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Hyponatraemic convulsions and fatal head injury secondary to desmopressin treatment for enuresis

EDITOR:

Desmopressin analogues (DDAVP) are licensed for the treatment of enuresis and are commonly prescribed by general practitioners and urologists for patients with nocturnal enuresis which is unresponsive to alternative treatments. Although generally well tolerated, these agents may have serious side-effects such as hypotonic hyponatraemia. DDAVP-induced hyponatraemia has been reported in adults treated for bleeding disorders and in children treated for enuresis but to date there have been few reports of symptomatic hyponatraemia developing in adults treated with DDAVP for enuresis. We describe a case of desmopressin-induced severe hyponatraemia in an adult being treated for nocturnal

In conclusion, we report a case where the use of

TEA in combination with antihypertensive therapy

may have caused a serious adverse event. Several lessons can be learned from this case report: firstly, in

patients with hypertension, starting two antihypertensive drugs at the same time may be dangerous. In

our patient, this was justified because of the severity

of the hypertension in combination with the urgent

need for the operation. However, starting two drugs

at the same time may influence BP too much, so it

seems prudent to start a beta-blocker first and even-

tually add an ACE-inhibitor later. Secondly, caution

should be taken when resuming antihypertensive

therapy in patients with TEA. In the absence of lit-

erature evidence, our recommendations in patients

on epidural analgesia are to resume antihypertensive

therapy only if the mean BP is within 20% of the

preoperative BP. Finally, in the direct postoperative

period, frequent BP recordings are very important,

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in particular in patients with epidural analgesia.

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enuresis which led to the development of seizures and a subsequent fatal traumatic brain injury.

A 27-year-old male was transferred to our neurosurgical intensive care unit (ICU) for management of a traumatic brain injury. He had developed seizures at home and subsequently fell off a chair injuring his head. His seizures continued and on admission to a local hospital he was fitting and deeply comatose with a Glasgow Coma Score (GCS) of 4. Intravenous diazepam and phenytoin were administered, his trachea was intubated, and an urgent computed tomography (CT) brain scan was performed. This showed a left fronto-temporal contusion with mass effect, and a small subdural haematoma (Fig. 1). Of note, he was hyponatraemic on admission with a serum sodium of 116 mmol L^{-1} and a calculated serum osmolality of $254 \operatorname{mosm} \mathrm{kg}^{-1}$. He was subsequently transferred to our neurosurgical ICU for further management.

His family revealed that he had been treated with desmopressin nasal spray for enuresis for the previous



Figure 1. CT brain showing a left fronto-temporal contusion with mass effect and a small subdural haematoma.

8 years. Enuresis seems to have been a problem only when he consumed alcohol. He had two previous admissions to another hospital in the previous 3 years with seizures associated with hyponatraemia. The first of these occurred when after consuming alcohol and cocaine he developed seizures and required tracheal intubation and ICU admission for 2 days. His sodium on this occasion was 112 mmol L^{-1} and a CT brain was normal. A further admission for seizures occurred a year later. Again alcohol had been consumed and he was noted to be hyponatraemic (Na⁺ 117 mmol L⁻¹). A diagnosis of probable 'alcohol-induced seizures' was made on that occasion and the patient was discharged. The history of desmopressin use was not obtained during these two previous admissions.

On arrival in our neurosurgical ICU an intracranial pressure (ICP) monitor was inserted and his head injury was managed according to our standard protocol aiming to maintain ICP <20 mmHg and cerebral perfusion pressure (CPP) >60 mmHg. Further laboratory tests confirmed the presence of hypotonic hyponatraemia. On clinical examination the patient was euvolaemic and his hyponatraemia was felt to be due to a combination of desmopressin treatment and excess fluid intake. As cerebral oedema secondary to traumatic brain injury is exacerbated by the presence of hyponatraemia, correction of his low sodium was imperative. Using a combination of hypertonic saline and fluid restriction his sodium rose from $116 \text{ mmol } \text{L}^{-1}$ to $130 \text{ mmol } \text{L}^{-1}$ over 24 h. Despite careful correction of his low sodium, and appropriate management of his head injury, he developed severe cerebral oedema and raised ICP necessitating a craniotomy and partial left frontal lobectomy. Postoperatively the patient continued to deteriorate, his ICP continued to rise and he died 4 days after admission from his head injury.

