Medical Memoranda

Fatal Hypernatraemia after a Saline Emetic

Hypertonic saline can be used to provoke vomiting in cases of acute poisoning in attempted suicide.¹ In certain circumstances this may lead to dangerous side-effects as illustrated by the following report.

CASE REPORT

A 74-year-old man was admitted to hospital, having taken 60 mg. of perphenazine ("fentazin") and 750 mg. of imipramine ("tofranil"). This quantity had been intended to represent a ten-day supply. He had been prescribed these tablets by his general practitioner the previous day for what was considered to be mild depression. Apart from having had a transvesical prostatectomy for benign prostatic enlargement in 1957 there was no relevant history of organic disease.

On examination he appeared to be well nourished. He could respond to simple questions and obey simple commands, and could hold a tumbler and drink on request. Agitation and a coarse Parkinsonian tremor of the hands were conspicuous.

The pulse rate was 84/min., regular, and blood-pressure 115/80 mm. Hg (a recording the previous day by his general practitioner gave 170/90 mm. Hg). Crepitations were present at both lung bases. The pupils reacted sluggishly to direct light; there was no neck stiffness, and Kernig's sign was negative. The patient was able to move all limbs equally. Tendon jerks in upper and lower limbs were brisk. Clonus was absent but both plantar responses were extensor.

An attempt to pass a stomach-tube was unsuccessful because of resistance by the patient. To provoke vomiting a tablespoonful of NaCl (30 g.) in 300 ml. of warm water was given and the patient drank this but no vomiting occurred. The dose was repeated, and only when he lay flat did he vomit, approximately 150 ml. being recovered. There was no retching. The vomit was discarded.

An intravenous infusion of NaCl 0.18% in dextrose 4.3% for the purpose of blood lavage,² and a course of penicillin, were begun. Urethral catheterization was required 10 hours after admission for acute retention of urine. The urine output for the first 24 hours was 2,100 ml. The patient's condition was unchanged for approximately 20 hours. From this time his condition deteriorated. A tachycardia with frequent ventricular ectopic beats accompanied signs of increasing pulmonary congestion, raised jugulo-venous pressure, and the development of sacral oedema. The systolic blood-pressure remained around 115 mm. Hg until shortly before death. Serial biochemical estimations are shown in the accompanying Table.

	Na (mEq/l.)	Cl (mEq/l.)	K (mEq/l.)	Bic. (mEq/l.)	Urea/mg. 100 ml.
On admission	143	120	4.3	26	37
24 hours after admission	174	152	3.7	25	45
27 hours after admission	172	152	3.7	25	45

The patient died 32 hours after admission.

The post-mortem findings confirmed the clinical diagnosis of pulmonary oedema. There were lesser degrees of oedema in other organs.

COMMENT

The cause of death in this patient was pulmonary oedema secondary to hypernatraemia, which in turn was caused by the absorption of a large quantity of hypertonic saline used in an attempt to produce vomiting. This attempt failed

because the patient had taken an overdose of perphenazine, a chlorpromazine derivative, which is a potent anti-emetic. The Parkinsonian state³ and hypotension⁴ are well-recognized side-effects of phenothiazine drugs.

Imipramine has no anti-emetic effect and may even cause nausea and vomiting as a side-effect.⁵ It can cause a Parkinsonian tremor.⁶

The anti-emetic effect of chlorpromazine is well documented⁷ and according to Wang⁸ perphenazine is 16.6 times more potent as an anti-emetic than the former drug and is more widespread in its anti-emetic action.

The rapid increase in levels of serum sodium and chloride could not be explained by the 10.8 g. of NaCl present in 6 litres of 4.3% dextrose and 0.18% NaCl which the patient received intravenously.

The total intake of NaCl was approximately 70.8 g. (60 g. orally and 10.8 g. intravenously). This is equal to 1,180 mEq Na.

Assuming a total body water of 50 litres, the expected rise in serum sodium would be 23.6 mEq. The observed rise, as the Table shows, was 30 mEq. In view of the possible loss of sodium in the vomit it is suggested that a complex interplay of osmotic forces of sodium in the gut and in the circulation must account for the observed rise in serum sodium.

Hypertonic saline—1 oz. (31 g.) of NaCl to 8 fl. oz. (227 ml.)—is listed in "Drugs of Special Value" section in the H.M.S.O. (1962) publication.¹ That this treatment carries a considerable risk where the new anti-emetic drugs are concerned is illustrated by this case report.

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Foetal Death after Pethidine and Promazine

Encouraged by reports on the value of promazine ("sparine") in obstetrics (Donald, 1959; MacVicar and Murray, 1960; etc.), we have made increasing use of this drug in the maternity department at St. George's Hospital over the past two years. During the five months preceding the admission of the case described below, 160 patients had received one or more injections of promazine 50 mg. with pethidine 150 mg. intramuscularly during the first stage of labour. No ill effects to any mother or child had been observed, and it was our general impression that labour was considerably less of an ordeal for a patient under the influence of this combination of drugs than with pethidine alone. Apart from intramuscular sedation in labour we have also successfully used an intravenous mixture of pethidine, promazine, and levallorphan on many

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occasions to produce a state of "hypo-aesthesia" before performing delivery under pudendal block (Crawford, 1958a, 1958b). In addition, intravenous pethidine and promazine alone had often been given, with gratifying results, either in a particularly painful first stage or as a premedication before surgical induction of labour.

