CHLORPROMAZINE IN THE MANAGEMENT OF PRE-ECLAMPTIC TOXAEMIA

(A Critical Review of 243 Cases)

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Chlorpromazine, a phenothiazine derivative, popularly known as Largactil or Thorazine, though introduced in the medical profession only recently since 1953, is remarkably known amongst others for its sedative, hypotensive, hypothermic and potentiating action of other sedative drugs. Very few drugs in medicine have been attributed to possess so many properties and recent literatures flourish with widely varying reports concerning its clinical application in different conditions. A fair trial of the drug had been given in cases of eclampsia by Aoustin, Grasser and Elmendorff and in this country by Mitra and Menon with appreciable reduction in maternal mortality and pulmonary complications. The encouraging results so far reported prompted us to study the effect of the drug not only in eclampsia but also in pre-eclamptic toxaemia from the point of view of preventing such cases to reach to the stage of eclampsia or in bringing down severe cases of pre-eclampsia to milder ones with reduction of hypertension.

Paper read at the 10th All India Obstetric & Gynaecological Congress at Hyderabad in January 1959.

During the years 1956 and 1957—3474 cases of pre-eclamptic toxaemia had been treated and delivered in Eden Hospital, while the total number of obstetric admissions during the same period had been 30,362—thus giving an incidence of the complication as 11.4%. The cases received treatment on the usual lines of bed rest, salt restriction, sedatives with/-out hypotensives and diuretics. The maternal mortality had been 0.54% and uncorrected foetal mortality of 5.7%.

243 consecutive cases of pre-eclamptic toxaemia were studied and cases were grouped as follows and results compared. A blood pressure of 130/90 mm. Hg. associated with oedema and/or albuminuria was taken as the criterion of pre-eclamptic toxaemia in the series.

The distribution of the cases in different groups according to the grade of severity of the triad of symptoms of toxaemia are arranged in Table No. I.

In all the groups, the patients received a salt restricted diet, rich in protein and diuretics; haemopoetics were used as conditions demanded.

Analysis of Results: (Tables II, III and IV)—In the whole series, 52.7% cases were below 24 years of age. 37% were primigravidae and 69.1% between 36-40 weeks of pregnancy. 8.6% of the cases were calculated to be post-mature from the menstrual history.

TABLE I

Distribution of Cases According to Symptom Triad of Toxaemia

	Group I	Group II	Group III (Control)
Total no. of cases 243	84	99	60
B.P. mm. Hg.			
130-160	54	58	37
160-200	28	37	22
Above 200	2	4	1
Oedema			
+	62	71	42
++	15	17	12
+++	7	11	6
Albumin			
Trace	17	25	14
Moderate	6	10	5
Solid on heating	1	3	1
Anaemia			
10 gms. + %	16	19	12
7-10 gms. %	63	71	46
Below 7 gms. %	5	9	2

Group I—84 cases: The patients received 50 mgm. Chlorpromazine and 50 mgm. of Promethazine intramuscularly 8-hourly.

Group II—99 cases: The cases received 100 mgm. of Pethidine hydrochlor. intramuscularly in addition to the above. In both the groups injections of chlorpromazine were replaced by tablets when B.P. came down to 120/90 mm. Hg.

Group III—60 cases as control receiving sedatives like morphine, mag. sulph., barbiturates and bromides.

TABLE II

Age Group

Age in years	Group I	Group II	Group III	Total cases
15-19	21	27	15	63
20-24	26	21	18	65
25-29	16	20	21	57
30-34	13	15	3	31
35-39	6	12	2	20
40-44	2	3	1	6
45 and above	—	1	—	1
Total	84	99	60	243

TABLE III

Period of Gestation in Weeks.

Weeks	Group I	Group II	Group III	Total
28-31	2	6	3	11
32-35	20	15	8	43
36-40	53	69	46	168
40 & above	9	9	3	21
Total	84	99	60	243

TABLE IV

Parity.

Parity	Group I	Group II	Group III	Total
0	32	39	19	90
1	14	18	12	44
2	5	10	8	23
3	7	3	5	15
4	10	4	6	20
5	3	5	2	10
6	8	6	2	16
7	5	8	3	16
8	—	3	2	5
9 & above	—	3	1	4
Total	84	99	60	243

Severe headache and sleeplessness were the chief complaints in 36.4% and 61% cases respectively (Table V) but quick relief was noted in Groups I and II. Sleep was quiet and adequate after therapy and maximum effect was noted in Group II, where the duration of sleep even lasted for 16 hours. Hang-over was minimum in Group I. 32% of the cases in Groups I and II, however, who received prolonged and inten-

TABLE V

Analysis of Symptoms.

