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REVIEW

Treatment of diabetic ketoacidosis in children and adolescents

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Abstract. Diabetic ketoacidosis (DKA) may be defined as a metabolic derangement characterized by hyperglycemia, acidosis and ketonuria. It is a crucial pediatric medical emergency. DKA may occur in children with diabetes at onset due to severe insulin deficiency, in established patients from failing to take insulin, acute stress, and poor sick-day management. The treatment of DKA has undergone a radical transformation over recent years. Among the major innovations the early adjustment of the hydroelectrolyte imbalance and the continuous I.V. infusion of microdoses of insulin are the most interesting. Despite appropriate use of insulin and fluids, and continuous clinical observation, the mortality rate has not improved, and has remained the same as that reported in the 1970s. DKA can be prevented by shortening the period of carbohydrate intolerance that usually precedes the diagnosis of Type 1 diabetes. Its prevention decreases morbidity and mortality and allows to save on the hospital costs. The aim of this paper is to review the main aspects of the treatment and prevention of DKA.

Key words: Type 1 diabetes, diabetic ketoacidosis, DKA, adolescents, ketonemia, beta-hydroxybutyrate

Introduction

Diabetic ketoacidosis (DKA) is the most important pediatric metabolic emergency. Twenty to forty per cent of children with Type 1 diabetes at onset present with DKA, but it may also occur in established patients failing to take insulin, or from acute stress with elevated counter-regulatory hormones, or from poor sick-day management (1, 2).

If DKA is recognized on time and adequately treated it generally disappears without complications. However, it may lead to death if it is associated with cerebral oedema (3). Despite appropriate use of insulin and fluids, and continuous clinical observation, mortality has not improved and has remained the same as that reported in the 1970s, i.e. 1-2% of newly diagnosed diabetic children (2, 4). In the USA, it was calculated that more children die each year from DKA than from childhood cancer (5). The aim of this paper is to review the main aspects of treatment and prevention of DKA in children and adolescents.

Definition and Pathogenesis

DKA may be defined as a metabolic derangement characterized by hyperglycemia (>250 mg/dl), acidosis (arterial pH <7.3 and/or bicarbonate < 15 mEq/l) and ketonuria (4,6). In very young newly diagnosed diabetic patients and in diabetic children with brain disorders unable to recognize and express "thirst", DKA may be complicated by hyperosmolar coma due to extreme hyperglycemia (> 1000 mg/dl), severe dehydration, and increased serum osmolarity without significant ketonuria (2, 7). These metabolic abnormalities may also occur in children when vo-

miting due to Type 1 diabetes at onset is confused with a ketosis induced by inadequate carbohydrate intake and treated with the ingestion of a large amount of high-carbohydrate-containing fluids (8).

Diabetic ketoacidosis is the result of insulin deficiency associated with increased levels of counter-regulatory hormones, which determine modifications of the glucidic, lipidic and proteic metabolism.

Insulin stimulates the uptake of glucose in muscle and adipose tissue through specific transporters. In the muscle and liver, lipogenesis and storage of glycogen are favoured. In the liver and in the renal cortex, insulin reduces the activity of enzymes which play a key role in gluconeogenesis. Furthermore, insulin inhibits endothelial lipolysis reducing circulating free fatty acids.

Hyperglycemia, due to insulin deficiency, determines osmotic diuresis with subsequent hypovolemia. If an adequate hydration is not maintained, a reduction in the glomerular filtration rate and in the renal clearance of glucose with subsequent extreme hyperglycemia and hyperosmolarity occurs (9).

