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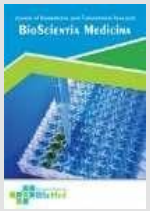

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Management of Critically Ill Patients with Severe Diabetic Ketoacidosis and Acute Renal Failure: A Case Report

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A B S T R A C T

Background: Diabetic ketoacidosis (DKA) is one of the hyperglycemic crises related to diabetes. The main problem in DKA is ketogenesis, a metabolic process that increases the production and decreases the utilization of ketones. DKA is characterized by a biochemical triad such as hyperglycemia, ketonemia, and high anion gap metabolic acidosis. Management of DKA needs to be carried out appropriately and immediately because it may lead to diabetic coma and death. **Case presentation**: A 38-year-old woman had decreased consciousness due to metabolic encephalopathy as a complication of severe DKA. The metabolic derangement shows an overlapping high anion gap metabolic acidosis and non-anion gap metabolic acidosis. This case is complicated by acute renal failure. The patient also had been in a hypovolemic state, causing pre-renal acute kidney injury. We treat the patient using a balanced solution to correct hypovolemia. Sonography of the vena cava and blood lactate levels are used to guide fluid resuscitation. We intubate and control the patient's breathing to reduce the metabolic demand. We titrate the insulin infusion until the ketogenesis process is abolished. Antibiotics are given based on sputum culture. **Conclusion:** Acute renal failure (ARF) is a rare but potentially fatal complication of diabetic ketoacidosis (DKA). Early recognition and aggressive treatment of ARF during DKA may improve the prognosis of these patients.

1. Introduction

Diabetic ketoacidosis (DKA), a severe complication of diabetes mellitus (DM), is the leading cause of hospitalization, morbidity, and mortality in patients with DM. DKA is associated with hyperglycemic crises and features metabolic acidosis, the production of ketoacids, volume depletion, and electrolyte imbalance, causing diabetic coma. Due to glucose-induced osmotic polyuria and even emesis, volume depletion is a major cause of acute kidney injury (AKI) in DKA patients. It is now well-accepted that AKI is an important factor that influences long-term morbidity and mortality. The clinical manifestations of AKI range from a mild increase in serum creatine (SCr) to anuric renal failure requiring dialysis. Most of the available studies focused on patients with acute renal failure (ARF) caused by DKA, and those with mild renal impairment who did not meet the criteria of ARF were overlooked. Brenden E et al. found that 44 of 106 (41.5%) DKA combined with AKI patients did not have documentation of AKI resolution prior to discharge. To date, no study has investigated the effect of AKI on long-term renal outcomes in DKA patients after discharge.[1-5] In this study, we reported a case of a DKA patient with complications who received haemodialisa in the intensive care unit.

2. Case Presentation

A 38-year-old woman was referred from the district hospital with a decrease in consciousness one day

before hospital admission. The patient had undiagnosed diabetes and showed no classic symptoms or significant family history. The patient had a high blood sugar level (reaching more than 800 mg/dL) after the decrease of consciousness proceeds. The patient denies a prior and family history of diabetes. The patient's consciousness began to decline one day before she was admitted. The patient was suspected of having DKA and had been resuscitated with 1000 mL of intravenous fluid in the emergency department. The patient denies prior surgeries, any cough and runny nose for the past two weeks, diarrhea, allergies, asthma, hypertension, and other systemic conditions.

