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Mortality and Prognostic Factors of Diabetic Ketoacidosis in Children in the Intensive Care Unit (About 142 Cases)

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Abstract **Original Research Article**

Diabetic ketoacidosis is a metabolic emergency and one of the main causes of morbidity and mortality in diabetic children due to its formidable complications. The severity of the evolution is essentially related to the initial clinical state, hence the interest of an early diagnosis and a correct management. In this work we tried to make a global analysis of this disease. We conducted a retrospective study of 122 cases admitted to the pediatric intensive care unit at the Ibn Rochd University Hospital in Casablanca between January 2010 and January 2020. The different variables collected at admission were analyzed and compared between two groups: patients who died and those who survived. 122 cases of diabetic ketoacidosis were identified. 68 boys and 74 girls with a sex ratio of 0.91. The average age was 7.61 years. Ketoacidosis was inaugural in 62% of cases, polyuoro-polydipsic syndrome was found in all patients followed by digestive disorders and 55.6% of cases. The average GCS on admission was 12. Shock was found in 17.6% of the cases and polypnoea with Kussmaul type respiration in 71.12% of the cases. The mean values of kalaemia and natraemia were close in both groups. Bicarbonates were below normal in all patients with an average of 6.37 mmol/l. The mortality was 15%. The treatment consisted of adequate rehydration associated with insulin therapy, following the protocol of the department. Our study shows that the diagnosis of DKA must be made early and requires a well codified management. Hence the interest in raising awareness and educating physicians and the population about the signs of diabetes in children in order to reduce the frequency and severity of pediatric DKA.

Keywords: Ketoacidosis, diabetes, child death, cerebral edema.

INTRODUCTION

Diabetes is a group of metabolic diseases characterized by a state of chronic hyperglycemia, linked to a relative or absolute deficiency of insulin or to a defect in its action or both. It is the most frequent chronic pathology in children after asthma.

It presents great geographical disparities throughout the world, with extreme values in Japan where the incidence is 0.8 per 100,000 for the lowest values and 40 per 100,000 for the highest values in Filand [1].

Furthermore, diabetes is on the rise all over the world, as evidenced by the latest figures, this pandemic requires rigorous efforts to provide solutions to this global health crisis [2].

Type 1 diabetes is an autoimmune disease corresponding to the destruction of the ß-cells of the islets of Langerhans, which normally synthesize insulin, leading to an absolute deficiency of insulin. Hyperglycemia occurs when about 90% of the ß-cells have been destroyed. The development of insulin-dependent diabetes requires predisposing genetic factors, triggering factors and the development of the autoimmune process.

Diabetic ketoacidosis remains a relatively frequent complication of childhood diabetes, representing the first cause of mortality in children. Its incidence has been increasing in recent years. It represents the main cause of hospitalization of diabetic children (14-20%), all forms of severity combined, in developed countries, whereas it is the first sign of diabetes in about 50% of cases in Africa [3].

Ketoacidosis in children remains a potentially fatal medical emergency (0.4-2%), with no significant decrease in mortality rates in recent years [2]. The

severity of the evolution is essentially related to the initial clinical state, hence the interest of an early diagnosis, and to the complications of the treatment, essentially acute cerebral edema leading to death in 70% of cases [3]. However, it has been established that the frequency becomes almost nil when the treatment is carried out according to protocols based on the knowledge of the pathophysiological mechanisms of CAD and codified in advance.

The aim of this work is to determine the prognostic factors and causes of mortality of this condition in the polyvalent pediatric intensive care unit of the children's hospital ABDERAHIM HAROUCHI within the CHU IBN ROCHD of Casablanca, in order to improve the management of patients.

MATERIAL AND METHODS

This is a retrospective study of 142 cases of patients admitted with inaugural diabetic ketoacidosis or complicating a known diabetes, based on a chart exploration and analysis.

This is a descriptive cross-sectional study of two groups of patients:

- A group of patients who died after at least 24 hours of hospitalization
- A group of patients admitted and then transferred to their respective departments or to a medical department for further management (survivor group)

The cases were collected in the pediatric intensive care unit of the ABDERAHIM HAROUCHI children's hospital at the IBN ROCHD University Hospital in Casablanca, between January 2010 and January 2020 (10 years).

