigravidas, it remains the commonest cause of maternal mortality and substantial cause of neonatal morbidity and mortality. Pre-eclampsia is complex & still incompletely understood.

Patients and methods: This prospective study had been conducted in a maternity hospital in Baghdad, between November 1993 and September 1994.Fifty women with antepartum or intrapartum diagnosis of severe pre-eclampsia were invited to participate on voluntary base in this study. Those 50 cases divided randomly into two equal groups the first group treated by nefipidine and the second group was given hydralazine.

Results: The first group was put on Nifedipine treatment, two (8%) of the patients given 10mg of nifedipine sublingually and only one patient (4%) required 40mg capsules to reach a safe level of blood pressure. The second group was put on Hydralazine treatment; Only 10(40%) of them required one dose (20 mg) in order to decrease their blood pressure to the safe level and 4(16%) of patients needed three doses (60 mg).

Conclusion: Both drugs are efficient in controlling the BP in severe hypertension, although Nifedipine showed a more rapid onset of action and it is self-administered orally.

Introduction:-

Raised arterial blood pressure is common in pregnancy. when the pregnancy ends the problem resolves within days or weeks [(1)]. Pre-eclampsia is primarily a disease of primegravidas, it is diagnosed in women who developed hypertension and proteinuria during pregnancy rarely before the 20 weeks of gestation [(2)].

Pregnancy induced hypertension with proteinuria occur in 5% of primigravidas, itremains the commonest cause of maternal mortality and substantial cause of neonatal morbidity and mortality [(3)].

Pre-eclampsia is complex & still incompletely understood. The disease is associated with inadequate adaptation of the maternal circulation to the implantation of the trophoblast, with some immunological changes [(4,5)]. Vascular

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endothelial dysfunction in the motherand fluid retention are the commonest pathophysiological changes occur in pre-eclampsia [6].

Management:-
Management strategies have aimed at trying to control BP in order to reduce the serious hazards. Drugs have therefor been used hopefully to prevent pregnancy induced hypertension when it develops and to slow or prevent a supposed progression to preeclampsia and to treat sever hypertension [7].

Prevention:-
Both anti platelet (aspirin 150 mg/dipyridamole 300 mg) daily have been tried for the prevention of pre-eclampsia and intra uterine growth retardation. They are used daily from the third month gestation until term [8].

Other studies showed that treatment with diuretic reduced the incidence of hypertension and oedema but did not prevent pre-eclampsia or reduce perinatal mortality. And the use of diuretics worsens the established pre-eclampsia [4,6]. Antihypertensive drugs remain the mainstay of treatment in hypertension in pregnancy whatever the cause.

Aim of the study:-
The aim of this study to show the effect of Nifedipine and Hydralazine in controlling the blood pressure in case of severe hypertension in preeclampsia during the perinatal period. And to compare treatment by Nifedipine vs treatment by Hydralazine in controlling hypertension in sever pre-eclampsia.

Patients and Methods:-
This prospective study had been conducted in AL-Elwiya maternity hospital in Baghdad, between November 1993 and September 1994.

Fifty women with antepartum or intrapartum diagnosis of severe pre-eclampsia were invited to participate in this study.

Case definition:-
Systolic BP > 160 mmHg or Diastolic BP > 110 mmHg on one occasion or systolic BP between 160 and 180 mmHg or Diastolic BP between 110 and 120 mmHg that persisted more than 2 hours despite bed rest. In addition to proteinuria > 2 mg/dl.

Sampling:-
Patients recruited to participate in the study according to certain inclusion and exclusion criteria.

Inclusion criteria:-
A primigravida pregnant patients aged 16-35 years their gestational age between 35-41 weeks were selected. They should be conscious, have not passed in eclamptic fit. On the other hand, the exclusion criteria were any hypertensive patients prior to pregnancy, diabetes mellitus, hyperthyroidism, cardiovascular disease, history of epilepsy, any other chronic disease under treatment, or patients with clinical signs of infection particularly urinary tract infection. In addition, cases with intra-uterine growth retardation, any congenital abnormalities of the fetus, or any evidence of fetal distress were also excluded.

Those 50 cases divided randomly into two equal groups (25 cases for each).

The first group (study group) was treated by using nifedipine capsule with a starting dose of 10 mg sublingual (instruction was given to bite the capsule between their molars and if possible to avoid swallowing in order to facilitate its absorption sublingually), this dose was repeated on need every 20 Min. until diastolic BP ranging between 90-95 mmHg and in some cases in whom their hypertension persisted we need 40 mg as a max. dose.

