Management of diabetic ketoacidosis in children and spectrum of complications in the pediatric intensive care unit


ABSTRACT

Diabetic ketoacidosis (DKA) is an acute and severe condition that can occur in diabetic patients. It is characterized by hyperglycemia, dehydration, and metabolic acidosis that develops from hyperproduction of ketones. This condition results in further complications such as cerebral edema that is more severe and common among the children. The current review was aimed to overview the spectrum of pediatric ketoacidosis and its management. The online databases PubMed and Google Scholar were used to perform a literature search for publications published between 2008 and 2019, without any date or language restrictions. We used a combination of relevant search terms “DKA, Children, Prevalence, Complications, Management.” We independently identified publications and systematically screened titles, abstracts, and full texts of the collected publications. Among 40 articles, initially selected based on the title and abstract, 31 articles were excluded as they were either duplicate of existed articles, or case reports, or articles published before 2000 or conducted on adults. Finally, nine review articles were selected and included in the systematic review. DKA was found as one of the leading causes of morbidity and mortality in diabetic children, especially those with type 1 diabetes due to the development of cerebral edema as a complication of DKA.

Keywords: DKA, children, prevalence, complications, management.

Introduction

There are three types of diabetes, type 1, type 2, and gestational diabetes, and other forms result from other conditions, such as consumption of large doses of exogenous steroids and pancreatitis [1]. Diabetic ketoacidosis (DKA) is a major life-threatening complication of diabetes; it is an acute metabolic state that is characterized by massive elevation of glucose and ketones in blood [2]. DKA occurs in both types of diabetes; type 1 and type 2 [3]. DKA results from relative or absolute lack of insulin combined with the effects of increased counter-regulatory hormone levels, including glucagon, growth hormone, catecholamines, and cortisol. The accelerated catabolic state leads to the classical DKA picture with hyperketonemia, hyperglycemia, and hyperosmolality [4], as episodes of DKA involve abnormal processes of the body including deranged pH, fluid shifts, and decreased perfusion that affect many functions and lead to electrolyte abnormalities [5]. The severity of DKA can be defined by the results of blood gas as mild, moderate, and severe, the mild DKA is defined when pH is less than 7.3 and bicarbonate is less than 15 mmol/l, whereas moderate DKA is defined when pH is less than 7.2 and the bicarbonate level is less than 10 mmol/l and severe DKA is defined at pH less than 7.1 and bicarbonate level less than 5 mmol/l [6]. Patients mostly present with polydipsia, abdominal pain polyuria, and vomiting. The resultant metabolic acidosis and dehydration can lead to confusion, hyperventilation, tachycardia, and severe forms of coma and death [2]. DKA can be the first presentation for non-diagnosed type 1 diabetic patients, one-third of diabetes mellitus (DM) patients’ admission to intensive care units is due to DKA.
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care units returns to severe DKA, and responsible for 13% of in-hospital mortality [7]. In diabetic children, DKA is the leading cause of morbidity and mortality [8]. DKA is a common pediatric emergency; it is the major cause of both morbidity and mortality in type 1 diabetes mellitus (T1DM) children [9]. In contrast to adults, the mortality in the pediatric population occurs mainly due to cerebral edema development [3]. The diagnosis of DM is often delayed in younger children and euglycemic ketoacidosis is rarely seen; however, it can be presented in children partially treated or those who had minimal carbohydrate intake [4]. This review was conducted to overview the complication spectrum of DKA and its management in the pediatric population.

Database Search

The online databases PubMed and Google Scholar were used to perform a literature search for publications published between 2008 and 2019, without any date or language restrictions. We used a combination of relevant search terms “DKA, Children, Prevalence, Complications, Management.” We independently identified publications and systematically screened titles, abstracts, and full texts of the collected publications. Among 40 articles, initially selected based on the title and abstract, 31 articles were excluded as were either duplicate of existed articles, or case reports, or articles published before 2000 or conducted on adults. Finally, nine review articles were selected and included in the systematic review.

Discussion

Ketoacidosis prevalence

According to the IPS registry in 2012, DKA occurs in more than half of children and adolescents with T1DM (60.56%) [10]. A study from King Abdul Aziz medical city showed that the average annual incidence of DKA onset was 6.2% with a mean age of 22.82-year old with more prevalence among females [1]. DKA incidence is higher among type 1 diabetes in both presentation and setting of established disease [11]. The incidence of DKA for type 1 diabetes (T1D) was 15%–70% for patients under 5 years of age, and its incidence is lower in type 2 diabetes (T2D) 5%–25% as reported from Europe and USA [3,4]. The risk of DKA is 1%–10% per patient per year in T1D and lower incidence regarding T2D [3]. The incidence variation of DKA among both sub-types is affected by the frequency of diabetes in a given population and the availability of healthcare [4]. Regarding the pediatric population, DKA was prevalent mostly among patients newly diagnosed with T1DM [12].

Ketoacidosis complications

DKA is an acute, life-threatening disease; it may be associated with acute and chronic complications. Acute complications include cerebral edema, deep vein thrombosis (DVT), hypokalemia, and death [9]. Other complications of DKA include cardiopulmonary, renal vascular, and other complications [13]. DKA can result in medium and chronic morbid conditions, such as neurological dysfunction [14]. Cerebral edema is a rare complication, its incidence ranges from 0.5% to 0.9% [15]. The mortality rate of cerebral edema in children with DKA is 40% [16]. Another study reported that the cerebral edema accounts for 57% and 89% of all DKA deaths [17]. Children and adolescents with DKA are at increased risk of DVT when they undergo replacement of central venous catheters [18,19]. DVT in DKA children and catheter placement is more common in children with age less than 3 years [18]. Low-molecular-weight heparin is required for children with DVT associated with DKA until ultrasound confirmation of DVT resolution occurs and this can take up to 6 months [18]. Another complication of DKA is pulmonary edema which occurs in children and adults. Some children suffer hypoxemia that requires oxygen supplementation or intubation [20]. A study conducted on children reported that hyperchloremia and other electrolyte abnormalities, cerebral edema and acute kidney injury (AKI) were the most common complication of severe DKA, the complications were present among patients as follows: 35.94% had hyperchloremia, 30.81% had hypokalemia, 26.70% had hyponatremia, 16.43% had cerebral edema, and 10.27% had AKI [5].

