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A Review on Euglycemic Diabetic Ketoacidosis

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ABSTRACT

The endocrine disease euglycemic diabetic ketoacidosis (EDKA) is a life-threatening emergency condition. The presence of ketone bodies in the blood or urine, as well as blood glucose levels of more than 200-250 mg/dL, metabolic acidosis (pH 7.3 and serum bicarbonate of fewer than 15 mEq/dL), and metabolic acidosis (pH 7.3 and serum bicarbonate of less than 15 mEq/dL) are all indicators. The use of sodium-glucose co-transporter-2 inhibitors in the treatment of diabetes mellitus has increased the incidence of diabetic ketoacidosis in the euglycemic state. Here it is addressed about both diabetic ketoacidosis and euglycemic diabetic ketoacidosis in pathophysiology, as well as the many causes of both. A diagnosis of exclusion, euglycemic diabetic ketoacidosis should be considered in the differential diagnosis of alcoholic ketoacidosis and starvation ketoacidosis. On the same principles as diabetic ketoacidosis, euglycemic diabetic ketoacidosis is treated. Preventive measures of Euglycemic diabetic ketoacidosis associated with sodium-glucose co-transporter-2 inhibitors (SGLT2i) is discussed.

KEYWORDS: *Euglycemic diabetic ketoacidosis, Alcoholic ketoacidosis, Starvation ketoacidosis, sodium-glucose co-transporter--2 inhibitors*

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INTRODUCTION

Diabetic ketoacidosis (DKA) is one of the most severe diabetic complications.(1) Diabetic ketoacidosis is a life-threatening emergency which can impact people with both type 1 and type 2 diabetes.(2) Hyperglycemia, anion gap metabolic acidosis, and ketosis are all symptoms of diabetic ketoacidosis, an endocrine emergency.(3-5) Euglycemic diabetic ketoacidosis (EDKA) is defined as relative euglycemia (serum glucose 250 mg/dL) with metabolic acidosis (serum bicarbonate 18 mEq/L and pH 7.3) and ketosis in patients with diabetic ketoacidosis who have normal serum glucose.(6) The absence of hyperglycemia can mask the underlying Diabetic ketoacidosis, causing a diagnostic dilemma, particularly in the emergency department, which is linked to worse outcomes.(1,2) The use of sodium-glucose co-transporter-2 (SGLT2i) inhibitors in insulin-deficient patients with chronic type 2 diabetes, type 1 diabetes, or latent auto immune diabetes has enhanced the detection and incidence of Euglycemic diabetic ketoaciosis in recent years.(6) Just around 6% of patients have blood glucose levels below 300 mg/dL, and only around 1% have levels below 180 mg/dL.(3) The newest class of antihyperglycemic drugs, sodium-glucose co-transporter-2 (SGLT2i) inhibitors, were authorised in 2013 for the treatment of type 2 diabetes.(8) Sodium-glucose co-transporter-2 (SGLT2i) inhibitors, a new class of oral Type 2 Diabetes Mellitus(T2DM) drugs, have recently been related to rare cases of kidney damage a possibly deadly and life-threatening complication involves mild - to - moderate glucose elevation and ketoacidosis. Euglycemic ketoacidosis is a condition that occurs when blood sugar levels were high (Euglycemic diabetic ketoacidosis).(9) Canagliflozin, dapagliflozin, and empagliflozin are some of the drugs in this class that show similar or increased efficacy in reducing bodyweight, serum glucose, haemoglobin A1c levels, and blood pressure.(6) As a result, the true incidence of Euglycemic diabetic ketoacidosis is unknown.(22) There have been several case reports and case series published describing Euglycemic diabetic ketoacidosis (EDKA) patients treated with sodium-glucose co-transporter-2 inhibitors (SGLT2i) in therapeutic practise for type 2 Diabetes Mellitus therapy.(7) Primarily treating

diabetic ketoacidosis, limiting food intake, consuming alcohol, and inhibiting gluconeogenesis are all suggested to assist Euglycemic diabetic ketoacidosis.(3) Treatment consist of stop inciting agent, start fluid replacement and continuous insulin infusion.

