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A study comparing efficacy of low dose Regimen (Dhaka) & standard dose regimen (Pritchard) in Eclampsia patient at Umaid Hospital, tertiary care centre of western Rajasthan

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I. Introduction

Safe pregnancy is beautiful voyage ending with birth of two lives. But, some co morbidities can affect this target like hypertensive disease of pregnancy.

Hypertensive disorder remains the most significant and intriguing unsolved problems in obstetrics. These disorders complicate 5 to 10 percent of all pregnancies; together they are one of the Deadly triad- along with the haemorrhage and infection that contribute greatly to maternal morbidity and mortality rates [(1)]. Hypertension is diagnosed empirically when appropriately taken blood pressure exceeds 140 mm of Hg of systolic or 90 mm of Hg diastolic pressure [(2)]. Hypertensive disorders during pregnancy can be included into four well defined groups according to International society for the study of hypertension in pregnancy **(ISSHP**) [(3).] Gestational hypertension, Pre Eclampsia and Eclampsia, Chronic hypertension, Pre Eclampsia superimposed on chronic hypertension Eclampsia is derived from the Greek word meaning "**flash of light, to shine forth or bolt of the blue"**[(5)]. It is defined as the new onset of seizures (convulsions) or unexplained coma in a woman with pre Eclampsia during pregnancy or postpartum. In some cases seizures and coma may be the only sign that a pregnant woman develops.

II. Pathophysiology:-

The pathophysiology of Eclampsia is still not conclusively elucidated. Posterior part of brain is mainly affected in Eclampsia than anterior part of brain because anterior circulation of brain is much better supplied by sympathetic innervations and therefore better protected against the effect of hypertension.

In case increased cerebral perfusion pressure, the main auto regulatory response to elevated BP is lost; vasodilatation occurs inspite of vasoconstriction. This leads to hyper perfusion, causing endothelial capillary damage and interstitial vasogenic oedema. This leads to brain irritation and cause convulsions.

But in case of Normal brain perfusion pressure, seizures are the result of abnormal auto regulatory response consisting of aggregated vasoconstriction and ischemic changes with rupture of vascular endothelium and pericapillary haemorrhage with development of foci of abnormal electrical discharge that generalise and cause convulsions.

Principles of management

1. General management
2. Control of seizures
3. Control of blood pressure
4. Obstetric management
5. Early detection, timely and appropriate management of complication.

CONTROL OF SEIZURES

Magnesium sulphate-

Mechanism of action

The precise mechanism of action of magnesium sulphate in eclampsia is not clear with great deal of controversies still existing. The postulated mechanisms include [(5)]:

- Blockade of NMDA (N Methyl D Aspartate) subtype of glutamate channel receptor in a voltage dependant manner.

 Peripheral action - At the neuro-muscular junction causing blockage of calcium entering the cell and blocking calcium at the intra cellular sites/membranes, reducing the pre-synaptic acetyl choline release at the end plate, reducing the motor end plate sensitivity to acetyl choline (reducing Neuro-muscular irritability).

 Direct action of a neuro muscular block though suggested seems unlikely, as the serum concentration for its anti-convulsive action is well below that needed for neuro muscular block.

 Central action: - Preferential uptake by the hippocampus and cerebral cortex rich in NMDA receptors (Hallak M et al [(6)] 1992). Lipton and Resenberg [(7)] (1994) showed that with potent cerebral vasodilatation demonstrated by Doppler (Belfort and Boise [(8)] 1992). Increased magnesium sulphate concentration was demonstrated in CSF after infusion (Thurnau [(9)] et al).

Conventional western regimen cannot be given worldwide in obstetric care unit because of its higher dose, need of consistent supervision and more side effects and requirement of trained persons. Since every individual is different so same dosage protocol may not be appropriately plan for all.
In recent years Andrea in her review article on Eclampsia commented
"One may also speculate that MgSO4 dosage should vary according to weight or body mass indices". This researcher showed the way for low dose protocol of MgSO4 regimen.
Various regimens with different dosages have been used over the years; question still remains about the 'minimum effective dose' of magnesium sulphate.