Symptoms	Group I	Group II	Group III	Total
Headache	45	48	40	133
Swelling of limbs	70	93	50	213
Sleeplessness	52	57	39	148
Pain abdomen	14	16	10	40
Scanty urine	50	56	35	141
Nausea & vomiting	14	21	6	41
Palpitation	5	8	7	20
Visual disturbances	—	2	1	3
Vaginal bleeding	1	—	1	2
Constipation	28	36	29	93
Burning sensation all over body	20	28	16	64
Loss of foetal movement	2	1	—	3

sive therapy were unable to get up from bed due to giddiness.

Nausea and vomiting were easily controlled in Groups I and II cases but in the control group it was sometimes increased. Burning sensation of the body was found in 26.3% of all cases. Low nutritional condition associated with vitamin deficiency might be a reason for the same. One amongst the cases who had a still-born baby (Group I) however, showed a raised glucose tolerance. Other symptoms like oedema feet, pain in abdomen, scanty urine, constipation, etc., responded equally well to treatment in all the three groups.

A fall in blood pressure was noticed almost every time after the first injection where the drug was used either alone or in combination. Drop in the range of 20-40 mm-Hg. was noticed in 48% cases in the therapy group against the 32% of the control cases.

The reduction of pressure was more marked in the systolic than in the diastolic pressure and depended on the initial level of pressure—the higher the initial pressure, the greater the fall.

The beneficial hypotensive effect was also noticed in a milder group of cases where there was some psychic factor playing in the form of anxiety and fear tension complex over the existing toxaemic syndrome.

The fall in blood pressure though fairly quick in manifestation, yet was not much prolonged in action. The average duration varied from 6-8 hours and was most marked in Group-II.

In 22 cases it was found that prolonged use of the drug gradually required a higher dosage to keep the patients at a controlled level of blood pressure. It was also noted in 10 cases, if the patients were kept at a fixed dosage of the drug, the blood pressure gradually went up till a larger dosage of chlorpromazine or suitable hypotensive, e.g. Serpasil was used.

In 7 cases only other hypotensive drugs were used in synergism and a relatively smaller dosage of these drugs (mainly Serpasil) were able to produce a desired beneficial effect.

In 16 patients sudden abrupt fall in systolic pressure of more than 50 mm.Hg. was noted but spontaneous recovery occured in each. Similar observances have been reported by Mitra and Menon in the treatment of eclampsia with Chlorpromazine.

The quick, abrupt, short acting action of the drug may be attributed to (a) anti pressor amine, (b) mild ganglion blocking, (c) vasodilating activity of the drug. The variations in the blood pressure can be seen in Table IV.

Urinary excretion improved with rest and salt restriction in all the cases on the average by 600-1000 c.c. But Chlorpromazine had no appreciable effect on the increase of the urinary output. Oedema was rapidly controlled but it appeared to be more due to rest and use of diuretics rather than to Chlorpromazine therapy. Weight gain was in no way different in Chlorpromazine treated cases than in the control group. No case of frequency of micturition or incontinence had been recorded after use of Chlorpromazine though reported by Lehman and Dobkin in normal persons.

TABLE VI

Variations of Blood Pressure.

Mm. Hg.		Group I	Group II	Group III
Systolic	0-10	14	9	11
	11-20	17	18	29
	21-30	21	32	17
	31-40	15	23	2
	41-50	8	10	1
	51-60	5	3	—
	61-70	3	3	—
	71-80	1	1	—
Diastolic	0-10	21	24	25
	11-20	39	46	33
	21-30	19	22	4
	31-40	5	6	—
	41-50	—	1	—

Albuminuria was present in 1/3rd of the cases and in five cases it was copious (2 gms./litre). Quicker disappearance of albumin from urine was noted along with fall of blood pressure in Groups I and II than in the control group.

About 72% of the cases were moderately anaemic (Hb. below 10 gm.%); 95% of nutritional type. Chlorpromazine offered no hindrance to the antianaemic treatment and improvement was equally noticed in all the groups after haematinic therapy. None of the patients treated with Chlorpromazine developed jaundice.