Glucagon is also involved in the development of DKA. High levels of glucagon favour gluconeogenesis and stimulate glycogenolysis; the result is an increased production of glucose with a further worsening of hyperglycemia. Furthermore, glucagon stimulates muscular proteolysis providing additional substrates for gluconeogenesis. The latter is stimulated by epinephrine, cortisol and GH, with a mechanism similar to that of glucagon. Epynephrine increases glucagon and stimulates lipolysis. Cortisol stimulates proteolysis. GH stimulates lipolysis and inhibits the transport of glucose in adipose tissue, reducing peripheral lipogenesis. Hyperglycemia is the result of the increased production of glucose in the liver and kidney, and of the reduced clearance in the muscle and adipose tissue. The hyperketonemia resulting from peripheral lipolysis, increased renal and liver production of ketone bodies, and the reduced use of ketones in the muscle, determines metabolic ketoacidosis (when the concentration of beta-hydroxybutyrate is about 6 mmol/L). Finally, osmotic diuresis induced by glucosuria determines secondary dehydration. In the initial phases of ketoacidosis excess glucose, accumulated in the extracellular compartment, has an osmotic action and retains water from the intracellular compartment with subsequent reduction in intracellular liquid and expansion of the extracellular volume. This dilutes sodium with subsequent low or normal blood levels. Osmotic diuresis causes a loss of sodium and water in the urine (if blood glucose level is > 250-300 mg/dl the capacity of renal concentration is further reduced and massive osmotic diuresis occurs), with excess of water with respect to sodium. Later, the loss of liquid also concerns the extracellular compartment and dehydration of the two compartments, intra and extracellular, with similar results in percentage. The loss of potassium is approximately 5-7 mEq/Kg. Despite this severe loss, blood potassium levels are normal or even increased at DKA diagnosis. This phenomenon is due to the passage of potassium from the intra-to the extracellular compartment due to the osmotic effect of hyperglycemia (10).

Presentation

A wide range of signs and symptoms may indicate DKA in children (Table 1).

The most obvious and precocious sign is the onset of an unaccountable nocturia in a child usually “dry”. Unfortunately, only in a minority of cases is this immediately linked to hyperglycemia/glucosuria. According to some authors, secondary enuresis prompts pediatric examination in 57% of cases, but the consultant associates this symptom with a latent hyper-

Table 1. Frequency of signs and symtoms of ketoacidosis in the newly diagnosed diabetic children admitted to the Departments of Pediatrics of the Universities of Parma and Chieti, Italy, from 1990-2000

Polyuria, nocturia	88%
Thirst, Polydipsia	84%
Signs of dehydration	78%
Abdominal pain, vomiting	14%
Acidotic breathing	6%
Alteration of consciousness	6%
Coma	2%

glycemia only in 13% of the subjects (11). The most frequent mistakes in the diagnosis are a urinary tract infection (misinterpreted polyuria), bronchitis and pneumonia (misinterpreted Kussmaul breathing) and meningitis (misinterpreted ketoacidosis with cerebral affection) (12). This may help to explain why, in many cases, the diagnosis of Type 1 diabetes continues to be markedly delayed.

Hyperglycemia causes intra-cellular fluid loss, osmotic diuresis and dehydration. Dehydration can be present with thirst, decreased turgor, soft eye balls, and hypotension. Confusion, stupor and coma are characteristic of a severe hyperosmolar state and are rarely observed in pure DKA (7).

DKA per se is never a cause of fever. If fever is present, it indicates that the patient has an infection and blood and urine cultures, and a chest X-ray are useful for the diagnosis. An elevated white blood count is usually reported as a result of a stress response to DKA, and therefore is not helpful to diagnose an intercurrent infection. Pneumonia may not be apparent on initial chest X-rays because of dehydration, but may become visible following hydration (4). Subclinical interstitial pulmonary oedema may frequently occur in children and adolescents with severe DKA and may be present prior to treatment (13).

The presence of deep, forced Kussmaul breathing is indicative of a pH below 7.1. In two adolescents with retrosternal pain, dyspnea and subcutaneous emphysema during severe DKA a pneumomediastinum due to alveolar rupture from hyperventilation was observed (14). Vomiting and abdominal pain usually develop in the late stages of DKA and these symptoms may also be the effect of severe ketoacidosis.

