Inappropriate antidiuretic state in long-term psychiatric inpatients

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Summary

To investigate the occurrence of an inappropriate antidiuretic state in a long-term psychiatric inpatient population, 690 patients underwent serum sodium determination. Forty-four patients (6.4%) had levels < 133 mmol/l. Fifteen of these patients could be investigated further and the biochemical findings in all were consistent with an inappropriate antidiuretic state. Evidence of previous episodes of water intoxication was found in 80% of these patients. Although more than one possible cause was present in most patients, the two factors most strongly incriminated in the pathogenesis of the inappropriate antidiuretic state were the drugs carbamazepine and hydrochlorothiazide.

Water intoxication is a well-recognised complication in certain patients with psychiatric disorders. The condition is characterised by seizures and confusion, and may progress to coma and death. Most of the cases appear to be 'self-induced', i.e. associated with polydipsia. However, polydipsia alone does not usually appreciably dilute body fluids because of the great excretory capacity of the kidneys, and it is now increasingly recognised that impairment of excretory capacity may be an additional necessary factor for the development of water intoxication. In this regard, an inappropriate antidiuretic state, manifest by polyuria and polydipsia, has been clearly documented in a number of such patients. Factors incriminated in the pathogenesis of the antidiuretic state in psychiatric patients include psychosis, alcohol withdrawal, psychotropic medication, carbamazepine, thiadie diuretics and smoking.

A study was undertaken to investigate the occurrence of an inappropriate antidiuretic state in long-term psychiatric inpatients, and to identify factors of pathogenic significance.

Patients and methods

All long-term inpatients at Stikland Psychiatric Hospital between the ages of 18 years and 70 years were screened for possible dilutional hyponatraemia. Blood samples for serum sodium estimation were obtained between 14h00 and 17h00, for one ward (containing usually between 30 and 50 patients) at a time. Serum sodium levels were determined on the same day using a Beckman Klina flame photometer.

Patients with hyponatraemia, i.e. serum sodium levels < 133 mmol/l, were kept recumbent, given nothing by mouth and abstained from smoking overnight.

Of 690 patients who underwent serum sodium determination, 44 (6.4%) had levels < 133 mmol/l. Twenty-nine of the 44 were excluded from further study for the following reasons: (i) inability to provide informed consent or to co-operate sufficiently (N = 14); (ii) concomitant physical illness (N = 4); and (iii) resolution of hyponatraemia before further studies could be carried out (N = 11). The remaining 15 patients, or 2.2% of the total population screened for hyponatraemia, had biochemical findings consistent with the diagnosis of an antidiuretic state (Table 1).

The following criteria were used as indicative of an inappropriate antidiuretic state: (i) body fluid hypotonicity, as indicated by a serum sodium value < 133 mmol/l; (ii) concomitant non-maximal dilution of urine, i.e. urine osmolality > 100 mmol/kg H2O; and (iii) no evidence of oedema, hypovolaemia, hypotension, hypoglycaemia, nausea or abnormal cardiac, renal, hepatic, adrenal or thyroid function.

Results

Of 690 patients who underwent serum sodium determination, 44 (6.4%) had levels < 133 mmol/l. Twenty-nine of the 44 were excluded from further study for the following reasons: (i) inability to provide informed consent or to co-operate sufficiently (N = 14); (ii) concomitant physical illness (N = 4); and (iii) resolution of hyponatraemia before further studies could be carried out (N = 11). The remaining 15 patients, or 2.2% of the total population screened for hyponatraemia, had biochemical findings consistent with the diagnosis of an antidiuretic state (Table 1). Other blood investigations indicated that no other recognised causes of impaired excretory capacity were present.

In order to establish whether factors implicated in the pathogenesis of the inappropriate antidiuretic state occurred more frequently in these patients, the following comparisons were made: using a chi-square test the 15 patients with an inappropriate antidiuretic state were compared with the 646 patients with normal serum sodium values for the following factors: diagnosis of schizophrenia, smoking, and the taking of psychotropic medication, carbamazepine or hydrochlorothiazide. The only significant differences found were that the patients with an inappropriate antidiuretic state were more often receiving the drugs carbamazepine (chi-square 8.40; df = 1; P < 0.005) and hydrochlorothiazide (chi-square 3.92; df = 1; P < 0.05). These two drugs were then discontinued in the 13 patients with an inappropriate antidiuretic

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Patients with an inappropriate antidiuretic state are at serious risk for the development of water intoxication — as demonstrated by the fact that 80% of cases in this study had evidence in their clinical files of previous episodes of water intoxication. While previous studies have highlighted the risk of water intoxication in patients with polydipsia, we in this study 12 of the 15 patients did not display excessive fluid intake. This would indicate that even more patients are at risk for developing water intoxication than was previously recognised. Considering the possible consequences (water intoxication may cause irreversible brain damage) and was found to be responsible for nearly one-fifth of deaths in schizophrenics aged < 53 years in a state hospital, the implications for clinical psychiatry would seem considerable.

Identification of these patients is important, since water intoxication, once diagnosed, can be effectively treated simply by restricting fluid intake. We suggest, therefore, that all long-term psychiatric inpatients at risk for the development of water intoxication be periodically screened for hyponatremia.

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REFERENCES


Discussion

In this study, evidence of an inappropriate antidiuretic state was found in 2,2% of long-term psychiatric inpatients. The actual incidence is likely to be considerably higher, however, since it was not possible to investigate almost two-thirds of the hyponatremic patients.

In most of the patients more than one possible cause of an inappropriate antidiuretic state was present, suggesting the possibility of a multifactorial aetiology. Cigarette smoking has been associated with vasopressin hypersecretion, as have neuroleptic drugs and schizophrenia. However, the two factors disproportionately over-represented in these patients compared with other long-term psychiatric patients were the drugs carbamazepine and hydrochlorothiazide. Furthermore, the fact that serum sodium levels returned to normal soon after their discontinuation indicates an important pathogenic role for these drugs.

Various mechanisms whereby these drugs induce an inappropriate antidiuretic state have been proposed. Carbamazepine may stimulate vasopressin release, enhance renal sensitivity to the hormone or have a direct effect on the renal tubule. Hydrochlorothiazide may cause an antidiuresis by reducing free-water clearance as a direct consequence of natriuresis or by stimulating the release of vasopressin.