Management of diabetic ketoacidosis in a patient with Chronic Kidney disease under maintenance hemodialysis: A case report and review of literature

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Abstract
Diabetic ketoacidosis (DKA) is a potentially fatal metabolic complication observed in individuals with type I DM or type II DM under stress, such as infections and treatment non-compliance. DKA in chronic kidney disease (CKD) patients undergoing maintenance hemodialysis presents challenges due to unique pathophysiology and the absence of specific management guidelines. This case report highlights the importance of tailoring the treatment of DKA based on the specific requirements of CKD patients on hemodialysis. The presented case involves a 47-year-old female with type II diabetes mellitus and CKD who developed DKA in the context of a urinary tract infection. Management included insulin infusion, cautious fluid replacement therapy, electrolyte monitoring, and identifying precipitating factors like an infection. The case highlights the complexity of DKA management in CKD patients and the necessity of individualized approaches. More studies and guidelines are needed to optimize the proper management of DKA in CKD patients.

Categories: Endocrinology/Diabetes/Metabolism, Nephrology  
Keywords: electrolyte in dka, fluid management in dka, insulin therapy, maintenance hemodialysis, chronic kidney disease, diabetic ketoacidosis

Introduction
Diabetic Ketoacidosis (DKA) is a common and potentially fatal metabolic abnormality in insulin-dependent Diabetes Mellitus [1,2]. DKA occurs commonly in Type 1 Diabetes mellitus (DM) but can occur in Type 2 DM under stressful conditions like infections, noncompliance to treatment, and insulin omission, of which infection is the most common precipitating factor [2-4]. Among all cases of DKA, about 1/3rd are due to DM Type 2 [5]. Management of DKA in the general population is established, but in a patient with renal failure under maintenance hemodialysis (MHD), no specific guidelines are available [6-8]. There are marked differences in the pathophysiology of DKA in a patient with Chronic Kidney Disease (CKD) from DKA in the general population with normal renal function, so management of DKA in CKD should differ and be tailored accordingly from established guidelines for appropriate management [9]. Also, a patient with DKA and CKD under MHD has a higher incidence of volume overload, hypoglycemia, longer stay, and need for ventilation than a patient with normal renal function [10].

Very few articles are related to managing DKA in a patient with CKD. Even in the tertiary center, we get to see very few cases. Our case report highlights the importance of calibrating treatment according to the need of patients with CKD under MHD.

Case Presentation
A 47-year-old female diagnosed with Type II Diabetes mellitus and chronic kidney disease on maintenance hemodialysis presented to the Emergency Department with bilateral swelling of lower limbs for 15 days, nausea for 5 days, and altered sensorium for 1 day. She was diagnosed with Type II Diabetes Mellitus 20 years back and was under metformin for the first 11 years, followed by insulin therapy for the past 9 years. She is hypertensive, has been under medication for 12 years, and has had a history of hypothyroidism for the past 2 years, for which she has been taking levothyroxine. She last had her hemodialysis session 3 days before the presentation. She had no history of missed insulin doses.

Her GCS was 13/15, E4, V4, and M4 on examination. Vitals were within normal range with a pulse of 84 beats/min, a respiratory rate of 22 breaths/min, and oxygen saturation maintained at room air, except for high blood pressure of 160/90 mmHg. Bilateral pitting pedal edema was present. Systemic examination
showed no significant findings, and she had no flapping tremors.

Her investigations showed increased creatinine of 718 umol/L, urea of 35 mmol/L, plenty of RBCs, and pus cells in urine with 3+ albumin. Hematological investigation shows Hemoglobin of 9.7 g/dL with normal total leukocyte count and platelets. Arterial Blood Gas (ABG) showed pH: 7.202 with HCO3: 6 mmol/L, PCO2: 22, K+: 3.5 mmol/L and Na: 135 mmol/L. Lactate was 9.2 mmol/L with urine analysis positive for acetone and fasting blood glucose of 27.1 mmol/L. Blood and urine cultures were sent. RT-PCR for SARS-CoV2 was negative. ECG was normal, and Chest X-ray showed no signs of pulmonary edema or pneumonia.

