Antidepressants, thiazide diuretics and alcoholism: central pontine myelinolysis waiting to happen?

Introduction

Hyponatraemia is a recognized complication in patients with excessive alcohol intake. Unfortunately it is not uncommon for patients with such a dependence to also suffer with depression. This article details the dangers of prescribing thiazide diuretics and tricyclic antidepressants in the alcoholic patient.

Discussion

Central pontine myelinolysis was first described by Adams et al in 1959 in patients with alcohol dependency and malnutrition. It is characterized by spastic quadriplegia, pseudobulbar palsy and varying degrees of encephalopathy. The patient can become drowsy and experience visual problems. In severe cases the patient can develop a 'locked-in' syndrome, with complete paralysis apart from blinking. Initial symptoms can appear within 2–3 days, with new problems continuing to arise over a 2–3-week period.

The myelin sheaths of the nerve cells in the pons become damaged and destroyed. The process is non-inflammatory and can also occur in the mid brain, thalamus, basal nuclei and cerebellum. The cause of this is severe and prolonged hyponatraemia, particularly if corrected too rapidly (Kleinschmidt-DeMasters and Norenberg, 1981). Cellular oedema is significant, with the intracellular components unable to compensate quickly enough when sodium is corrected. The principal diagnostic test is magnetic resonance imaging which shows areas of high signal on T2-weighted images in the pons.

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Alcohol and malnutrition are significant risk factors for central pontine myelinolysis, but it can result from any cause of hyponatraemia. Drugs which lower sodium are important, particularly in patients who are already at risk. There is an 11% incidence of some degree of hyponatraemia in elderly patients receiving a thiazide (Byatt et al, 1990). Patient age, body weight and serum potassium are independent risk factors (Chow et al, 2003). Selective serotonin-uptake inhibitors result in increased risk, with an odds ratio of 3.3 (95% confidence interval 1.3–8.6), as do tricyclic antidepressants (Tamres et al, 1995). Risk also increases with age (Movig et al, 2002).

The key to management of hyponatraemia is slow correction. For chronic onset it is felt that the sodium level should not rise by more than 12 mmol in 24 hours. A formula can be used to calculate how much saline can be safely given:

Change in serum [sodium] = Infulsate [Na] – serum [Na] / total body water +1

where concentrations are measured in mmol/litre and total body water = 0.5–0.6x the total body weight in kg (Russell et al, 2003).

However, many physicians feel it is safer to simply stop the offending drugs and to restrict fluid intake until the deficit has resolved unless the patient is having hyponatraemia-induced seizures.

Treatment is supportive, with an unpredictable outcome. Maximum recovery may take several months. Steroids have been tried without benefit. Mortality was thought

Case Report

A 50-year-old man, with a known weekly alcohol intake of almost 100 units, presented to his GP feeling drowsy. Routine blood tests revealed a profound hyponatraemia of 100 mmol/litre, and he was referred to hospital for investigations. On admission he was drowsy, but had a Glasgow Coma Scale score of 15, an abbreviated mental test score of 10/10 and an entirely normal neurological examination. Liver function tests were consistent with excessive alcohol consumption. He had been prescribed bendroflumethazide and clomipramine (a tricyclic antidepressant) by his GP. In view of their potential to cause hyponatraemia these were subsequently withheld and he was fluid restricted to 1.5 litres per day. His sodium level rose gradually and on day 5 of admission it had increased to 122 mmol/litre. He was discharged on day 8 having been advised to stop drinking.

Less than a week after discharge he represented to his GP with symptoms of excessive sweating, shaking, constipation, disorientation and dysarthria. He was febrile at 38.6°C , and had a blood pressure of 180/90 mmHg. Electrolytes were normal (Na+ 135 mmol/litre). Although he denied consuming any alcohol since his initial admission, his symptoms were consistent with acute alcohol withdrawal and he was treated accordingly. He failed to improve on two attempts at reducing doses of chlordiazepoxide. His dysarthria progressed until his speech was difficult to understand and his swallow became unsafe. He continued to spike temperatures throughout the admission and although a catheter specimen of urine was positive for enterococcus, treatment with a prolonged course of antibiotics had not resolved his fever.