Desmopressin (DDAVP) is a synthetic structural analogue of antidiuretic hormone (ADH) licensed for the treatment of cranial diabetes insipidus, nocturia associated with multiple sclerosis and primary nocturnal enuresis. Compared with ADH, desmopressin has a longer lasting and more potent antidiuretic effect and is devoid of vasopressor effects. When used for the treatment of nocturnal enuresis, intranasal desmopressin can induce water intoxication with profound hyponatraemia and resultant seizures if water intake is not restricted.

There have been numerous case reports of desmopressin-induced symptomatic hyponatraemia in children treated for enuresis [1-6] but only a few case reports of this complication occurring in enuretic adults [7-9]. A recent review and metaanalysis of trials looking at the use of desmopressin in older adults with nocturia found the pooled estimate for the incidence of hyponatraemia was 7.6% [10]. This suggests that hyponatraemia as a complication of desmopressin treatment is relatively common. However in most cases the hyponatraemia is mild and asymptomatic. In a large randomized trial investigating desmopressin for long-term treatment of nocturia in 249 patients, the incidence of hyponatraemia was 14% but was clinically significant in only 0.8% [11].

The risk of developing hyponatraemia associated with desmopressin therapy is higher in those patients with above average fluid intake. In the case described above, the use of desmopressin followed by excessive alcohol intake precipitated a fall in serum sodium. Although the patient's demise was not directly due to the presence of desmopressin-induced hyponatraemia, it played a pivotal role leading to seizure activity and a subsequent fall resulting in a traumatic brain injury. The cerebral oedema which resulted was further exacerbated by the presence of hyponatraemia and ultimately proved fatal.

Due to the potential for serious adverse effects, desmopressin should not be considered as the first choice treatment for primary nocturnal enuresis. Careful selection of patients who will comply with instructions regarding restriction of fluid intake and who understand the potential serious adverse effects is necessary prior to commencing therapy with desmopressin. When therapy is commenced it is essential to monitor the patient's daily fluid intake and serum sodium periodically. These measures may help to prevent the development of this serious and potentially fatal iatrogenic condition.

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Total spinal anaesthesia following epidural test dose in an ankylosing spondylitic patient with anticipated difficult airway undergoing total hip replacement

EDITOR:

The use of regional anaesthesia in patients with a recognized difficult airway does not solve the problem of difficult airway; the difficult airway is still present. We report a case where giving regional anaesthesia in a patient with difficult airway, required emergency securing of the airway.

A 58-yr-old male patient (55 kg, 160 cm, ASA II) suffering from ankylosing spondylitis for 25 yr was scheduled for total hip replacement. Airway examination revealed interincisor distance of 4 cm, normal dentition, and reduced mentosternal distance of 6 cm due to fixed flexion deformity of neck. X-ray revealed ankylosis of spinous processes showing posterior joint involvement, resorption of the anterior surfaces of the vertebral bodies and ossification of the posterior ligaments and surrounding soft tissues. Anaesthesia was planned with a combined spinal epidural (CSE), separate needle technique, with difficult intubation cart ready. Premedication consisted of diazepam 10 mg orally the previous night and oral ranitidine 150 mg with metoclopramide 10 mg 2 h before surgery. On arrival in the operating room, routine monitoring was applied and an intravenous (i.v.) line was secured. The epidural block was

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attempted by the para-median approach through L_{3-4} space with the patient in the sitting position but the space could only be localized in the third attempt. While threading the epidural catheter, some initial resistance was met at the 10-cm mark but was overcome. Later, multiple attempts were made with 26-G Quinke's needle to locate the subarachnoid space, but free flow of cerebrospinal fluid could not be obtained and the procedure was abandoned. We decided to proceed with epidural block alone. Before fixing the epidural catheter, basal readings of heart rate (HR) and blood pressure (BP) were recorded and a test dose of lidocaine 2% 3 mL with epinephrine 15 µg (1:200 000) was injected, after negative aspiration, to confirm the position of catheter in the epidural space. Soon after the test dose the patient complained of dizziness and weakness. He was asked to lie down in the supine position and oxygen provided by face mask. Within a couple of minutes the patient became unconscious, apnoeic and BP dropped to 80/50 mmHg with severe bradycardia (heart rate $< 36 \text{ min}^{-1}$). Immediately atropine 0.6 mg and mephentermine 6 mg were given i.v. and attempts at mask ventilation with 100% oxygen were made. The patient's HR increased but it was not possible to mask-ventilate despite inserting an oral airway. An attempt to intubate the trachea with direct laryngoscopy also failed. By this time the patient had started desaturating with SPO2 reading 80%. However, we were able to place a size 4 laryngeal

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