other than metoclopramide and, in particular, had not received aspirin. There was a past history of asthma controlled in recent years by inhaled salbutamol. On admission he was vomiting, confused and irritable. Except for typical varicella skin lesions and clinical evidence of dehydration, there were no abnormal signs. Intravenous normal saline was given. After a few hours combative behaviour necessitated sedation with intravenous diazepam (and chlorpromazine). At this time bilateral extensor plantar responses were found. CT head scan and CSF examinations were carried out. Intravenous fluids were continued but no other medication was given. By the following day he was alert, cooperative and orientated and without abnormal neurological signs. A prompt and complete recovery was made and he remained well two months later.

Initial hospital investigation gave the following results: haemoglobin 16.4 g/dl, white cell count 12,200 × 10^9/l (62% polymorphs, 36% lymphocytes), platelet count 47,000 × 10^9/l, plasma glucose 6.1 mmol/l, urea 8.1 mmol/l, sodium 142 mmol/l, potassium 3.5 mmol/l, total bilirubin 13 μmol/l, aspartate aminotransferase activity 165 IU/l (normal 13–38), alkaline phosphatase activity 396 IU/l (normal range 75–245) and plasma ammonia 248 μmol/l (normal range 10–47). Clotting studies were normal. Two days later the platelet count was normal and the sole biochemical abnormality was aspartate aminotransferase activity 395 IU/l. Lumbar puncture on the second day of admission gave an opening pressure of 230 mm of water. The CSF contained no cells and protein content was 150 mg/l. CT head scan was normal. EEG performed on the third day of admission showed a mild bilateral excess of theta activity. Serum CFT to varicella zoster was positive at a titre of 1:320. Convalescent biochemical tests, including aspartate aminotransferase, were normal.

Perhaps due to wider recognition of the condition, mild cases of Reye's syndrome in children have been noted with increasing frequency. This case associated with an otherwise uncomplicated varicella infection indicates that mild cases also occur in adults. We suspect that Reye's syndrome may go unrecognised and emphasise the importance of measuring plasma ammonia levels in cases of acute encephalopathy with profuse vomiting. Prompt diagnosis is important because the mitochondrial changes and metabolic defects are normally self-limiting provided that the systemic biochemical disturbances particularly dehydation, hypoglycaemia and cerebral oedema, can be controlled.

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References


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Thiazides, compulsive water drinking and hyponatraemic encephalopathy

Sir; Compulsive water drinking frequently defies diagnosis until the patient develops hyponatraemic encephalopathy. This complication most often arises when normal homeostatic mechanisms are deranged.1 When such mechanisms are preserved, additional factors must be sought, one of which is the use of a thiazide diuretic.1 To our knowledge, there have been 11 detailed case reports of hyponatraemic encephalopathy in patients with compulsive water drinking taking a thiazide diuretic.1–7 The infrequency of this association was felt to merit a further addition to this literature.

A 48-year-old female was admitted to hospital in 1982 with a 7 day history of progressive confusion and restlessness. She had had a 20 year history of alcohol abuse. In 1972 she underwent uncomplicated aneurysm surgery for subarachnoid haemorrhage. Four years later she had a single generalised seizure, since when she had taken phenobarbitone 90 mg per day. For one year she had taken Moduretic (hydorchlorothiazide 50 mg and amiloride hydrochloride 5 mg) 1 tablet per day for hyper tension. On admission, she was restless, irritable and disorientated. There were no psychotic features. Physical examination was unremarkable. A provisional diagnosis of alcohol withdrawal was made and diazepam, 15 mg per day, and multivitamins were prescribed. The Moduretic and phenobarbitone were continued. Within 2 days her abnormal mental state had resolved, at which time blood biochemistry was normal.

Three weeks after admission, she came to be explained as insatiable thirst and was noted to be drinking large volumes of water. Symptoms of headache and vomiting were followed by confusion, coma and a single generalised seizure. At this time the serum sodium was 119 mmol/l; the potassium 3.3 mmol/l; bicarbonate 81 mmol/l; the creatinine 4.3 mmol/l; and the urea 4.9 mmol/l. The plasma osmolality was 237 mOsm/kg H_2O with coincident urine osmolality of 169 mOsm/kg H_2O, urine sodium of 24 mmol/l and urine potassium of 17 mmol/l. Other relevant investigations were normal.

Moduretic was discontinued and phenobarbitone was withdrawn 4 days later. Restriction of water intake resulted in rapid clinical recovery and return of biochemical parameters to normal. Shortly thereafter, a further episode of excessive water drinking occurred. Intake was restricted and there were no sequelae. Five weeks later she was discharged on phenobarbitone, 300 mg per day, having displayed no further desire to drink excessively.

There are at least three mechanisms whereby thiazides could have contributed to the hyponatraemia in our patient and the 11 other reported cases.1–7 First, as a direct consequence of natureresis. Second, as a result of reduced free water clearance. These mechanisms may have greatest relevance to the three patients who developed
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Hyponatraemic encephalopathy within 1 week of taking thiazides,\(^6\) since (with a constant intake) an “escape” from negative sodium balance can occur after 5 days of constant thiazide administration.\(^6\) Finally, thiazides have been implicated as a cause of the syndrome of inappropriate secretion of antidiuretic hormone.\(^1\) In our patient and in seven of the previously reported cases,\(^1\) biochemical findings at the time of hyponatraemic encephalopathy were compatible with Syndrome of inappropriate secretion of antidiuretic hormone (though thiazides may have contributed directly to the urine tonicitics)\(^6\).

Fichman et al\(^1\) proposed that thiazides stimulate release of antidiuretic hormone by extracellular volume contraction which in turn results from thiazide-induced potassium depletion. Such a mechanism of antidiuretic hormone release may be specially important in the development of hyponatraemic encephalopathy in patients with compulsive water drinking, since Hariprasad et al\(^1\) recorded hypokalaemia in 17 of such patients who were not taking diuretics. Thus in the four patients\(^1\) who were known to have either continuous or periodic compulsive water drinking, the introduction of thiazides may have acted as a further stimulus to antidiuretic hormone release and have been the critical factor in precipitating hyponatraemic encephalopathy. Also, it may be relevant that in six of the reported cases,\(^1\) serum potassium was <3.0 mmol/l at the time of hyponatraemic encephalopathy. In our patient, however, other mechanisms seem likely since she was also taking a potassium sparing diuretic and the serum potassium was 3.3 mmol/l.

As in all previously reported cases (with one possible exception)\(^1\) our patient had another illness or was taking another drug implicated in Syndrome of inappropriate secretion of antidiuretic hormone.\(^6\) Thus the precise role of thiazides in the development of hyponatraemic encephalopathy in these patients with compulsive water drinking remains uncertain. However, the very occurrence of such an association seems good reason to caution the use of thiazides in those patients at known risk for other causes of Syndrome of inappropriate secretion of antidiuretic hormone.

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References


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