The selection criteria of the patients are:

- Hyperglycemia ≥ 2.5 g/l
- Glycosuria ≥ 2 crosses
- Ketonuria ≥ 2 crosses
- Presence of clinical signs pointing to a state of diabetic ketoacidosis (AEG, DHA, consciousness disorder, kussmaul dyspnea , digestive signs ...)

The AR level was not included in the criteria because it was not available in all patients.

The exclusion criteria are:

- Patients who died within 24 hours of admission
- Patients for whom the records were not usable

The records were collated in the form of a multiparametric database established using Microsoft Excel.

We conducted a comparative study between 2 subgroups:

- Survivors group
- Deceased group

We first proceeded with an overall descriptive analysis of the population and then with an analytical study using several successive uni-variate analyses.

RESULTS

In our study we divided the patients into two groups:

Survivors: n=121

Deceased: n=21

We compared different parameters for each of these two groups. The average age of the survivors was 7.55 years and of the deceased was 7.94 years. Among the deceased, 8 cases were male and 13 cases were female, compared to 62 cases and 59 cases respectively in the survivor group.

Our study did not reveal any difference in demographic parameters between the two groups.

In the group of deceased patients, 12 patients (8.45%) came from the pediatric endocrinology service (P2), 8 patients (5.63%) came from the pediatric emergency department (PED), and 1 patient (0.70%) came from a private facility.

In the survivor group, 65 patients (45.7%) came from the pediatric endocrinology department (P2), 47 patients (33.09%) came from the pediatric emergency department (PACU), and 9 patients (6.33%) came from a private facility. There was no significant difference between the 2 groups regarding origin (p=0.147).

Among the deceased 11 cases were of rural origin and 10 cases of urban origin, compared to 53 cases and 68 cases respectively in the survivors group. The difference between the two groups was not statistically significant (p=0.466).

Statistical analysis between the 2 groups in relation to the period of admission to the service during the year did not reveal any significant difference (p=0.756).

Consanguinity was found in 2 patients in the deceased group and in 17 patients in the survivor group. The difference between the 2 groups was not significant (p=0.739).

In the survivor group, 17 patients (9.8% of the survivors) had a history of surgery, compared with 6 patients (4.22%) in the deceased group. The presence of a medical and surgical history was not associated with mortality.

In the deceased group, 2 patients (1.40%) had a family history of diabetes. Whereas in the survivors group, 17 patients (12%) had a family history of diabetes. The difference between the 2 groups was not significant (p=0.178).

Diabetes was inaugural in 10 patients while 11 patients were known to have diabetes in the deceased group, whereas in the survivor group diabetes was inaugural in 78 patients and 43 patients were known to have diabetes. The difference was not significant (p=0.152).

16 cases (11.26%) presented shock in the deceased and 9 cases (6.33%) in the survivors. The difference between the two groups was significant (p=0.001).

82 patients had polypnoea with Kussmaul-like breathing in the survivors' group versus 19 patients in the decedents' group. The difference between the 2 groups was not significant.

The mean Glasgow score in the survivors was 13 and in the decedents it was 7.90. There was a significant difference in the GCS score between the two groups (p=0.001).

71 survivors (50%) presented with digestive disorders against 8 deceased (5.63%). The difference was not significant (p=0.098).

24 patients (16.90%) were febrile in the survivors group versus 16 cases (11.26%) in the decedents group. The difference between the 2 groups was significant (p=0.002).

Table 1: Results of univariate analysis of demographic and clinical parameters

Variables	**Survivors *(n=121)***	**Deceased *(n=21)***	***P***
Age	7.55	7.94	NS
Sex (M / F)	62/59	8/13	NS
Origin (Rural /Urban)	53/68	11/10	NS
Consanguinity	17	2	NS
Medical and surgical history	17	6	NS
Family history	17	2	NS
Age of diabetes Inaugural/known diabetes	78/43	10/11	NS
State of consciousness (GCS)	**13**	**7.90**	**0.001**
Shock	**9**	**16**	**0.001**
Fever	Fever	Fever	Fever
Polypnea Kussmaul type	82	19	NS
Digestive signs	71	8	NS

In the deceased group, 11 patients (52.4% of all deceased patients) developed cerebral edema during their stay in the ICU. In the survivor group, 22 patients (18.2% of survivors) developed this complication. Disturbed consciousness was the clinical manifestation in all cases.