Table 2. Protocol for the treatment of DKA

First hour
Minimum I.V. treatment (rehydration only)
Saline solution 0.9%
5-8 ml/kg/hour
↓
From the 2nd hour onwards
Complete I.V. treatment (rehydration + insulin)

↓	↓
Rehydration Saline Solution 0.9% (1) + Potassium (2) Max. 4 l/m² in 24-36 hours (3)	Fast-acting insulin - glycemia >250 mg/dl 0.1–0.075 IU/Kg/hour (4) - glycemia <250mg/dl 0.05–0.025 IU/kg/hour + 10% Glucose Solution 1 ml/kg/hour (5)

1) If corrected blood sodium levels are > 150 mEq/l, 0.45% saline solution may be used.

(2) Add K+ to the saline solution (if the patient is not anuric) in order to infuse 0.1-0.2 mEq/Kg/hour (never more than 0.4 mEq/Kg/hour): the calculated dose must be divided into 50% K-phosphate and 50% K-cloride.

(3) Calculation of the volume of liquids to be infused in 24-36 hours, according to body weight and chronological age:
Kg 14-21 (age: 3-6 years): 2200 ml/m²
Kg 22-29 (age: 7-9 years): 1800 ml/m²
Kg 30-55 (age > 10 years): 1500 ml/m²

(4) If pH> 7.25: 0.075 IU/Kg/hour should be used.

(5) Maintain the combined infusion until beta-hydroxybutirate blood levels are normalized. Regulate the velocity of the two infusions in order to maintain blood glucose levels within 150-180 mg/dl.

Treatment

The treatment of DKA has undergone a radical transformation over recent years. Among the major innovations the precocious adjustment of the hydro-electrolyte imbalance and the continuous I.V. infusion of microdoses of insulin are the most interesting ones (15, 16).

At present, the cornerstones of the treatment of DKA are rehydration, insulin therapy, and removal of the electrolyte disorders with particular attention to potassium, sodium and phosphate, as shown in Table 2. In single cases, alkali administration might be taken into consideration.

Monitoring

Before considering in detail the above-mentioned points, a general introduction regarding the monitoring of children presenting with DKA is advisable. These patients need, at regular intervals, a careful clinical, laboratory and instrumental assessment. A schedule for monitoring is summarized in Table 3.

Frequent monitoring is a key component of successful treatment and must concern neurologic condition and mental status, blood glucose levels, serum electrolytes, blood pH and ketone bodies.

Table 3. Monitoring of DKA

a) clinical	neurological status (pupillary responses, reflexes) cardic rate respiratory rate
b) biological	blood glucose blood sodium (*) blood potassium blood chloride
c)instrumental	ECG blood pressure
On admission and every 3 hours	haemogasanalysis creatinine blood level blood beta-hydroxybutyrate

(*) The value of blood glucose must be corrected, each time, on the basis of blood glucose levels adding to the blood sodium level 2.75 mEq every 100 mg/dl of glucose above 100 mg/dl base-line.

In contrast to the advances obtained in the 1990s in the approach to bedside glucose monitoring by fingerstick in the emergency diagnosis and management of DKA, the concentration of ketone bodies has not changed significantly in the same period of time. Ketone determination was traditionally performed on the urine, but this conventional testing has been associated with several problems. At first, nitroprusside test strips only detect acetoacetate (AcAc) in the urine and not 3 β-hydroxybutyrate (β-HBA) which is the predominant ketone body in DKA (17). Furthermore, ketone test based on the nitroprusside reaction has been reported to be falsely positive in the presence of drugs containing sulfhydryl groups and to produce false-negative readings when the strips have been exposed to air for a long time.

A system for the precise quantification of β-HBA levels in capillary blood (MediSense Optium Ketone Sensor) has been recently introduced in the clinical practice by Abbott Laboratories (Bedford, MA, USA). This has to be considered an important progress in the management of DKA because the method allows to measure quantitatively the major ketone in the circulation during DKA which correlates better than AcAc with changes in acid-base status during the course of treatment for DKA (17 bis).