EPIDEMIOLOGY:

Euglycemic patients occur for about 2.6 % to 2.4 % of diabetic ketoacidosis admissions. (10,11) Patients with type 1 diabetes who had diabetic ketoacidosis while taking sodium-glucose co-transporter-2 inhibitors had rates ranging from 5 to 12 percent; however, euglycemia has not always been present.(12)

ETIOLOGY:

There are multiple known causes of Euglycemic diabetic ketoacidosis in diabetic people. The entire mechanism is predicated on a condition of general starvation, which results in ketosis while maintaining normoglycemia. As a result, conditions (Table 1) such as anorexia, gastroparesis(2,22), fasting, a ketogenic diet, and alcohol use disorder can cause carbohydrate deficiency and ketosis.(2) Pregnancy, acute pancreatitis(22), glycogen storage problems, surgery(22), infection, cirrhosis, and insulin pump use are all additional Euglycemic diabetic ketoacidosis causes.(13,14,22), cocaine intoxication (2,22), sepsis(16,17), and so on. Type 1 diabetes, sodium-glucose co-transporter-2 inhibitors, and prolonged preoperative fasting during bariatric surgery all increase the risk of Euglycemic diabetic ketoacidosis.(18,19,)

➢ Anorexia/fasting state (pre-operative)
➢ Gastroparesis
➢ Glycogen storage disease
➢ Infection/sepsis
➢ Insulin pump use
➢ Intoxication/Ingestion (alcohol, cocaine)
➢ Intra-abdominal pathology (gastroenteritis, pancreatitis, etc.)
➢ Ketogenic diet
➢ Liver disease
➢ Pregnancy
➢ Renal disease
➢ Self-treatment with insulin for diabetic ketoacidosisprior to presentation
➢ Sodium-glucose co-transporter-2 inhibitor (SGLT2i) use
➢ Surgery

Table 1: Conditions associated with Euglycemic diabetic ketoacidosis.(6)

CLINICAL MANIFESTATION:

Euglycemic diabetic ketoacidosis patients can present with

- Nausea
- Vomiting
- Shortness of breath
- Generalized malaise
- Lethargy
- Loss of appetite
- Fatigue
- Abdominal pain
- Since serum glucose is normal, patients may or may not experience polydipsia or polyuria(20)

PATHOPHYSIOLOGY:

The pathophysiology of diabetic ketoacidosisis well-known, with a relative or absolute lack of insulin and an over abundance of counter regulatory (or counter-responsive) hormones such as glucagon, corticosteroids, catecholamines, or growth hormones.(1,3) Hyperglycemia is caused by a hormonal imbalance that produces increased glycogenolysis, hepatic gluconeogenesis, and reduced peripheral glucose use.(1) It also increases gluconeogenesis and ketogenesis by mobilising free fatty acids through adipose tissue lipolysis and amino acid proteolysis.(3) Metabolic acidosis is caused by ketone bodies (beta-hydroxybutyrate, acetoacetate, and acetone), whereas dehydration and hypovolemia are caused by hyperglycemia caused by glycosurias and osmotic diuresis (Figure 1).