A computed tomography scan of his head and a lumbar puncture were performed. Other than cortical atrophy in keeping with alcohol abuse, neither investigation provided any answers. It was considered that his symptoms could be explained by autonomic dysfunction. In view of his corrected hyponatraemia, central pontine myelinolysis was suggested and a magnetic resonance imaging head scan was performed (*Figure 1*). This confirmed the presence of central hyperintensity on the water sensitive sequences within the central pons, in keeping with an osmotic demyelination syndrome. Additionally these changes were identified within the caudate nuclei, possibly accounting for the patient's inability to fully control voluntary movement. The ongoing temperatures without sepsis suggested hypothalamic involvement.

Following diagnosis this patient failed to improve. Treatment became supportive, and he died 7 weeks later.

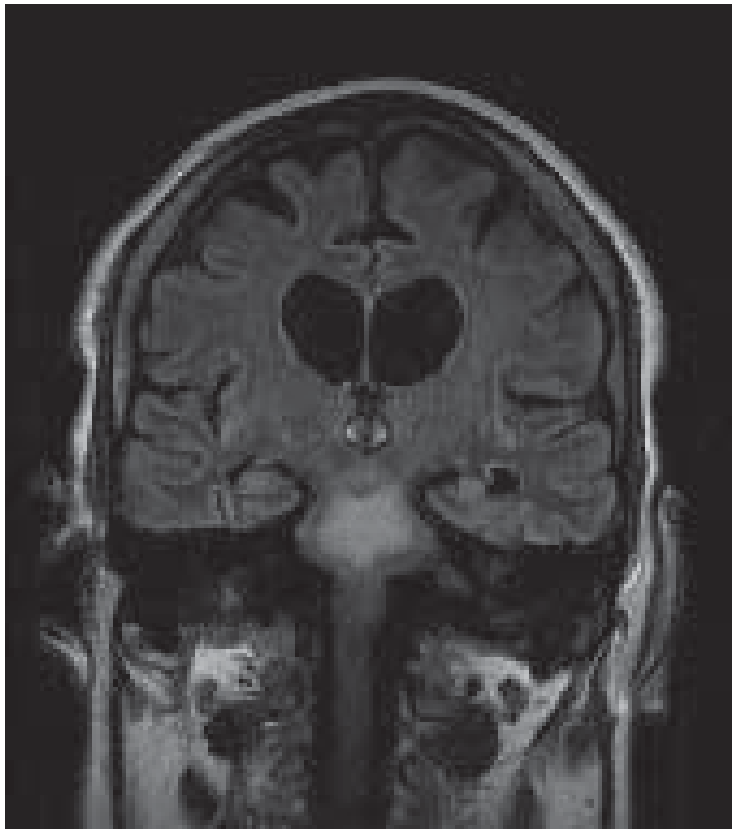

Figure 1. Magnetic resonance imaging demonstrating high signal in the pons consistent with demyelination.

to be as high as 50%, but death and disability are not invariable, and a study by Menger and Jörg (1999) showed a death rate of 19%. Of the survivors, 34% completely recovered, 34% had some deficit but were independent and 32% were left dependent, either from cognitive deficit, tetraparesis, ataxia or polyneuropathy. Surprisingly, the extent of the initial lesion was not correlated with the severity of the clinical findings. They felt that survival was more dependent on the management of secondary complications, such as aspiration pneumonia, septicaemia and pulmonary embolism.

Conclusions

This case highlights the importance of care in prescribing for patients with chronic alcohol-related problems, and the potentially catastrophic consequences which can occur from commonly used drugs. When correcting hyponatraemia care must be taken not to let the sodium rise too quickly. However, as seen in this case there is no guarantee that central pontine myelinolysis will be avoided. **BJHM**

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