Case report

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Restrictive fluid and fluid removal approach in diabetic ketoacidosis with septic AKI: A case report

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Abstract

Diabetic ketoacidosis is a life-threatening complication that requires a rapid restoration of intravascular volume usually with aggressive administration of intravenous fluid with 0.9% sodium chloride as recommended by the American Diabetes Association. We report a 50-year-old obese female patient with a history of diabetes mellitus (DM) since 20 years ago and routinely using insulin. She experienced dyspnea and presumably was caused by diabetic ketoacidosis. The patient was given fluid resuscitation with normal saline, but the dyspnea did not resolve and the work of breathing increased further, so the patient was intubated and admitted to the intensive care unit. Aggressive fluid resuscitation carries potential adverse effects such as hyperchloremic metabolic acidosis, interstitial multi-organ edema, and increased incidence of acute kidney injury. The first day of ICU treatment, positive cumulative fluid balance occurred and fluid removal was indicated. Fluid removal using diuretic or ultrafiltration is a part of the treatment of organ congestion and fluid overload after the initial phase of shock resuscitation to achieve negative fluid balance. This case showed that restricted fluid and fluid removal improve the patient outcome, especially in diabetic ketoacidosis and septic AKI patients.

Key words: Diabetic ketoacidosis, septic AKI, restricted fluid, fluid removal, negative cumulative balance.

Introduction

Diabetic ketoacidosis (DKA) is a life-threatening complication that can occur in patients with diabetes mellitus. Diabetic ketoacidosis patients with another condition such as acute kidney injury (AKI) and sepsis are considered critically ill and require treatment in an intensive care unit (ICU). (1) Recent guidelines from American Diabetes Association (ADA) recommend fluid resuscitation using normal saline 15-20 ml/kg/hour (1-1.5 liter) in the first one hour and continue with 250-500 ml/hour as maintenance. This approach is still controversial because this type of fluid overload could induce hyperchloremic metabolic acidosis. (2) Positive fluid balance and vein congestion may worsen critically ill patients' outcomes and induce multiple organ failures such as lungs, renal, liver, and gastrointestinal. (3) Active fluid removal using diuretic and ultrafiltration could be used to treat organ congestion and fluid overload after initial resuscitation. We present a DKA with septic AKI case with a restricted fluid approach and active fluid removal which improved patient outcomes.

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Case presentation

We report a 50-year-old obese female patient with a history of diabetes mellitus (DM) since 20 years ago and routinely using insulin. First, she had myalgia, nausea, and vomitus during the first day in the general ward. The patient had normal vital signs, leukocytosis, high blood glucose (358

mg/dl), normal urea-creatinine, normal chest X-ray, and normal electrocardiography (ECG). On the second day of treatment, she experienced dyspnea, tachypnea, increased blood pressure (193/79 mmHg), tachycardia 142 beats/min, and presumably caused by diabetic ketoacidosis. The patient was given fluid resuscitation with normal saline 1500 ml and further consulted with the cardiologist. The cardiologist performed echocardiography, found there were no abnormalities, then gave diuretic (furosemide), nitrate, and antihypertensive agent to treat for the possibility of pulmonary edema. One hour later, the dyspnea did not resolve and the work of breathing increased, so the patient was intubated and admitted to the intensive care unit (ICU).

In the ICU, the patient got mechanical ventilation and a central venous catheter was inserted. During treatment, the patient tended to have tachycardia (120-140 beats/min), fever, and elevated blood pressure (120-160 mmHg), so the patient was given nicardipine in titrated dose. Central venous pressure (CVP) was maintained around 6-8 mmHg. Additional examination showed the patient had an increased level of ketones and creatinine, leukocytosis, metabolic acidosis, but ECG and chest X-ray did not show anything abnormal. The working diagnosis was diabetic ketoacidosis with septic acute kidney injury (AKI).

