THE
Journal of Obstetrics & Gynaecology of India

VOLUME XV, No. 3 JUNE 1965

MANAGEMENT OF ECLAMPSIA

(At the Patna Medical College Hospital from 1954 to 1963)

by

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This paper is at best an apology, because the treatment of eclampsia is still in the dark, and the disease continues to take a heavy toll of life in our part of the world. Varieties of hypotensive, sedative and anti-convulsant drugs have been employed for the treatment of eclampsia with varying results. Unfortunately the aetiology of eclampsia continues to remain evasive and the treatment as empiric as ever. We have made an attempt to review the management of eclampsia in our hospital during the past 10 years.

The incidence of eclampsia at the Patna Medical College Hospital during the period 1954 — 1963 was found to vary between 0.38 and 0.78%, as detailed below in Table I.

TABLE I

Incidence of Eclampsia at the Patna Medical College Hospital

Year	Total No. of cases of eclampsia	Total No. of deliveries	Incidence %
1954	25	3826	0.67
1955	17	4491	0.38
1956	23	5276	0.42
1957	37	4700	0.78
1958	35	6110	0.57
1959	43	7210	0.52
1960	33	6727	0.49
1961	33	7235	0.45
1962	40	8171	0.48
1963	53	8712	0.60

Mitra (1951) worked out the incidence of eclampsia at 1.1%, and Krishna Menon (1961) found the incidence as 2.1% during the years

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Received for publication on 29-1-65.

1923 and 1929, and 1.6% during the years 1953 and 1958. The incidence at the Patna Medical College Hospital was found to be significantly lower.

It is interesting to review the type of people who are prone to fall a victim to the disease. It would appear from the census report of this State that 28.5% of our female population residing in rural areas are labourers earning their daily wages through hard manual work in fields and homes. Such women assimilate their food well, enjoy open air and sunshine, and seldom suffer from metabolic disorders and toxaemia. It was found that most of the eclamptics were anaemic and had sedentary habits and less opportunity for fresh air and sunshine. This lends support to the theory advocated by Theobald (1955) that eclampsia was a disease of disturbed metabolism which in turn resulted in deficiency of vitamins *a, b, c, d,* iron and calcium and that the deficiency adversely affected the endocrine glands and lead to disturbed hormonal balance and sensitization of the vascular system of the body. That the metabolic disorder has some bearing on the aetiology of eclampsia can be further supported by the fact that toxaemia is more commonly associated with diabetes which is a disease of disturbed metabolism with vascular complications and consequent hormonal imbalance.

For the treatment of eclampsia. varieties of sedatives have been used in different institutions. It must be, however, admitted that the so-called modern treatment of eclampsia is essentially based on the principles laid down by Stroganoff (1930) more than three decades ago. The two main principles of his regime of treatment were: (1) prevention of external stimuli by suitable nursing, and (2) reduction of sensitivity of the central nervous system by the use of sedatives. These principles have remained the sheet anchor of modern treatment of eclampsia, and sedatives, basal narcotics and hypotensive drugs have been employed for the the purpose.

Morphia was the main drug in the Stroganoff regime of treatment and continues to enjoy the place of pride in many institutions. Stroganoff used morphia in combination with chlora! hydrate and reduced maternal mortality to 2%.

In the present investigation we have used morphia in combination with one of the phenothiazine derivatives, viz. chlorpromazine (Largactil) which possesses hypotensive and, to some extent, anticonvulsant properties. Largactil is said to enhance the action of other sedatives, hypnotics, analgesics and general anaesthetics. Aoustin (1953), Grasset et al, (1953) and Baccaglind (1953) also reported successful employment of this drug in cases of eclampsia. Schmidt Elmendorft (1963) reported his experience of treating eclampsia with chlorpromazine in combination with diethazine and phenobarbitone. More recently, Mitra (1955) reported briefly his results of the treatment of 46 cases of eclampsia with chlorpromazine. Krishna Menon (1956) treated 28 cases with promethazine and phenobarbitone and did not find the results encouraging.

Aguero (1957) injected, intravenously, a mixture of 25 mgs. of chlor-

promazine, 50 mgs. of promethazine (Phenargan) and 100 mgs. of pethidine in 8 c.cs. of 5% glucose solution, as many times as seemed necessary to control fits, in 56 cases. The maternal mortality was 5.4% in the series presented by Mitra et al, (1958). In an earlier series consisting of 125 cases, Mitra and Das Gupta (1957) gave intravenous injection of 12.5 mgs. of chlorpromazine and 12.5 mgs. of promethazine in 50 c.cs. of 5% glucose drip containing 50 mgs. each of chlorpromazine and promethazine in 540 c.cs. of the solution. Fits were checked in most of the patients by injecting a pint of the mixture in 5 hours. They also injected 100 to 200 mgs. of pethidine in 13 patients and thiopentone in two patients of status eclampticus.

