The Management of Eclampsia and Severe Pre-eclampsia with Diazepam and Dihydralazine

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SUMMARY

A study of the use of diazepam and dihydralazine in the management of 10 patients with eclampsia and 29 patients with severe pre-eclampsia was carried out in Central Africa. The results of this method of treatment are compared with the use of barbiturates or the lytic cocktail on a similar group of patients during the period immediately preceding the introduction of this regimen.

An improvement was noted both in the perinatal mortality rate (18% compared with 30% previously) and in the prevention of eclamptic fits. No maternal death occurred in patients treated with diazepam and dihydralazine, while two mothers died after eclampsia during the preceding period. The independent control of the blood pressure and level of sedation provided by this regimen facilitated the management of eclampsia and severe pre-eclampsia.

S. Afr. Med. J., **48**, 1459 (1974).

Pre-eclampsia and eclampsia are common and serious problems in tropical Africa, and are responsible for a considerable proportion of both perinatal and maternal mortality. Although rapid termination of pregnancy is the best way to control the eclampsia,[1] operation is frequently refused by the patient or her relatives, and a medical regimen, together with stimulation of labour, has to be used. At three hospitals in northern Zambia a variety of treatments were in use until mid-1970, generally relying upon sedation with barbiturates or mixtures of pethidine, promethazine and promazine (the lytic cocktail). In view of the continuing high perinatal mortality rates and the poor control of both hypertension and eclamptic fits, a different medical regimen was studied, using diazepam as an anticonvulsant and dihydralazine, a hypotensive with spasmolytic effects. Separate drugs are used because the hypertensive and convulsive effects of the eclamptic process are often unrelated. Favourable results with similar regimens have been reported.[2,3]

PATIENTS AND METHODS

The study extended over a period of 18 months, from September 1970 to March 1972, during which time 29 patients with severe pre-eclampsia (blood pressure exceeding 150/100 mmHg with albuminuria) and 10 patients with eclampsia, were treated. The results are compared with those of the preceding 2 years, during which traditional methods were used. This group included 27 patients with severe pre-eclampsia and 13 with eclampsia.

Sedation

Each patient received an initial dose of 10 mg diazepam given slowly intravenously, and at the same time a continuous intravenous infusion containing another 40 mg diazepam in 500 ml 5% dextrose was set up and adjusted so that the patient was kept in a sedated state from which she could easily be roused.

Hypertension

Each patient was given an initial intravenous injection of 6,25 mg dihydralazine, repeated after 20 minutes if the blood pressure remained elevated. Further doses of 6,25 - 12,50 mg dihydralazine were given whenever the diastolic blood pressure exceeded 100 mmHg. (An initial injection of 12,5 mg dihydralazine was used for the first 2 cases.)

Diuretics

In patients with gross oedema an immediate injection of furosemide 40 mg was given intravenously and repeated as necessary.

Analgesia

If the patient appeared restless during uterine contractions, intramuscular pethidine was given. Occasionally this augmented the effects of the other drugs, necessitating an adjustment of dosage.

Obstetric Management

Termination of pregnancy by the safest and quickest route was the aim. However, in an area where fear and tribal superstitions frequently held sway, consent for Caesarean section was often withheld. Under such circumstances labour was stimulated by rupture of the forewaters and an intravenous infusion of oxytocin.

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Date received: 7 January 1974.

The blood pressure, pulse rate and level of consciousness were noted every 5 minutes. The urinary output was recorded by measurements from an indwelling catheter. Whenever possible, vaginal delivery was further expedited by the use of the vacuum extractor or, during the second stage of labour, the obstetric forceps.

RESULTS

In Table I the series of patients given diazepam and dihydralazine is compared with a preceding group who received barbiturates or the lytic cocktail. Accurate assessment of the duration of gestation and even the maternal age was not usually possible in this region of Africa, and has not been included.