On the first day in the ICU, this patient had positive fluid balance and was indicated for fluid removal. On the third day, the patient got continuous veno-venous hemofiltration (CVVH) and on the fourth day negative cumulative fluid balance reached, the vital sign was stable (CVP around 0-6 mmHg), and the level of creatinine and ketones were significantly decreased. The CVVH was performed until the sixth day to maintain negative fluid balance. Finally, on the seventh day, the patient got extubation and transferred into the general ward with a cumulative fluid balance of -5172 ml.

Discussion

Diabetic ketoacidosis is defined by the triad of hyperglycemia, metabolic acidosis, and ketonemia. Hyperglycemia and ketones may induce osmotic diuresis, leading to hypovolemia and decreased glomerular filtration rate (GFR). Progressive volume depletion caused a decrease in GFR, and a further decrease in clearance of glucose and ketone resulting in subsequent hyperglycemia, hyperosmolality, and metabolic acidosis. (2) Patients with ketoacidosis also have a tendency to experience sepsis and AKI. (4)

Fluid resuscitation protocol according to ADA in 2009 is the administration of 1000-1500 ml of initial normal saline for the first hour. Excessive administration of normal saline has the potential to cause hyperchloremic metabolic acidosis. (2) A recent study suggested that administering a balanced electrolyte solution can prevent hyperchloremic metabolic acidosis. (5)

KAD is an acute inflammatory condition and may promote further increase in inflammatory mediators. Patients who are free from the shock phase will experience inflammatory mediator homeostasis within three days, characterized by hemodynamic stabilization and restoration of plasma oncotic pressure, diuresis, mobilization of extravascular fluid, and negative fluid balance, which is known as the flow phase. Contrary to usual inflammatory patients, this patient developes persistent systemic inflammation, plasma leakage, and flow phase fails to be reached, so that fluid accumulation increases, results in positive cumulative fluid balance. Cordeman, et al introduced the term global increased permeability syndrome (GIPS), which denotes the third hit of shock after injury and multi-organ dysfunction syndrome (MODS). GIPS can be caused by hypervolemia and can be implemented as cerebral edema, lung edema, kidney edema, intestinal edema, and peripheral edema. (6) At the time of admission to the ICU, this patient had entered the third hit phase and GIPS already occurred, which was marked by positive cumulative fluid balance.

Fluid removal was performed with diuretics to achieve negative fluid balance. Fluid removal using diuretic or ultrafiltration is a part of the treatment of organ congestion and fluid overload after the initial phase of shock resuscitation to achieve negative cumulative fluid balance. In addition to diuretics, ultrafiltration was also performed in order to remove the cytokines and also the fluid. Initial CVP monitoring ranged from 8-12 mmHg and reached 0-4 mmHg when the negative cumulative fluid balance was achieved. Legran, et al found there was a linear relationship between CVP values, and the risk of AKI. This suggests a role for venous congestion in the pathophysiology of AKI in sepsis. (3) Multicenter observational studies found the use of diuretics was associated with better survival in critically ill patients with AKI. (7) In 2017 European Society of Intensive Medicine recommended the use of diuretics to control and prevent fluid overload in patients who were responsive to diuretics. The use of diuretics can improve AKI including tubular obstruction, reducing medullar oxygen consumption, and increasing renal blood flow, reducing fluid overload, and venous

congestion. Although there is no single parameter for fluid overload, increased CVP, peripheral edema, and increased intra-abdominal pressure can be used as surrogates. (8) Negative fluid balance has a linear correlation with mean CVP and creatinine value, where the more negative fluid balance results in the lower mean CVP and creatinine value (**Figure 1**).

