

Protocol Summary Paragraph

Study Title: Fluid Therapy and Cerebral Injury in Pediatric Diabetic Ketoacidosis (Fluid Therapy in DKA)

Study Details Table

Protocol Version	v4.00; dated June 27, 2013
ClinicalTrials.gov	URL: https://clinicaltrials.gov/ct2/show/NCT01365793?cond=DKA&draw=1&rank=16
Study Type	Interventional (Clinical Trial)
Funding Source	NICHD (Eunice Kennedy Shriver National Institute of Child Health and Human Development)
Study Period	February 2011 – January 2017
Enrollment	1389 distinct episodes of DKA were enrolled (composed of 1255 distinct patients) from February 2011-September 2016
Consent	Yes

Purpose: To determine whether variations in fluid treatment protocols affect acute neurological outcomes of DKA and long-term neurocognitive function. This was accomplished by evaluating the effects that variations in intravenous fluids (IV) administration rates and sodium content had upon the frequency of mental status abnormalities and cerebral edema symptoms during DKA treatment and upon neurocognitive outcomes 3 months after discharge.

Design: This was a multi-center, factorial-design, randomized controlled trial of children less than 18-years of age who presented/transferred to the emergency department with a diagnosis of DKA (defined by (1) a serum or fingerstick glucose concentration >300 mg/dL AND (2) a venous pH < 7.25 OR serum bicarbonate concentration < 15 mmol/L.). Participants were randomized into one of four fluid treatment protocols in order to evaluate the effect of rehydration rates (rapid vs slower) and rehydration fluid concentrations (0.45% saline or 0.9% saline), as detailed below:

1. **Rapid** rehydration using 0.45% saline replacement fluid
2. **Rapid** rehydration using 0.9% saline replacement fluid
3. **Slower** rehydration using 0.45% saline intravenous fluid
4. **Slower** rehydration using 0.9% saline intravenous fluid

Treatment arms were compared using a comprehensive set of assessments for neurological injury and measures of long-term neurocognitive function.

Hypotheses: The study hypothesized that in children:

1. Untreated DKA results in cerebral hypoperfusion and cytotoxic cerebral edema and the extent of cerebral injury may in part be determined by the duration of hypoperfusion.
2. During DKA treatment, reperfusion of previously hypoperfused cerebral tissue results in hyperemia and vasogenic cerebral edema, and the extent of injury caused by reperfusion may also be correlated with the duration of prior hypoperfusion.
3. More rapid rehydration protocols using higher sodium content fluids may promote more rapid reperfusion of hypoperfused brain tissue and result in decreased risk of neurological injury compared with slower rehydration protocols using lower sodium content fluids.