Total serum protein could be estimated in 180 cases and the average figure varied between 5.2 to 6.8 gm./100 c.c. Very little changes in protein content were noticed in Chlorpromazine treated cases as also corroborated by Lehmann (1954). In only one case there had been alteration in Alb./glob. ratio without any liver damage. Blood chemistry was within normal limits in nearly all the cases—one case only in the control group showed retention of urea (45 mgm.). Retinal examination revealed vasospasm in 39 cases in total but noted more in Group III. Relief of spasm was marked after therapy in cases belonging to both Group I and Group II.

History of previous toxaemia and eclampsia was suggested in 16 cases in the series of which 5 belonged to the last group. Induction of labour was necessary in 18% of Groups I and II, and 25% of Group III cases. The methods of induction were medical with castor oil, enema and Pitocin drip in 40 cases and surgical with low rupture of membranes in 28 cases; while high rupture was carried out in 20. No undue prolongation of labour was experienced with Chlorpromazine therapy and forceps rate was rather less by about 5% than in the control group (Table VII). Lower segment caesarean section was performed in 1 case belonging to Group II and that due to definite cephalopelvic disproportion.

TABLE VII

Effect of Labour.

Groups	Medical induction	Surgical induction	Average duration of labour	Forceps	C.S.	3rd stage complications	Maternal mortality	Foetal mortality
I	12	16	15.0 hrs.	15	x	2 (manual removal of placenta)	x	3
II	18	20		18	1	x	x	3
III	18	12	15.3 hrs.	14	x	1 (Cardiac failure)	x	5

Eclampsia developed in 3 primigravidae in the series. One belonging to Group II had convulsions shortly after the beginning of the treatment. She had initially a pressure of 210/130 mm.Hg. with severe oedema and heavy albuminuria (solid on boiling). The other two cases belonged to Group III. One of them had the initial blood pressure at 180/110 mm.Hg., moderate oedema with heavy albuminuria. She had the first fit 24 hours after admission though B.P. was 160/110 mm.Hg. only at that time. The other patient had the first fit in the second stage of labour though her blood pressure was brought down to the level of 130/100 mm.Hg. from 170/116 mm. Hg. on admission. There was only slight oedema but no albuminuria.

Accidental haemorrhage was noted in 2 cases—one in Group I and the other in Group III. In neither was the blood pressure raised to more than 150/100 mm.Hg. Cardiac failure was encountered in one case in the control group, the patient having suffered from rheumatic heart disease for a long time, and improved with treatment. No mother was lost during treatment in the series. 82% of the babies were above 5 lbs. and 17% between 3-5 lbs. The increased number of premature babies was probably due to inclusion of cases of more severe degree of toxaemia and also due to increased incidence of twin pregnancy in the series (4%). Four of the babies were still-born; foetal movements disappeared during treatment in 2 cases in Group I and in one in Group II. In one of the cases a raised glucose tolerance was noted though no sugar could be detected in the urine. There had been 7 neonatal deaths of which 5 were due to prematurity thereby giving a total foetal mortality of 4.5%. Foetal loss was greater in the control group of cases. No significant variation was noted in the rate of the occurrence of asphyxia or in its severity in study groups.

Only 106 cases turned up for check-up 3 weeks after delivery and in 25 the blood pressure was recorded to be above 140/90 mm.Hg. The cases were equally distributed among the three groups.

Though the number of cases studied in each of the groups is comparatively small, in conclusion the following observations may well be drawn:

(i) The drug is able to bring

down the blood pressure and the effect is more pronounced in patients with a relatively higher blood pressure.

(ii) The fall of blood pressure is transient and requires a prolonged and frequent administration of the drug.

(iii) An increasing dosage of the drug is required in a few patients for the control of the blood pressure as the treatment proceeds.

(iv) Water excretion, change in weight gain and control of oedema, etc., do not differ significantly from the control group.

(v) No hepato-toxic and allergic manifestations developed even with prolonged course of treatment.

(vi) Patients (8 cases of group III) who did not favourably respond with routine treatment (as in control group) showed satisfactory results when transferred to Chlorpromazine and Pethidine regime.

(vii) No pulmonary complications were generally noted even in the cases who developed eclampsia.

(viii) There were no untoward effects on labour or on the new-born. On the contrary this was found more suitable for its tranquilising effect or in alleying vomiting, restlessness, etc., and instrumental delivery was rather less frequent.

I take this opportunity to thank Dr. Sobhen Ghosh, the Research Assistant for the help I received from him in following up the above series of cases.

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