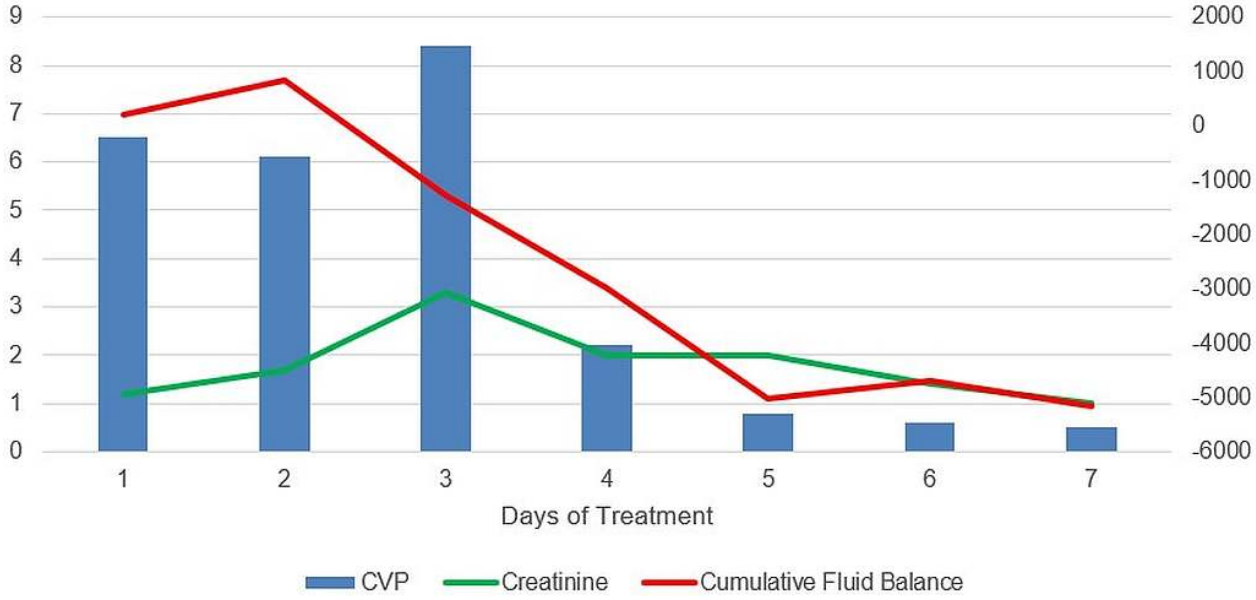
Based on Guyton's approach, the cardiovascular hemodynamic system depends on cardiac output (CO) and venous return. Venous return is determined by the difference between the venous stress volume creating the mean circulatory filling pressure (MCFP) and CVP. Therefore, MCFP is one of the major contributors to the hemodynamic system. Normal MCFP level ranges from 8-10 mmHg while normal values for CVP are 0-2 mmHg. (9) When the CVP value is too high, the pressure gradient difference between MCFP and CVP will decrease, which can decrease venous return and CO. This patient was given diuretic and CVVH to achieve a negative cumulative fluid balance, reduce CVP levels, and increase MCFP coherent with improvement in hemodynamic status.

In addition to fluid removal, ultrafiltration is also useful for eliminating cytokines. Patients with DKA may experience increased plasma levels of glucose, fatty acids, proinflammatory mediators, and oxidative stress. In uncontrolled diabetic patients, there is an increase in interleukin (IL)-6, IL-1B, IL-8, tumor necrosis factor (TNF)-α, and also the counter-regulating hormones so that ketoacidosis can occur. (10) The patient's ketone value improved on the second day and the creatinine value increased on the third day but normalized after CVVH. The patient was extubated and moved to the general ward after the seventh day of treatment in the ICU.

Conclusion

This case highlights the importance of fluid restriction and fluid removal in critically ill patients especially those with diabetic ketoacidosis and septic AKI. Fluid resuscitation in diabetic ketoacidosis must be monitored cautiously to prevent GIPS. Fluid removal using diuretic and ultrafiltration may improve hemodynamic status and patient outcome.

Figure 1. Cumulative fluid balance, CVP, and creatinine relationship



Legend: CVP=central venous pressure.

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