TABLE I. COMPARISON OF THE RESULTS OF TREATMENT

	Diazepam/ dihydralazine regimen	Barbiturates or lytic cocktail series
Total No. of patients	**39**	**40**
Cases of eclampsia	**10**	**12**
Eclamptic fits occurring after the onset of treatment	**1**	**4**
Maternal deaths	**0**	**2**
Perinatal deaths	**7 (18%)**	**12 (30%)**

No maternal death occurred in patients treated with diazepam and dihydralazine, whereas 2 mothers died after eclampsia during the earlier period when treatment with barbiturates or the lytic cocktail was in use. Only one eclamptic fit occurred after the commencement of treatment in this series, while during the earlier period reviewed it was noted that although the lytic cocktail was frequently successful in lowering the blood pressure, recurrent eclamptic fits occurred four times, and on two of those occasions the diastolic blood pressure was below 90 mmHg at the time of the fit. The average fall in blood pressure recorded 30 minutes after the injection of dihydralazine was 50 mmHg systolic and 40 mmHg diastolic.

There were 7 perinatal deaths in the 39 patients treated with diazepam and dihydralazine (18%), compared with a perinatal loss of 30% during the period before the introduction of this regimen. Two perinatal deaths which occurred in the presence of severe pre-eclampsia might have been prevented had the mothers (or their relatives) consented to Caesarean section early in labour. An intrauterine death which may have been the result of an abrupt fall in blood pressure after an initial injection of 12,5 mg dihydralazine, is discussed below.

DISCUSSION

Any comparison of the results of treatment of pre-eclampsia and eclampsia is made difficult by the wide variations in the duration and severity of the condition. An attempt has been made here to compare groups that are essentially similar in race, background, and in the severity of eclamptic process. The majority of these patients had received no antenatal care and some had been in labour for several days by the time they were admitted to hospital. After treatment with diazepam and dihydralazine improvement was noted in both the maternal and perinatal mortality and in the prevention of eclamptic fits. The size of the groups is too small for the results to show statistical significance.

Diazepam was used as an anticonvulsant and the level of sedation was readily adjusted by the nursing staff so that the woman could be aroused easily and there was no loss of reflex activity. Such ease of control is an important factor in areas where specialised nursing facilities are not always available. No excessive sedation of the fetus by the diazepam was noted. By contrast, depression of both the mother and fetus often occurred when the lytic cocktail was used in those dosages necessary to reduce the higher blood pressures to acceptable levels.

Hydralazine derivatives have the theoretical advantage of promoting dilation of the cerebral, renal and placental blood vessels,[4] where vasoconstriction has been held responsible for some of the clinical effects of eclampsia.[5] Dihydralazine reduced the blood pressure in every case in this series, and on only two occasions was the diastolic pressure above 100 mmHg 30 minutes after the second injection. Tachycardia frequently followed its use but the pulse rate rarely exceeded 110 beats/minute.

On one occasion an abrupt fall of blood pressure to 90/40 mmHg occurred after an intravenous injection of 12,5 mg of dihydralazine given to a woman soon after her admission to the unit with severe pre-eclampsia (blood pressure 170/120 mmHg) and complaining of frontal headache. The fetal heart, which had been heard on admission, was subsequently inaudible. Although it could not be established whether the hypotension or the pre-eclamptic process was responsible for this fetal death, the regimen was thereafter modified by halving the initial dose of dihydralazine to 6,25 mg intravenously to act as a test dose, and the same amount was repeated after 20 minutes if necessary. Subsequent amounts, which were rarely necessary within 3½ - 4 hours, were gauged according to the initial responses. A minor degree of tachyphylaxis to the dihydralazine was sometimes noted.

Lack of information regarding the aetiology of the eclamptic process has meant that treatment is largely empirical and is directed at the effects of the condition rather than at its underlying cause. The hypertensive and convulsive effects are frequently disproportionate and independent control of these two factors provides a more balanced form of therapy.

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