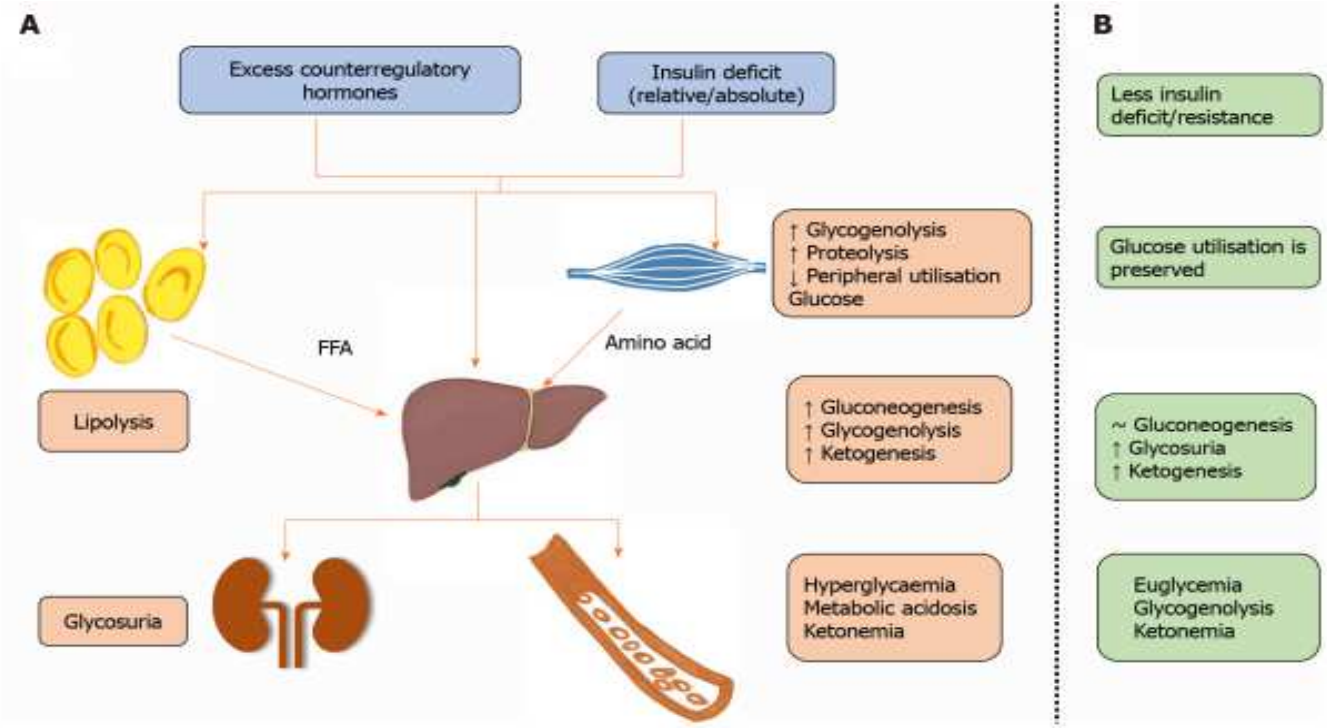

Figure 1: Metabolic acidosis is induced by ketone bodies (beta-hydroxybutyrate, acetoacetate, and acetone), while dehydration and hypovolemia are caused by hyperglycemia caused by glycosuria and osmotic diuresis. A: Pathophysiology of diabetic ketoacidosis; B: Pathophysiology of Euglycemic diabetic ketoacidosis. FFA: Free fatty acids; ↑: Increase; ↓: Decrease; ~: No change.(22)

Carbohydrate deficiency plays a major role in the pathophysiology of Euglycemic diabetic ketoacidosis, whereas due to insulin resistance or resistance is secondary (Figure 1B). The synthesis of the counter regulatory hormones, on the other hand, continues unabated, resulting in an elevated glucagon/insulin ratio and triggering ketogenesis with no change in hepatic gluconeogenesis or peripheral glucose utilization.(22) Fasting or extended physical activity with depleted hepatic glycogen reserves and thus impaired glycogenolysis are the triggering factors of Euglycemic diabetic ketoacidosis.(1,25) When glycolysis intermediates are unavailable due to lower intracellular glucose oxidation, increased glucagon stimulates lipid oxidation, generating acetyl-CoA and ketone bodies. Euglycemic (or hypoglycemia) diabetic ketoacidosis is caused by uncontrolled ketonemia and glycosuria (often seen with SGLT2i). (2,25)

The other possible causes and pathogenetic mechanisms of Euglycemic diabetic ketoacidosis are shown in Figure 3.

Other common causes of euglycemic diabetic ketoacidosis:

- Sodium-glucose co-transporter-2 inhibitors (SGLT2i): sodium-glucose co-transporter-2 inhibitors are the most recent addition to the treatment arsenal for diabetic patients. Clinical trials have shown that they protect against significant adverse cardiovascular events and minimise hospitalisation for heart failure and fatalities in people with type 2 diabetes.(27,28) They also appear to be linked to modest weight and systolic blood pressure decreases.(29)

