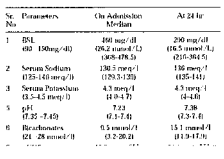
The Indian Journal of Pediatrics



ORIGINAL ARTICLE
Year : 2007 | **Volume** : 74 | **Issue** : 6 | **Page** : 551-554

Management of diabetic ketoacidosis in PICU

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Date of Submission	24-Jul-2006
Date of Acceptance	13-Dec-2006

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Source of Support: None, **Conflict of Interest:** None

» Abstract

Objective. This study was undertaken to analyze the outcome of children with DKA treated with a modified protocol at a tertiary level teaching hospital PICU in Pune, Maharashtra.
Methods. We retrospectively analyzed case records of 12 patients (8 males and 4 females) with DKA (11 new and 1 readmission) admitted in our PICU from January 2005 to June 2006. Patients were managed according to a modified protocol (that is with less intensive biochemical monitoring when compared with standard book protocols). Laboratory parameters measured were blood glucose, urinary ketones, electrolytes, urea creatinine, arterial blood gas (ABG) and infectious screen. Treatment included fluid therapy and insulin infusion- 0.1 u/Kg short acting intravenously followed by 0.1 u/Kg/hr. No bicarbonate was administered as a bolus.
Results. Total fluid deficit was corrected slowly over a period of 36 hr. The median time to normalize ABG was 19 hr (5.3-39) while the median time for the urinary ketones to disappear was 1day (1-3). The child to nurse ratio was 1:2, there were 2 pediatric residents in house all 24 hr with an intensivist and pediatric endocrinologist on call.
Conclusion. We have shown that when DKA is managed in a PICU setting using modified protocol, the outcome is good and complications such as brain edema can be prevented.

Keywords: *Diabetic Ketoacidosis; Children; Pediatrics Intensive Care Unit*

How to cite this article:
Jahagirdar RR, Khadilkar VV, Khadilkar AV, Lalwani SK. Management of diabetic ketoacidosis in PICU. Indian J Pediatr 2007;74:551-4

How to cite this URL:
Jahagirdar RR, Khadilkar VV, Khadilkar AV, Lalwani SK. Management of diabetic ketoacidosis in PICU. Indian J Pediatr [serial online] 2007 [cited 2008 Jan 31];74:551-4. Available from: http://www.ijppediatricsindia.org/text.asp?2007/74/6/551/33065

Type 1 diabetes is being increasingly reported from many centers in India and the rise in incidence could be

apparent due to improved diagnostic facilities such as routine use of glucometers or it could be a reflection of true increase in the incidence as seen in the western world.[1] Diabetic ketoacidosis (DKA) is one of the major complications of type 1 diabetes in childhood associated with increased risk of morbidity and mortality. About 25-40% of newly diagnosed type 1 diabetes patients present with DKA especially under the age of 5 years[2] . Although the European Society for Pediatric Endocrinology, Lawson Wilkins Society and the American Diabetic Association have consensus guidelines available for managing DKA in children, practices in India vary from unit to unit and as per individual preferences. [3] ,[4] At our institute we have been following a modified standard protocol (with less biochemical monitoring) for managing children with DKA since the inception of the Paediatric Intensive Care Unit (PICU) in August 2003. This retrospective study was undertaken to analyze the outcome of patients with DKA treated with a modified standard protocol at a tertiary level care teaching hospital PICU in Pune, Western Maharashtra. This study shows that although less intensive biochemical monitoring was performed in our setup as compared to most of the western data, the outcome was good and very few complications were seen, suggesting positive effect of PICU setting, better patient-nurse, patient-doctor ratio and close clinical and vital signs monitoring.