One of the advantages of the use of β-HBA assay concerns the opportunity to monitor hourly the patients' ketotic status. According to one recent study the goal may be achieved in all patients monitored with β-HBA independently from their dehydration degree. On the contrary, the dehydration status affected the regular collection of urine specimen in half of the patients monitored with urine ketone bodies (17 bis).

The availability of β-HBA dosage since admission can be a useful parameter a well as the traditional sensitive markers of metabolic decompensation such as serum bicarbonate and anion gap, to program the initial therapeutic plan for DKA management, and insulin therapy. Beta-Hydroxybutyrate levels at diabetes diagnosis was found to be correlated with HbA1c values, latency before diagnosis of diabetes

and insulin dose infused during the first hours of treatment. Based on these observations, high levels of β-HBA at diagnosis can throw light on a long-standing insulin deficiency state and a possible insulin resistance due to a prolonged metabolic derangement. In this perspective, β-HBA levels can be considered as a sensitive metabolic marker of insulin requirements during the first hours of treatment (17 tris).

Beta-Hydroxybutyrate levels at admission may also be useful to forecast the required time to achieve the definitive resolution of DKA. In the patients with higher values of β-HBA this time is longer than that seen in the patients presenting lower values (Figure 1). A low β-HBA level on admission (indicative of a short metabolic derangement time) could then be used to select the patients with DKA that can be managed in out-patient clinic.

The normalization of β-HBA levels may be used as a primary endpoint for reducing the length of stay in the intensive care unit for the patients with severe DKA (17 bis). This saving is of about 5 hours compared with the stay in the same intensive care unit of the patients monitored with urine ketone bodies (UKB) determination (Figure 2). The early discharge led to a saving in time and money for clinical assessment and laboratory investigations, and to a reduction in the professional burden on nurses and physicians in the management of DKA. A total saving for managing DKA in the patients monitored with β-HBA of 2,940 € was calculated including the costs for laboratory tests (29.8%) and for clinical assessment in an intensive care unit (70.2%) (17 bis).

From an economic perspective, these results can contribute in reducing the increasing pressure on healthcare resources as far as costs of managing diabetes and its complications are concerned.

Rehydration

The restoration of an adequate intravascular volume is the first priority in the treatment of DKA. An adequate rehydration determines a spontaneous fall in the blood glucose levels, probably due to a dilution effect but also by improving renal glucose clearance and increasing tissue perfusion. Concomitantly insulin

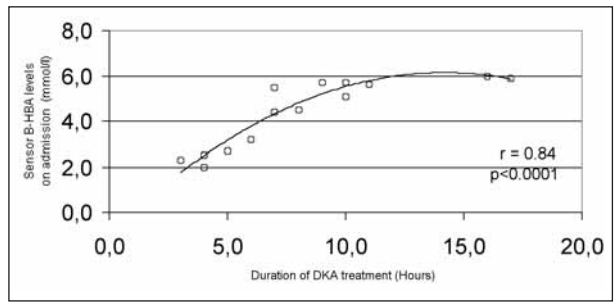

Figure 1. The required time to achieve the resolution of ketosis (β-HBA values <1.00 mmol/l) in patients monitored with β-HBA appeared to be related to the values of β-HBA levels on admission. In the patients with higher values of β-HBA this time was longer than that found in the patients presenting lower values (17 tris).

sensitivity is improved while the concentration of counter-regulatory hormones is reduced (18).

An average fall of 30.4±15.5% in the blood glucose levels may occur after 1 hour of rehydration: in sporadic cases up to a 53% decrease has been observed (11). The drop is more pronounced when arterial pH is not far from the physiological value. This spontaneous fall in blood glucose levels constitutes a simple and effective way to avoid an excessively rapid fall in blood glucose concentration under the effect of insulin in the following hours of treatment. It's highly advisable to delay the beginning of insulin therapy after