Physical examination finding was 160 cm woman with normal BMI (23.4 kg/m^2). Physical examination results were as follows; central nervous system: Glasgow Comma Scale E3VxM4, pupils are equal (3 mm in size) and reactive to light; Respiration: chest expansion is symmetrical, respiratory rate 18-20, rhonchi and wheezing are absent, peripheral oxygen saturation 95-97% on ventilator portable PCV Pinsp 16, FiO_2 50%, Ps 10; Cardiovascular: normal heart sounds with no murmur and no gallop, heart rate 99 bpm, blood pressure 125/88 mmHg; Gastrointestinal: bowel sounds are normal, no distension; Urogenital: spontaneous micturition; Musculoskeletal: neck flection and deflection are good, Mallampati II, warm extremities, no edema on both legs, capillary refill time <2 seconds. Complete blood count showed a leukocytosis on 1st, 7th, and 9th day (18.39 x 10^9/L, 13.44 x 10^9/L, 19.37 x 10^9/L respectively), anemia on 6th and 10th day (hemoglobin 8.9 g/dL, hematocrit 26.4% and hemogloblin 7.8 g/dL, hematocrit 24.3% respectively), high blood urea nitrogen and serum creatinine levels on 1st, 4th, 5th, 7th, and 8th day (72.70 mg/dL and 3.06 mg/dL; 85 mg/dL and 3.79 mg/dL; 58.8 mg/dL and 2.86 mg/dL; 53.5 mg/dL and 1.49 mg/dL; 23.50 mg/dL and 0.65 mg/dL respectively), hypoalbuminemia on 10th day (2.19 g/dL). Blood gas analysis showed low pH levels on the 1st, 2nd, 3rd, 4th, and 7th day (6.97, 7.17, 7.13, 7.1, and 7.29 respectively), low HCO_3^- levels on 1st, 2nd, 3rd, 4th, and 5th day (3.20 meq/L, 6.20 meq/L, 6.30 meq/L, 9.6 meq/L, and 14.9 meq/L respectively), low total CO_2 levels on 1st, 2nd, 3rd, 4th, 5th, 6th, 7th, and 8th day (3.6 meq/L, 6.7 meq/L, 6.9 meq/L, 10.6 meq/L, 15.6 meq/L, 18.9 meq/L20.4 meq/L, and 21.5 meq/L respectively) indicating metabolic acidosis. Chest X-ray on 6th day revealed pneumonia, right pleural effusion, attached CVC with distal tip projecting at CV Th-7 level, impression of cavoartrial junction, Attached RTT with distal tip projecting at CV Th 3 level. A urine culture on 3rd day was negative. Sputum culture on the 5th day was positive for *Acinetobacter baumannii* sensitive to trimethoprim/sulfamethoxazole, amikacin, and tigecycline, adjusting the dose.

3. Discussion

Ketoacidosis is a medical emergency with significant morbidity and mortality. It should be diagnosed promptly and managed intensively. The specialist diabetes team should always be involved as soon as possible and ideally within 24 hours because this has been demonstrated to be associated with a better experience for the intensivist and reduced length of stay. The lack of renal insulin clearance means that ketoacidosis is much less likely to occur. It may also be difficult to determine because of the chronic metabolic acidosis associated with advanced chronic kidney disease (stages 4 and 5). Intensive data suggest that those presenting with ketoacidosis with end-stage renal disease have lower ß- hydroxybutyrate concentrations and higher glucose and anion gaps than those with preserved renal function. Bicarbonate and pH were not significantly different When ketoacidosis does occur in end-stage renal disease.[6-8]

A meta-analysis of observational studies conducted by Tza-maloukas et al. in 2008 found that serum tonicity was lower in the dialysis group than in those with preserved renal function. They suggested that when hyperglycaemia contributes to increased extracellular tonicity, the fluid shift increases extracellular fluid volume. When DKA occurs in people with preserved renal function, this results in osmotic

diuresis and a net loss of water, which increases extracellular tonicity. In people on maintenance with hemodialysis, there is no osmotic diuresis, resulting in increased extracellular volume and reduced extracellular tonicity compared with those without renal failure.[9]

In this case report, the patient lost consciousness as a result of a complication of DKA, namely metabolic encephalopathy. Metabolic dysregulation that occurs during DKA will mediate neuroinflammation and cerebral oxidative stress, resulting in neuronal injury. Indications for intensive care in this patient are Hyperkalemia, acute renal failure, and coma mental status. The patient had severe DKA with serum bicarbonate level <10 mmol/L (3.20) and arterial pH < 7 (6.97).[3,9] People with acute kidney failure are at a higher risk of hyperkalaemia. An observational study by Tzamaloukas et al. reported higher initial serum potassium levels compared with patients on peritoneal dialysis who presented in DKA. The frequency of hyperkalaemia was also higher in DKA than in non-ketotic hyperglycaemia.[10-11]

DKA is a volume-depleted state with a total body water deficit of approximately 6L. Therefore, the initial fluid therapy is directed toward the expansion of intravascular volume and securing adequate urine flow. The initial fluid of choice is isotonic saline at the rate of 15–20 ml /kg body weight per hour or 1–1.5 L during the first hour. The goal is to replace half of the estimated water and sodium deficit over a period of 12-24 hours.[12-13] The initial hydration in this patient was 1000 mL/hour was not given fluids containing chloride, so it did not worsen the acidosis in DKA. Resuscitation was carried out with ultrasound guidance (IVC distensibility), which led to worse acidotic conditions in DKA.