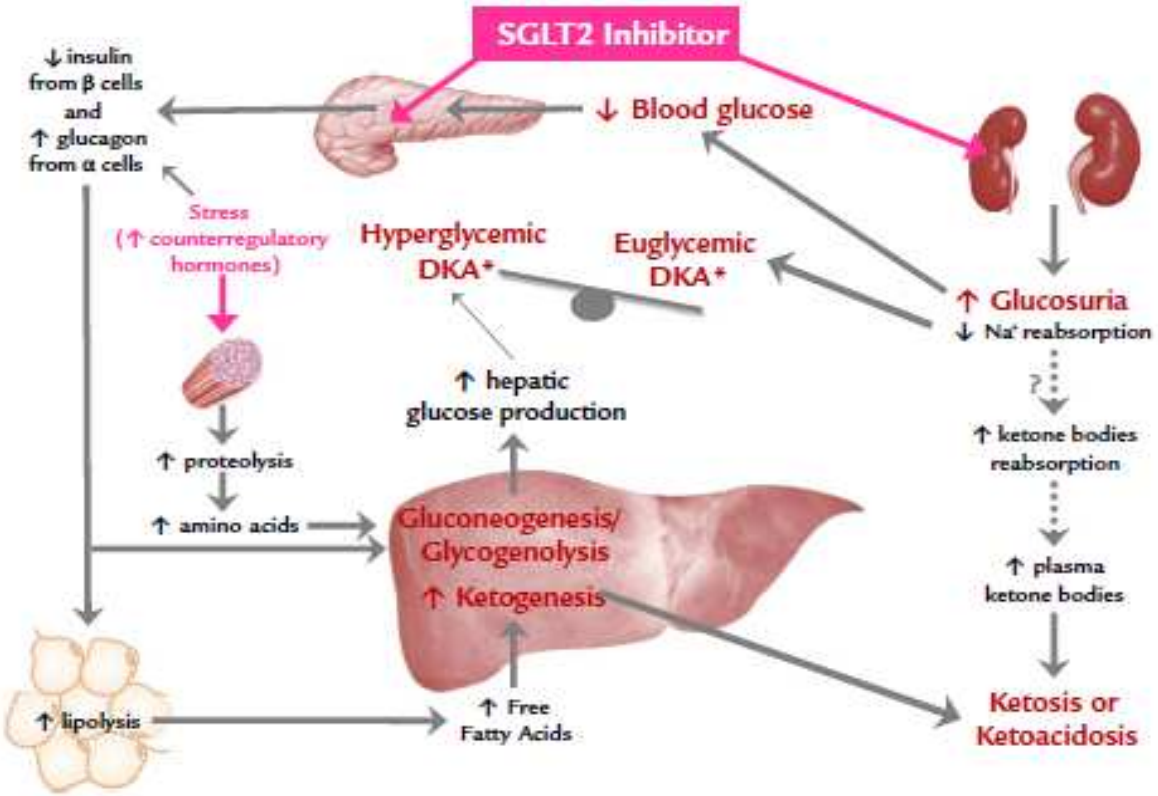

Figure 2: Mechanism of sodium-glucose co-transporter-2 inhibitor (SGLT2i) – associated diabetic ketoacidosis. * The balance between hepatic glucose production and glucosuria determines whether diabetic ketoacidosis is euglycemic or hyperglycemic.(12,26)

Figure 2 depicts the possible methods by which sodium-glucose co-transporter-2 inhibitors causes Euglycemic diabetic ketoacidosis. It work by increasing glucosuria in the kidney to lower blood glucose levels. They also appear to induce the production of glucagon in the pancreas.(30) Ketone accumulation with sodium-glucose co-transporter-2 inhibitor–associated diabetic ketoacidosis is similar to classic diabetic ketoacidosis in that it occurs as a result of insulin deficiency and glucagon increase, which promote lipolysis and hepatic ketogenesis.(12) It enhanced glucosuria efficiently lowers plasma glucose levels, reducing pancreatic cell insulin production. It's been suggested that sodium-glucose co-transporter-2 inhibitor-induced glucosuria and reduced salt reabsorption in the kidneys could help to enlarge the ketone reservoir indirectly by increasing renal ketone reabsorption.(12)

Insulin also increases the activity of acetyl-CoA carboxylase, which produces malonyl-CoA, a powerful inhibitor of carnitine palmitoyl transferase–I(CPT-I). The decrease in the circulating amount of insulin boosts the formation of ketone bodies by activating carnitine palmitoyl transferase–I(CPT-I), which promotes the transport of fatty acids into mitochondria and thus raises the rate of beta oxidation. Moreover, data suggests that sodium-glucose co-transporter-2 inhibitors enhance glucagon secretion(31), which could be a secondary impact mediated by the reduction in insulin secretion or a direct effect of sodium-glucose co-transporter-2 inhibitors on pancreatic a-cells.(31) Because glucagon inhibits acetyl-CoA carboxylase and hence increases carnitine palmitoyl transferase–I activity in the liver, increased glucagon secretion is likely to contribute to ketone body over production.

One of these factors can cause diabetic ketoacidosis in people on sodium-glucose co-transporter-2 inhibitors(Table2). Excessive insulin dose reduction (> 50%) or omission, insulin pump failure or malfunction, a low carbohydrate diet, nausea and vomiting caused by other drug combinations such as glucagon-like peptide 1 agonists, excessive alcohol consumption, acute stressful conditions such as myocardial infarction, heart failure, infections or fever, trauma, and surgery.(22)

Risk factors	Pathophysiology
Infection	Insulin resistance due to counterregulatory hormones (adrenaline, glucagon, *etc.*), increased peripheral glucose utilization, decreased intake (nausea, vomiting)
Surgery	Perioperative fasting, gastrointestinal surgery has increased incidence as fasting is prolonged and/or gut absorption is slow
Fasting	Decreased glycogen stores, increased risk with SGLT-2 inhibitors and type 1 DM
Alcohol intake	Deceased carbohydrate intake, osmotic diuresis, increased ketogenesis (beta hydroxybutyrate) due to altered NADH/NAD ratio, increased risk in patients on SGLT-2 inhibitors
Acute vascular events (ACS or stroke)	Increased counterregulatory hormones, decreased oral intake
Trauma	Decreased oral intake, increased counterregulatory hormone, blood glucose dilution by large fluid shifts during resuscitation
Prolonged physical activity or exercise	Increased counterregulatory hormones, increased peripheral glucose utilization, decreased carbohydrate intake