MAGNESIUM SULPHATE MONITORING- magnesium sulphate toxicity can be monitored by clinical sign because particular sign present at specific serum magnesium concentration. No serum magnesium concentration monitoring is required.

a) Knee jerk (deep tendon reflex) should be present.
b) Urine output should be more 30ml per hour (more than 100 ml in 4 hours).
c) Respiratory rate should be at least 14 per minute (12-20/min).

Therapeutic level of magnesium sulphate is 4-7 mEq/L (2-3.5 m mol/L)
ANTIDOTE - Calcium gluconate 10%, 10ml (1gm) slowly IV over 3 minutes.

RESEARCH QUESTION:- What are the benefits of Dhaka regimen over Pritchard regimen?
HYPOTHESIS- Dhaka regimen is better than Pritchard regimen in efficacy of controlling convulsion, preventing recurrence of convulsions and incidence of complications.

AIMS AND OBJECTIVES

1. To study the efficacy of low dose MgSO4 (DHAKA) regimen in Eclampsia
2. To study the efficacy of high dose MgSO4 (PRITCHARD) regimen in Eclampsia
3. To compare the efficacy of MgSO4 regimens- Dhaka regimen with Pritchard regimen

a) Proportion of controlling convulsions.
b) Proportion of preventing recurrent convulsions.
c) Proportion of the incidence of complication

III. Material And Methods

STUDY DESIGN: -
Hospital based case control prospective study
STUDY SETTINGS:-
The study was conducted in department of obstetrics and gynaecology, Umaid hospital, Dr S.N. Medical College, Jodhpur.
STUDY DURATION- 1 Year
CASE – Patients who received Dhaka regimen.
CONTROL: - Patients who received Pritchard regimen.
INCLUSION CRITERIA:- Patients presenting with Eclampsia irrespective of parity and gestation age.

EXCLUSION CRITERIA

1. Referred patient who received MgSO4 loading dose before admission.
2. Fits after 7 days of delivery.

IV. Methodology:-

History:- A detailed history regarding age, parity, last menstrual period, gestational age, obstetric history, time of onset and duration of convulsion, number of convulsions before admission, any treatment taken for fits(MgSO4, antihypertensive), symptom and duration of pregnancy induced hypertension, fits in previous pregnancy, history of imminent symptoms taken from close relatives and also from patient if she was conscious. Any past history of epilepsy, renal disease, hypertension, diabetes mellitus, and asthma also elicited. Maternal family history of Eclampsia and HDOP.

Vital parameters like Blood pressure, pulse rate, respiratory rate and temperature were noted. Systemic examination included Cardiovascular, Central nervous system, Respiratory system.

 Patient was catheterised for urine output measurement, spot urine albumin test done. Particular MgSO4 regimen was started and hourly urine output was measured. Half hourly pulse, temperature, and respiratory rate, two hourly blood pressure was taken. Knee jerk, Urine output, Respiratory rate assessed before next dose of MgSO4. It is discontinued 24 hr after delivery or last seizures whichever is late

Per abdominal examination: - After stabilizing the patients, a detailed obstetric examination according to Leopold's manoeuvres was done. Per vaginal examination was done and bishop score was calculated. Mode of termination was decided according to the gestational age, viability of fetus and bishop scoring.

HIGH DOSE REGIMEN

PRITCHARD REGIMENS (1955 Parkland hospital)[10] :

Jack. A. Pritchard gets the credit for popularizing magnesium sulphate for Eclampsia /pre-Eclampsia in modern obstetrics in 1955. He initiated the parkland hospital Eclampsia protocol which came to be popularly known as the 'Pritchard regimen'

- INITIAL DOSE- Magnesium sulphate 4 gm is given IV slowly over 3to 4 minutes as 20ml of 20% MgSO4 immediately; followed by 5gm in each buttock intramuscularly as 10ml of 50% magnesium sulphate (Total 14g).
- FURTHER DOSE - A total 5gm of MgSO4 is given IM in alternate buttocks 4 hourly. It is discontinued 24 hr after delivery or last seizures, whichever is late.

DHAKA REGIMEN OF MAGNESIUM SULPHATE REGIMEN [11]:

Loading Dose:

- 4gm of magnesium sulphate given intravenously slowly over 15minutes.
- 3gm given intramuscularly in each buttock.