While the second group (control group) treated by hydralazine which was given by intravenous infusion of 20 mg diluted in 200 ml normal saline, starting at a flow rate of 2 mg/hour and doubling every 30 minute until diastolic BP back to 90-95 mmHg or a maximum dose rate of 20mg/hr is reached and in some patients this regimen (20 mg in 200 ml normal saline) repeated three times i.e. up to 60 mg as a maximum dose. If diastolic BP fall below 90 mmHg

the drip rate is halved and if necessary halved again every 30 min, so that diastolic BP maintained between 90-95 mmHg.

As regard to the maintenance dose in the study group on nifedipine, the route of administration was changed to oral (swallowing), in a dose of 10 mg every 4 hours before labour, which was changed after labour to 10 mg eight hourly.

All the patients received diazepam (valium) in form of intramuscular injection as prophylactic anticonvulsant.

Monitoring of the fetal heart by using sonicaid, and uterine activity was reported on partogram during labor.

Patients were positioned in left lateral recumbence for cardiovascular measurement uniformly. Pulse rate and BP had been measured every 20 Min using the standard sphygmomanometer (phase 4 of the korotkov sound for the diastolic BP). Mean arterial BP is calculated with standard formula.

Measurement of the blood loss after delivery was done by using any container to collect blood loss, then measuring the amount of blood by using a collecting bag (1000 cc), added to it 50 cc for undetected blood loss.

Laboratory investigations was done for each patient, which include: general urine examination for albuminurea and pus cells. Haemoglobulin percent and packed cell volume random blood sugar measured twice: first on admission; and second one after 12 hrs. and lastly 24 hours post-natal.

Statistical issues:-
The data is presented by using frequency and percentage. Chi-square and t-test were used to find the significance of the relationship.

Results:-

The age of all participants ranged between 16-35 years. The mean age of patients in first group on nifedipine treatment was (24.48 + 4.95), the mean age of patients in second group on hydralazine treatment was (25.72 + 4.85) there was no significant difference between the mean of the two groups (P=0.376). Distribution of patients in both groups according to age categories was shown in (table -1). Patients in both groups have their highest rate in the age categories of 30-30 year.

Dose effect in both groups:-
Treatment was started in both groups at the same time. In first group on nifedipine treatment, it was found that; 2(8%) of the patients required 10 mg of nifedipine sublingually, 10(40%) required 20 mg, 12(48%) patients required 30 mg, and only one patient (4%) received 40 mg capsules to reach a safe level of blood pressure. In the second group, who were on Hydralazine treatment; the highest rate of cases 44% (eleven patients) received two doses (40 mg) initially in order to decrease their blood pressure to the safe level, 10(40%) patients required one dose (20 mg), and the lowest number of cases 4(16%) needed three doses (60 mg) at the start in order to decrease BP to the safe level (Table-2).

Blood pressure remain stable with normal limits (before and after labour) in all the cases in thefirst group except one patient, the BP rose again after initial falling and sustained at 170/120 mmHg. This was considered the only treat-ment failure before labour, in this case we returned to give 20 mg nifedipine sublingually to control the blood pressure. Also there were two patients in which their BP rose within first 24 hrs after labour, it reaches up to 170/110 mmHg, again we returned to 20 mg nifedipine sublingually to decrease BP down to its safe level.

Following the maintenance dose in the secondgroup of patients, BP remain stable (with the help of intravenous slow drip infusion of hydralazine), in one patient the BP raised again reaching 160/110 mmHg within the first 24 hours postnatal, so we returned to increase the rate or the concentration of hydralazine drug.

There were no resistant cases among the study groups neither to nifedipine nor to hydralazine medication.

In nifedipine group the fall in systolic BP in the first 20 min was significant ($P < 0.05$), by a range of 25-30 mmHg and average (27.4). Similar1y the diastolic BP was reduced significantly ($P < 0.05$) with a range of (15-25) mmHg

and average of (21.3). Twenty minutes following administration of hydralazine treatment, only 8 cases (32%) had their systolic & diastolic BP lowered by (15-20 mmHg), (5-10 mmHg) respectively. The majority of cases 21(84%) achieved the safe level of BP (diastolic BP below 110 mmHg) after 60 mint of treatment. Hypertension persisted in four cases, for those additional dose had been used to reach a maximum dose of 60 mg (table 3).

