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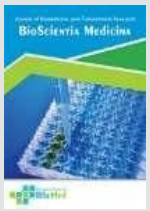

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Alcohol-Induced Hyperosmolar Hyperglycemic State in Type 1 Diabetes Mellitus: A Case Report

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A B S T R A C T

Background: Adolescents with diabetes mellitus who consume alcohol increase the risk of developing diabetic ketoacidosis (DKA) and HHS. In addition, alcohol consumption has long-term adverse effects on the glycemic control of type 1 diabetes mellitus. This study aimed to describe cases of alcohol-induced hyperosmolar hyperglycemic state in adolescents with type 1 diabetes mellitus. **Case presentation:** A teenage boy, aged 15 years, came with his family to the ER with complaints of weakness. The patient also complained of persistent tingling in the legs for the last two weeks. Three days before entering the hospital, the patient also felt blurred vision that disturbed him while studying at school. The results of the physical examination stated that the general condition was weak, compos mentis, pulse 80x/minute, blood pressure 110/70 mmHg, respiratory rate 20x/minute, axillary temperature 36ºC, weight 65 kg, and height 165 cm. Examination of the extremities showed a slow return of skin turgor. Laboratory evaluation showed an increased leukocyte count (10.45x10^3/µL), and blood gas analysis showed mild acidosis (HCO_3 24.3 mmol/L, PCO_2 38.6 mmHg, PO_2 82 mmHg, tCO_2 26 mmol/L, pH 7.4, and SaO_2 96%), HbA1c 14.2%, glucose at 621 mg/dL (hyperglycemia), C-peptide 0.87 ng/dL. The patient was diagnosed with hyperglycemia, hyperosmolar state, type 1 diabetes mellitus, and mild dehydration. **Conclusion:** The main management of alcohol-induced hyperosmolar hyperglycemic state in type 1 diabetes mellitus is fluid resuscitation to achieve hemodynamic stability, correction of electrolyte abnormalities, gradual reduction of blood sugar levels, and hyperosmolality. Insulin administration to lower blood sugar levels is done after stable hemodynamics.

1. Introduction

Hyperosmolar hyperglycemic state (HHS) is a rare complication of diabetes mellitus (DM).[1] HHS is characterized by hyperglycemia less than 600 mg/dL, hyperosmolality greater than 330 mOsm/L, and mild metabolic acidosis (pH>7.2). HHS generally occurs in patients with type 2 DM, but in some cases, it is also found in patients with type 1 DM. HHS causes a high mortality rate in children of 10%-35%.[1]

Most people with type 1 diabetes mellitus have a history of an acute clinical course.[2] Polyuria, polydipsia, polyphagia but accompanied by rapid weight loss within 2-6 weeks before diagnosis and accompanied by visual disturbances. Data for 2021, there are 1220 children with type-1 DM in Indonesia.[3] The incidence of type 1 DM in children and adolescents increased sevenfold from 3.88 to 28.19 per 100 million population in 2000 and 2010.[4]

The population of type 1 DM adolescents who consume alcohol increased from 19.3% to 26%.[5] The lack of parental supervision and the absence of an age limit on purchasing alcohol increases the accessibility of alcohol to adolescents. Adolescents with diabetes mellitus who consume alcohol increase the risk of developing diabetic ketoacidosis (DKA) and HHS.[6-8] In addition, alcohol consumption has long-term adverse

effects on the glycemic control of type 1 diabetes mellitus.[7] This study aimed to describe cases of alcohol-induced hyperglycemic hyperosmolar state in adolescents with type 1 diabetes mellitus.

2. Case Presentation

A teenage boy, aged 15 years, came with his family to the ER with complaints of weakness. The patient also complained of persistent tingling in the legs for the last two weeks. Three days before entering the hospital, the patient also felt blurred vision that disturbed him while studying at school. In the last six months, the patient's weight has drastically reduced by 20 kg. The patient also complained of frequent urination at night and being easily hungry and thirsty since 1 month ago. One day before admission to the hospital, the patient consumed a large amount of alcohol (2 bottles). The patient has regularly consumed cigarettes and alcohol since he was 13 years old. Based on family history, the patient's grandmother, biological mother, and sister died from complications of diabetes mellitus.

