Protecting the Brain During Pediatric DKA Treatment

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The most feared complication when treating diabetic ketoacidosis (DKA) is sudden onset of neurologic deterioration, which may include central herniation. Clinical brain swelling complicates 0.5% to 1% of pediatric DKA episodes, and when it occurs, permanent morbidity and mortality are common. However, children in DKA are known to have subclinical brain edema. Factors that lead to clinical edema and neurologic abnormalities are not clear. The key issue is to determine the best way to manage these patients, who are dehydrated, severely hyperglycemic, and may have hypo or hypernatremia and severe acidosis.

In this issue of Pediatrics, Glaser et al provide clinically helpful and reassuring findings in a comparison of 4 intravenous infusion protocols, with varying sodium concentrations and differing rates of rehydration. There was no difference in rates of neurologic dysfunction or clinically apparent brain swelling in any of the groups. Even more reassuring, there were no significant differences in these outcomes among those whose serum sodium remained stable or increased versus those whose sodium fell during the first 12 hours of therapy. An important clinical lesson is that this study prospectively demonstrated that rehydration over 1.5 to 2 days does not increase the risk of neurologic injury.

Prevention of DKA is difficult because just over half of episodes are the initial presentation of diabetes. Assessment of sensorium can be challenging because headache, throat pain, difficulty waking, and cooperation in infants and younger children can be difficult to judge. The primary study from which Glaser used data included 1389 episodes of DKA in 1255 children. There were 48 episodes (3.5%) when the Glasgow Coma Score was <14 for 2 assessments, and clinically apparent brain injury occurred in 12 episodes (0.9%). However, they did not find a significant difference in depression of Glasgow Coma Score or in clinically apparent brain injury among the 4 rehydration protocols.

Neuroimaging with MRI and apparent diffusion coefficient (ADC) of water, diffusion weighted images, and spectroscopy reveal that DKA is associated with increased water content in brain tissues supplied by the anterior and middle cerebral arteries with increased perfusion; however, the mean ADCs are abnormally elevated. This differs from what would be predicted by the osmotic disequilibrium theory because the ratio of extracellular volume to total tissue volume determines in part the ADC and should decrease. Clinical features that were significantly associated with severity of ADC increases during DKA were hypocarbia and elevated serum urea nitrogen but not glucose, sodium, or osmolality.

Previous studies with serial neuroimaging of children receiving...
faster versus slower rehydration during DKA did not differ significantly in the risk of brain edema. This previous work, also conducted by Glaser, helped to establish the foundation for this current study to assess different strategies for rehydration.

What other pathophysiology occurs that might lead to neurologic injury and brain edema? The brain autoregulates blood flow to meet metabolic needs across a wide range of blood pressure but cerebral blood flow is highly responsive to partial pressure carbon dioxide (paco2). Acute hyperventilation causes vasoconstriction and severe hypocarbia can cause brain ischemia. Although the hypocarbia during DKA causes a compensatory respiratory alkalosis to increase blood pH, the cerebrospinal fluid (CSF) pH typically is normal before treatment. As blood ketosis decreases and the blood paco2 increases, the CSF becomes acidic. It is important to remember that administration of bicarbonate exacerbates the CSF acidosis associated with DKA treatment. Likewise, a sudden relative increase in paco2 will increase intracranial pressure and CSF acidosis. Airway manipulation should include targeting the child’s baseline paco2 rather than normal values.

The current state-of-the-art method to prevent neurologic abnormalities and clinical brain swelling in DKA is not dependent on specific fluid administration but instead on earlier recognition and treatment to avoid profound acidosis and hyperventilation. Current imaging data do not implicate rehydration regimens or changes in blood glucose or sodium with progression to clinical brain edema. The astute clinician will need to rehydrate carefully while paying attention to neurologic status, sustained ventilation, and acid–base status to protect the brain from worsening edema.

**ABBREVIATIONS**

ADC: apparent diffusion coefficient
CSF: cerebrospinal fluid
DKA: diabetic ketoacidosis
paco2: partial pressure carbon dioxide

**REFERENCES**

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