PAPERS

Neurological aspects of hyponatraemia

PETER DAGGETT*
M.R.C.P.

JOHN DEANFIELD
M.R.C.P.

FIONA MOSS
M.R.C.P.

The Central Middlesex Hospital, Acton Lane, London NW10

Summary

Hyponatraemia is a common biochemical finding, but clinical features due to it are infrequent. They are most likely to occur when the plasma sodium concentration has fallen quickly to below 120 mmol/litre. In a study of 73 hyponatraemic individuals, it was possible to identify four categories of patient, the clinical features becoming more severe as the sodium level fell. In 25 instances there were no effects (mean plasma sodium 118.3 mmol/litre), in a further 25 cases there was confusion only (mean plasma sodium 117.1 mmol/litre), in 13 there were focal neurological signs and in 10 there were convulsions (mean plasma sodium 110.8 mmol/litre). In the group with convulsions there were six deaths, the four survivors all being young women. The 13 cases of 'focal' neurological signs included three instances each of hemiparesis and monoparesis, seven of extra-pyramidal disturbance and six of cerebellar ataxia. All these abnormalities resolved when the plasma sodium concentration rose to 125 mmol/litre.

Active measures to raise the plasma sodium level are only needed when there have been convulsions and the aim should be to achieve a value no higher than 120 mmol/litre. In other cases, the only treatment required is to restrict fluid intake.

Introduction

Disturbances of the plasma sodium concentration are frequent in hospital in-patients and we have reported previously the clinical associations of hyponatraemia (Daggett *et al.*, 1979). Hyponatraemia is a commoner biochemical abnormality, which has been studied by other groups (Thomas *et al.*, 1978; Kennedy, Mitchell and Hoffbrand, 1978), but it is noteworthy that clinical effects from this are uncommon. When they do occur, the nervous system is most

prominently involved (Janakiraman, 1974) and may be damaged irreversibly. Neurological disease caused by a lowered plasma sodium concentration is protean and influenced by the severity of the abnormality and by its speed of development. We have made a study of patients with a plasma sodium level below 121 mmol/litre and we report here details of their neurological findings.

Patients and methods

During a prospective, year-long study of disturbances of plasma sodium concentration, 92 patients were identified, with a level below 121 mmol/litre on at least two occasions separated by 24 hr. Nineteen of these had major neurological disease before the development of the biochemical abnormality and were excluded from this report. The remaining 73 individuals had no identifiable structural lesion of the nervous system, but were suffering from a variety of conditions, listed in Table 1. The mortality of these patients was generally associated with the underlying disorder, rather than with the hyponatraemia.

TABLE 1. Conditions associated with hyponatraemia

Associated disease	Number of cases	Deaths in this group
Renal impairment	18	7
Chest infection*	18	12
Inappropriate ADH secretion	14	2
Iatrogenic fluid overload	10	1
Obstetric causes	4	0
Drug induced	4	0
Addison's disease	2	0
Hypothyroidism	2	0
Liver disease	1	1

*Includes six patients with lobar pneumonia (who all survived) and twelve in whom bronchopneumonia occurred as a terminal event in other illnesses.

*Present address: Staffordshire General Infirmary, Stafford ST16 2PA.

TABLE 2. The neurological categories of hyponatraemic subjects

	No apparent effect	Confusion only	Focal signs	Convulsions
Number of cases	25	25	13	10
Deaths	10	8	3	6
Mean age (years)	57.1	71.6	65.2	63.9
Mean plasma sodium (mmol/litre)	118.3	117.1	115.9	110.8
Range of plasma sodium (mmol/litre) ¹	115-120	111-120	101-120	104-118

Liver function was assessed in the 73 patients by measuring bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase. No patient had values for any of these of more than twice the upper point of the reference ranges. Renal function was assessed by measuring the serum creatinine on two occasions 24 hr apart. In the 18 patients with renal impairment, the values were between 200 and 500 μ mol/litre; in the remaining 55 subjects, they were below 150 μ mol/litre.

The patients' state of hydration was assessed clinically in the usual way and the jugular venous pressure or measurements of central venous pressure were used to judge the circulating volume. The observer who made all the neurological examinations was aware of the plasma sodium concentration at the time. The examination was made at the time of maximal biochemical disturbance, but in patients who had convulsed it was deferred for 24 hr. The patient was judged to be confused if disorientated in time and space, and when replies to standard questions were inappropriate. Ataxia was judged to be of cerebellar origin when there were associated features, such as dysidiadokokinesia and past pointing. Extrapyramidal dysfunction was diagnosed when there was rigidity of lead pipe or cogwheel type, or when there were involuntary movements or tremor, which could be minimized by volition.

Results

The neurological findings fell into four categories, the abnormalities becoming more severe as the mean plasma sodium for the group fell (Table 2). In 25 instances there were no neurological abnormalities and the hyponatraemia had no apparent effect upon the outcome of the illness. In another group the most prominent feature was confusion, often associated with confabulation, resolving when the plasma biochemistry returned to normal; there was no evidence that hypoxia played any role in these cases.