» Materials and Methods

We retrospectively analyzed case records of 12 patients (8 males and 4 females) with DKA (11 new and 1 readmission) admitted in PICU from January 2005 to June 2006. All children received intensive care therapy and flow sheet was maintained for monitoring progress of each child. Patients were managed according to our protocol as follows:

(1) History and clinical examination: Abdominal pain, vomiting, breathlessness, polyuria, polydipsia, polyphagia, height and weight, acetone breath, air hunger, dehydration, altered sensorium, vitals and systemic examination were noted.

(2) Laboratory parameters: Blood glucose, urinary ketones, electrolytes, urea and creatinine, arterial blood gas (ABG), electrocardiogram (ECG), and infectious screen [hemogram, blood culture and chest X-ray] was performed. Blood sugar level (BSL) was performed 2 hourly for 1st 8 hr, 4 hourly for next 16 hr and 6-8 hourly until acidosis resolved. Urinary ketones were measured 4 hourly, ABG 6 hourly and serum electrolytes 12 hourly until transfer out to the ward. Blood glucose was performed by glucometer and in the laboratory (Glucose oxidase and peroxidase method).Urinary ketones were measured by Ketostix (KetoDiastix Bayer the range in mg/dl is trace(5), small(15), moderate(40) large(80-160)).

(3) Treatment: Precise treatment was individualized.

A) Fluid balance and electrolytes: Fluid therapy: maintenance = 1000 ml/m^2 /day, deficit = assumed to be 10% of body weight. For the first 2 hr normal saline (0.9%), then 0.45% saline till blood glucose dropped to 220 mg% or 12.5 mmol/l was given. At this stage the fluid was changed to 5% dextrose with half normal saline which gives an osmolarity of 406mmol/L Potassium was given in the second hr preferably after urine was passed or creatinine was available, whichever was earlier. KCL was added to the drip in a dose of 30-40 milli equivalents/ liter/day. Total fluid requirement was calculated for 36 hr. Of the total fluid volume 1/3 was given in 1st 6 hr, 1/3 in next 12 hr and 1/3 in next 18hr.

(B) Insulin Therapy: Priming - 0.1 u/Kg short acting intravenously followed by 0.1 u/Kg/hr as infusion was given (Human Actrapid 40 IU/ml Novo Nordisk). Insulin was administered as a continuous IV infusion using a syringe pump (TOP model no. 5330). Insulin infusion was continued until acidosis resolved and ketone bodies had disappeared. 0.2 - 0.4 u/Kg of subcutaneous short acting insulin was given 1/2 hr prior to stopping insulin infusion. Before starting the insulin, the insulin binding sites on the tubing were saturated by running about 50 ml of insulin infusion through the tubing.

(C) Antibiotics: All patients received antibiotics in the form of Ceftriaxone in a dose of 100mg/Kg/day for a period of 7 days.

(D) Bicarbonate: No bicarbonate was administered as a bolus. Bicarbonate was given when pH was below 7.0 as a slow infusion in a dose of 0.3 x base deficit x body weight in Kg over 2-4 hr.

Patients were monitored hourly by clinical assessment, vital signs (pulse, BP, temp, pulse oximetry, respiration, cutaneous perfusion, level of consciousness) pulse oximetry and continuous ECG. Patients were shifted out of the PICU when they were clinically stable and off the insulin pump, with normal sensorium and had adequate oral intake and acidosis was completely resolved.

» Results

The median age at presentation was 7.9 yr (IQR 5.0-12.1) and duration of illness prior to admission was 15.2 days (3-32). The median height was 126.3 cm (103.3-138), median weight was 21 Kg (12.8-26.5) and the median body mass index was 13.1Kg/m^2 (11.3-14.8). The most common presenting complaint was polyuria (10/12,

83.3%). Vomiting was the presenting complaint in 6(50%), and 2(16.6%) patients each presented with polydipsia, polyphagia and abdominal pain. Seven patients (58.3%) were moderately dehydrated on admission, 3 (25%) had severe dehydration while 2(16.6%) were mildly dehydrated. The blood pressure was normal in all but one patient who presented in shock. Median body temperature was 98.8°F (98.5-99), the median respiratory rate was 29 (24.5-41.3). ECG was normal in all patients. The laboratory parameters at admission and at 24 hr are shown in [Table - 1]. All patients had large amount of urinary ketones at admission while at the end of 24 hr 1 patient had no ketones, 10 had a small amount of ketones and only one patient had a large amount of ketone bodies in the urine. Two patients had high urea and creatinine levels which returned to normal after adequate hydration. Acidosis had completely resolved with normal blood pH when patients were shifted to the ward.