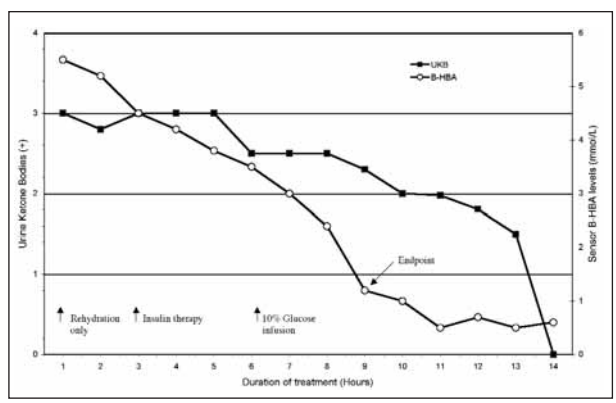

Figure 2. In response to therapy, β-HBA (white circles) levels begin to decline sooner than UKB levels (black squares). Furthermore β-HBA dosage informs on the definitive resolution (Endpoint) of ketosis many hours in advanced compared with UKB test (17 tris).

starting of the correction of the fluid deficit (above all in hyperosmolar patients), because glucose and water may shift from the vascular space into the cells causing vascular collapse, shock, and death (7).

A rehydration protocol for a 5-10% fluid deficit is reported in the appendix of Table 2. This scheme prevents exceeding 4 l/m^2/24 hours fluid administration, which is considered the safety limit (19).

At the beginning of rehydration, a normosaline solution is usually recommended for two main reasons: the plasma of a child with DKA has a relatively increased osmolarity (therefore, an isotonic saline solution turns out to be hypotonic); the restoration of normal osmolarity in plasma must be gradual, to avoid the risk of cerebral oedema due to hypo-osmolarity. If the serum sodium level is elevated, the initial fluid replacement should be carried out as one half of normal saline followed by normal saline when the serum sodium levels return to normal. In fact, as acidosis decreases, a recovery of sodium from the intracellular compartment takes place. A slow recovery of pure metabolic acidosis (i.e when the anion gap is increased) may result from a too rapid infusion of fluids. In this case, the forced loss of ketone bodies in the urine leads to a deficit of "fuel" for the production of bicarbonates (20, 21).

Insulin therapy

Insulin therapy has the primary role to promote a correction of the metabolic derangement occuring in DKA by suppressing hepatic production of both glucose (22) and ketone bodies (23), in addition to an increased glucose utilization (24) and ketone body clearance (25).

The subcutaneous administration route is no longer used, for two reasons. First, the risk of a slow, variable and consequently unpredictable absorption, especially in patients with severe acidosis and advanced dehydration. Second, the prolonged half-life of subcutaneous insulin when compared to intravenous, with the consequent risk of hypoglycemia due to an overlapping effect of single injected doses.

In the modern schemes, a continuous I.V. infusion of microdoses of insulin is recommended (16, 26). Low-doses of I.V. insulin infusion (0.05 - 0.1 U/kg/h) are able to increase peripheral insulin levels to 50-100 mU/l, which are sufficient to inhibit lipolysis and ketogenesis and to suppress glyconeogenesis and glycogenolysis (25, 27, 28).

Some Authors suggest a preliminary bolus of 0.1 U/kg before continuous insulin infusion especially when blood glucose levels exceed 500 mg/dl (1). Others do not agree with this procedure because of the overwhelming evidence that even small quantities of insulin are able to saturate cellular receptors. If these doses are exceeded, no further effect is observed in blood glucose levels (29). Treatment of DKA must not be a race to the normalization of blood glucose and ketone body levels, and of acid-base balance. On the contrary, the metabolic equilibrium must be restored gradually, without abrupt accelerations.

Most Pediatricians agree with the principle of infusing insulin at the rate of 0.1 U/kg/h (1, 10, 17, 31). Some recommend the use of even lower doses (from 0.05 to 0.075 U/kg/h), especially in patients with a venous pH > 7.25 (11, 32) because of the inverse correlation ($r=-0.79$; $p<0.0001$) reported between venous pH at diagnosis and requirement of insulin during the first 12 hours of treatment (11). In other words, the closer pH is to normal, the smaller the quantity of insulin required to stabilize blood glucose levels is needed.