The presence of cerebral edema on the CT scan was statistically significant between the two groups (p=0.009).

The other abnormalities observed on the brain scan: meningeal hemorrhage - inactive tri ventricular hydrocephalus - calcifications of the basal ganglia, were not significant.

Chest X-ray was requested in all our patients in the group of deceased, it revealed a focus of pneumopathy in 9 patients.

In the survivor group, 101 patients were submitted for a chest X-ray, which revealed pneumonia in 9 patients.

The presence of a focus on the admission chest X-ray was not significant between the two groups (p=0.06).

In the group of deceased patients, all patients received antibiotic therapy. The latter was directed in 3 patients and probabilistic in 18 patients.

In the survivors group, 42 patients received antibiotic therapy on admission. This antibiotic therapy was directed in 4 patients and probabilistic in 38 patients and then adjusted according to the antibiogram after the infectious workup.

The initiation of antibiotic therapy on admission was statistically significant between the two groups (p=0.001).

In the group of deceased, 21 patients were put on mechanical ventilation. The mean value of the duration of ventilation was 9 days with extremes ranging from 1 day to 22 days.

In the survivor group, 8 patients were put on mechanical ventilation. The mean value of the duration of ventilation was 6 days with extremes ranging from 2 to 26 days.

The use of mechanical ventilation was statically significant between the two groups (p=0.000001). However, the duration of ventilation was not significant.

The use of vasoactive drugs was necessary in 16 patients (11.26%). 14 patients in the deceased group and 2 in the survivor group.

The use of vasoactive drugs was statistically significant between the two groups (p=0.000001), while the duration was not significant.

In the deceased group, 16 patients had a central venous catheter with a mean duration of 6 days.

In the survivors group, 3 patients had a KTC with a mean duration of 8 days. Placement of a central venous catheter was statistically significant between the two groups (p=0.001).

Table 2: Results of the analysis of the therapeutic parameters

Variables	Survivors *(n=121)*	Deceased *(n=21)*	*P*
Antibiotic therapy on admission	**42**	**21**	**0.0001**
Mechanical ventilation	**8**	**21**	**0.000001**
Vasoactive drugs	**2**	**14**	**0.000001**
Vascular catheterization	**3**	**16**	**0.0001**

3 cases of the survivors had presented a nosocomial infection compared to 16 cases of the deceased. The difference between the two groups was significant (p=0.0002).

10 cases of the deceased patients presented hypokalemia against 21 cases in the survivors group. Hypokalemia was characterized by its depth in the deceased patients (less than 2.5 mmol/l). The difference between the two groups was not significant (p=0.104).

11 patients of the deceased group and 18 patients of the survivors group presented this complication during their stay in the intensive care unit. It is characterized by its depth in the deceased group with a mean value of 0.49 mmol/l. In the survivors group the mean value of hypoglycemia is 0.52 mmol/l. The difference between the 2 groups was not significant (p=0.36).

Table 3: Results of the analysis of complications

Variables	Survivors *(n=121)*	Deceased *(n=21)*	*P*
Nosocomial pneumonia	**3**	**16**	**0.0002**
Hypokalemia	21	10	NS
Hypoglycemia	18	11	NS

A multivariate analysis by logistic regression was conducted on the factors associated with ICU mortality.

Taking into account characteristics measured at admission and during the immediate course, 5 of them were significantly associated with mortality: low Glasgow score (less than 9), brain edema, nosocomial infection, need for endotracheal intubation, and use of vasoactive drugs.

Table 4: Variables considered in multivariate analysis

Variable	**Odds Ratio**	**P value**	**IC 95%**	
			Lower	**Upper**
Glasgow score	0.450	0.001	0.6782	1.800
Cerebral edema	6.424	0.009	2.333	17.687
Mechanical ventilation	56.433	0.000001	7.9874	864.600
Vasoactive drugs	*21.09*	0.000001	5.778	315.456
Nosocomial infection	*0.7781*	0.0002	0.354	1.058

DISCUSSION

According to the latest WHO and IDF estimates (year 2017), the continued rise in the incidence and prevalence of diabetes is evident. Indeed, 425 million people worldwide have diabetes; this figure could rise to 629 million by 2045, or one in ten people.

In addition, according to these estimates, one in two people is undiagnosed and the number of children and adolescents under 20 years of age with type 1 diabetes exceeds one million [2].

