Ketoalkalosis in Diabetics: A Diabetic Ketoacidosis Alkalemic Variant Commonly Overlooked in Relation to Mixed Acid-Base Disorders

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Abstract

It is discussed a case of diabetic ketoacidosis that presented with alkalemia (pH 7.61) rather than acidemia (pH 7.35). Even though ketosis is present, severe vomiting causes electrolyte depletion and hypovolemia, which in turn causes bicarbonate reabsorption and an alkaline state. Alkalemia can also arise from severe respiratory alkalosis. The implementation of the appropriate treatment will result from the identification of alkalemia and its cause.

Alkalaemia and diabetic ketoacidosis in two type 1 diabetic patients are described by us. Twenty-three cases have been reported, and vomiting, taking alkali, and taking diuretics were the main causes of alkalaemia. Patients with poorly controlled diabetes who already had autonomic neuropathy, according to our report, are at risk.

Keywords: Diabetic ketoacidosis; Diabetic patients; Metabolic acidosis

Introduction

A serious and potentially fatal diabetes mellitus complication is diabetic ketoacidosis (DKA). Its prompt treatment necessitates an immediate diagnosis [1]. The American Diabetes Association published the guidelines for hyperglycemic crises in adult diabetes patients. These crises typically occur in patients taking sodium-glucose cotransporter-2 inhibitors or when starvation causes confusion.

Mixed acid-base disorders are frequent in DKA patients. Patients with DKA frequently have volume contraction primary metabolic alkalosis, Kussmaul breathing-related primary respiratory alkalosis, or respiratory muscle fatigue-associated respiratory acidosis in addition to an increased anion gap metabolic acidosis [2]. Blood pH and bicarbonate are ultimately affected by this combination of acid-base disturbances. Consequently, in clinical practice, patients who present with diabetes, elevated serum ketones, and increased anion gap metabolic acidosis but with a pH greater than 7.3 or bicarbonate greater than 18 mmol/L fall outside the current diagnostic criteria for DKA. Amazingly, diabetic keto alkalosis is a condition in which patients present with alkalemia with a pH greater than 7.4. Diabetic keto alkalosis was initially thought to be a rare clinical presentation until it was first observed in case reports and literature reviews.

An important clue for identifying occult acid-base disorders, anion gap can help doctors make the right diagnosis [3]. In addition, measuring serum beta-hydroxybutyric acid (-OHB), the major ketone body, has become easier to do, making it easier to use serum ketone measurement as a separate parameter for detecting DKA. In order to examine the spectrum of DKA presentations, including traditional acidemic DKA, DKA with mild acidemia (7.3 ≤ pH ≤ 7.4), and diabetic keto alkalosis (pH > 7.4), we examined three years' worth of cases of patients with diabetes, positive serum ketones, and elevated anion gap metabolic acidosis at a single institution.

Methods

A retrospective, descriptive case-control study was conducted at Tays, a tertiary hospital in Pirkanmaa, Finland, and used a case-control design. Clinical qualities, treatment methodology, and the reasons for ketoacidosis of all patients (≥15 years old) with DKA treated at Tays were tentatively gathered into a neighborhood vault of endocrinological patients (Endo Library).

Age at DKA onset, gender, BMI, duration, type of diabetes (type 1, type 2, monogenic, or secondary diabetes), insulin replacement therapy (no insulin, multiple daily injections, or pump therapy), and blood glucose monitoring or self-monitoring were all included in the Endo Registry data. We evaluated patients with DM1 in addition to those with monogenic or secondary diabetes for the statistical analysis. Additionally, the data included the most obvious DKA causes. At the time of the DKA, a specialist evaluated and recorded the causes of the condition using six predefined categories: as of late analyzed diabetes, unimplemented insulin treatment, disease or drug debilitating glucose resilience, mechanical issues with gadgets, denatured insulin, and other or obscure causes. The following four groups were further subdivided into for implemented insulin therapy: unawareness, learning difficulties, other illnesses, and social factors such as alcohol abuse that lead to neglecting insulin therapy or a lack of self-care commitment [4]. The Endo Registry also provided us with the number of DKA episodes that occurred during the time period. Due to a lack of specific data on DKA episodes, patients who moved to another hospital district during this follow-up period were excluded.