Krishna Menon (1960, 1961) treated 402 cases of eclampsia during the years 1955 to 1961. He gave 25 mgs. of chlorpromazine and 100 mgs. of pethidine in 20 c.cs. of 5% glucose solution intravenously and 50 mgs. of diethazine intramuscularly. He then started drip infusion of 20% glucose solution containing 200 mgs. of pethidine per litre. In addition 20 mgs. of chlorpromazine and 50 mgs. of diethazine were injected alternately through the intramuscular route. The maternal mortality was 2.2%. It suggests therefore, that Largactil has been increasingly employed in recent years in combination with different drugs.

Management of Cases in the Present Series

During the period under study 339 cases of eclampsia were treated in this hospital. Out of these cases, 264 received injections of Largactil and morphia (Group I) and 75 cases were treated with magnesium sulphate and morphia (Group II), according to the schedule detailed below.

Regime of Treatment for Group I

0 hour	Morphia ¼ gr.	IM. +	Largactil 50 mgs. IM.
0 + 4 hours	Nil	+	—do—
0 + 8 hours	Morphia ¼ gr.	+	—do—
0 + 12 hours	Nil	+	—do—
0 + 16 hours	Morphia ¼ gr.	+	—do—
0 + 20 hours	Nil	+	—do—
0 + 24 hours	S.O.S.	+	—do—

Regime of Treatment for Group II

0 hour	Morphia ¼ gr.	IM.	
0 + ½ hour	Nil	+	Mag. sulph. 16 c.cs. (25%) IM.
0 + 1½ hours	Morphia ¼ gr.	+	Nil
0 + 5½ hours	Nil	+	Mag. sulph. 16 c.cs. if fit recurred otherwise 12 c.c.
0 + 11½ hours	Nil	+	—do—
0 + 19½ hours	Nil	+	—do—

The blood pressure, respiration and pulse rate were recorded every hour before and after medication. If the blood pressure at any scheduled time of medication was found to be 120/80 mm. Hg. or below, the administration of the drug was withheld. For Group II cases the knee jerk was tested as a

routine before repeating magnesium sulphate and in the absence of knee jerk the drug was withheld and 10 c.cs. of 10% calcium gluconate solution was injected intravenously. Not more than 20 gms. of magnesium sulphate was given during 24 hours in any case. The hypotensive and sedative line of treatment was followed for 48 hours after the cessation of fits or after delivery when it was felt that there was less danger of recurrence of fits. Crystalline penicillin (5 lac units) was injected intramuscularly every four hours in all cases as a prophylactic measure.

In addition to the above treatment the patients were meticulously nursed in order to cut off all external stimuli, and they were handled as little as possible. An indwelling catheter was used to assess total urinary output and urinary albumin and sugar. Repeated catheterization was avoided to minimise the risk of fits. Wooden mouth gags were used when fits were imminent to avoid injury to the tongue. In the presence of pulmonary secretion a suction appartus was used to clear bronchial congestion. Oxygen was administered after each fit to combat asphyxia. In unconscious patients two pints of 25% glucose solution were infused in drip for maintenance of nutrition and fluid balance during 24 hours; 10 c.cs. of 10% calcium gluconate solution was injected intravenously in all patients to prevent liver damage.

Among the 339 cases treated by us 200 were antepartum, 109 intrapartum and 30 postpartum. Out of the 109 patients admitted in labour, 60 delivered normally, in 28 cases the second stage of labour had to be cut short with the help of forceps, and in the remaining 21 cases membranes were ruptured to expedite labour.

Among the 200 cases of antepartum eclampsia, 22 delivered spontaneously. The remaining 178 cases posed the obstetric problems. In 138 cases with ripe cervix and vertex presentation, pregnancy was terminated by artificial rupture of membranes. In 4 of them, pitocin drip infusion was used in addition. The period of gestation in these cases varied between 36 to 40 weeks in 38 cases, 32 to 36 weeks in 90 and 32 to 36 in 10 cases. The remaining 40 cases had intrauterine death of the foetus and pregnancies were terminated by pitocin drip infusions. We did not have the necessity to resort to caesarean section in any of our cases.