All patients received 0.9% normal saline (NS) as initial hydration therapy in a dose of 10-20 ml/Kg. The fluid was changed to 0.45% NS with dextrose at average BSL of 178mg/dl (10.1 mmol/L). Average fluid received in first 24hr was 3.1 L/m ^{2} . The initial dose of insulin was 1.3 u/Kg/day. Sodium bicarbonate was given in infusion to one patient who had severe acidosis (pH 6.9). The median time taken to normalize blood gas was 19 hr (5.3-39) while the median time for the urinary ketones to disappear was 24 hr (24-72 hr 1-3). The median time to shift patient to subcutaneous insulin was 1 day (1-2) while the median time to shift patient out of the PICU was 1.2 days (1.2-3.8). None of the patients developed brain edema and the median number of days for patients to be discharged was 13(IQR 9.5-15). The median dose of insulin at discharge was 19.5 units (11.5-29)(0.93 u/Kg/day). The median BSL at discharge was 176.5 mg/dl (10.1mmol/L) (range 143.5-214.5mg/dl).

» Discussion

In this retrospective study of 12 patients admitted to our PICU we used a modification of the standard textbook protocol to manage DKA. The main difference in our hospital ICU protocol and standard textbook protocol is in the monitoring schedule, as financially it is often not possible to perform such frequent tests. We evaluated clinical signs such as reduction in the respiratory rate and heart rate to interpret reduction in acidosis rather than performing blood gases two hourly. The number of times blood sugars and electrolytes were estimated was also less. We used deterioration in the level of consciousness to determine brain edema rather than serial CT scans.

Biochemical monitoring was done as per the protocol, which is much less intensive when compared with the western protocols. Most western Protocols advise that capillary blood glucose should be measured at hourly intervals and that the electrolytes, blood urea and blood gasses measured every four hourly. [2] Such intensive monitoring is often not possible in the Indian scenario. We performed less tests but at regular intervals and each patient was monitored hourly for clinical signs, vital signs (pulse, BP, temp, pulse oximetry, respiration, cutaneous perfusion, level of consciousness) pulse oximetry and continuous ECG. The child to nurse ratio was 1:2 and there were 2 pediatric residents in house for the PICU all 24 hr with an intensivist and pediatric endocrinologist on call all the time. None of our patients developed brain edema probably due to slow rehydration, avoidance of bicarbonate and careful biochemical, clinical monitoring in PICU and early referral.

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Diabetic ketoacidosis is diagnosed when blood glucose is more than 300 mg% (17.1 mmol/L), blood pH is less than 7.3, serum bicarbonate is under 15 mmol/L and serum acetones are present.[5] If it is not diagnosed and treated promptly it can lead to serious neurological damage or even death. The typical clinical features are polyuria despite dehydration, Kussmaul respiration, vomiting, abdominal pain, and distension of abdomen, acetone breath, drowsiness and coma. Insulin deficiency and surge of counter-regulatory hormones lead to hyperglycemia, ketonemia, hyperosmolarity, diuresis, dehydration, acidosis, cerebral oedema and eventually coma. Tissue hypoxia and shock lead to secondary lactic acidosis.

The principles of management of DKA in a child are prompt recognition of the problem, adequate but cautious fluid replacement, provision of insulin, treatment of associated infections, careful monitoring of glucose, electrolytes, vitals and blood gases in an intensive care unit and prevention of complications in particular cerebral edema.