Maintenance Dose:

- 2.5gm every 4 hours given intramuscularly in alternate buttocks, until 24hrs after delivery or last seizures, whichever is later.

V. Observations

TABLE 1: AGE DISTRIBUTION

Age (years)	Dhaka		Pritchard	
	Number	Percentage	Number	Percentage
<20	5	11.12	3	6.67
20-24	24	53.33	32	71.10
25-29	10	22.22	3	6.67
≥30	6	13.33	7	15.56
Total	45	100.0	45	100.0
Mean+SD	23.42+3.84		23.6+4.66	

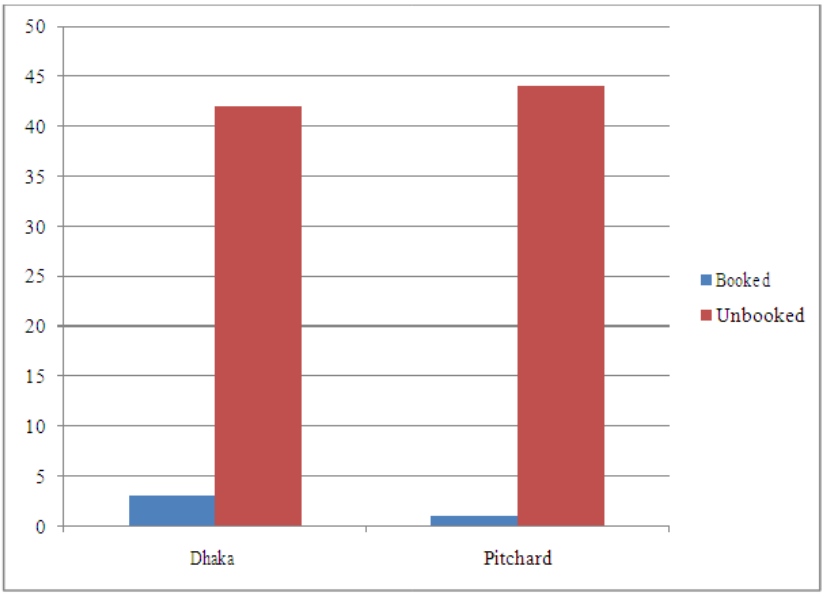
Mean age in our study was 23.52±3.84 (range 20-24 year).

TABLE 2:- PARITY

Parity	Dhaka		Pritchard	
	Numbers	Percentage	Numbers	Percentage
Primi	31	68.89	29	64.44
Multi Gravida	14	31.11	16	35.56
Total	45	100	45	100

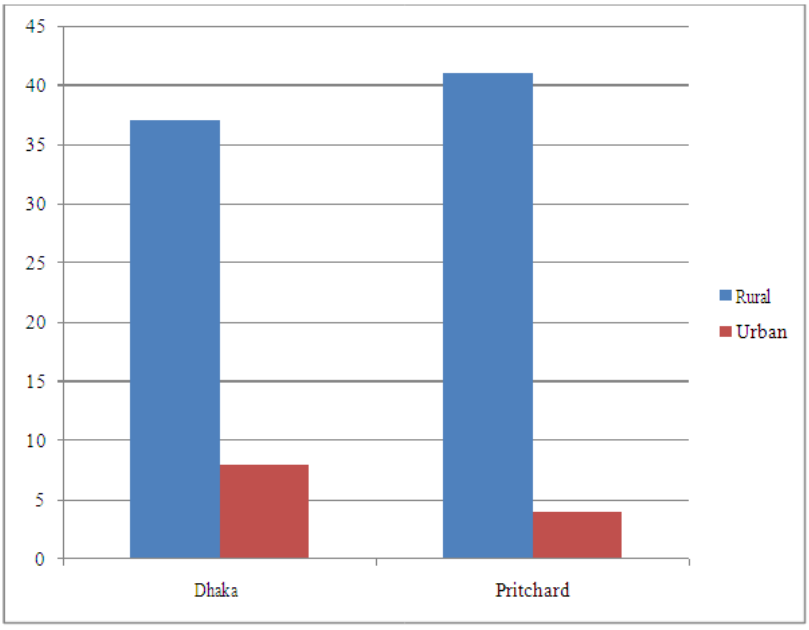
In Dhaka group 68.89% and in Pritchard group 64.44% were primigravida. In Dhaka group 31.11% and in Pritchard group 35.56% were multigravida.