As soon as blood glucose falls below 250 mg/dl the general agreement is to halve the rhythm of insulin infusion (e.g. 0.05 U/kg/h) and to integrate the infusional program with a 5% glucose solution (2 ml/kg/h) or 10% glucose solution (1 ml/kg/h) to avoid hypoglycemia.

It is well known that ketosis may persist for many hours after correction of hyperglycemia (32, 33). This suggests the continuation of the combined infusion of glucose and insulin until hyperketonemia has disappeared. This extended regimen was reported to produce a more rapid resolution of ketosis than the conventional regimen (34). To avoid hypoinsulinemia is usually suggested that this regimen should continue until the patient is eating again, and has begun subcutaneous insulin injection therapy (11, 35).

Electrolytes

a) Potassium

Upon diagnosis of DKA the plasma concentration of potassium is increased since acidosis determines the passage of potassium from the intra to the extracellular compartment. With the progressive correction of both acidosis and hyperglycemia by rehydration and insulin therapy, potassium returns to the cellular compartment and its blood level begins to decrease. The fall may be so rapid as to alter electrical activity of cell membranes and to provoke cardiac arythmias and respiratory arrest (4).

If the diuresis is conserved and in the absence of remarkable hyperkalemia, it is advisable to associate the administration of potassium immediately from the beginning of the insulin therapy. As soon as blood glucose falls under 250 mg/dl the requirement of K+ increases, due to the progressively increased endocellular uptake. It is not recommended to give more than 0.5 mEq/kg/h. In any event, the dose should be adjusted hourly or every 2 hours depending on the modifications of kalemia and or on electrocardiography. Such a procedure leads to the maintainance of a stable level of blood potassium during all the treatment of DKA (16).

The kind of potassium salt to be infused is important. For a long time, potassium phosphate was the most commonly used; however it may cause hypocalcemia if given in excess. Therefore, the infusion of a mixture of 50% phosphate and 50% chloride is preferable (36).

b) Sodium

Sodium is generally reduced because of dehydration. The depletion is mainly due to increased natriuresis and, to a lesser degree, to a loss through vomiting. The deficit of sodium and the reduction of the extracellular volume stimulates the synthesis of aldosterone, which increases the reabsorption of sodium and causes a further loss of potassium. Blood sodium may vary from 120 to 130 mEq/l; but the blood level of sodium does not reflect the true deficit of this electrolyte. In fact, hyponatremia can originate from the dilution of extracellular sodium due to the fluid coming out of the cellular compartment as a consequence of hyperglycemia.

In practice, considering that hyponatremia will be more pronounced where hyperglycemia is more severe, it is prudent to correct the value of blood sodium according to the blood glucose level (calculated adding to the blood sodium level, 2.75 mEq every 100 mg/dl above 100 mg/dl-base line), before deciding on the quantity of normal saline solution to be infused. The monitoring of serum sodium corrected for the blood glucose levels should be performed hourly and the trend of serum sodium concentrations during the treatment must be carefully evaluated. An abrupt serum sodium decline may occur in children with DKA who have or are developing cerebral oedema (44). This phenomenon may be due to an unidentified alteration in sodium homeostasis as a consequence of the cerebral injury rather than an excess of free water administration (36 bis).

c) Phosphorus

During the treatment of DKA an important loss in phosphate and a reduction in 2.3 diphosphoglycerate (2,3-DPG) in red blood cells have been reported (37). 2,3-DPG plays an important role in the haemoglobin-oxygen dissociation curve and its depletion increases the affinity of haemoglobin for oxygen. Consequently less oxygen is available for the tissues, resulting in an increase of anaerobic metabolism and of lactic acid production. Generally it is unnecessary to use phosphate salts in the treatment of DKA. The administration of half of the required potassium as a phosphate salt is more than enough to prevent hypophosphatemia.

d) Alkali

Metabolic acidosis disappears spontaneously within 14.4±8.2 hours using the scheme of treatment outlined so far (11). Bicarbonate administration on a routine basis may lead to sodium overload and hypernatraemia, rebound metabolic alcalosis, and to an excessively rapid return of potassium to the intracellular compartment resulting in hypokalemia (4). In addi-

tion, alkali therapy may impair oxyhaemoglobin dissociation leading to increased anaerobic glycolysis and giving origin to tissue hypoxia with elevated lactate levels (12, 16). Bicarbonate may induce a paradoxical fall in cerobrospinal fluid pH (39), and increase both acetoacetate (AcAc) and hydroxybutyrate production (β-HBA), and β-HBA / AcAc ratio (39).