Tables-4 showed the systolic and diastolic BP continued decreasing by (15-20 mmHg), (10-15 mmHg) respectively, to reach the safe level in all cases after 60 mint. of treatment, so no patient needs more than 40 mg as a maximum dose. And the BP remains stable even after 2 hr, and still so for 8 hr, and 12 hr.

Table-5 represented types of delivery in both groups. In nifedipine treated group; 19 patients (76%) delivered by normal vaginal root, while 6 patients (24%) delivered by caesarian section (Two cases were breech presentation, one transfers lie, and the remaining three cases had cephalo-pelvic disproportion and fetal distress). On the other hand, in hydralazine group; 18(72%) patients were delivered by normal vaginal delivery, and 7(28%) were delivered by caesarian section (two cases had placentaprevia, one case breech presentation, two cases cephalo-pelvic disproportion, one case pregnant with twin both were breech presentation, and the last one was cord prolapse). There was no significant difference in between the two groups on different medications (P = 0.747).

The amount of blood loss after labour in both groups were studied and represented again in table 5. In nifedipine treated group, six patients (24%) lost 250 cc of blood, 17(86%) patients lost 350 cc blood, and two patients (8%) lost more than 550 cc blood. In hydralazine treated group the blood loss was 250 cc. in 10 cases (50%), 14 patients (65%) lost 350 cc. & only one patient lost more than 500 cc. of blood. There was no significant difference in amount of blood loss between the two groups on different medications (P= 0.44).

APGAR score assessment had been performed at five mint and shown in (table 6). Although there was no significant difference in APGAR score among infants born to mothers in the two groups. The APGAR score of 9/10 had been observed in highest rate of infant (80%) from mothers treated by nifedipine drug. Mothers who were treated by hydralazine 16 (64%) of their infants had APGAR score 9/10, eight infants (3%) had APGAR score between 7-8/10 (from which 2 babies were admitted to the baby care unit for further observation). There was no significant difference in APGAR score between those patients on nifedipine treatment and those on hydralazine therapy (p = 0.411).

Table 1:-Distribution of patients on both types of treatment according to age group.

Age group	Hydralazin n(%)	Nifedepin n(%)	total
16-20	5(20)	8(32)	13
21-25	6(24)	4(16)	10
26-30	9(36)	10(40)	19
31-35	5(20)	3(12)	8
total	25	25	50

Table 2:-Dose needed to reach safe BP in both groups

Doses	Hydralazin n(%)	Nifedepin n(%)	total
10 mg	-	2(8)	2
20 mg	10(40)	10(40)	20
30 mg	-	12(48)	12
40 mg	11(44)	1(4)	12
60 mg	4(16)	-	4
Total	25	25	50

Table 3:-Effect of treatment by hydrazine and nefideipine on systolic and diastolic blood pressure within the first 20 minutes.

Mean blood pressure	Hydralazin	t-test p-value	Nifedepin	t-test p-value
Systolic BP before treatment	175.6	1.567	170.4	4.7024

Systolic BP After treatment	166.6	0.124	143	0.0004
Diastolic BP before treatment	112.6	7.8501	110.6	5.4486
Diastolic BP after treatment	104.2	0.0001	86.6	0.0001

Table 4:-Changes in systolic and diastolic blood pressure with time after starting treatment

	Time	Systolic BP (mean±SD)	Diastolic BP (mean±SD)
Before nifedipine	-	173 ± 9	110 ± 5
After nifedipine	5 min	154 ± 18	96 ± 5
	10 min	144 ± 14	92 ± 6
	20 min	140 ± 14	86 ± 7
	30 min	135 ± 16	80 ± 7
	1 hr	134 ± 16	79 ± 6
	2 hr	133 ± 12	83 ± 8
	3 hr	131 ± 16	83 ± 11
	4 hr	135 ± 14	82 ± 15
	5 hr	137 ± 11	85 ± 15
	6 hr	136 ± 7	87 ± 11
	7 hr	134 ± 16	87 ± 16
	8 hr	138 ± 11	83 ± 10
	9 hg	130 ± 18	80 ± 18
	10 hr	136 ± 14	85 ± 14
	11 hr	140 ± 6	88 ± 5
	12 hr	139 ± 12	86 ± 8
BP:blood pressure, SD: Standard deviation.			