TABLE 3: ANTENATAL STATUS



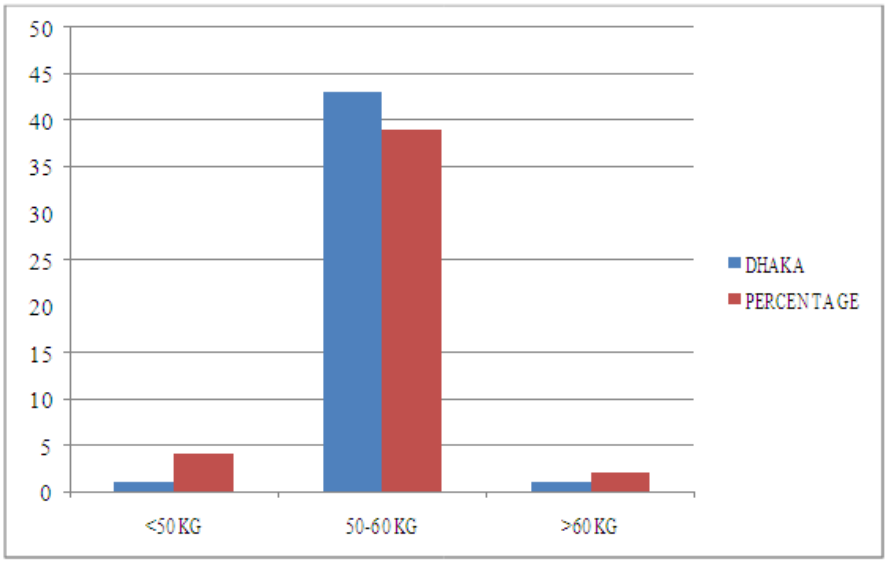
In our study 6.67% patients were booked and 93.33% patients were unbooked.

TABLE 4: GEOGRAPHICAL DISTRIBUTION



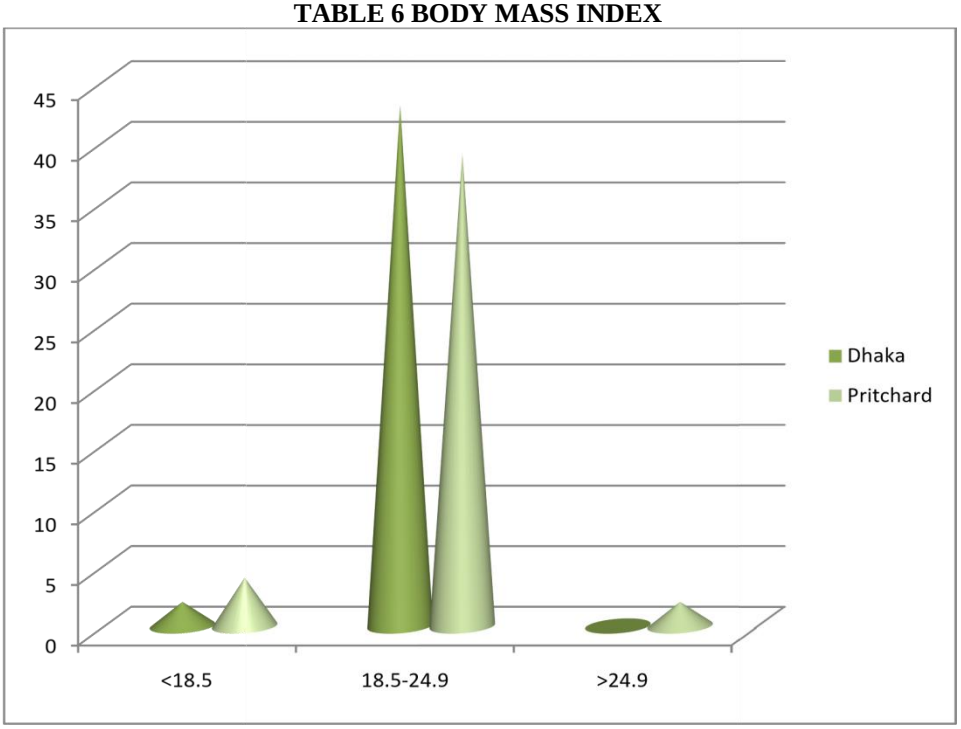
This table denotes distribution of cases according to geographical area.91.11% .