Thirteen patients showed a variety of focal neurological signs, summarized in Table 3. In the 10 survivors from this group, the signs all remitted when

the plasma sodium rose to and remained above 125 mmol/litre. The fourth category contained 10 patients who had sustained a generalized convulsion. In each case, the fit had been preceded by a period of confusion, tremulousness and muscular twitching and was followed by prolonged stupor. Six patients failed fully to recover and eventually died of respiratory complications, despite the maintenance of normonatraemia and measures to reduce cerebral swelling. The four survivors were all young women, whose hyponatraemia had been induced by an infusion of oxytocin in 5% dextrose, used to accelerate labour. All recovered over periods of 1 to 12 months and details of their illnesses will form the subject of a separate report (Daggett and Shields, in press).

TABLE 3. Focal neurological abnormalities associated with hyponatraemia

Abnormality	Number of instances
Hemiparesis	3
Monoparesis	3
Rigidity (leadpipe/cogwheel)	3
Extrapyramidal type of tremor	4
Cerebellar ataxia	6
Horizontal nystagmus	4
Pupillary inequality	2

In some patients, more than one abnormality occurred. Ten of the 13 patients in this group survived, and in these cases, the neurological abnormalities resolved when the plasma sodium concentration rose to 125 mmol/litre.

In the group of patients who were judged clinically to be fluid overloaded, there was no apparent relationship between the degree of overload and neurological features, including confusion. Similarly, in patients with renal impairment there was no correlation between the physical signs and parameters of renal function.

Discussion

There is great variation in the clinical consequences of hyponatraemia. There may be no apparent effects at all, a predominantly psychiatric presentation with psychosis (Burnell, 1972; Ralston, Fogelman, and Lowe, 1982), or with one of several

neurological syndromes (Taclob and Needle, 1973; Glasser, 1971). Symptoms are most likely when the fall in plasma sodium concentration has been rapid (Thompson, 1979), but in any case they are uncommon until levels fall below 120 mmol/litre (De Troyer and Demanet, 1976). Cerebral oedema alone is usually responsible for the clinical features (Arora *et al.*, 1971), but this may result in occlusion of cerebral blood vessels.

Confusion is the commonest clinical abnormality (Arieff and Guisado, 1976) and with levels above 115 mmol/litre is usually the only problem. Convulsions are the next commonest mode of presentation, but only occur with values below 115 mmol/litre. A generalized fit is usual, but occasionally Jacksonian attacks occur (De Troyer and Demanet, 1976). The electroencephalogram shows high voltage delta and theta waves, but has no diagnostic features distinguishing the condition from other metabolic disorders (Schwartz *et al.*, 1969). When the illness is sufficiently severe for there to be fits, there is a 50% mortality (Thompson, 1979; Arieff and Guisado, 1976; Arieff, Llach and Massry, 1976), with the possibility of permanent disability in the survivors (Lipsmeyer and Ackerman, 1966).

Between the extremes of simple confusion and convulsions there exist several syndromes which, broadly speaking, occur with a plasma sodium concentration in the middle ground of 112 to 118 mmol/litre. They are uncommon and are associated with rapid changes in plasma electrolyte levels. Coma and stupor are probably part of the same spectrum of illness as confusion, occurring when the biochemical abnormality is more severe, but being consistent with full recovery (De Troyer and Demanet, 1976; Arora *et al.*, 1971). Paralyses, including hemiparesis (Ruby and Burton, 1977; Gilbert, 1966) and monoparesis occur rarely, but are also compatible with complete resolution. Extrapontine disturbances which have been described include tremor and rigidity (De Troyer and Demanet, 1976). Ataxia of cerebellar type, sometimes with nystagmus, has also been reported (Arieff and Guisado, 1976). The brain stem may be damaged by hyponatraemia and central pontine myelinolysis has been noted (Burcan, Norenberg and Yarnell, 1977) but, interestingly, the spinal cord and peripheral nerves appear to be unaffected by a low plasma sodium level. It is, however, possible that the muscular twitchings sometimes seen (Arieff and Guisado, 1976) originate peripherally, although myoclonic jerks (Gilbert, 1966) are almost certainly centrally mediated. The role of hyponatraemia in causing muscular cramps (Gotloib and Servadio, 1972) is largely anecdotal and we have not seen any examples in our series.

The wide spectrum of clinical features in our series and in the literature indicates that the hypo-osmolal-

ity consequent upon hyponatraemia can affect any part of the central nervous system. Clinical effects are usually only found when the plasma sodium concentration (and hence the osmolality) has fallen rapidly to below 120 mmol/litre (corresponding to an osmolality of 240 to 250 mmol/litre), and it is in such cases that therapeutic intervention is sometimes required. Chronic hyponatraemia, on the other hand, is seldom symptomatic, even when severe, and for practical purposes hardly ever causes problems when the plasma sodium level is above 120 mmol/litre. We have adopted the policy of using corrective measures to restore the plasma sodium only when there have been convulsions and the plasma sodium level is below 115 mmol/litre. This action will, of course, have no effect on the underlying cause and it should be remembered that energetic treatment may do more harm than good. In this small, selected group of patients, we infuse 5% saline in 100 ml aliquots over 30 min until the plasma sodium concentration reaches 120 mmol/litre; the infusion should then be discontinued (Daggett, 1979). We combine this treatment with dexamethasone by i.v. injection to reduce cerebral swelling and with phenytoin, to forestall further convulsions. In six patients so treated we have not seen further fits, nor have there been any unwanted effects. Lesser degrees of acute hyponatraemia and all chronic cases should be managed with fluid restriction alone.

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