Case Report

Hyponatraemic seizures resulting from inadequate post-operative fluid intake following a single dose of desmopressin

Zoltán Molnár¹, Viktor Farkas¹, László Nemes², György S. Reusz¹ and Attila J. Szabó¹

¹First Department of Pediatrics, Semmelweis University, Budapest and ²National Haemophilia Center, National Medical Center, Budapest, Hungary

Keywords: desmopressin; hyponatraemia; seizure

Introduction

1-Deamino-8-D-arginine vasopressin (desmopressin, DDAVP), a selective agonist of type 2 vasopressin receptors, has been widely used to treat enuresis. The early works of Manucci et al. have established that infusion of DDAVP elicits a rapid, transient rise in the levels of both plasma factor VIII (FVIII) and von Willebrand factor (vWF) [1]. This effect provides an approach to the treatment of mild haemophiliaacs, and, according to recent guidelines, DDAVP is the treatment of choice in these patients prior to minor surgical procedures.

The administration of DDAVP is often accompanied by headache, facial flushing, a drop of blood pressure and a secondary increase in heart rate. Moreover, since free water reabsorption in renal collecting ducts is enhanced, water intoxication and dilutional hyponatraemia may result. Though this effect can be easily prevented by water restriction, the ignorance of medical personnel or the inadequate compliance of patients may lead to severe hyponatraemia and the neurological sequelae that accompany it. The control of fluid intake during DDAVP treatment is therefore of utmost importance.

Here we present the case of a 3.5-year-old girl with mild haemophilia A who received a single intra-venous dose of DDAVP prior to adenotonsillectomy. Hypotonic fluid intake in the early post-operative period led to the patient rapidly developing hyponatraemia and its associated neurological symptoms. Correcting electrolyte abnormality with hypertonic saline stopped the recurrent convulsions, and the patient recovered without any residual neurological sequelae.

Case

The father of the index patient suffered from severe haemophilia A; the medical history of the patient’s mother was negative. According to the report of the comprehensive haemophilia care centre, the girl was a symptomatic carrier with a slightly reduced FVIII level (49 IU/dl). Though she was not tested genetically, the most plausible explanation for this symptomatic carrier state is non-random X chromosome inactivation (lyonization) in her liver cells. Aside from this, her medical history was unremarkable.

At the age of 3.5 years, she was considered a candidate for elective adenotonsillectomy because of chronic adenoid hypertrophy. To prevent perioperative haemorrhage, the patient received 250 mg of tranexamic acid (Exacyl, Sanofi-Chinoin) orally every 6 h and 0.3 mg/kg desmopressin (Octostim, Ferring) intravenously 30 min prior to the adenotonsillectomy. We found no history of any previous exposure to DDAVP. The patient’s serum sodium (Na⁺) was not checked in the morning of surgery, but her serum concentration ([Na⁺]) was 139 mmol/l 6 days before the operation. The operation was performed under intratracheal narcosis without any notable complications. Bleeding was within the normal range during surgery, and no excessive haemorrhage was observed in the early post-operative period. She was allowed to take fluids ad libitum; her total intake was roughly 600 ml in the first 10 post-operative hours. Approximately 12 h after the surgery, the girl was awoken by a mild headache and nausea; she later also vomited. Then she had a generalized, tonic-clonic seizure of 3 min duration, which resolved spontaneously. As a result, she was transferred to our department for further evaluation and treatment. While being transferred, the patient received 300 ml of 5% dextrose in half isotonic saline intravenously.

Correspondence and offprint requests to: Zoltán Molnár, MD, PhD, First Department of Pediatrics, Semmelweis University, Budapest, Bókay János u. 53, H-1083 Budapest, Hungary. Email: zmolnar77@hotmail.com