Results

Effect of the Treatment on the Control of Fits

The efficiency with which fits could be controlled by treatment is detailed below in Table II.

It is obvious from Table II that in Group I. under Largactil-morphia treatment, fits could be controlled completely in 23% of the cases, and though fits recurred in 77% of the cases, their frequency was much reduced, the number of fits varying between 1 to 5 in 75% of the cases. Convulsions could not be controlled in two patients who later responded to pentothal sodium. Pulmonary secretion was remarkably absent in all cases.

In Group II, under magnesium sulphate-morphia treatment, fits were

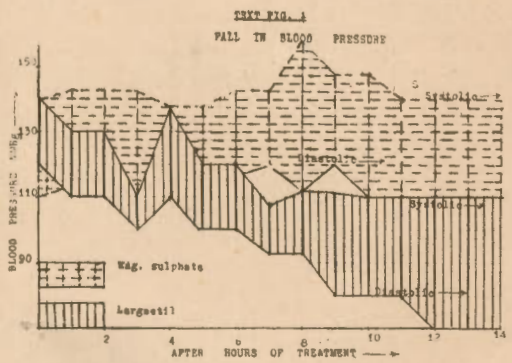
TABLE II

Distribution of Cases Before and After Treatment According to the Number of Fits

No. of fits	Largactil				Magnesium Sulphate			
	Before treatment		After treatment		Before treatment		After treatment	
	No. of cases	% of total 264 cases	No. of cases	% of total 264 cases	No. of cases	% of total 75 cases	No. of cases	% of total 75 cases
0	0	0	60	23	0	0	5	7
1 to 5	150	57	198	75	55	73	65	86
6 to 10	54	20	6	2	5	7	5	7
11 to 15	30	11	0	0	0	0	0	0
16 to 20	18	7	0	0	10	13	0	0
21 to 30	12	5	0	0	5	7	0	0
Total	264	100	264	100	75	100	75	100

completely controlled in 7% and recurred in 93% of the cases. The frequency of fits was reduced by this regime of treatment also, as 1 to 5 fits recurred in 86% of the cases. There were four patients in low condition having had 30 fits before admission and they did not survive.

The effect of both the regimes of treatment on blood pressure has been presented in Table III and IV and the typical fall in blood pressure at hourly intervals in the two regimes of treatment is graphically illustrated in Fig. 1.



From Tables III and IV it would appear that the maximum and the minimum drop in the systolic blood pressures in the Largactil treatment was 53 mm. Hg and 44 mm. Hg respectively as compared to the corresponding drop of 37 mm. Hg and 36 mm. Hg in the magnesium sulphate treatment. Similarly, the maximum and the minimum drop in the diastolic blood pressure in the Largactil treatment was 37 mm. Hg and 34 mm. Hg. respectively as compared to the corresponding figures of 30 mm. Hg and 23 mm. Hg in the magnesium sulphate treatment.

The drop in the blood pressure during the first 24 hours of the treatment was maintained for three hours in 90% of the cases with Largactil, and, therefore, administration of the drug every fourth hour ensured the maintenance of the lowered blood pressure for a longer period. In two of the cases in the Largactil group the blood pressure fell suddenly to 90/68 mm. Hg and 90/60 mm. Hg from 160/110/mm. Hg and 150/100 mm. Hg respectively but no adverse effects were noticed and the blood

TABLE III

Effect of the Treatment on Blood Pressure (MM. Hg.) During the first 24 Hours of Treatment

Regime of treatment	Type of eclampsia	Maximum		Minimum		Range	
		Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic
Largactil 264 cases	Ante-partum	160	115	116	81	44	34
	Intra-partum	164	112	111	75	53	37
	Post-partum	159	115	114	78	45	37
Magnesium sulphate 75 cases	Ante-partum	158	117	122	87	36	30
	Intra-partum	143	90	107	67	36	23
	Post-partum	145	90	108	60	37	30

TABLE IV

Average Daily Blood Pressure (MM. Hg.) Under the Treatment

Particulars of B.P.	Largactil								Magnesium sulphate	
	Ante-partum		Intra-partum		Post-partum		Average			
	Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic
Initial	160	110	163	110	160	110	160	110	158	112
1st day	136	100	133	90	134	94	135	96	132	90
2nd day	125	90	123	80	135	92	126	90	138	110
3rd day	123	84	123	80	130	90	125	89	130	99
4th day	115	80	123	80	130	88	120	81	130	90
5th day	120	75	123	80	124	90	120	82	126	86
6th day	123	70	120	78	125	85	122	80	128	88
7th day	124	82	120	78	124	85	123	80	126	87
On the day of discharge	122	78	120	78	124	80	123	80	125	90

pressure gradually rose and stabilized at normal levels.