DKA treated

Tays during person-time were divided to determine the overall incidence. The sum of the time each person was observed was used to calculate person time. Additionally, the annual incidence of DKA in Tays was calculated in relation to the total number of diabetic patients in the Pirkanmaa hospital district. All DKA patients, as well as DM1 and DM2, had their annual incidences separately calculated.

From the pilot version of the Finnish National Diabetes Registry, three controls for each DKA patient were collected [5]. These controls

were adjusted for age, gender, diabetes type, and municipality and did not have any DKA episodes during the follow-up period. In the event that no control patient could be found in the same municipality, they were taken from the same hospital district. To ensure that there were enough controls, the ages of three patients were changed to +/- 1 year.

Clinical data

Using routinely collected clinical data, laboratory values, other diagnoses, and mortality among patients and controls were gathered from the Finnish National Diabetes Registry for the period. For the patients and a few controls, the index date was the day of the patient's first day of ketoacidosis.

Patients with diabetes were identified using the Finnish version of the 10th revision of the International Classification of Diseases (ICD-10) in the pilot version of the Finnish National Diabetes Registry. Since, diabetes was defined as any patient who had an E10–E14 diagnosis and was included in the Care Register for Health Care (HILMO) or the Register of Primary Health Care Visits (Avohilmo). The statutory data for all Finnish residents who have been discharged from any Finnish hospital's inpatient care as well as outpatient visits to public health care are collected in these registers, which are kept up by the Finnish Institute of Health and Welfare (THL). During the follow-up period, prevalences of mental and behavioral disorders, such as ICD-10 diagnoses of dementia, alcohol or drug addiction, psychoses, bipolar disorder, intellectual disability, depression, and eating disorders (F50), were gathered [6]. The analyses included both the primary and secondary diagnoses.

For both patients and controls, HbA1c (mmol/mol), estimated glomerular filtration rate (eGFR, ml/min/1.73 m2), low-density lipoprotein cholesterol (LDL, mmol/l), urine albumin-creatinine ratio (U-ACR, mg/mmol), and urine albumin (cU-Alb, mg/mmol) values were collected less than a year prior to the index date and less than a Using the CKD-EPI equation, the eGFR was determined. The following three categories of albuminuria were used in the statistical analysis: none, a high level of albuminuria, or a very high level of albuminuria.

Patients with recurring DKA and those with only one episode were compared in terms of their characteristics, treatment options, and DKA causes. In patients with recurring and single DKA, the differences in glycaemic control, comorbidities, and mortality between the patients and their matched controls were examined separately.

Register-based research is exempt from ethical approval and informed consent requirements under Finnish law. This study is thought to be important to public health because it is based solely on registry data and does not involve any contact with the study participants. The study protocol was approved by the National Institutes of Health and Welfare. Throughout the study, the Declaration of Helsinki, good clinical practice, and the new EU regulation on data protection were adhered to.

Statistical analyses

Stata Statistical software, version 17.0 (Stata Corporation, College Station, Texas, USA), and IBM SPSS Statistics for Windows, version 26.0, were used for statistical analyses. Continuous variables were compared between groups using the Student's t-test, Kruskal-Wallis, Mann-Whitney U test, and categorical variables were compared using the 2 or Fisher's exact test [7]. For the matched case-control data, a conditional logistic regression model was utilized. P-values of less than 0.05 were considered to be statistically significant.

Result and Disccusion

282 DKA patients treated at Tays and 846 control diabetics without DKA from the Finnish National Diabetes Registry were included in the study's findings. During the course of the study, Tays treated a total of 324 DKA patients. One patient was left out due to non-diabetic ketoacidosis, and 41 patients were left out because they didn't live in the Tays catchment area for the whole time they were followed up.

