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LETTER TO THE EDITOR

Cerebral oedema in adult diabetic ketoacidosis: the importance of effective serum osmolality

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Dear Editor,

We compliment Haringhuizen and colleagues on their case containing the important message that (fatal) cerebral oedema can also occur during treatment of diabetic ketoacidosis (DKA) in adults.[1] We wish to add the following points.

First, we beg to differ that the fall in effective serum osmolality from 391 to 369 mOsm/kg was insufficient to contribute to brain cell swelling. Previously, we have shown that in children an average drop in effective serum osmolality of 9±2 mOsm/kg was associated with cerebral oedema.[2] The clinical deterioration at the time of lowest effective serum osmolality also suggests a causal relationship.[1]

Second, the authors state that 'progressive hypernatraemia was not completely understood'.[1] The course of serum sodium during treatment of DKA is determined by three factors, I) decreasing glycaemia implies the loss of an effective osmole resulting in less water movement from the intracellular to the extracellular compartment resulting in a rise in natraemia, II) the tonicity of the administered intravenous fluids, (III) the ongoing osmotic diuresis, which usually contains more water than sodium. Using a validated formula,[3] the fall in serum glucose from 84.9 to 43.2 mmol/l should have led to a rise in serum sodium of ~18 mmol/l, whereas the observed rise was only 10 mmol/l. This implies that the infusate was hypotonic relative to the urine.[4] Large infusions are known to induce a natriuresis, a phenomenon referred to as 'desalination' and may prevent the necessary rise in serum sodium to prevent a drop in effective serum osmolality.[2,5]

These physiological considerations boil down to the following practical points. First, the effective serum osmolality should be used as the primary parameter to guide therapy, as this is the only measure reflecting the opposite trends in glycaemia and natraemia. Second, when the effective serum osmolality falls by ~9 mOsm/kg or more, the risk of cerebral oedema should be anticipated and the infusion rate of insulin and/or saline should be reduced, or, counterintuitively, hypertonic saline should be administered.[6] Although the hypertonic state should also be corrected during DKA treatment, the potential complications of cerebral oedema probably outweigh the risks of a hypertonic state in the early phase of treatment. Finally and more generally, this case illustrates that the recommended rates for saline and insulin in the national DKA treatment guidelines are rather high and should be tailored to each individual patient.[7]

REFERENCES

1. Haringhuizen A, Tjan DH, Grool A, van Vugt R, van Zante AR. Fatal cerebral oedema in adult diabetic ketoacidosis. Neth J Med. 2010;68:35-7.
2. Hoorn EJ, Carlotti AP, Costa LA, MacMahon B, Bohn G, Zietse R, et al. Preventing a drop in effective plasma osmolality to minimize the likelihood of cerebral edema during treatment of children with diabetic ketoacidosis. J Pediatr. 2007;150:467-73.
3. Hillier TA, Abbott RD, Barrett EJ. Hyponatremia: evaluating the correction factor for hyperglycemia. Am J Med. 1999;106:399-403.
4. Hoorn EJ, Betjes MG, Weigel J, Zietse R. Hypernatraemia in critically ill patients: too little water and too much salt. Nephrol Dial Transplant. 2008;23:1562-8.
5. Steele A, Gowrishankar M, Abrahamson S, Mazer CD, Feldman RD, Halperin ML. Postoperative hyponatremia despite near-isotonic saline infusion: a phenomenon of desalination. Ann Intern Med. 1997;126:20-5.
6. Kamat P, Vats A, Gross M, Checchia PA. Use of hypertonic saline for the treatment of altered mental status associated with diabetic ketoacidosis. Pediatr Crit Care Med. 2003;4:239-42.
7. Lutterman JA, Elving LD, van Haeften TW, Verschoor L, Jorna AT. Richtlijn voor de acute ontregeling van diabetes mellitus – diabetische ketoacidose en hyperosmolair hyperglycemisch non-ketotisch syndroom. Richtlijn Nederlandsche Internisten Vereeniging 2005.