

Hypokalaemia in Patients with Diabetic Ketoacidosis (DKA): A Literature Review

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Abstract

Diabetic ketoacidosis (DKA) is one of the acute complications of diabetes mellitus (DM) that can involve patients from all types of DM. DKA-associated electrolyte imbalance is the main contributor to morbidity and mortality in diabetic patients with potassium being the most affected electrolyte in DKA. The aim of this study is to provide an overview of the prevalence, pathogenesis and management of hypokalemia in DKA. For that, we performed an extensive literature search of the Medline, Cochrane, and EMBASE databases 25 October 2019 using the medical subject headings (MeSH) terms. Papers discussing the prevalence, pathogenesis and management of hypokalemia in DKA were screened for relevant information. The prevalence of hypokalemia in patients with DKA to be ranging from 0% to 4%, during different stages of DKA management. However, a higher (5.6%) and lower (1.3%) prevalence of hypokalemia has been also reported. The lack of insulin, the renal loss of potassium, diarrhea and vomiting are all major contribution factor in the complex pathogenesis of hypokalemia. The American Diabetic Association (ADA) and Joint British Diabetes Societies (JBDS) guidelines are recommending intravenous fluid resuscitation and measuring the potassium levels prior to insulin initiation. Once the normal saline has been used for initial resuscitation and the potassium level is back to normal, the potassium replacement therapy should be started. This replacement therapy is required for patients with for all patient with serum potassium level between 3.3 and 4.5 mmol/L.

Keywords: *Diabetic Ketoacidosis (DKA); Diabetes Mellitus (DM)*

Introduction

Diabetic ketoacidosis (DKA) is one of the acute complications of diabetes mellitus (DM) that can involve patients from all types of DM [1]. It is more common in type 1 diabetes compared to type 2 diabetes. DKA is the first presentation in about one-third of the newly diagnosed type 1 DM patients and a higher percentage can be noticed within the low socioeconomic groups [2,3]. A significant increase of 54.9% in DKA-related hospitalization has been recorded between 2009 and 2014 only [4,5]. DKA is reported to be responsible for about 500,00 days of hospital stay per year with overall cost of 2.4 billion US dollars [4,6,7]. The pathogenesis of DKA is quite simple; a decline in the insulin will decrease the glucose entry to the cells with subsequent hyperglycemia [8]. Accordingly, a series of triglycerides breakdown starts to give free fatty acids that can be used as a source of energy [1,9,10]. Ketones, as the end product of this metabolic plateau, will cause blood acidification with hemostasis disruption [8]. The treatment of DKA is usually a straight forward process with insulin, colloid or crystalloid administration to correct hyperglycemia, hypovolemia and electrolyte disturbance [1,9,11]. However, the patient usually seeks medical care when these simple derangements have gone far away [12,13].

DKA-associated electrolyte imbalance is the main contributor to morbidity and mortality in diabetic patients with potassium being the most affected electrolyte in DKA [8,14,15]. An expected drop of total potassium up to 3 - 6 mEq/kg is usually expected at presentation; however, serum potassium will not be very low due to the extracellular shift induced by acidosis and insulin deficiency [8,9,15]. This decline in total body potassium is mainly caused by vomiting, excessive urination, and secondary hyperaldosteronism [8,9,15]. Following insulin treatment, the serum potassium level will drop due to the resulting intracellular shift [3]. The mandatory potassium replacement therapy is a standard in DKA management to prevent hypokalemia and associated fatal complications including arrhythmias and respiratory failure [3].

Aim of the Study

The aim of this study is to provide an overview of the prevalence, pathogenesis, and management of hypokalemia in DKA.

Methods

We performed an extensive literature search of the Medline, Cochrane, and EMBASE databases on 25 October 2019 using the medical subject headings (MeSH) terms "Diabetic Ketoacidosis" [Mesh] AND "Hypokalemia" [Mesh]. Papers discussing the prevalence, pathogenesis, and management of hypokalemia in DKA were screened for relevant information. There were no limits on date, language, age of participants or publication type.

Prevalence of hypokalemia in DKA

Many studies in the literature have reported the prevalence of hypokalemia in patients with DKA to be ranging from 0% to 4%, during different stages of DKA management [16,23]. Accordingly, the American Diabetic Association (ADA) and Joint British Diabetes Societies (JBDS) guidelines are recommending intravenous fluid resuscitation and measuring the potassium levels prior to insulin initiation [24,25]. In the same context, a higher prevalence of hypokalemia (5.6%) was reported among 54 studied DKA patients [26]. In contrast, a large multi-center cross-sectional study of 537 DKA patients has found a much smaller prevalence of hypokalemia with only 1.3% [27]. Moreover, none of the patients was presenting with significant hypokalemia (< 3.3 mmol/L) that may necessitate potassium supplementation prior to insulin treatment [27]. They considered this difference mainly due to the changing demographics of diabetes with further recent large scale studies needed [27].