Hence, alkali should not be used as a routine, but must be restricted, to the most severe cases of DKA (pH<7.0 or bicarbonates < 8 mEq/l), and given cautiously, diluted in saline solution (11, 12). The recommended dose of sodium bicarbonate is 1-2 mmol/kg, half infused slowly over 60 minutes, the remaining half over 1-2 hours after checking haemogasanalysis. Treatment should be supplemented with potassium (0,1 mEq/Kg/h).

Complications

Most of the deaths occurring during ketoacidosis are due to complications related to treatment. The most feared complication is cerebral oedema which is frequent in very young children at their very first episode of ketoacidosis. One must bear in mind that:

- All children with ketoacidosis are at risk of developing cerebral oedema;
- The danger is greater before the beginning of treatment and up to 48 hours after the diagnosis;
- Neurological signs and symptoms should be constantly monitored (Table 4);
- Mannitol and the instruments for hyperventilation and intubation must always be at the patients bedside;
- Among the different factors which may contribute to a cerebral oedema the following are particularly important: initial severe hyperglycemia (>500 mg/dl) followed by an excessively rapid normalization; severe hyponatraemia; excessive infusion of liquids during the first hours; rapid alcalinization with a worsening of acidosis and cerebral hypoxia which may derive from the first (19).

Headache is the first premonitory symptom of this severe situation, although it is not always present.

Table 4. Signs and symptoms of cerebral oedema during treatment of DKA

- Sudden headache
- Vomiting
- Disorientation, agitation
- Change in vital signs
- Papillar asymmetry
- Papilloedema
- Seizure

Other signs are a sudden alteration of the state of consciousness associated with neurological signs related to the involvement of the truncus, mydriasis and respiratory arrest which may occur within a few minutes. If this condition is recognized early, an immediate reduction in the infusion of liquids and the admnistration of mannitol 0.5-1 g/Kg i.v. within 2 hours from the appearance of symptoms, represent an effective remedy. To be effective, mannitol must be administered during the first ten minutes (40). JR Curtis et al. have recently reported a successful treatment of oedema in a newly diabetic adolescent with a combination of mannitol and hypertonic saline (5 mL/kg of 3% saline) rapidly infused (41).Vascular thrombosis secondary to excessive dehydration, infections and rabdomyolisis are other relevant complications of DKA (42). Low flow oxygen delivery may decrease cerebral oedema associated with DKA, and fundoscopy must be performed both initially and at intervals during the treatment to recognise precociously cerebral oedema (43). Despite therapeutical attempts, cerebral oedema may cause some permanent neurological damage or may even lead to death.

Finally, reversible posterior hemispheric swelling is reported in children with DKA if an increased serum osmolarity is associated (43).

Conclusions

Since most early diabetes-related deaths are attributable to DKA (4, 45), prevention of this condition should lower mortality (45). Vanelli et al. were

able to prevent most episodes of DKA at disease onset by shortening the period of carbohydrate intolerance that usually precedes the diagnosis of Type 1 diabetes (46). In this field, they obtained highly satisfying results by providing medical information on DKA to teachers, students and parents in schools and in the private offices of general pediatricians as well as giving the opportunity to pediatricians to measure blood glucose levels and glycosuria in their clinics. Thanks to this prevention program, none of the newly diagnosed diabetic children aged 6-14 years, originating from the area where the campaign for the prevention had been carried out, were ever admitted to hospital for DKA after 1992 (46). One could reasonably speculate that children being diagnosed today with Type 1 diabetes face an even more optimistic future.

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