The results of the physical examination stated that the general condition was weak, compos mentis, pulse 80x/minute, blood pressure 110/70 mmHg, respiratory rate 20x/minute, axillary temperature 36ºC, weight 65 kg, and height 165 cm. Examination of the extremities showed a slow return of skin turgor. Laboratory evaluation showed an increased leukocyte count ($10.45x10^3/\mu L$), and blood gas analysis showed mild acidosis (HCO_3 24.3 mmol/L, PCO_2 38.6 mmHg, PO_2 82 mmHg, tCO_2 26 mmol/L, pH 7.4, and SaO_2 96%), HbA1c 14.2%, glucose at 621 mg/dL (hyperglycemia), C-peptide 0.87 ηg/dL. Urinalysis showed urine glucose +3, pH 5.5, negative ketones, urea 68.1 mg/dL, and creatinine 1.46 mg/dL. The patient was diagnosed with hyperglycemia, hyperosmolar state, type 1 diabetes mellitus, and mild dehydration.

Management of this patient included loading IVFD NaCl 0.9%, 1200 mL for 2 hours, and maintenance IVFD NaCl 0.9% 95 mL/hour for 48 hours. After 48 hours of hydration, give fluids based on random blood sugar levels. Novorapid insulin drip administration (325 units in 50 mL NaCl; rate 0.5 mL/hour) was started after fluid loading. After 48 hours of insulin drip, insulin administration was changed to subcutaneous insulin (Novorapid 8 units before meals and Lantus 14 units before bedtime). Observation of vital signs and blood sugar is done regularly (when waking up, in the morning before eating, 2 hours after breakfast, before lunch, 2 hours after lunch, before dinner, 2 hours after dinner, and before going to bed). After 7 days of intensive care, the patient was discharged with improvement. Patients and families are encouraged to control routines and educated on self-monitoring of blood sugar. HbA1c and C-peptide re-examination will be evaluated in the next 3 months.

3. Discussion

Hyperosmolar hyperglycemic state (HHS) and diabetic ketoacidosis (DKA) are emergencies and complications in diabetes mellitus.[1] HHS occurs after a prolonged and gradual increase in polyuria and polydipsia, resulting in severe dehydration.[9] This is accompanied by severe electrolyte loss because of the longer duration of osmotic diuresis. Hypovolemia eventually results from prolonged osmotic diuresis, causing a progressive decrease in the glomerular filtration rate and exacerbating hyperglycemia. The hyperglycemia and increased plasma protein concentration following the loss of intravascular fluid result in a hyperosmolar state. A hyperosmolar state will trigger the secretion of anti-diuretic hormones and cause thirst or dehydration due to the increased frequency of urination. The state of glucosuria will cause failure in the ability of the kidneys to concentrate urine and exacerbate the degree of water loss.[9,10]

Dehydration in HHS can affect the skin and integumentary system. Decreased blood flow to the brain due to severe dehydration can cause focal neurological deficits and disturbances in visual acuity to coma.[1] Diabetes mellitus complications are divided into two, namely microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular

(cardiovascular disease and peripheral arterial disease), both of which are responsible for the morbidity and mortality in patients with diabetes mellitus.[1,11] In this patient, there was no disturbance of consciousness. There was only visual acuity disturbance where the patient complained of blurred vision 3 days before entering the hospital. Diabetes complications were also found in patients, namely, tingling and numbness in the feet (peripheral neuropathy) and blurred vision (retinopathy).