During the management of DKA first priority is to replenish fluids.[6] ,[7] The initial fluid should be an isotonic solution like normal saline. Subsequent fluid therapy can be given with normal or half normal dextrose saline or ringer lactate solution. It is important not to infuse hypotonic fluid as it increases the chance of cerebral edema. The speed of fluid replenishment is a critical factor in determining cerebral edema and hence overzealous fluid replacement in too short a time is best avoided.[2]

Antibiotics were used in all patients because full blood count is often high in DKA due to acidosis and many markers of sepsis are not immediately available.

Insulin infusion is the gold standard of insulin therapy. Subcutaneous insulin should be avoided because acidosis leads to cutaneous vasoconstriction and insulin does not get absorbed in a reliable manner from subcutaneous sites.[8] Studies have shown that there is not much benefit of giving intravenous bolus of insulin at the beginning of therapy either.[9] Since insulin deficiency is the primary pathology in type 1 diabetes and particularly in DKA, it is best not to titrate insulin infusion with the blood glucose level but to titrate the amount of glucose that is infused so that adequate amount of insulin and substrate is provided to the child. It is also necessary to saturate insulin-binding sites on the tubing by running about 50 ml of insulin infusion through the tubing before starting

the infusate. It is important not to stop insulin infusion early based on the glucose value alone. It should ideally be continued for about 12-24 hr after acidosis has resolved and ketone bodies have disappeared.[8] If the blood glucose continues to fall glucose concentration of the infusate can be increased from 5% to 10% and accordingly half normal saline can be given instead of normal saline. With adequate insulin and glucose, lactate gets converted into bicarbonate in liver resolving acidosis.[4]

Measurement of ketone bodies in the urine can be tricky. Ketodiastics, which are routinely used for measurement of ketones in the urine, do not measure betahydroxybutyrate but are sensitive to acetone and acetoacetic acid. In the initial phase of DKA as there is more betahydroxybutyrate in the urine the test may be weakly positive and as the patient improves and more of acetone and acetoacetic acid starts coming out in the urine the test becomes strongly positive giving a false impression of deterioration of the patient's condition.[10]

There is no role for routine use of bicarbonate in DKA.[11],[12] Metabolic acidosis, which is often profound, should not be treated with bicarbonate and usually settles down with adequate fluid and insulin therapy. When fluid and insulin are provided ketones and lactic acid are metabolized to bicarbonate thus correcting the acidosis. Bicarbonate on the other hand worsens cerebral acidosis, leads to hypernatremia and hypokalemia and this leads to poor oxygen delivery to the tissues due to shift of the oxygen dissociation curve. Bicarbonate may be used only if there is symptomatic hyperkalemia, cardiovascular instability or pH below 7.0. If bicarbonate is used it should be used as an infusion slowly over a period of 2-4 hr and should not be given as a bolus.

Cerebral edema is the most dangerous complication of DKA and is often precipitated by overzealous fluid replacement. Therefore, slow rehydration over 36 hr is recommended. Isotonic and not hypotonic fluids should be used for rehydration. Other complications include electrolyte imbalance and hypoglycemia, which can be prevented by careful monitoring. None of our patients at the time of admission were in moribund state. All patients were conscious and no signs of brain oedema were present. We thus had patients referred to our hospital at a stage where irreversible damage had not already occurred. This is an important point in good outcome observed in our study.

Our study has a number of limitations. The number of patients is small. We have not been able to measure serum ketones and perform a CT scan of the brain for our patients.

» Conclusion

It has been shown that when DKA is managed in a PICU setting using modified standard protocol the outcome is good and complications such as brain edema can be prevented. Due to economic reasons it may not always be possible to perform rigorous biochemical monitoring in every child as suggested by most western literature yet clinical observations, adequate tests and PICU set up seems to be the key to successful management of DKA.

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