Table 5:-Types of delivery and blood loss in both groups

Type of delivery	Hydralazine n(%)	Nifedipine n(%)	Total n(%)	Chi-sq P-value
Caesarian section	7(28)	6(24)	13	0.104
Normal vaginal delivery	18(72)	19(76)	37	0.747
Total	25	25	50	
Blood loss				
200+50 ml	10(40)	6(24)	16	1.6237
300+50 ml	14(56)	17(68)	31	0.44
400+50ml	0	0	0	
>550 ml	1(4)	2(8)	3	
Total	25	25	50	
Corrected Chi-square test (Pooling of last two rows				

Table 6:-APGAR score in babies born to patients on different treatments

APGAR SCOR	Hydralazine n(%)	Nifedipine n(%)	Total n(%)	Chi-sq P-value
9/10	16(64)	20(80)	36	1.778
7-8/10	8(32)	4(16)	12	0.411
<5/10	1(4)	1(4)	2	
Total	25	25	50	
Death report: one infant in Hydralazine group				

Discussion:-

Hypertension continues to complicate a significant number of pregnancies, and it remains our commonest cause of materna1 mortality and a substantial cause of neonatal morbidity & mortality [(1)].

Over the past thirty years a number of drugs have been used as antihypertensive alone or in combination. Many drugs like Diazoxide, Labetalol and Hydralazine were most widely used for the treatment of severe hypertension episodes in pregnancy, but these need to be given parenterally and they have a high incidence of side effects [(7)]. Calcium channel blockers like nifedipine and nicardipine exhibits a greater selectivity for its antihypertensive effect [(7)].

The safe use of antihypertensive agents in perinatal period should be given only for those cases with high BP otherwise such treatment may interfere with placental circulation; gradual cessation and/or changing the route of the therapy when the blood pressure adjusted to the safe level [(4)].

In this study Nifedipine has a great effect on blood pressure, it significantly decreases BP rapidly and smoothly within the first 28 mint of administration and still so at 60 mint, 2 hr, 4 hr, 8 hr, and 12 hr. This finding matching the work of Walter and Redman in 1984 [(7)], Greer in 1985 [(9)], and Seabe et al study in 1989 [(10)]. These studies found that there were a significant falling of the blood pressure following nifedipine treatment. This effect most probably due to the mode of action ofnifedipine as a calcium channel blocker it affects the contractility of smooth muscle cells of the blood vessels especially the arterioles, result in vasodilatation lead to rapid decrease in BP, this work done by Edvinssonin 1979 [(11)] and Ahokas et al. in 1986 [(12)]. Also an increase of intracellular ions activates vascular smooth muscle & prevent vasoconstriction of the arterioles which are more sensitive than venules, causing dilatation of the arteriolar bed & decrease peripheral resistance [(13)].

In comparing the mode of action of nifedipine with hydralazine, the later when was usedto lower BP takes longer period of time (30 mint & more) in a majority of patients, this result goes with the finding of Seabe et al. study in which they concluded that, both drugs were found to be equally efficacious, but nifedipine however showed an earlier onset of action in lowering the blood pressure [(10)].

Also we observed that the BP progressively drops as long as the patient on hydralazine infusion, this Means that continuous monitoring of the patient is highly required, while in nifedipine treatment the BP remains stable on the safe level in spite of continuing the treatment, this finding is in consistent with the finding of Davey study [(4)].

The current study could not detect any significant relationship between the type of treatment and the amount of blood loss during and after labour. This result supported by the finding of Anderson et al in 1989, who detect that nifedipine can cause uterine relaxation, but none of the patients treated by this drug had an excess uterine bleeding [(7)]. This could be attributed to absence of the cumulative effect of nifedipine, being used for a short period of time, beside that a precaution had been taken to perform a continuous uterine massage from the end of the second stage till the end of the third stage.

Regarding the APGAR score, in the current study there is no impact of nifedipine on the APGAR score of the babies. This finding is in agreement with Hanretty et al. 1989, this condition was attributed to the effect of nifedipine on placental circulation, in which there is no reduction of utero-placental blood flow, so this will preserve the placental circulation and in turn will give no effect on the fetal wellbeing [(15)].

Conclusion:-

Both drugs are efficient in controlling the BP in severe hypertension, although Nifedipine showed a more rapid onset of action and it is self-administered orally. Nifedipine did not show the acute hypotensive effect even on maintenance treatment, while hydralazine effect to lower blood pressure below normal if not well controlled.

Both antihypertensive agents have no significant effect on postpartum blood loss.

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