The HHS criteria are plasma glucose concentration > 33.3 mmol/L (> 600 mg/dL), venous pH > 7.25, arterial pH > 7.3, serum bicarbonate > 15 mmol/L, ketonuria or ketonemia, serum osmolality >320 mOsm/kg and altered consciousness or seizures. In this case, the blood glucose test result for the first time was 620 mg/dL.[1] Based on the results of the blood gas analysis, serum bicarbonate was found to be 24.3 mmol/L, pH 7.41 (mild acidosis). From the calculation of osmolality, it was found to be 33.8 mOsm/kg (hyperosmolar). Higher serum osmolality is associated with changes in consciousness. From the urinalysis, there was glucosuria +3 and negative urine ketones, urea 68.1 mg/dL, and creatinine 1.46 mg/dL. An increase in BUN and creatinine in HHS indicates prerenal azotemia, whereby hydration and insulin therapy are performed, and values usually decrease to normal.

The HbA1c examination result was 14.2% (normal value <7%). HbA1c values reflect glycemic control over the previous 2-3 months. C-peptide examination showed a result of 0.87. C-Peptide is also used as an indicator to determine whether a patient has type 1 DM or type 2 DM.[12] C-Peptide is better used to determine insulin production and assess beta cell function clinically. The lower the C-peptide is also used as an indicator of the severity of the disease in children with hyperglycemia.[12]

Determination of type 1 DM and type 2 DM in adolescents is quite difficult, so it is necessary to trace the history of DM in the family, measurement of autoantibodies, and plasma C-peptide concentrations.[12,13] In this case, the results of the C-Peptide examination were within normal limits, where the diagnosis of diabetes mellitus led to type 2 DM. The patient's family has a history of diabetes mellitus, namely the patient's grandmother, biological mother, and older sister. All three died due to complications of diabetes mellitus type 2 (mother and grandmother) and type 1 (siblings).

HHS is rare in type 1 diabetes mellitus. The incidence of HHS at a young age has a high morbidity and mortality rate. Mortality due to HHS is 50% to 60%.[14] HHS is caused by a deficiency of insulin in the blood circulation and an increase in counter-regulatory hormones such as catecholamines, glucagon, cortisol, and growth hormone, which stimulate gluconeogenesis and glycogenolysis. HHS, in this case, was induced by heavy alcohol consumption. Alcohol intake is associated with insulin sensitivity in adolescents. High alcohol consumption is also associated with poor glycemic control, risk of DKA, HHS, and high HbA1c.[7,8]

The goals of HHS therapy are rehydration to achieve hemodynamic stability, correction of electrolyte abnormalities, gradual reduction of blood sugar levels and hyperosmolality, detection of triggering factors for HHS, and prevention of complications. In HHS, fluid resuscitation aims to expand intra and extravascular volume, restore renal perfusion, and promote a gradual decrease in sodium concentration and serum osmolality. Generally, the degree of dehydration in HHS is greater than in DKA, so a more aggressive fluid resuscitation of 20 ml/kg BW is performed until adequate peripheral perfusion, followed by fluid deficit replacement for 48 hours. After fluid resuscitation is expected to reduce serum glucose by 75-100 mg/dL per hour.[15,16]

Insulin drip should be administered after fluid rehydration because it can cause a rapid decrease in serum glucose levels and cause cerebral edema. It is recommended to be a glucose level of around 300 mg/dL. Insulin drip is started at a dose of 0.05-0.1 units/kg/hour. During treatment, regular monitoring of blood sugar is carried out after 72 hours of giving insulin by drip followed by subcutaneous

administration of insulin with novorapid 8 IU before eating and then 14 IU before going to bed. The blood sugar target before eating is 90-110 mg/dL, and the blood sugar target 2 hours after eating is <180 mg/dL.

4. Conclusion

The main management of alcohol-induced hyperosmolar hyperglycemic state in type 1 diabetes mellitus is fluid resuscitation to achieve hemodynamic stability, correction of electrolyte abnormalities, gradual reduction of blood sugar levels, and hyperosmolality. Insulin administration to lower blood sugar levels is done after stable hemodynamics.

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