In Morocco, more than 2 million people aged 18 and over have diabetes, 50% of whom are unaware of their disease, and the number of diabetic children is estimated at more than 15,000. Moreover, according to the global annual report established by the ANAM for the year 2016, 48% of the total expenses are generated by long-term conditions (ALD) and diabetes represents 11% of these expenses.

Diabetic ketoacidosis is the most frequent and most serious metabolic complication in children. Its incidence in known diabetics is 1-10% per year per patient [7, 8].

The risk factors are infection, which increases the need for insulin, corticosteroid therapy, adolescence with rejection of treatment and dietary instructions, psychiatric disorders, omission of insulin, malfunctioning of an insulin pump... [4, 8, 9].

There are wide geographic varieties in the frequency of DKA in early diabetes. Rates are related to access to medical services and inversely proportional to the regional incidence of diabetes.

It remains important in Africa: it is seen in 20-50% of known diabetic children [10], and is low in the West where it complicates diabetes in 0.3-1.3% and inaugurates it in 25-30% of cases [11, 12].

There does not seem to be a predilection age for diabetic ketoacidosis. It occurs at any time in life, from children under 5 years of age to patients over 60 years of age [13].

CAD is the leading cause of hospitalization, morbidity and mortality in children with type 1 diabetes. It is responsible for 50% of all deaths in young diabetics under 24 years of age.

Cerebral edema, a formidable complication of ketoacidosis, occurs unpredictably in 0.5 to 3% of cases, frequently resulting in death (25%) or major neurological sequelae (20 to 35% of cases). Preventing acidotic decompensation is therefore a public health priority in order to avoid the morbidity and mortality associated with childhood diabetes [24].

The diagnosis of diabetes should normally be made at the stage of hyperglycemia without ketosis, i.e. when the cardinal signs of insulin-dependent diabetes appear or reappear (polyuro-polydipsic syndrome + weight loss contrasting with a preserved appetite or polyphagia), which has been evolving for a few days to a few weeks.

In the absence of treatment, the clinical evolution is towards a phase of simple ketosis or ketoacidosis. In children, ketoacidosis can develop very rapidly [4].

Secondary to hyperglycemia and osmotic diuresis, dehydration predominates in the extracellular sector and associates a skin fold, arterial hypotension and tachycardia. Intracellular dehydration characterized by dry mucous membranes, intense thirst and hypotonia of the eyeballs may be associated. Despite the extent of the dehydration, diuresis remains preserved, which is why the existence of anuria requires the search for an organic cause and the careful introduction of rehydration. The evolution towards a cardiovascular collapse is to be feared in case of intense dehydration (intra and extra cellular). The water deficit is estimated at: 5 - 10% [8, 17].

Digestive disorders (nausea, vomiting and abdominal pain) are present in 50 to 75% of cases, and can simulate a surgical abdomen by their intensity. This underlines the importance of a meticulous interrogation, which easily finds polyuria and weight loss in the previous days or weeks, provided they are mentioned.

The mechanisms of abdominal pain are poorly understood, and can be explained by a decrease in mesenteric perfusion [6, 8], delayed gastric emptying, ileus or subacute pancreatitis [18].

The respiratory rate must be measured accurately and in the absence of any additional respiratory abnormality, particularly a pulmonary infection, as it is a true reflection of the severity of ketoacidosis [4, 19].

The respiratory signs are variable and proportional to the metabolic acidosis. They are either a wide and noisy polypnoea without intermediate pause (30 to 40 cycles/min), or a 4-stroke Kussmaul dyspnoea (with inspiratory and expiratory pauses) [16, 19].

The state of consciousness must be precisely assessed during the initial examination, according to the standard or adapted GCS score for the young child, in order to follow its evolution during the treatment, in particular to detect the first signs of cerebral edema. Generally, consciousness remains normal for a very long time, obnubilation is possible.

True coma concerns less than 10% of patients [20], a calm, variable depth, flaccid coma with osteo-tendinous areflexia without any sign of localization on neurological examination.

The diagnosis evoked by the clinic is confirmed by the demonstration of hyperglycemia by evaluation of capillary glycemia, glycosuria and ketonuria on urine strips. In some diabetes centers,

ketones can be measured in the blood using strips or in the laboratory. This first diagnostic step is simple and easily performed at the patient's bed. It allows to orient the diagnosis and to quickly start the therapeutic management, without waiting for the results of the complementary examinations which will allow to confirm and to appreciate the gravity of the ketoacidosis and to search for its cause.

