

FRUSEMIDE (LASIX) IN THE TREATMENT OF TOXAEMIA OF PREGNANCY AND PREMENSTRUAL TENSION

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Toxaemia of pregnancy contributes to a great extent to perinatal mortality and also to maternal mortality and morbidity. It complicates 5-10% of pregnancies and early puerperium. Pre-eclampsia and eclampsia are believed to be two stages of the same disease. There is no denying the fact that these are largely preventable with good antenatal care and timely treatment results in a substantial lowering of maternal and perinatal morbidity and mortality.

Abnormal weight gain is one of the earliest signs and a gain of more than 2 pounds in any one week should be looked upon with suspicion. The next important sign is a rise of blood pressure. Albuminuria is usually the last sign to appear. Headache, visual disturbances, epigastric pain and vomiting are signs of impending eclampsia.

The exact etiology of pregnancy toxæmia is still not known, hence therapy is purely symptomatic. Salt restriction, diuretics and anti-hypertensive agents form the backbone of therapy in pre-eclampsia. Sedatives and anticonvulsants are additionally used in cases of eclampsia.

Since 1967, a short acting, very effective diuretic Frusemide (Lasix), which

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can be used by oral or parenteral route has been available in India. Since Lasix is reported to be effective even when glomerular filtration is markedly impaired, the present study was undertaken to evaluate its efficacy in toxæmia of pregnancy.

Material and Methods

Frusemide was evaluated in 50 patients. Thirty-two cases were of pre-eclampsia, 11 of eclampsia (9 antepartum, 2 postpartum) and 7 of premenstrual tension. Patients suffering from pregnancy-toxæmia were all hospitalised, while those suffering from premenstrual tension were treated as out-patients.

On admission, a detailed history was taken regarding date of last menstrual period, presence of nausea, vomiting, visual disturbances, oedema, bleeding, etc. A detailed clinical examination was then carried out and the findings recorded in a standard proforma. A daily record of cardiac rate, blood pressure, oedema, body weight and urine output was maintained.

Urinalysis, haemoglobin estimation and serum Na & K estimations were done in all patients. Urine analysis was done every day, while serum Na and K levels were repeated at the end of the trial.

Frusemide was made available as tablets of 40 mg. each and in ampoules of 2 ml. each containing 20 mg. In pre-

eclampsia, 40-80 mg of the drug was given daily orally; in addition, all patients received phenobarbitone 60 mg twice daily. A few cases were also given antipyretic-analgesics, antispasmodics, or antiemetics, if indicated. Salt and water restriction was observed in all cases.

In eclampsia, frusemide 40 mg was given intramuscularly daily for the first few days and then reduced to 20 mg intramuscularly daily. In addition to fluid and sodium restriction, patients were also treated with intramuscular paraldehyde and magnesium sulphate. The results in pregnancy-toxaemia were evaluated at the end of 10 days therapy.

In cases of premenstrual tension, 40 mg. of frusemide was given orally on alternate days, beginning one week prior to menstruation upto the end of the cycle.

The results were graded as good (complete relief), fair (partial relief) or poor (no relief) depending on the degree of improvement in clinical and laboratory findings.

Results

Table I summarizes the results obtained.

(A) *Pre-eclampsia*: The average weight loss in 10 days was 2.5 lb. although some patients lost as much as 6 to 8 lbs. within

10 days. The average blood pressure was 144/94 mm Hg. before therapy; by the tenth day it had fallen to 127/87 mm Hg. The fall in blood pressure was highly significant ($P < 0.01$) for both systolic and diastolic.

The mean pre-treatment serum Na level of 150 meq/l had fallen to 146.5 meq/l ($P < 0.001$) by the tenth day; however, the fall in serum K was insignificant from 3.8 meq/ initially to 3.6 meq/l on the tenth day. On the basis of overall response, 27 cases (84%) were judged to have obtained complete relief, while 5 cases (16%) had only partial relief.

(B) *Eclampsia*: There were 9 cases of antepartum and 2 cases of postpartum eclampsia. The blood pressure fell from the initial average of 165/115 mm to 135/95 mm by the tenth day. Serum Na level fell from 148.3 meq/l initially to 145.6 meq/l by the tenth day. The initial and final average values of serum K were 4.1 meq/l and 3.6 meq/l respectively.

All the 11 cases had marked clinical and biochemical improvement.