In a retrospective study of the pediatric population, 114 children with DKA have been screened for hypokalemia and possible precipitating factors [28]. This study showed a prevalence of 13.8% at presentation and 92.5% during the treatment of DKA [28]. The study also concluded that duration of the metabolic acidosis is the most important risk factor for developing hypokalemia and other possible factors include younger age, higher urine output, lower body weight, lower mean plasma bicarbonate at presentation, lower potassium

serum level at presentation, higher potassium supplementation was given before nadir of potassium (Kn), and shorter time lag of starting potassium supplements [28].

Pathogenesis of potassium loss during DKA

The lack of insulin can cause a major disturbance in the electrolytes and potassium is the most impacted one [13,16]. Insulin promotes the intracellular influx of potassium and from the extracellular space [8,16,29,30]. The stress-induced cellular insensitivity makes it impossible for cells to uptake potassium through the catecholamine-induced mechanism [8,30,31]. The aforementioned mechanism would cause an increase in serum potassium that be evident as false hyperkalemia in some cases [8,32,33]. Moreover, the hyperglycemia-induced diuresis with subsequent water and sodium retention, as a compensatory mechanism, at the expense of potassium excretion [8,9]. In a similar mechanism, acidosis-induced compensation by preserving the hydrogen of bicarbonate would do that at the expense of potassium excretion [8,9].

Besides the renal loss of potassium, a significant amount is lost through the gastrointestinal tract [1,8,34]. The protective nature of the human body would maintain balanced osmotic pressure at expense of electrolytes (both serum and tissue) [8]. As previously mentioned, there is a hyperkalemic state which induces preservation of hydrogen ions by gastric cells [1,8,34]. Accordingly, the associated epigastric stress would induce vomiting and diarrhea with further potassium loss [1,8,34].

Overview of hypokalemia management and potassium resuscitation

Most morbidity and mortality in DKA managements is a result of mismanagement of potassium replacement. Insulin therapy, volume resuscitation and correction of acidosis decrease serum potassium concentration. Patients with low serum potassium concentration on admission have severe total-body potassium deficiency and require potassium replacement and cardiac monitoring because treatment lowers potassium and can provoke cardiac dysrhythmia. As mentioned before, the patients usually seek treatment after deterioration, which makes the DKA management a complex process [8,12,13]. When is patient is not comatose, fluid resuscitation and bolus insulin are started as soon as possible [8]. The ADA and JBDS guidelines are recommending intravenous fluid resuscitation and measuring the potassium levels prior to insulin initiation [24,25]. Once the normal saline has been used for initial resuscitation and the potassium level is back to normal, the potassium replacement therapy should be started [8,9,25,35]. This replacement therapy is required for patients with for all patients with serum potassium levels between 3.3 and 4.5 mmol/L [8,9,25,35]. If serum potassium less than 3.3 meq/l, insulin should be postponed temporarily until potassium concentration increase above 3.3 meq/l in order to prevent cardiac arrhythmia and respiratory muscle weakness. Serial monitoring of serum potassium level is crucial during the management of DKA. The recommendations of the most used guidelines are summarized in figure 1 [9,11,35,36].

A recent case report of a 39-year-old African-American female, with DKA and hypokalemia, has shown a possible promising treatment for persistent cases [4]. Correction of the patient's serum potassium has initiated through intravenous route; however, all efforts have failed [4]. A more aggressive approach has been used with veno-venous hemodialysis (CVVH) using a 4 mEq/L K dialysate bath along with aldactone and low-dose insulin infusion for 24 hours [4]. On follow up, the patient showed normalization of potassium levels, correction of acidosis, and improvement in conscious level [4].

Conclusion

DKA-associated hypokalemia is a fatal complication that should be monitored and corrected as soon as possible. Following the initial resuscitation with normal saline and the potassium level is back to normal, the potassium replacement therapy should be started. CVVH should be considered for persistent cases of DKA-associated hypokalemia.