A study by Fisher JN that investigated the optimum route of insulin therapy in DKA demonstrated that the time for resolution of DKA was identical in patients who received regular insulin via intravenous, intramuscular, or subcutaneous routes.[14] In DKA, we recommend using intravenous (IV) starting with a regular insulin dose of 0.1 units/kg, followed by a continuous infusion of 0.1 units/kg/hour of regular insulin. The patient, in this case report, was given insulin drip at a dose of 4 units/hour. Metabolic targets that need to be achieved after insulin administration are an increase in bicarbonate concentration to 3 mmol/L per hour, a decrease in blood glucose levels to 3 mmol/L per hour, and a decrease in the concentration of ketones in the blood by 0.5 mmol/L per hour while maintaining potassium levels normal.[5]

The patient was suspected of pneumonia, which was confirmed by chest X-ray, and the sputum culture was positive for *Acinetobacter baumannii*, which is sensitive to trimethoprim/sulfamethoxazole, amikacin, and Tigecyc. The patient was treated with ceftriaxone 2 g/24 hours IV and levofloxacin 750 mg/24 hours IV. On the 5th day, after the culture results came out, antibiotics were changed to a tigecycline 200 mg loading dose, finished in 1 hour, and then continued with a tigecycline 100 mg/12 hours IV. Another complication encountered in this patient is acute renal failure (AKI). The creatinine level in this patient met the RIFLE criteria for AKI, where there was a 2-fold increase in creatinine level, and then the patient got haemodialysis in the intensive care unit.

During haemodialysis lower glucose dialysates may influence glucose control and increase the risk of hypoglycaemia due to the movement of glucose down a concentration gradient. There are also concerns that haemodialysis may cause a rapid reduction in hypertonicity in DKA, which could potentially lead to adverse neurological outcomes. In one case report by Gupta et al., haemodialysis caused a rapid reduction in tonicity (14.5 mOsm/kg/h) and was stopped 1.5 h after initiation due to fears that this is approximately five times faster than the recommendation. Another complication that should be considered with haemodialysis, especially in patients who have reduced GCS at presentation or have missed sessions of dialysis, is dialysis disequilibrium syndrome (DDS). The pathophysiology of DDS is unclear, but it is proposed that there is a reverse osmotic shift due to

the rapid removal of small solutes, such as urea, which causes cerebral oedema.[10,15]

Key recommendations on the medical management of DKA in renal replacement therapy. First, a reduced rate of insulin infusion to mitigate the risk of hypoglycaemia. Insulin infusion rates should be adjusted in relation to haemodialysis timing. Second, careful monitoring of potassium, with replacement only if serum potassium is <3.5 mmol/L and acidosis is corrected. Medical management of hyperkalaemia should be adapted in the context of hyperglycaemia if there is a delay in haemodialysis. Third, carefully assess fluid volume status, with small boluses (250 mL) of intravenous fluids if deemed hypovolaemic, and frequent re-assessment to avoid fluid overload. Invasive monitoring and vasopressor support in a critical care setting may be required in complex sepsis cases. Fourth, as there are concerns regarding rapid reduction in hypertonicity in DKA, haemodialysis should be considered in cases with severe hyperkalaemia with ECG changes or severe pulmonary oedema.[12] The AKI observed in these patients may result from pre-renal treatment and is resolved by fluid resuscitation with guiding IVC distensibility and hemodialysis support to improve renal shutdown. has been successful with twice haemodialisa, such as hypovolemia induced by polyuria or emesis.[6]

4. Conclusion

Diabetic ketoacidosis (DKA) is characterized by a biochemical triad such as hyperglycemia, ketonemia, and high anion gap metabolic acidosis. Indications for intensive care in DKA, in this case, coma mental status, end-stage renal failure, and hyperkalemia.

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