Hyperglycemia, which is constant in the state phase of diabetic ketoacidosis [22], is often higher than 400 mg/dl, and can reach more than 1000mg/dl. When higher figures are reached, it is mostly a case of decompensation in the hyperosmolar mode [6], which is rare in children. It should be noted that a patient with an elevated blood glucose level above 2.5g/l (14 mmol/l) can be neither in ketosis nor in ketoacidosis. Conversely, ketosis or ketoacidosis may be observed with low blood glucose levels, especially in patients treated with insulin pumps [4, 15]. The blood glucose value alone does not exclude or make the diagnosis of ketoacidosis [23].

The combination of hyperglycemia above 2.5 g/l, glycosuria and ketonuria greater than or equal to two crosses on the urine dipstick in a polypneic patient is sufficient for the diagnosis.

To avoid these errors, it is currently recommended to perform the test on fresh urine and preferably to measure ketonemia with a combined ketonemia and blood glucose meter.

Additional tests are prescribed but should not delay treatment:

♦ Natremia: Before treatment, the natraemia may be normal (¼ of cases), low (⅔ of cases), or high, depending on the extent of respective water and salt losses [22, 24]. In its interpretation, one should beware of false hypo natremia related to:

- Hyperglycemia: this is a dilution hyponatremia by outflow of water from the intracellular sector [5].
- Hypertriglyceridemia: due to the inactivation of lipoprotein lipase secondary to insulinopenia, it leads to hyponatremia by reduction of the volume of water per liter of plasma [4, 25].

Hence the interest in measuring corrected natraemia. A high value of corrected natraemia (Na©) indicates associated intracellular dehydration and a mixed form of diabetic coma (ketoacidosis + hyperosmolarity) [26].

In general, hyponatremia does not need to be corrected due to the use of SS for rehydration. But, when introducing SG one enriches this solute by: 30-60 mEq/m²/24h i.e. 4g/l Na Cl. The use of isotonic saline solutions corrects the body loss but at the cost of an "overcorrection" of the chlorine deficit which contributes to the appearance of a hyperchloremic state.

♦ Kalemia: Ketoacidosis is constantly responsible for a marked potassium loss essentially intracellular. In general, it is estimated at 3 - 5 mEq/l but it can reach 10 mEq/l. The main mechanism is a passage of K+ ions from the intracellular to the extracellular medium favored by hypercatabolism, dehydration and acidosis, but the origin of potassium depletion is renal and is explained by osmotic polyuria, elimination of organic acids and hyperaldosteronism [17, 4]. Indeed, all these elements accentuate potassium output while poor renal function (impaired glomerular function and tubular function) limits its urinary loss.

Hypokalemia on admission indicates a profound potassium deficit secondary to recurrent vomiting, or to a large diuresis in children [25].

Insufficient potassium intake may induce hypokalemia with cardiac risk, hence the interest of close monitoring (every 4 hours) of signs of hypokalemia by ECG and repeated potassium determinations with secondary adaptation of potassium supplementation. The study of signs of dyskalemia focuses on the measurement of T-wave amplitude and the search for cardiac conduction abnormalities. The ECG may show [21]:

- Decreased or flattened T waves in D2, AVR.
- ST-segment undershift.
- An appearance of U wave.
- QT: prolonged.
- Atrial (supraventricular tachycardia) and ventricular rhythm abnormalities are much more severe and exceptional.
- Prolongation of the P-R interval (at an advanced stage).

In case of hyperkalemia:

- T waves: wide, sharp and symmetrical.
- QT: shortened.

♦Osmolarity in plasma: Most often moderately increased, rarely exceeds 320 mosmol/l. It is calculated according to the formula: osmolarity (mosm/l water): 2 x Natremia mmol/l + 13 + Blood glucose mmol/l. Thus, an increase in this value reflects relative dehydration, a decrease reflects hyperhydration.

♦ Arterial pH: The measurement of pH on arterial blood is potentially difficult and may be accompanied by risks and complications, its measurement on venous blood has been proposed as an alternative (easier method) especially since studies have shown that venous pH correlates well with arterial pH in the diagnosis and evaluation of ketoacidosis. It is normal or lowered depending on the stage. 20 A pH < 7.3 with an alkaline reserve < 15 m E q/l confirms the presence of acidosis.