In 16 cases out of 264 under the Largactil treatment and in 15 cases out of 75 under the magnesium sulphate treatment the blood pressure remained high at 140/90 mm. Hg even at the time of discharge.

Effect of the Treatment on Urinary Output, Oedema and Albuminuria

Though no diuretic property has been ascribed to chlorpromazine, urinary excretion improved in 90% of the cases in Group I and 60% of the cases in Group II after 24 hours of treatment. Krishna Menon (1961) remarked that in 95% of his cases good urinary output was maintained. With improved urinary excretion oedema gradually disappeared in all cases; proteinuria persisted in 20 patients on Largactil and 25 patients on magnesium sulphate at the time of discharge.

Effect of the Treatment on Pulse Rate, Temperature and Respiration

With both regimes, pulse rate came down to normal in three days. Tachycardia was observed only in 48 out of 264 cases, pulse rate being raised by about 11 beats. In the fatal cases, however, the pulse rate steadily increased. Krishna Menon (1956) and Mitra and Das Gupta (1957) observed tachycardia following the administration of chlorpromazine.

Rise of temperature in eclampsia may be attributed to infection of the genito-urinary tract or pulmonary infection. We administered antibiotics prophylactically in all our cases to prevent infection. Temperature came down to normal in all our cases. It is difficult to say if Largactil or antibiotics were responsible for lowering of the temperature. Krishna Menon (1955) noted a marked fall in temperatures of eclamptic patients.

We could not find any significant change in respirations after administration of the drug as other workers have.

Effect of the Treatment on Maternal and Foetal Mortality

In Group I, 8 patients out of 264, died; 4 of them were received in a moribund condition with 30 or more fits before admission. The failure of treatment in these cases is attributable to the fact that the drug had no time to act. Such mortalities are conventionally ascribed to the regime of treatment under trial, but in fact it should not be so. The blood pressure could not be brought down in 4 patients who died of sudden cardiac failure. They were all cases of postpartum eclampsia. The overall maternal mortality comes to 3% but the corrected mortality is 1.5% in this series.

Ten patients out of 75 died in Group II a mortality rate of 13.3%. Among these 10 patients, 4 had blood pressure of 190/120 mm. Hg and developed deep coma. Two patients developed pulmonary oedema and died of respiratory failure. Fits could not be controlled in three patients. One patient with postpartum eclampsia had 105°F temperature and the patient died of cardiac failure.

Discussion

As indicated earlier majority of the patients were anaemic and of sedentary habits. This indicates that

eclampsia is a disease of disturbed metabolism as suggested by Theobald (1955). As the exact aetiology of the disease is unknown, the treatment still remains symptomatic and various hypotensives, sedatives and narcotics have been employed for the purpose.

We had been using magnesium sulphate and morphia in eclamptic patients as advocated by Stroganoff and Davidovitch (1937). As the results were not encouraging, with the advent of chlorpromazine we started using it in combination with morphia. Robson and Keele (1958) used 2 gms. of chlorpromazine without any adverse effect. Krishna Menon (1960, 1961) used 200 mgs. of chlorpromazine per day and the initial dose was used intravenously. We, however, used 300 mgs. in divided doses of 50 mgs. each, intramuscularly in 24 hours, the consideration being that the number of fits should be controlled even where highly skilled medical aid is not available.

Efficiency of any line of treatment is judged by the effectiveness with which fits are controlled as in the words of Stroganoff and Davidovitch (1937) "each fit brings the patient a step towards the grave". In the simple regime of treatment presented here the greatest advantage is that chlorpromazine had a potentiating action with morphine sulphate and deep sedation could be achieved in the patient with complete stoppage of fits in 23% of the cases and though fits recurred in 77% of the cases, the number of fits was much reduced, varying between 1 to 5 only.

It is obvious from the results that fits were checked in the magnesium sulphate treatment also but with less effectiveness.

The effect of the treatment on blood pressure was quite satisfactory as it came down in 90% of the cases. Krishna Menon (1961) noticed a satisfactory drop in the blood pressure in 60% of his cases. In our series the blood pressure remained low for only about three hours and so it was necessary to repeat the drug every four hours. This tendency of blood pressure to rise was noticeable during the first 24 hours only. The blood pressure, however, came down effectively within 48 hours. The hypotensive effect of chlorpromazine was more marked in antepartum and intrapartum as compared with postpartum eclampsia.