TABLE 5: BODY WEIGHT



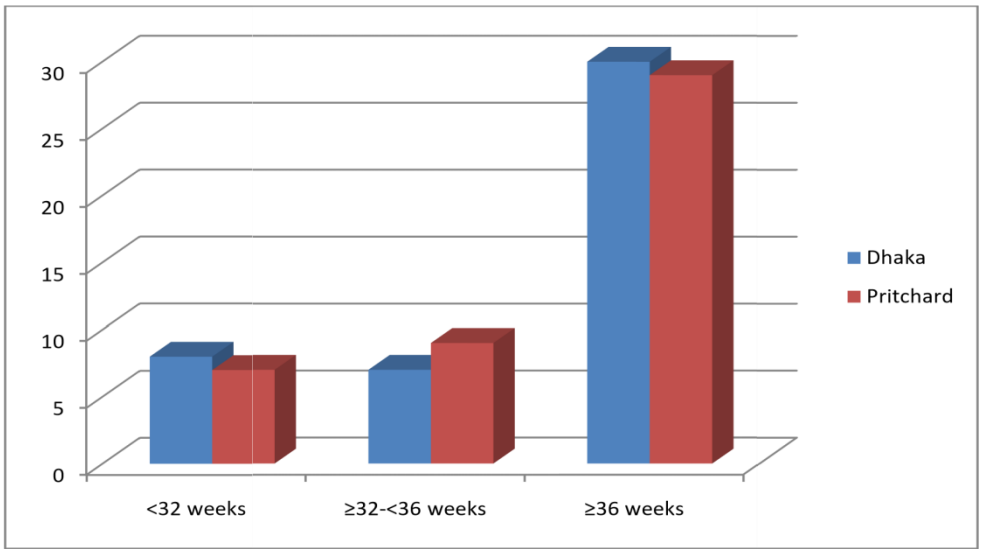
This table denotes cases distribution according to body weight. Most patients had average weight between 50-60kg (in Dhaka group 95.56% and in Pritchard
86.67%).

TABLE 6 BODY MASS INDEX



In this study most of patients (91.11%) had normal BMI (18.5-24.9) {in Dhaka group 95.56%, and in Pritchard group 86.67%

TABLE 7: GESTATIONAL AGE



The mean gestation age was ≥36 week.

TABLE 8: TYPE OF ECLAMPSIA

Type	Dhaka		Pritchard	
	Numbers	Percentage	Numbers	Percentage
Antepartum	40	88.89	44	97.78
Intrapartum	1	2.22	1	2.22
Postpartum	4	8.89	0	0.00
Total	45	100	45	100

In this study most common type of Eclampsia was antepartum Eclampsia, in which 88.89% had in Dhaka group, 97.78% in Pritchard group

TABLE 9: RECURRENCE OF CONVULSION AFTER STARTING REGIMEN

Convulsions after starting Regimen	Dhaka		Pritchard	
	Numbers	Percentage	Numbers	Percentage
Nil	44	97.78	45	100
≥ 1	1	2.22	0	0
Total	45	100	45	100

Recurrence of convulsion was seen in only 2.22% in Dhaka group and there was no recurrence in Pritchard group.

TABLE 10: KNEE JERK REFLEX

Knee Jerk	Dhaka		Pritchard	
	Numbers	Percentage	Numbers	Percentage
Present	43	95.56	41	91.11
Absent	2	4.44	4	8.89
Total	45	100	45	100

Knee jerk reflex was absent in 4.44% in Dhaka group, 8.89% in Pritchard group.

TABLE 11: OLIGURIA

Urine Output	Dhaka		Pritchard	
	Numbers	Percentage	Numbers	Percentage
<30ml/hr	2	4.44	4	8.89
>30ml/hr	43	95.56	41	91.11
Total	45	100	45	100

In this study 6 patients had oliguria, in which 2 cases (4.44%) belong to Dhaka group and 4 cases (8.89%) belong to Pritchard group.