© The Author [2005]. Published by Oxford University Press on behalf of ERA-EDTA. All rights reserved.
For Permissions, please email: journals.permissions@oupjournals.org
At presentation in our department, the patient did not show any focal neurological signs. She still had headache; we also found her hard to arouse, but she withdrew from noxious stimuli. Her vital signs showed no significant deviations; her blood pressure was 110/70 mmHg and body weight 15.3 kg (based on her history, her body weight was 15.0 kg 12 h earlier). Serum glucose, calcium, magnesium and C-reactive protein were within normal limits; serum $[\text{Na}^+]$ was at 121 mmol/l. Serum osmolality was calculated to be 250 mosmol/l. At admission and in the first hour of hospitalization after transfer, the girl experienced more seizures and emesis. Having assumed that the observed neurological sequelae were due to acute hyponatraemia, we started to correct the electrolyte anomaly by infusing 3% NaCl solution, until the neurological symptoms disappeared (serum $[\text{Na}^+]$ was 129 mmol/l by that time). We also administered an intravenous bolus of $\sim 1$ mg/kg furosemide (Furon, Ratiopharm) at the beginning of our electrolyte therapy, to bring about a net water loss. The serum $[\text{Na}^+]$ rose to 137, 135 and 137 mmol/l 8, 14 and 30 h after admission, respectively. Ophthalmological investigation did not reveal papillary oedema, and the girl’s neurological examination was normal on the following days. Although a slight, generalized slowing of the background electroencephalographic (EEG) activity was observed on the first day, EEG records normalized within 10 days. The girl was doing well at her follow-up several weeks later and had no neurological abnormalities. Our patient’s medical history, laboratory data and fast response to treatment all indicate that she suffered from water intoxication. Her severe neurological symptoms were the consequence of cerebral oedema resulting from DDAVP-associated dilutional hyponatraemia.

**Discussion**

Information in the current literature suggests that mild, asymptomatic hyponatraemia should be considered a common side effect of DDAVP treatment [2,3]. A symptomatic form is much less frequent, though numerous papers report such cases. Hyponatraemia causes headache, nausea, vomiting and slightly altered mental status, which may turn into seizures, dramatically altered mental status and coma, as cerebral oedema progresses. These symptoms, signs and neurological sequelae are mainly associated with and follow chronic use or, at least, repeated doses of DDAVP [4]. Few papers report cases like ours, in which severe neurological symptoms were due to only a single dose of desmopressin [3,5–7]. Excess fluid intake, young age, overdosage and the potentiating effect of other drugs have all been identified as factors contributing to DDAVP-associated hyponatraemia [4]. In our case, the intake of hypotonic fluid seemed to underlie the development of hyponatraemia; and the occurrence of neurological symptoms was most probably the consequence of the rapid decrease of serum $[\text{Na}^+]$ and the delayed adaptation of neurons to the lowered extracellular tonicity. In addition, children are also known to be at a higher risk of hyponatraemic encephalopathy, because the brain-to-skull ratio in children is greater than in adults, providing less room for brain expansion [9].

Given the neurological symptoms of our patient, we administered hypertonic saline, although rapid and exaggerated correction of hyponatraemia is known to be associated with osmotic demyelination of the pontine area, especially in patients with chronic hyponatraemia. Factors such as a hypoxic event during hyponatraemia, the presence of severe liver disease and the correction of plasma $[\text{Na}^+]$ by a rate $> 25$ mmol/l in 48 h or creating hypernatraemia during correction may also increase the risk of myelinolysis [9]. In view of the absence of these predisposing factors, and considering that the child was without any neurological abnormalities at her follow-up 3 weeks later, we chose not to do a brain magnetic resonance imaging (MRI) examination to exclude myelinolysis.

In summary, our case highlights the importance of fluid restriction and regular checking of serum $[\text{Na}^+]$ when intravenous DDAVP is used, especially in children. Since even a single dose of the drug may induce symptomatic hyponatraemia within 12 h, serum $[\text{Na}^+]$ and urine output must be checked every 6 h for the first 24 h after administering DDAVP, as suggested by Sutor [8]. Taking this information into account will help to prevent this serious adverse effect of DDAVP, and will provide additional safety and effectiveness in its clinical use.

**Acknowledgements.** This work was supported by grants from OTKA (T 046155) and DAAD (2005–2006 13).

**Conflict of interest statement.** None declared.

**References**

5. Garcia EB, Ruitenbergen A, Madretsma GS, Hintzen RQ. Hyponatraemic coma induced by desmopressin and ibuprofen


Received for publication: 6.1.05
Accepted in revised form: 17.3.05