<table>
<thead>
<tr>
<th>Test</th>
<th>On arrival</th>
<th>After two episodes of dialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea</td>
<td>35 mmol/L</td>
<td>16 mmol/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>718 umol/L</td>
<td>482 umol/L</td>
</tr>
<tr>
<td>Sodium</td>
<td>128 mmol/L</td>
<td>135 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.5 mmol/L</td>
<td>3.5 mmol/L</td>
</tr>
<tr>
<td>pH</td>
<td>7.2</td>
<td>7.46</td>
</tr>
<tr>
<td>HCO3</td>
<td>6.0 mmol/L</td>
<td>18.9 mmol/L</td>
</tr>
<tr>
<td>pCO2</td>
<td>15.2 mmHg</td>
<td>26.2 mmHg</td>
</tr>
<tr>
<td>Fasting sugar level</td>
<td>27.1 mmol/L</td>
<td></td>
</tr>
<tr>
<td>Urine acetone</td>
<td>Positive</td>
<td>Positive</td>
</tr>
</tbody>
</table>

**TABLE 1: Laboratory parameters on arrivals and after two episodes of hemodialysis**

A diagnosis of Diabetes Ketoacidosis, secondary to urinary tract infection, was made. Initially, the patient was managed with two 500ml of normal saline, each infused with 20mEq of KCl at 100ml/hr. The fluid was titrated with urine output which was 350ml/day initially. Regular insulin of 0.1U/kg/hr was given by infusion pump. 100mEq of IV NaHCO3 and antibiotic coverage were given for Urinary Tract Infection (UTI). Her insulin infusion was titrated with a level of K+ and random blood sugar. Insulin infusion was withheld for 4 hours if the K+ level was below 3mmol/L, and 50ml of 50% dextrose was given if the blood sugar level was below 150mmol/L. Her output decreased to 100ml/6 hours with a rise in potassium and creatinine levels following the next day of treatment, and hemodialysis was done. Following hemodialysis, she had one episode of hypoglycemia with a random blood sugar of 2.3mmol/L, for which she was given 50ml of 50% dextrose. She was continued on insulin infusion and subcutaneous insulin given before each meal after she started taking meals. Her insulin infusion was kept at 0.05U/kg/hour. She was planned for alternate-day dialysis to prevent fluid overload and uremic complications. After resolving acidosis, she was kept in ICU and shifted to the nephrology ward.

**Discussion**

The management principles of DKA in a patient with End-stage Renal Disease (ESRD) on maintenance hemodialysis is complex and determined by various factors. Each patient should be tailored according to volume status, serum glucose level, serum osmolality, serum potassium level, and general condition. Unlike the general population, it is difficult to generalize the treatment of DKA in anuric patients. The following recommendations are drawn from the literature we reviewed.

1. Hyperosmolar state

Pontine myelinolysis and cerebral edema are the most critical fatal complications that can be prevented by properly managing the hyperosmolar state. Hyperglycemia-induced osmotic diuresis is absent in an anuric patient, so they rarely present with dehydration and shock [8]. Most, not all, patients have low serum sodium associated with hypertonicity, and this patient gets better with insulin infusion along with close monitoring of blood glucose, electrolyte, and volume status [8]. Sometimes, emergency hemodialysis may be needed if the initial presentation is associated with extreme hyperglycemia, hypertonicity, and a low serum sodium level. This doesn’t indicate that we can perform early dialysis without proper indications; if done can lead to cerebral edema due to a rapid decrease in serum osmolality [8, 11]. The recommended reduction rate of serum glucose level varies, but most believe it to be around 50-75mg/dl/hr [8]. In our case, fluid therapy was initially titrated, considering the urine output and the possibility of developing pulmonary edema.
2. Fluid management

Fluid management is a crucial step in managing DKA. A patient with normal renal function is expected to have around 5-8 liters of fluid loss, but in an anuric patient on HD, the scenario is different because of the absence of loss of osmotic diuresis [8]. So fluid replacement in DKA in CKD under MHD should include 250 - 500 ml boluses guided by the patient’s volume status; in case of significant fluid overload, it should be managed by HD [12,13]. In a patient with DKA with CKD, there will be no hyperglycemia associated with osmotic diuresis, which causes expansion of extracellular volume, unlike the general population. It is not recommended to resuscitate patients with fluid boluses if done, which can lead to fatal consequences [14,15]. Cautious fluid replacement should be done continuously, guided by the patient’s volume status, to prevent pulmonary edema [8]. Xue Meng Lim et al. stated that for the choice of fluid, we could use isotonic saline or dextrose normal saline if the blood glucose level drops [11].