The fall in blood pressure in patients under the magnesium sulphate regime was less marked than in patients under Largactil treatment.

We noticed in our cases that the urinary excretion improved after the lowering of the blood pressure. Consequently the oedema subsided and proteinuria disappeared. Pulmonary secretion was remarkably absent in patients under the chlorpromazine and morphia treatment. Krishna Menon (1961) was struck with the absence of pulmonary secretion in his patients and the pulmonary complication was reduced to a minimum. In none of our cases respiratory depression, attributable to morphia, was noticed.

Tachycardia was observed in only 48 out of 264 cases under the chlorpromazine and morphia treatment. Krishna Menon (1956) and Mitra and Das Gupta (1957) observed tachycardia following the administration of

chlorpromazine.

The placenta has been incriminated as one of the factors in the causation of eclampsia. On this assumption, termination of pregnancy by extracting the foetus through an incompletely dilated cervix was practised in the past. This resulted in high maternal mortality. Consequently this method of treatment fell into disrepute a long time back. Stroganoff (1928), in addition to his conservative management, terminated pregnancy by artificial rupture of the membranes when the fits persisted in spite of the treatment. He achieved improved results by the treatment. Krishna Menon (1938) ruptured the membranes as a routine in all cases, in addition to the sedative line of treatment.

We treated a total of 339 cases, and 109 of these were admitted in labour. Spontaneous delivery occurred in 60 patients and we had to cut short the second stage of labour with the help of forceps in 28 patients. We ruptured the membranes in 21 intrapartum cases and 138 antepartum cases of eclampsia with slight effacement of the cervix. The induction/delivery interval ranged from 10 to 12 hours and the delivery was uneventful. We had to infuse pitocin in 4 patients to accelerate uterine contractions after rupture of membranes and in 40 patients, with intrauterine death of the foetus, to induce labour. We were not in favour of doing caesarean section in patients having fits and in low physical condition for fear of losing the patients on the operation table. Greenhill is against routine caesarean section as this leads to high maternal mortality. Dieckmann (1950) performed caesarean section in cases of cephalopelvic disproportion and for closed and uneffaced cervix. Dewar (1947) recommended caesarean section when the induction was not successful after artificial rupture of the membranes. However, Krishna Menon (1961) performed caesarean section in 42 antepartum cases when fits could not be controlled in spite of the treatment. Only two of his patients had convulsions after the operation. The patients improved remarkably after 24 hours of delivery by caesarean section. We feel that he must have had patients in a much better condition to stand the operation.

The overall maternal mortality in the chlorpromazine treatment was 3% and as four patients were admitted in a moribund condition and could not avail of the treatment, the corrected maternal mortality comes to 1.5%. Krishna Menon (1961) noted maternal mortality of 2.2%. The overall maternal mortality in the magnesium sulphate treatment was 13.3%.

The foetal mortality under the two regimes of treatment, namely, chlorpromazine and magnesium sulphate, was 20% and 26.6% respectively. Krishna Menon (1961) noted a foetal mortality of 27.8%. The high foetal mortality rate in eclampsia is ascribed to prematurity and frequent use of sedatives, and under the treatment currently employed it appears unlikely that the two factors of foetal wastage can be eliminated.

On the whole we were impressed with the effectiveness of this simple regime consisting of chlorpromazine and morphia in the management of

eclampsia at the Patna Medical College Hospital.

Summary

1. The incidence of eclampsia at the Patna Medical College Hospital during the years 1954 to 1963 has been analysed. It has been noted that the disease was more prevalent in anaemic patients and patients with sedentary habits.

2. 264 cases of eclampsia were treated with chlorpromazine and morphia and 75 with magnesium sulphate and morphia. Chlorpromazine in combination with morphia had a more powerful hypotensive, sedative and anticovulsant effect than magnesium sulphate in combination with morphia.

3. No toxic or psychic effect of the prolonged use of chlorpromazine was noted.

4. The overall maternal mortality was 3%, and the corrected mortality, 1.5% under the chlorpromazine treatment. The overall mortality under the magnesium sulphate treatment was 13%.

5. The foetal mortality under the two regimes of treatment was 20 and 26.6% respectively.

6. Simplicity, safety and security were achieved by this treatment which could be adopted without any difficulty by doctors in villages where eclampsia is a major problem.

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