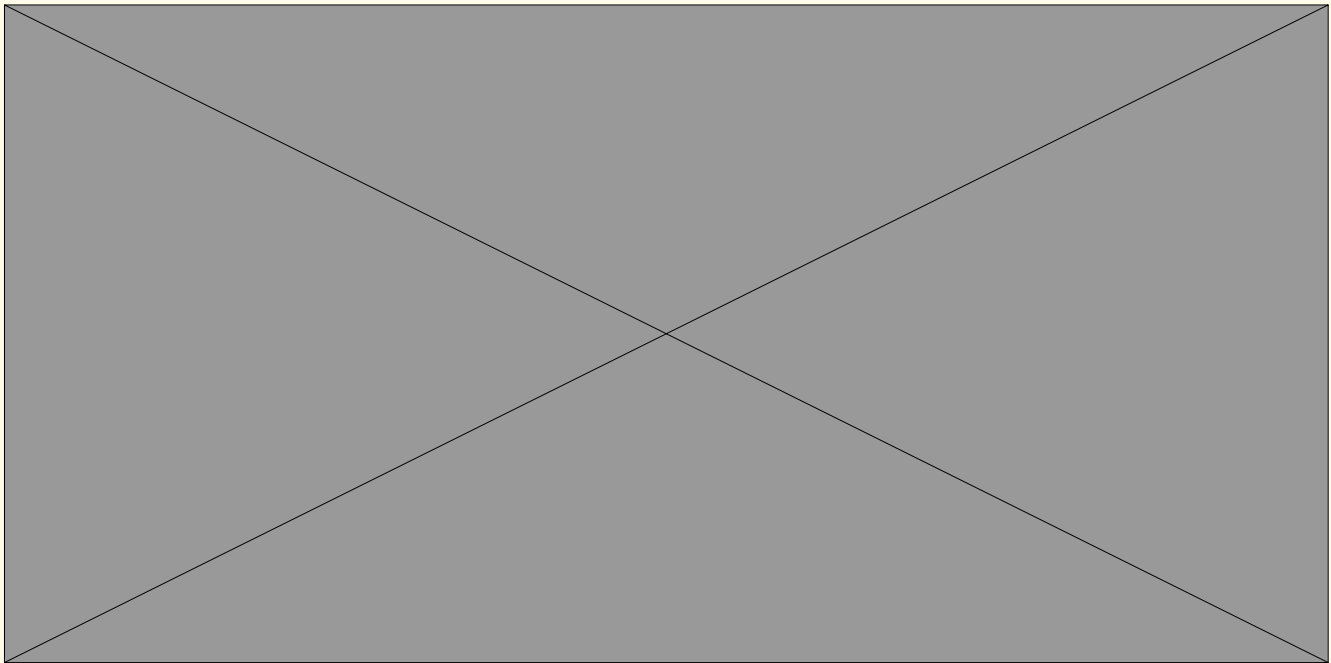


Figure 1: Recommendations of potassium replacement by different guidelines. NICE: The National Institute for Health and Care Excellence; JBDS: Joint British Diabetes Societies; CPG: Clinical Practice Guidelines [9,11,35,36].

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Conflicts of Interest

No conflicts related to this work.

Bibliography

1. Umpierrez GE and AE Kitabchi. "Diabetic Ketoacidosis: Risk Factors and Management Strategies". *Treatments in Endocrinology* 2.2 (2003): 95-108.
2. Dabelea D., et al. "Trends in the Prevalence of Ketoacidosis at Diabetes Diagnosis: The Search for Diabetes in Youth Study". *Pediatrics* 133.4 (2014): e938-e945.
3. Davis Shanlee M., et al. "Profound Hypokalemia Associated with Severe Diabetic Ketoacidosis". *Pediatric Diabetes* 17.1 (2016): 61-65.
4. Syed Zainab., et al. "Successful Use of Renal Replacement Therapy for Refractory Hypokalemia in a Diabetic Ketoacidosis Patient". *Case Reports in Critical Care* (2019): 6130694.
5. Benoit Stephen R. "Trends in Diabetic Ketoacidosis Hospitalizations and in-Hospital Mortality - United States, 2000-2014". *MMWR: Morbidity and Mortality Weekly Report* 67 (2018): 6712a3.