3. Insulin therapy

The mainstay of treatment of DKA is insulin therapy, which decreases the serum glucose levels, and synthesis of ketone bodies and corrects hyperkalemia [8,15]. Regarding insulin administration, an infusion is preferred over the subcutaneous route as it is easy to titer [8]. In a patient with DKA and ESRD, most studies recommend dose reduction of insulin as it is excreted renally [8,9]. The recommended infusion rate is 0.05 to 0.07 units/kg per hour to prevent rapid blood glucose levels and osmolality changes [8]. The rate of infusion can also be guided by a reduction of serum ketone level, which should be around 0.5mmol/h, a reduction of serum glucose level, which should be around 50-75mg/dl per hour, and an increase in serum bicarbonate level, which should be around 3mmol/hr [8]. Vigilant monitoring of capillary blood glucose is recommended as patients with DKA in ESRD have a higher incidence of hypoglycemic events and other adverse glycemic events than the general population [16]. So, a slower rate of insulin infusion is recommended by Kuverji et al. to prevent hypoglycemic episodes [12]. In our case, the patient received six days of insulin infusion at 0.1U/kg/hr initially, followed by 0.05U/kg/hr after dialysis until her glucose level was less than 200mEq/L with correction of acidosis. She was started on subcutaneous regular insulin and titrated accordingly after she tolerated the oral intake of meals. She developed one episode of hypoglycemia following hemodialysis, which was corrected with dextrose. Hypoglycemia is common after hemodialysis, depending on the glucose content in the dialysate.

4. Electrolyte Disturbances: Potassium

Hyperkalemia is a known complication in patients with hyperglycemia, even without acidosis, but severe hyperkalemia is usually absent in a patient with intact renal function by increasing renal loss of potassium [15]. However, Diabetic patients under MHD have severely impaired renal function, which increases the risk of fatal hyperkalemia associated with hyperglycemia [15]. Seddik et al. recommends not replacing potassium in a patient with DKA with ESRD on HD, even with the evidence of biochemical hypokalemia, as the total body potassium levels remain high due to the inability to excrete potassium renally [8]. Patients with a serum potassium level of > 5.5mmol/l should be on continuous cardiac monitoring; also, they may require emergency HD and insulin therapy for its management. Correction with 40mmol/L of KCl should be done to reach the target potassium level of <5.5mmol/l in patients with a serum potassium level of <3.5mmol/l [8,11]. Potassium replacement, if done at initial presentation without laboratory evidence of hypokalemia, might be fatal in the case of DKA with abnormal renal function. Insulin therapy alone can be used to treat the majority of hyperkalemia associated with DKA as studies have concluded that insulin deficiency is its major cause [15]. As the potassium level was 3.5mmol/L in our case, 40mEq/L of KCl was given with normal saline infusion at 100ml/hr to prevent hypokalemia. The potassium level was measured every four hours to monitor hypokalemia due to insulin and also for possible hyperkalemia that may require immediate management. Hemodialysis can be started when the potassium level crosses 5.5mmol/L despite insulin therapy.

5. Metabolic Acidosis

Severe metabolic acidosis can be seen at initial presentation in an anuric patient. Seddik et al. recommend emergency HD for correcting acidosis but have suggested against bicarbonate administration [8]. Lim et al. state ESRD patients are accustomed to acidosis and don’t recommend bicarbonate therapy [11]. In chronic renal failure patients, there is a lack of excretion of metabolizable acids and a lack of regeneration of bicarbonate to counteract the acidosis. Therefore, bicarbonate supplementation must be started when the PH is less than 7.2 or HCO3: 20-22mmol/L as the acidosis increases protein catabolism.

6. Identification and addressing precipitating factors: Infection

Identifying precipitating factors like missed insulin dosing and infection is an important step in managing and preventing the recurrence of DKA [11]. In our case, plenty of pus cells in urine analysis and high lactate levels in ABG analysis warranted using parental piperacillin and tazobactam for probable sepsis.
culture showed a growth of E.Coli, suggesting urinary tract infection, which was the precipitating factor of DKA.

Conclusions

The management of DKA in patients with CKD under maintenance hemodialysis has challenges as it is an uncommon presentation. The management requires specific approaches due to the risk of volume overload and hyperkalemia in an individualized manner. Critical factors such as hyperosmolar state, insulin therapy, electrolyte disturbances, and metabolic acidosis should be attended to carefully. Identifying and promptly managing inciting events like infection and dehydration is crucial for proper management of the condition and prevention in the future.

Due to the lack of literature on this topic, this case report highlights the importance of additional research and formulation of specific management protocols for this condition which can lead to improvement in management strategies and reduced complication rates in this unique but challenging medical scenario.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References