



# Recognition and Treatment of Cerebral Edema Complicating Diabetic Ketoacidosis

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## Introduction

Although early mortality is very low in children and teens with type 1 diabetes, DKA accounts for up to 80% of all deaths.<sup>1,2</sup> Cerebral edema (CE) is the leading cause (30–62%) of these DKA-related deaths. CE case fatality estimates range from 25 to 67%.<sup>3,4</sup> In the largest CE case series (N=69), the outcome was death in 64%, severe disability in 13%, mild disability in 8.6% and intact survival in only 14.5%.<sup>3</sup> Several case reports suggest that subclinical CE may be a common occurrence both before and during DKA treatment.<sup>5-7</sup> Clinically significant edema may occasionally be present at the time of presentation of the child with DKA to the hospital, but CE generally develops 2 to 24 hours after initiation of DKA treatment.<sup>3</sup>

## Risk factors for cerebral edema during DKA

- There is increased representation of **young children (< 5 years)**<sup>3,8</sup> and those with **new onset diabetes**<sup>1,3,9</sup> in reports of CE during DKA.
- There is no convincing evidence that initial acid-base status, glucose, electrolytes or effective osmolality are useful predictors of CE.<sup>3,9-11</sup> Thus, all paediatric DKA patients should be presumed to be at risk, independent of initial biochemical parameters.

## Signs and symptoms of cerebral edema

- Early warning signs of cerebral edema include headache (especially new onset of headache during treatment), irritability or altered behaviour.
- Drowsiness, decreasing level of consciousness.
- Abnormalities of the vital signs (bradycardia, hypertension) and blurred disc margins are late signs.

## Prevention of cerebral edema during DKA

- **Overzealous rehydration and hypotonic fluid use** have been implicated as possibly contributing to CE.<sup>10,12,13</sup> As a result, aggressive fluid therapy is not recommended except in the presence of shock. Although institutional treatment guidelines will vary, the following are the guidelines used by the investigating centres for this study:<sup>14</sup>



# RESOURCES

- Initially 0.9% NS at 10 mL/kg/hour x 1 hour, then 5 mL/kg/hour until acidosis is corrected. Dextrose is added when the blood glucose is <15-17 mmol/L.
- Ensure that the corrected Na does not decrease over the first 12 hours, then no faster than 1 mmol/L/hour. Decreasing levels of corrected serum sodium suggests an excess of hypotonic fluids. (Corrected serum Na: a 3.5 mmol/L increase in serum glucose depresses serum sodium by 1 mmol/L).

## Confirmation of the diagnosis

- A CT scan or MRI of the head is very helpful to confirm the clinical suspicion of cerebral edema.
- It can be difficult to distinguish if a decreased level of consciousness is caused by acidosis or by cerebral edema. This is particularly true in patients who do not show a clear deterioration in level of consciousness or who remain depressed despite biochemical improvement. In such cases, CT or MRI imaging can be especially helpful.

## Management of cerebral edema<sup>14</sup>

- CE is potentially reversible, but the time for effective treatment with mannitol and hyperventilation is very short.<sup>3,9,12,15-17</sup> If you think that cerebral edema is developing, **immediate treatment is essential rather than waiting for the results of diagnostic studies.**
- For headache alone:
  - Elevate head of the bed to 30 degrees, maintain head in midline.
  - Decrease fluids to maintenance.
  - Closely monitor Glasgow Coma Scale (GCS) and serum sodium.
- Decreasing level of consciousness:  
As for headache, plus:
  - Oxygen by mask.
  - Mannitol 0.2–0.5 g/kg IV (1–2.5 mL/kg/dose of 20% solution) over 10-30 minutes every 2 hours as needed.
- If GCS < 10:  
As above plus:
  - Decrease the IV to half maintenance.
  - Hyperventilate with bag and mask, then rapid sequence induction of anesthesia for intubation, with ICP precautions.<sup>†</sup>
  - Correct hyperosmolality over at least 48 hours.

<sup>†</sup> Lidocaine may prevent rise in ICP associated with intubation. Elective intubation should be carried out by personnel experienced in the use of anesthetic agents.



## **Recognition and treatment of cerebral edema complicating diabetic ketoacidosis (continued)**

### **References**

1. Scibilia J, Finegold D, Dorman J, Becker D, Drash A. Why do children with diabetes die? *Acta Endocrinologica*. Supplementum. 1986; 279:326-33.
2. Edge JA, Ford-Adams ME, Dunger DB. Causes of death in children with insulin dependent diabetes 1990-1996. *Arch Dis Child* 1999; 81:318-23.
3. Rosenbloom AL. Intracerebral crises during treatment of diabetic ketoacidosis. *Diabetes Care* 1990; 13:22-33.
4. Mel JM, Werther GA. Incidence and outcome of diabetic cerebral oedema in childhood: are there predictors? *Paediatr Child Health* 1995; 31:17-20.
5. Durr JA, Hoffman WH, Sklar AH, el Gammal T, Steinhart CM. Correlates of brain edema in uncontrolled IDDM. *Diabetes* 1992; 41:627-32.
6. Hoffman WH, Steinhart CM, el Gammal T, Steele S, Cuadrado AR, Morse PK. Cranial CT in children and adolescents with diabetic ketoacidosis. *Am J Neuroradiology* 1988; 9:733-9.
7. Krane EJ, Rockoff MA, Wallman JK, Wolfsdorf JI. Subclinical brain swelling in children during treatment of diabetic ketoacidosis. *New Engl J Med* 1985; 312:1147-51.
8. Anonymous. Coma at the onset of young insulin-dependent diabetes in Japan. The results of a nationwide survey. Japan and Pittsburgh Childhood Diabetes Research Groups. *Diabetes* 1985; 34:1241-6.
9. Bello FA. Cerebral oedema in diabetic ketoacidosis in children. *Lancet* 1990; 336:64.
10. Harris GD, Fiordalisi I, Harris WL, Mosovich LL, Finberg L. Minimizing the risk of brain herniation during treatment of diabetic ketoacidemia: a retrospective and prospective study. *J Pediatr* 1990; 117:22-31.
11. Duck SC, Wyatt DT. Factors associated with brain herniation in the treatment of diabetic ketoacidosis. *J Pediatr* 1988; 113:10-4.
12. Harris GD, Fiordalasi I. Physiologic management of diabetic ketoacidemia. A 5-year prospective pediatric experience in 231 episodes. *Arch Pediatr Adolesc Med* 1994 Oct; 148(10):1046-52.
13. Hale PM, Rezvani I, Braunstein AW, Lipman TH, Martinez N, Garibaldi L. Factors predicting cerebral edema in young children with diabetic ketoacidosis and new onset type I diabetes. *Acta Paediatrica* 1997; 86:626-31.
14. *The HSC Handbook of Pediatrics*, 9<sup>th</sup> ed. AI Dipchand (Ed). Mosby, Toronto, ON, 1997.
15. Metzger AL, Rubenstein AH. Reversible cerebral oedema complicating diabetic ketoacidosis. *Br Med J* 1970; 3:746-7.
16. Wood EG, Go-Wingkun J, Luisiri A, Aceto T. Symptomatic cerebral swelling complicating diabetic ketoacidosis documented by intraventricular pressure monitoring: survival without neurologic sequela. *Pediatr Emerg Care* 1990 Dec; 6(4):285-8.
17. Franklin B, Lui J, Ginsberg-Fellner F. Cerebral edema and ophthalmoplegia reversed by mannitol in a new case of insulin-dependent diabetes mellitus. *Pediatrics* 1982 Jan; 69(1):87-90.

**RESOURCES**