6. Kim S. "Burden of Hospitalizations Primarily Due to Uncontrolled Diabetes: Implications of Inadequate Primary Health Care in the United States". *Diabetes Care* 30.5 (2007): 1281-1282.
7. "Nhds - National Hospital Discharge Survey Homepage" (2019).
8. Usman Atif. "Initial Potassium Replacement in Diabetic Ketoacidosis: The Unnoticed Area of Gap". *Frontiers in Endocrinology* 9 (2018): 109.
9. Kitabchi AE., et al. "Hyperglycemic Crises in Adult Patients with Diabetes: A Consensus Statement from the American Diabetes Association". *Diabetes Care* 29.12 (2006): 2739-2748.
10. Kraemer FB and WJ Shen. "Hormone-Sensitive Lipase: Control of Intracellular Tri-(Di-)Acylglycerol and Cholesteryl Ester Hydrolysis". *Journal of Lipid Research* 43.10 (2002): 1585-1594.
11. Savage MW and A Kilvert. "Abcd Guidelines for the Management of Hyperglycaemic Emergencies in Adults". *Practical Diabetes International* 23.5 (2006): 227-231.
12. Usman Atif., et al. "Profiles of Diabetic Ketoacidosis in Multiethnic Diabetic Population of Malaysia". *Tropical Journal of Pharmaceutical Research* 14.1 (2015): 179-185.
13. Wong B., et al. "Examining the "Killer K" of Diabetic Ketoacidosis at a Tertiary Care Hospital: An Exploratory Study". *Canadian Journal of Diabetes* 40.3 (2016): 204-209.
14. Edge JA., et al. "Causes of Death in Children with Insulin Dependent Diabetes 1990-96". *Archives of Disease in Childhood* 81.4 (1999): 318-323.
15. Wolfsdorf JL., et al. "Ispad Clinical Practice Consensus Guidelines 2014. Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar State". *Pediatric Diabetes* 15.20 (2014): 154-179.
16. Adroque HJ., et al. "Determinants of Plasma Potassium Levels in Diabetic Ketoacidosis". *Medicine (Baltimore)* 65.3 (1986): 163-172.
17. Cohen AS., et al. "Diabetic Acidosis: An Evaluation of the Cause, Course and Therapy of 73 Cases". *Annals of Internal Medicine* 52 (1960): 55-86.
18. Beigelman PM. "Potassium in Severe Diabetic Ketoacidosis". *American Journal of Medicine* 54.4 (1973): 419-420.
19. Kitabchi AE., et al. "The Efficacy of Low-Dose Versus Conventional Therapy of Insulin for Treatment of Diabetic Ketoacidosis". *Annals of Internal Medicine* 84.6 (1976): 633-638.
20. Kitabchi AE., et al. "Thirty Years of Personal Experience in Hyperglycemic Crises: Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar State". *Journal of Clinical Endocrinology and Metabolism* 93.5 (2008): 1541-1552.
21. Beigelman PM. "Severe Diabetic Ketoacidosis (Diabetic "Coma"). 482 Episodes in 257 Patients; Experience of Three Years". *Diabetes* 20.7 (1971): 490-500.
22. Abramson E and R Arky. "Diabetic Acidosis with Initial Hypokalemia. Therapeutic Implications". *Journal of the American Medical Association* 196.5 (1966): 401-403.
23. Manzano F and GP Kozak. "Acute Quadriplegia in Diabetic Hyperosmotic Coma with Hypokalemia". *Journal of the American Medical Association* 207.12 (1969): 2278-2281.

24. Kitabchi AE., *et al.* "Hyperglycemic Crises in Adult Patients with Diabetes". *Diabetes Care* 32.7 (2009): 1335-1343.
25. Savage Mark., *et al.* "Joint British Diabetes Societies Guideline for the Management of Diabetic Ketoacidosis". *Diabetic Medicine* 28 (2011): 508-515.
26. Arora S., *et al.* "Prevalence of Hypokalemia in ED Patients with Diabetic Ketoacidosis". *American Journal of Emergency Medicine* 30.3 (2012): 481-484.
27. Jang TB., *et al.* "Hypokalemia in Diabetic Ketoacidosis Is Less Common Than Previously Reported". *Internal and Emergency Medicine* 10.2 (2015): 177-180.
28. Lee Lai Ka., *et al.* "Prevalence and Potential Risk Factors of Hypokalemia in Pediatric Patients with Diabetic Ketoacidosis". *International Journal of Pediatric Endocrinology* 1 (2015): P8.
29. Adroque HJ., *et al.* "Plasma Acid-Base Patterns in Diabetic Ketoacidosis". *New England Journal of Medicine* 307.26 (1982): 1603-1610.
30. Adroque HJ and NE Madias. "Changes in Plasma Potassium Concentration During Acute Acid-Base Disturbances". *American Journal of Medicine* 71.3 (1981): 456-467.
31. Kes Petar. "Hyperkalemia: A Potentially Lethal Clinical Condition". *Acta Clinica Croatica* 40.3 (2001): 215-225.
32. Joseph E Parrillo and R Phillip Dellinger. "Critical Care Medicine: Principles of Diagnosis and Management in the Adult". Elsevier Health Sciences (2013).
33. Liamis G., *et al.* "Spurious Electrolyte Disorders: A Diagnostic Challenge for Clinicians". *American Journal of Nephrology* 38.1 (2013): 50-57.
34. Schaefer TJ and RW Wolford. "Disorders of Potassium". *Emergency Medicine Clinics of North America* 23.3 (2005): 723-747, viii-ix.
35. Excellence, National Institute for Clinical. "Type 1 Diabetes: Diagnosis and Management of Type 1 Diabetes in Children, Young People and Adults" (2004).
36. Malaysia MOH. "Clinical Practice Guideline; Management of Type 2 Diabetes Mellitus. 5th Edition" (2015).

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