We therefore believe that the employment of pethidine-phenothiazine mixtures forms a considerable advance in obstetric analgesia. Nevertheless, among the mounting literature on the place of these substances in labour no account has so far appeared where foetal death was a direct consequence of their use, and the following case should therefore be placed on record.

CASE REPORT

A primigravida aged 22 went into spontaneous labour at 42 weeks after an entirely normal pregnancy. Her blood-pressure on admission to hospital was 130/85 mm. Hg and the urine for the first time contained a trace of albumin. Irregular weak contractions continued over the following 24 hours and the blood-pressure rose to 135/105; it was therefore decided to perform an artificial rupture of membranes.

Intravenous premedication was given consisting of pethidine 100 mg. with promazine 50 mg. dissolved in 20 ml. of saline, taking five minutes over the injection. Immediately before this the foetal heart rate was 140, the maternal pulse was 96, and the blood-pressure 130/100. Five minutes after the injection the patient was placed in the lithotomy position and the membranes were ruptured and the forewaters released. At the end of this procedure and 15 minutes after the injection the foetal heart rate was 72. The patient appeared pale and shocked, with a thready pulse of 120 and a systolic blood-pressure of 70 mm. Hg. She said afterwards she felt she had been given the biggest gin-and-tonic of her life. Over the next 15 minutes the maternal and foetal condition remained unchanged. It was thought that the foetal distress was secondary to the patient's collapsed condition and she was transferred to the operating-theatre, where mephentermine 15 mg. was given intravenously with atropine 0.6 mg. and anaesthesia was induced with nitrous oxide, oxygen, and halothane. A living female child was delivered by lower segment caesarean section approximately one hour after the original injection of pethidine and promazine. An intravenous drip of 5% dextrose had been set up during the operation but was discontinued on returning to the ward, when the blood-pressure was 150/100. By the following morning the blood-pressure was 120/80 and normal levels persisted thereafter.

The child weighed 8 lb. 10 oz. (3,910 g.). It was flaccid and asphyxiated at birth, with a heart rate of 40. After endotracheal intubation there was a slow response to mucus extraction and oxygen by catheter; nalorphine 0.5 mg. was injected via the umbilical vein and nikethamide 0.25 ml. given intramuscularly twice. Regular respirations were established only after 40 minutes and remained extremely shallow. The baby died 40 hours after delivery and a post-mortem examination showed the general features of an asphyxial death with no evidence of trauma or congenital defect.

COMMENT

Chlorpromazine ("largactil") was the first of the phenothiazines to be employed in obstetrics, but as intravenous techniques began to develop the drug was found to be too unpredictable and likely to cause alarming falls in blood-pressure, quite apart from its other toxic side-effects (Hershenson *et al.*, 1956; Kuntze and Sison, 1957). This led Crawford (1959) and O'Sullivan (1960, 1962) to recommend promethazine as a substitute which appeared to be much less liable than chlorpromazine to cause significant hypotension.

The first account of the use of promazine in labour was that of Sprague (1957), who used a combined intravenous

injection of pethidine 50 mg., promazine 50 mg., and scopolamine 0.6 mg. Investigating 677 patients, he found that any resulting hypotension was minimal and required no active therapy. From a study of 100 consecutive patients Kuntze and Sison (1957) concluded that intravenous promazine "appeared to satisfy all the criteria for adjunctive medication in obstetrics." None of their babies required even minimal resuscitation. A similar view was expressed by Wegryn and Marks (1958) after comparable experience, although they drew attention to the danger of producing severe hypotension in asthmatics. Both papers underlined the necessity for frequent recordings of blood-pressure and foetal heart rate. Sippel (1958) preferred to avoid the intravenous route. Nevertheless, he recorded an alarming episode 45 minutes after an intramuscular dose of only 25 mg. when the blood-pressure fell to 60/0. Recovery, however, was rapid and no resuscitation of the baby was required. In a more recent study of this subject MacVicar and Murray (1960) investigated a controlled series of patients with intravenous pethidine and promazine separately and in combination. Their general conclusion was that the giving of promazine reduced the amount of pethidine required.

Our own experience with both intramuscular and intravenous pethidine-promazine mixtures had been entirely without mishap until the case described here. We accept that either drug could be incriminated as responsible for the maternal collapse and that the dosage of each was large merely to prepare a patient for surgical induction of labour. Indications apart, it seems clear that an unexpectedly high potentiation of pethidine by any of the phenothiazines may occasionally take place even after a carefully controlled injection. From discussion with others and from a brief study of the literature we find considerable variation in the amounts of pethidine used intravenously, but many advocate a similar technique to ours and higher doses than 100 mg. are not uncommon.

Further study of the management of intravenous sedation in obstetrics would be valuable.

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A film intended for the interest and education of general practitioners, "Long-term Care After Partial Gastrectomy," sponsored by Glaxo Laboratories Ltd., has been made by Mr. J. A. Williams, of the Department of Surgery, Queen Elizabeth Hospital, University of Birmingham Medical School. The film, copies of which may be borrowed from Mr. Williams, is 16 mm. colour, with a sound commentary.