♦Phosphoremia [4]: Initial hyperphosphoremia may be observed during ketoacidosis. It is due to

transmembrane movements induced by hyperglycemia, insulinopenia, and the presence of ketone bodies on the one hand and to renal failure on the other. During treatment, there is a rapid and significant decrease in phosphorus entering the cells as a result of insulin therapy and the resumption of carbohydrate metabolism.

♦ Urea-Creatinine: Their increase reflects the extent of the water deficit leading to functional renal failure [4] and reflects very advanced acidotic decompensation or poor management.

♦ Protidemia and hematocrit: Reflect the intensity of extracellular dehydration. Their increase reflects hemoconcentration [5]. These biological parameters gradually correct with rehydration.

♦Blood count: A polynuclear hyperleukocytosis between 10,000 and 15,000 related to dehydration and leukocyte demargination is frequent without underlying infectious syndrome. However, a value > 25,000 may indicate infection and requires evaluation [27].

♦ HbA1C: May be useful in determining whether ketoacidosis is the culmination of progressive undiagnosed or poorly balanced diabetes, or secondary to a truly acute episode in a previously well-balanced patient [28, 33].

♦ Triglycerides: hypertriglyceridemia is common and may be the consequence:

- Of a defect in clearance of triglyceride-rich lipoproteins (chylomicrons and VLDL) by inactivation of lipoprotein lipase,
- And an increase in hepatic synthesis of VLDL.

♦ Transaminases: Are elevated in 25- 50% of cases without obvious hepatocellular damage.

♦Other complementary tests: Are requested to complete the etiological diagnosis:

- ECBU: in case of symptoms or positive strip for leukocytes or nitrites. However, urinary tract infection is rarely found in children initially, except in the case of catheterization, which should be avoided.
- Chest X-ray: should only be performed when the patient is rehydrated, even if there are major pulmonary symptoms. [29]
- Blood culture: is requested in case of fever.
- Fundus: can detect post-acidotic cerebral edema [31], especially in the event of a sudden onset of ICU during treatment or when a coma resists a well-conducted treatment.
- Ketoacidosis is a complication of type 1 diabetes. It can reveal the disease or occur during its evolution. It is due either to absolute or relative insulinopenia.

SITUATION OF ABSOLUTE INSULINOPENIA [4]:

- Ketoacidosis reveals type 1 diabetes in children in 15 to 70% of cases, depending on the country.
- In a known diabetic, the causes are essentially represented by eating disorders (especially in girls), socio-economic difficulties, and denial of the disease during the peripubertal period. These three factors are often found in recurrent episodes of ketoacidosis. Insulinopenia, in these cases, is secondary to voluntary discontinuation of insulin therapy by the patient or his family.
- Technical failure of insulin pumps or pens or lipodystrophies: can be responsible for glycemic instability with risk of diabetes decompensation. This underlines the importance of intensive education and better management of patients on insulin pens or pumps.

SITUATIONS OF RELATIVE INSULINOPENIA [4]:

These situations mainly concern known diabetic patients. They are responsible for a sudden and sometimes unpredictable increase in insulin requirements that are not or insufficiently compensated.

Infectious factors constitute the main circumstance favoring inaugural ketoacidosis in children, and are dominated by ENT infections, pneumopathy, and skin infections. Intercurrent pathologies: stress, trauma, surgery, etc. favor the occurrence of this complication. Hormonal pathologies (such as hyperthyroidism...) are likely to trigger ketoacidosis in diabetic patients.

Moderate and severe DKA require inpatient treatment and monitoring. On the other hand, in case of mild DKA in a cooperating patient, ambulatory management can be considered. The goal is to correct metabolic disorders and restore homeostasis while normalizing blood glucose levels.

The initial evaluation on admission allows for the detection of vital distress in order to manage it urgently. Thereafter, specific management based on rehydration and insulin therapy must be undertaken, associated with electrolyte and bicarbonate supplementation if necessary.

Clinical and biological monitoring (blood glucose and ketone levels) is used to monitor progress. DKA should be managed in a hospital setting with an intensive care unit and treatment should be started without waiting for the results of additional tests.