Cases and matched controls' baseline characteristics are shown. The majority of patients were male, with a mean age of 36 years. 79% of people had type 1 diabetes, 0.4 percent had monogenic diabetes, 6% had secondary diabetes, and 15% had type 2 diabetes.Patients treated for DKA in Tays' clinical characteristics, mortality, and mental and behavioral disorders, as well as their age, gender, type of diabetes, and municipality-adjusted control patients without diabetic ketoacidosis (DKA).

The information regarding the treatment options and causes of ketoacidosis in patients with a single DKA as opposed to recurrent DKA. There were 49 diabetics with ketoacidosis who had just been diagnosed. 229 of the 282 patients only had one DKA episode, and 53 of them had recurring DKA episodes, requiring an average of two (minimum 2, maximum 20) admissions per patient over the course of a three-year follow-up period. When compared to patients who had a single DKA, those with recurring DKA were younger (median age 23 vs. 38 years), had diabetes for a longer period of time (median duration of diabetes 12 vs. 9 years), and had diabetes for the first time earlier (median age 12 vs. 22 years) [8]. In the group with recurrent DKA, DM1 was more prevalent. Ketoacidosis recurrence was not correlated with gender, BMI, smoking status, treatment method, or glucose monitoring system. In both groups, social factors and non-adherence to insulin therapy were the most common causes of DKA. Recurrent DKA patients were statistically more likely than single DKA patients to be on insulin therapy, while individuals with only one DKA episode were more likely than single DKA patients to have recently been diagnosed with diabetes.

Two of the patients had T1DM, and four of them were taking insulin. Recurrent vomiting (6/13, 46%) and alkali ingestion (2/13, 15%) were the primary triggers. While none of the patients experienced DKA, three of them passed away from underlying conditions like pancreatic or lung cancer.

Using criteria and Fall, the coexistence of mixed acid–base disorder was examined. When the ratio of serum bicarbonate to the increase in AG (AG/HCO3) was nearly equal, metabolic acidosis was generally regarded as pure. A metabolic acid–base disorder was diagnosed when the AG/HCO3 ratio was less than or equal to 1.2. All of the patients in this case report presented with either respiratory or metabolic alkalemia. Regarding compensations for metabolic alkalosis, superimposing respiratory acidosis was diagnosed if the change in PCO2 was less than expected by 0.6 change in bicarbonate; On the other hand, superimposing respiratory alkalosis was diagnosed if the change was greater than anticipated. Regarding compensations for respiratory alkalosis, the expected 0.2 change in PCO2 was caused by a change in bicarbonate. Ten of the 15 cases, including the present two, had respiratory or metabolic alkalosis that was related to DKA [9]. Five of the cases had a triple acid-base disorder that was related to either respiratory alkalosis or respiratory acidosis that was related to DKA and metabolic alkalosis.

Recurrent vomiting may have been related to autonomic neuropathy, such as delayed gastric emptying. In previous cases,

there was insufficient information regarding diabetic complications; However, autonomic dysfunction was present in both of our patients, indicating either poor glycemic control or prolonged disease duration. Although only four of the patients, including ours, had their HbA1c measured, all of them had HbA1cs greater than 10%, indicating poor glycemic control and the possibility of delayed gastric emptying.

All of the patients in this case report had alkalemia upon admission. However, in order to avoid underdiagnosing metabolic acidosis, particularly DKA, clinicians must obtain arterial blood gas and calculate AG. Patients run the risk of developing unnecessarily complicated conditions if the presence of DKA is not detected promptly, delaying the necessary treatment [10]. The treatment of DKA with alkalaemia is the same as for pure DKA: DKA can be treated with intravenous insulin and enough fluid replacement, and nausea and vomiting go away in a few days.

Conclusion

In conclusion, our case report revealed that DKA with alkalemia can occur in poorly controlled diabetics with an HbA1c of more than 10%. With alkalaemia, autonomic neuropathy appeared to accelerate DKA and predicted additional admissions.

Acknowledgement

None

Conflict of Interest

None

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