VI. Discussion

AGE DISTRIBUTION –

Mean age in present study was 23.42±3.84 (20-24year).As this is maximum reproductive potential physiologically and usual age of child bearing according to culture background. As Eclampsia is more common in teenage mothers but in present study patients below 20 year of age were minimum (8 out of 90 patients), as there is improvement in literacy rate.

PARITY-

Eclampsia was more common in primigravida (66.66%). Majority of studies were depicted same results. However in study by Sanjeev et al[16] Eclampsia was more common in multigravida. Eclampsia is a disease of the first pregnancy as

- Women exposed to chorionic villi for the first time
- Immunological incompetence seen in first pregnancy between fetoplacental and maternal tissues.
- Primigravida had higher circulating sflt1 levels and sflt1/PIGF ratios than multiparous suggesting an association with an angiogenic imbalance.

ANTENATAL STATUS-

In present study majority of the patients had no antenatal visit. In developing country like India there is negative health seeking behaviour of patients due to ignorance and illiteracy, so early screening of pre Eclampsia and subsequent complications can't be prevented. Similar results were observed by the Ranjana et al[17], Anshu et al[15] studies.

GEOGRAPHICAL DISTRIBUTION-

Our hospital is a government hospital, major tertiary care centre, which caters referrals from major part of western Rajasthan. This is because in rural area, there is lack of awareness, lack of resources and health facilities and prevalence of various taboos and culture beliefs, preventing them from seeking medical health

GESTATIONAL AGE-

In present study Eclampsia was more common in rural area as compared to urban area. Because in Eclampsia as gestation age increases, blood flow to placenta decreases, resulting UPI and subsequent oxidative stress. Ranjana et al[17] and Bhagat et al[12] also observed similar results.

TYPE OF ECLAMPSIA-

As shown in Table 8 in present study ante partum Eclampsia was most common. Due to lack of awareness and illiteracy, patients do not access to health facility, so pre Eclampsia is not picked up early.

In recent years there is decrease in postpartum Eclampsia probably due to better antenatal care and prophylactic use of magnesium sulphate in severe pre Eclampsia during antepartum and intrapartum period. Eclampsia is a placental disease so after removal of placenta, ultimately the risk naturally reduces. Similar observations were made by Sanjeev et al[16], Sulatana et al[14] and Patil et al[13].

RECURRENCE OF CONVULSION AFTER STARTING TREATMENT-

In current study recurrence was observed in only 2.22% in Dhaka group and there was no recurrence in Pritchard group. Low dose of magnesium sulphate in Dhaka group may be responsible for slightly more recurrence. P value was 0.50, which is not statistically significant.

According to Table 10,11as dose of magnesium sulphate was high in Pritchard group, so all complications knee jerk reflex, oliguria were more in Pritchard group as compare to Dhaka group. Magnesium

sulphate toxicity correlate with its serum level which can be assessed clinically so as dose of magnesium sulphate increases probabilities of toxicity increases.

VII. Conclusion

Magnesium sulphate is Hobson's choice as an anticonvulsant for Eclampsia. It is a magical drug with tragic potential due to narrow therapeutic range.

It is speculated that dose of magnesium sulphate should vary according to body mass indices.

"If women appear to be small, the dose should be small."

This gave birth to the concept of low dose regimens for small size women.

Our study shows that low dose regimen (Dhaka) is equivalent to the high dose regimen (Pritchard) in controlling convulsions, preventing the recurrence of convulsion with slight difference in incidence of complications.

So with equivalent efficacy, favourable toxicity, complication rate and better perinatal outcome, the low dose $MgSO_4$ is a tenable alternative to standard dose regimen.

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ABBREVIATIONS

MgSO4	-	Magnesium Sulphate
ARF	–	Acute renal failure
HDOP	–	Hypertensive disease of pregnancy
DTR	–	Deep tendon reflex
BMI	–	Body mass index
NICU	-	Neonatal intensive care unit
LSCS	–	Lower sector caesarean section
IUGR	–	Intra uterine growth retardation

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