Diabetic ketoacidosis is a medical emergency [30-33] whose treatment is based on:

- Hemodynamic restoration.
- Insulin therapy to correct hyperglycemia, metabolic acidosis and ketonemia.
- Correction of fluid and electrolyte disorders.
- Treatment of a possible triggering factor

This treatment should be performed in an intensive care unit, if the child has:

1. A PH less than 7.
2. An initial kalemia of less than 4mmol/l.
3. Impaired consciousness.
4. Visceral failure.

Blood glucose and PH should be normalized slowly to avoid a sudden drop in blood osmolality that could lead to cerebral edema.

The initial biochemical assessment should include blood glucose, sodium, kalemia, chloremia, bicarbonates, urea, creatinine and venous PH measurement.

1- Hydroelectrolytic resuscitation:

- Constitutes the most delicate aspect of treatment. The goal is to restore circulating volume and improve tissue perfusion allowing insulin to interact with its receptors. Correction of hypovolemic shock by vascular filling with 10 to 20 ml/kg of 0.9% isotonic saline or colloids over 30 minutes by the intravenous route is essential and should be repeated if necessary [30].
- Rehydration is started with isotonic sodium chloride solutions at a dose of 10 ml/kg/h. This should be done during the first 2 hours of treatment [34-36]. To be discontinued before, if the blood glucose level, checked every 30 min (by dipstick), reaches less than 2.5g/l. When the blood glucose level falls below 2.5 g/l or systematically from the second hour onwards, SS is replaced by 10% SG [37, 38], with a total infusion rate of about 3 L/m²/24h without exceeding 4 L/m²/24h; above which the risk of cerebral oedema is important [37, 39].
- IV rehydration should be continued for at least 4-6 hours [30].
- Hypotonic solutions are not used because of the risk of cerebral edema [40].
- The volume to be infused should in principle take into account the weight loss if available, or the calculation of the water deficit in case of hypernatremia.
  [Water deficit=0.6 x weight (kg) x (1 - 140/corrected natremia)]

2-Insulin therapy

Its goals are to inhibit hepatic glucose production, increase peripheral glucose utilization, and arrest lipolysis and ketogenesis. It should be started at the same time as rehydration. Only rapid-acting insulin is used intravenously (immediate onset + short duration of action) because it allows for better glycemic control and more flexible dosage adjustment.

The current consensus is based on the use of insulin pumps that allow for continuous intravenous administration of low doses of insulin. This method seems more physiological than intramuscular or subcutaneous injections. It minimizes the risk of complications such as hypoglycemia, hypokalemia, and cerebral edema.

Two administration protocols are possible:

- Rapid insulin by self-propelled syringe [30, 41, 42] at a rate of: 0.05 IU/kg/h if age< 5 years 0.1 IU/kg/h if age> 5 years.
- Rapid insulin in infusion bottles [38, 43, 44]: 22 IU/l (saline, glucose) if age > 5 years, 11 IU/l (saline, glucose) if age < 5 years, and the tubing must be purged with the first 150 ml of solution to saturate the tubing, and repurge if the tubing must be changed [36, 45, 46, 47].

The initial insulin flow rate should be adapted according to glycemic fluctuations, with the aim of lowering blood glucose levels progressively at a rate of 0.5 g/l (without exceeding 1 g/l) during the first few hours, and then maintaining it between 1.6 - 1.8 g/l at 12 - 24 hours.

Indeed, too rapid a correction of blood glucose levels exposes the patient to excessive osmotic changes which would favor the development of cerebral edema [48].

All authors agree on the need for an available and easily accessible protocol, adapted to the requirements of the context.

- IV insulin therapy should be continued (for at least 12 hours) until:

Normalization of consciousness.
Correct hydration status.
Blood glucose < 2.5g/l.
Disappearance of ketonuria or remain a cross (or normalization of the anion gap).
Rise of the pH to 7.30 or alkaline reserve to 15 mEq/l.
And the patient able to feed.

Then.

- Switch to subcutaneous insulin therapy: (30' before stopping insulin infusion):

If insulin therapy is started at breakfast.

---- AT 8 H: give 2/3 of the daily dose (30-40% rapid insulin and 60-70% intermediate).

----- At 8 p.m.: give 1/3 of the daily dose (30 to 40% rapid insulin and 60 to 70% intermediate).

If insulin therapy is started at lunch.