(C) *Premenstrual Tension*: Out of 7 cases treated, 5 had dramatic relief of their symptoms, while 2 cases showed no improvement. In cases that improved, the duration of complaints ranged from

TABLE I
Results Obtained With Frusemide

	Number of cases	Number of patients with response to treatment		
		Good	Fair	Poor
Pre-eclampsia	32	27	5	-
Eclampsia				
Ante-partum	9	9	-	-
Post-partum	2	2	-	-
Premenstrual tension	7	5	-	2

8 months to 3 years. The patients who failed to improve were suffering since 6 months and 4 years respectively.

No adverse reactions were noticed in any of the patients. Hypokalaemia was not seen in even a single case.

Discussion

The exact etiology of toxæmia of pregnancy is still not known. Probably several factors operate at different organ levels to produce the total clinical picture. All investigators however agree that retention of sodium and water is the most important biochemical alteration present in all cases. Hence, a potent diuretic has a rightful place in the therapeutic schedule. In this respect frusemide is the diuretic of choice. It has a quick onset, the intensity of diuresis is directly proportional to the dose used and its relatively short duration of action does not inconvenience the patient.

In the present series, out of 32 cases of pre-eclampsia, good results were obtained in 27 cases (84%). Several authors Tanaka *et al.*, (1966), Wu *et al.*, (1966), Yuasa *et al.*, (1965) have reported elimination of oedema fluid in 67-100% of cases depending on the dose used. Kanda *et al.*, (1966) reported an average fall in body weight by 3.4 kg. with 80 mg. frusemide given in divided doses. Tanaka *et al.*, (1966) found an average weight reduction of 2 kg., while Wu *et al.*, (1966) report a fall in body weight by 1.5 kg. In our series the average weight lost was comparatively less, being about 1 kg.

Blood pressure was elevated in all our cases and it also significantly improved without the addition of any antihypertensive agents. This effect can be attributed to water and sodium elimination in addition to bed rest. Albuminuria was present in 10 cases and in 9 cases it cleared

up together with the improvement in other clinical and biochemical findings. Yuasa *et al.*, (1965) and Kanda *et al.*, (1966) did not find any improvement in albuminuria in their cases.

There was a definite fall in the serum Na level from an average of 150 meq/l to 146.5 meq/l, while the serum K was not altered. This finding is in agreement with that reported by De Cecco (1965). This characteristic of frusemide to have only a slight effect on potassium elimination in comparison with the magnitude of diuresis is a definite advantage. With the older diuretics one had also to bear in mind the possibility of iatrogenic hypokalaemia in a patient with a grossly disturbed 'milieu interior'.

There were 11 cases of eclampsia in our series and good results were obtained in all. What is also important is that all the 9 cases of antepartum eclampsia could be managed successfully on medical lines without having to terminate the pregnancy. In the series reported by Ratnam *et al.*, (1966), out of 92 cases with severe pre-eclampsia, pregnancy had to be terminated in 27 patients. Wu *et al.*, (1966) treated 2 cases of eclampsia with frusemide, with satisfactory results. However, it must be emphasized that medical treatment must be combined with good obstetrical judgement.

Premenstrual tension is the term used to describe a group of physical and mental symptoms commencing in the latter part of the menstrual cycle and ending with the onset of the menstrual flow. In most cases, psychoneurosis plays a prominent role. However, in some cases there is definite sodium retention and an increase in the extracellular body fluid, probably the result of excess oestrogens. These women may gain as much as 4-5 lb. instead of the normal $\frac{1}{2}$ -1 lb.

Jeffcoate (1962). In such cases, diuretics have a definite place in the treatment schedule, and give a dramatic relief in the symptoms. This is borne out in our series where 5 out of the 7 cases studied had complete relief irrespective of the duration of their symptoms. Of course, it is understood that the drug would have to be repeated in each subsequent menstrual cycle.

Summary

Out of 32 cases of pre-eclampsia, 27 (84%) cases had complete relief, while 5 cases (16%) had partial relief.

All the 11 cases (100%) of eclampsia had complete relief in their symptoms.

Hypertension improved without the use of any other antihypertensive agents. Albuminuria cleared up in 90% cases. There was a distinct fall in the serum Na levels, while the serum K levels were hardly altered.

In 5 cases of premenstrual tension,

there was a dramatic and complete amelioration of all the symptoms with the very first course of frusemide therapy. In 2 cases there was no improvement.

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