Ketoacidosis management in children

The principle goal for DKA management is to avoid any complications during the correction of the hydration status of the patients and other abnormalities present [21]. There are variations in the details of the DKA treatment protocol; however, its management requires frequent measuring of serum electrolytes, acid-base status, and glycemia to evaluate the efficacy of the treatment as well as its resolution [22]. Careful history taking of each patient should be performed with physical examination involving body mass index, circulatory and respiratory status, vital signs, hydration status, and level of consciousness [21]. The considerations for pediatric DKA management are in general similar to that for adults and include exogenous insulin intravenous (IV) fluid therapy and replacement of electrolytes. However, there are several important variations between both populations such as DKA of pediatrics is often greater in severity at presentations and children are more prone to develop cerebral edema; however, this edema can be exacerbated by the treatment [11].

Insulin therapy

Switching off lipolysis and ketogenesis requires insulin. It was suggested by one study [8] that a low dose of insulin (0.1 unit/kg hour) achieves a steady-state plasma level of 100–200 uU/ml within 1 hour. This level of plasma is sufficient to overcome insulin resistance and to inhibit ketone production and lipolysis as well as exerting a maximal effect on peripheral glucose uptake.
and suppression of gluconeogenesis [8]. It is unnecessary to take IV bolus of insulin at the beginning of therapy, as it may increase the risk of cerebral edema development [4], this may return to the activation of sodium ions and hydrogen ions in membrane exchange process leading to increase in sodium ions which associated with osmotic fluid shifts [23]. Recent guidelines suggested avoiding insulin boluses and delaying commencement of insulin infusion until 1–2 hours of fluid therapy [4].

**Fluid therapy**

The fluid therapy is applied to replace the deficit of fluids secondary to dehydration and to resuscitate in case of inadequate vascular volume [11]. Replacement fluid comprises normal maintenance and estimated dehydration. Hypotonic solutions must not be given as they may increase the risk of cerebral edema, so the standard therapy should be saline of 0.9% with a combination of glucose of 5%–10% in case of a reduction of plasma glucose to 15 mmol/l [23]. Judicious use of fluid boluses is advised as a shock with hemodynamic compromise is uncommon in DKA [8]. The current recommendation for the restoration of intravascular volume is to use saline of a concentration of 0.9% with a dose of 10–20 ml/kg that is given in the first 1–2 hours and repeated as necessary [4].

**Electrolyte replacement**

**Sodium**

It is the most important extracellular caution that is influencing intracellular volume. There are several factors in DKA cause a reduction in the level of sodium in plasma [4], this, in turn, may lead to depletion of sodium in tandem with water loss as a result of osmotic diuresis secondary to ketonemia and hyperglycemia. Osmotic movement of water occurs from the cells as a result of increased concentration of extracellular glucose leads to pseudo hyponatremia. Hence, the measured sodium will increase as plasma glucose decreases by the effect of insulin and fluid therapy; however, this can occur in the face of the dramatic reduction in effective osmolality [11].

**Potassium**

The deficit in the total body potassium in DKA children is estimated between 3 and 6 mmol/kg, from intracellular stores. There are several causes of loss of potassium such as deficiency of insulin, vomiting, metabolic acidosis, and volume depletion that leads to hyperaldosteronism [4]. All patients require potassium replacement; however, if the potassium in serum level is more than 5.5 mmol/l, then postpone giving potassium until it starts to decrease or in case of documentation of urine output [4].

**Phosphate**

Intracellular phosphate depletion occurs in DKA (hypophosphatemia) tends to occur when food intake is delayed above 1 day [4]. Hypocalcemia can be induced by IV phosphate, so it may be recommended in case of muscular weakness [11].

**Bicarbonate**

Bicarbonate treatment should be considered in case of extreme acidosis, as it is associated with cerebral edema which is the main cause of mortality in children. The treatment of bicarbonate involves administration of 1–2 mmol/kg added to 0.45% saline which should be provided over 1–2 hours [24].

**Conclusion**

DKA is the leading cause of morbidity and mortality in diabetic children, especially those with T1D due to the development of cerebral edema as a complication of DKA. DKA also leads to other complications, such as pulmonary and cardiovascular complications. The management of DKA is necessary, and in children, the management is similar to that of adults. Moreover, monitoring during treatment is also necessary.

**List of Abbreviations**

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<tr>
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<tr>
<td>AKI</td>
<td>Acute kidney injury</td>
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**Author details**

Mohammed Wasel H. Alsimail1, Meshari Fayez I. Aladhadh2, Ibrahim Hamad I. Erwe3, Abdulrahman Ahmed A. Alnaim1, Ali Majeed A. Almuzaini4, Qasem Ahmed Ali Almulhi5

1. King Faisal University, Al Ahsa, Saudi Arabia
2. King Saud bin Abdulaziz University for Health Sciences, Jeddah, Saudi Arabia
3. King Khalid University, Abha, Saudi Arabia
4. Taibah University, Medina, Saudi Arabia
5. Prince Saud Bin Jalawy Hospital, Al Mubarak, Saudi Arabia

**References**

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