- At 12 PM: give 1/3 of the daily dose of rapid insulin.
- At 8 p.m.: give 1/3 of the daily dose (30 to 40% rapid insulin and 60 to 70% intermediate).

3-Potassium supplementation:

Hypokalemia is probably the most frequent cause of death by cardiac rhythm disorders in adults on

the other hand in diabetic children, cerebral edema is the first cause of death [49].

Given the rapid onset of hypokalemia in ketoacidosis, it is recommended that potassium be added early to the infusion solution and that the kalemia be checked four hours after the start of treatment.

The quantity to be administered throughout the course of ketoacidosis depends on the evolution of the kalemia:

- When the kalemia is< 5mmol /l, correction of the potassium deficit should be started. The dosage is 1.5 to 2 g/l of rehydration fluid. The goal is to maintain a kalemia between 4 and 5 mmol/l [50].
- If initially the kalemia is < 3.3 mmol /l, insulin therapy should be started only after adequate correction of the potassium deficit.
- In case of kalemia < 4 mmol/l, monitoring of the heart rhythm is essential.

4-Phosphorus intake:

The contribution of phosphorus during treatment appears theoretical. However, recent studies have not shown any benefit from the correction of hypophosphatemia but, on the contrary, an increased risk of hypocalcemia responsible for tetany. Nevertheless, some authors recommend coupling the correction of hypophosphatemia and hypokalemia by using potassium phosphate.

5-Bicarbonate intake:

The use of this solution remains controversial despite the possible complications due to severe acidosis (ventricular rhythm disorders, negative inotropism, peripheral vasodilatation, hepatic and cerebral failure, etc [51].

The use of bicarbonates seems to be responsible for hypokalemia, paradoxical acidification of the central nervous system and decrease in ionized calcium with the risk of altering myocardial performance [52].

6-Treatment of the triggering factor:

Treatment of the triggering factor is imperative:

*Infectious causes (ENT, pulmonary, digestive, skin...): an adapted antibiotic therapy is prescribed after bacteriological samples.

*Resumption of education

*Psychotherapy for adolescents denying the disease, etc.

Clinical monitoring: must take into account hemodynamic status (BP, HR, diuresis), respiratory rate and state of consciousness. These parameters are monitored every 30 minutes for the first two hours, then once an hour for the next 4 hours, and finally every 2 to 4 hours until complete resolution of ketoacidosis [1].

It is imperative to monitor for neurological symptoms suggestive of cerebral edema.

Paraclinical monitoring includes:

- Capillary blood glucose and ketonuria are monitored every hour in order to adapt the insulin flow rate.
- Blood ionogram, kalemia and alkaline reserve every 4 hours until normalization of the parameters [53].
- Electrocardiogram should be checked regularly if abnormalities in kalemia are present.

If treated effectively, ketoacidosis usually resolves within 12 to 48 hours, which is the most frequent case.

However, the evolution can be unfavorable: secondary to several factors related to the ketoacidosis and/or the treatment. Mortality related to ketoacidosis is in the order of 1 to 2%. Three factors are involved: hypokalemia, inhalation of gastric fluid and cerebral edema.

CONCLUSION

Diabetic ketoacidosis is a real public health problem and is the most frequent acute complication of diabetes in children, responsible for a significant morbidity and mortality. It can be inaugural or occur at the time of a triggering factor in particular an infectious cause, a bad therapeutic observance or other.

It is the first cause of mortality in children because of its formidable complications, the main ones being cerebral oedema, dehydration, severe acidosis and hypokalaemia.

Management consists of rehydration and insulin therapy with correction of electrolyte disorders that may be associated with it.

A correct clinical and biological monitoring allows to evaluate the efficiency of the treatment and to avoid complications.

In our context, the main cause of the high mortality rate is the delay in diagnosis and the absence of a hospital structure adapted to take care of these cases. As a consequence, most patients are transferred to the university hospital at an advanced stage with the complications already installed.

The prevention of DKA is one of the objectives of the management of T1DM. In known diabetic patients, it is mainly based on the education of parents and children on the alarming functional signs and the conduct at home: capillary glycemia and ketonuria research by urine dipstick, knowing how to consult in time before the aggravation. Education on

injection techniques and insulin storage is also necessary.

A thorough training of physicians on childhood diabetes allows an early detection and a quick diagnosis before the onset of metabolic complications.

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