Table 2: Precipitating causes for Euglycemic diabetic ketoacidosis and their mechanisms.(22)

ACS: Acute coronary syndrome; DM: Diabetes mellitus; NAD: Nicotinamide adenine dinucleotide; NADH: Nicotinamide adenine dinucleotide hydrogen; SGLT2: Sodium/glucose cotransporter-2.(22)

PREGNANCY:

Due to the obvious physiologic state of hypoinsulinemia and increased hunger, pregnancy is a risk factor for Euglycemic diabetic ketoacidosis. Insulin resistance is determined by elevated cortisol and placental lactogen levels, and bouts of vomiting or fasting can lead to exacerbated starving ketosis.(33) Acidosis is exacerbated by respiratory alkalosis, which causes bicarbonate loss in the urine.(16) Diabetic ketoacidosis is more common in pregnant women than in non-pregnant women (8.9% vs. 3.1%), and is linked to lower blood glucose levels and greater perinatal morbidity and mortality.(13,34) Various case reports of Euglycemic diabetic ketoacidosis in pregnancy with type 1 diabetes, type 2 diabetes, and gestational diabetes have been published.(22) The respiratory alkalosis that occurs during pregnancy, as well as the compensatory loss of bicarbonate through urine, deprives the body's stores for buffering metabolic acidosis.(22) During the second and third trimesters of pregnancy, counter regulatory pregnancy hormones (progesterone, oestrogen, human placental lactogen, and tumour necrosis factor) promote insulin resistance. Due to physiological hemodilution of blood glucose and higher glomerular filtration rate with glucosuria, Euglycemia diabetic ketoacidosisis also common during pregnancy.(22) Any unexplained acidosis in a pregnant woman with a history of nausea, vomiting, and decreased intake should be suspicious of Euglycemic diabetic ketoacidosis.(2)

FASTING OR DECREASED CALORIC INTAKE:

Low-calorie diets, especially in combination with other illnesses in patients with type 2 diabetes, can cause diabetic ketoacidosis and euglycemia. Fasting causes a carbohydrate shortfall and glycogen depletion, resulting in the use of alternate energy sources such as free fatty acids and lipolysis.(38) Euglycemia is maintained by continued insulin consumption and depleted glycogen stores, while lipolysis and ketogenesis continue unabated, resulting in Euglycemic diabetic ketoacidosis. In people without diabetic ketoacidosis, an extremely low carbohydrate diet or fasting can trigger Euglycemic diabetic ketoacidosis.(2) Fasting-induced Euglycemic diabetic ketoacidosis must be distinguished from starving ketosis, which does not cause metabolic acidosis (serum bicarbonate > 18 mmol/L).(2,39) Ketogenesis is promoted by a carbohydrate deficit and an excess of fatty acids, which diverts ketones bodies as a source of nourishment. Reduced insulin requirements, ketone induced osmotic diuresis, and decreased oral intake due to ketonemia all contribute to weight loss. For a short period of time, the keto diet has been attempted successfully in type 2 diabetes, with weight loss benefits, improved glycemic control, and medication reduction.(22)

GLYCOGEN STORAGE DISEASE AND CHRONIC LIVER DISEASE:

Euglycemic ketoacidosis can be triggered by glycogen storage problems or chronic liver disease, both of which result in diminished glycogen levels. (36,45) Glycogen storage disorder type VI (Hers disease) is characterised by a lack of liver glycogen phosphorylase and is thought to be inherited in an autosomal recessive pattern with mutations in the PYGL gene. (46,47) Glycogen-induced hepatomegaly, liver dysfunction, fasting hypoglycemia, and ketosis with euglycemia are all clinical characteristics of patients with type 1 diabetes and glycogen storage disease type VI.(45)

COMORBID CONDITIONS:

Acute pancreatitis(22), Euglycemic diabetic ketoacidosis in patients due to heavy alcohol use (36), cocaine intoxication(2,22), Euglycemic diabetic ketoacidosis due to gastroparesis(22,23), Euglycemic diabetic ketoacidosis risk is higher in type 1 diabetes, patients on sodium-glucose co-transporter-2 inhibitors(SGLT2i), and prolonged perioperative fasting during bariatric surgery(18,19), and Duchenne muscular dystrophy are some of the less common(48,49).

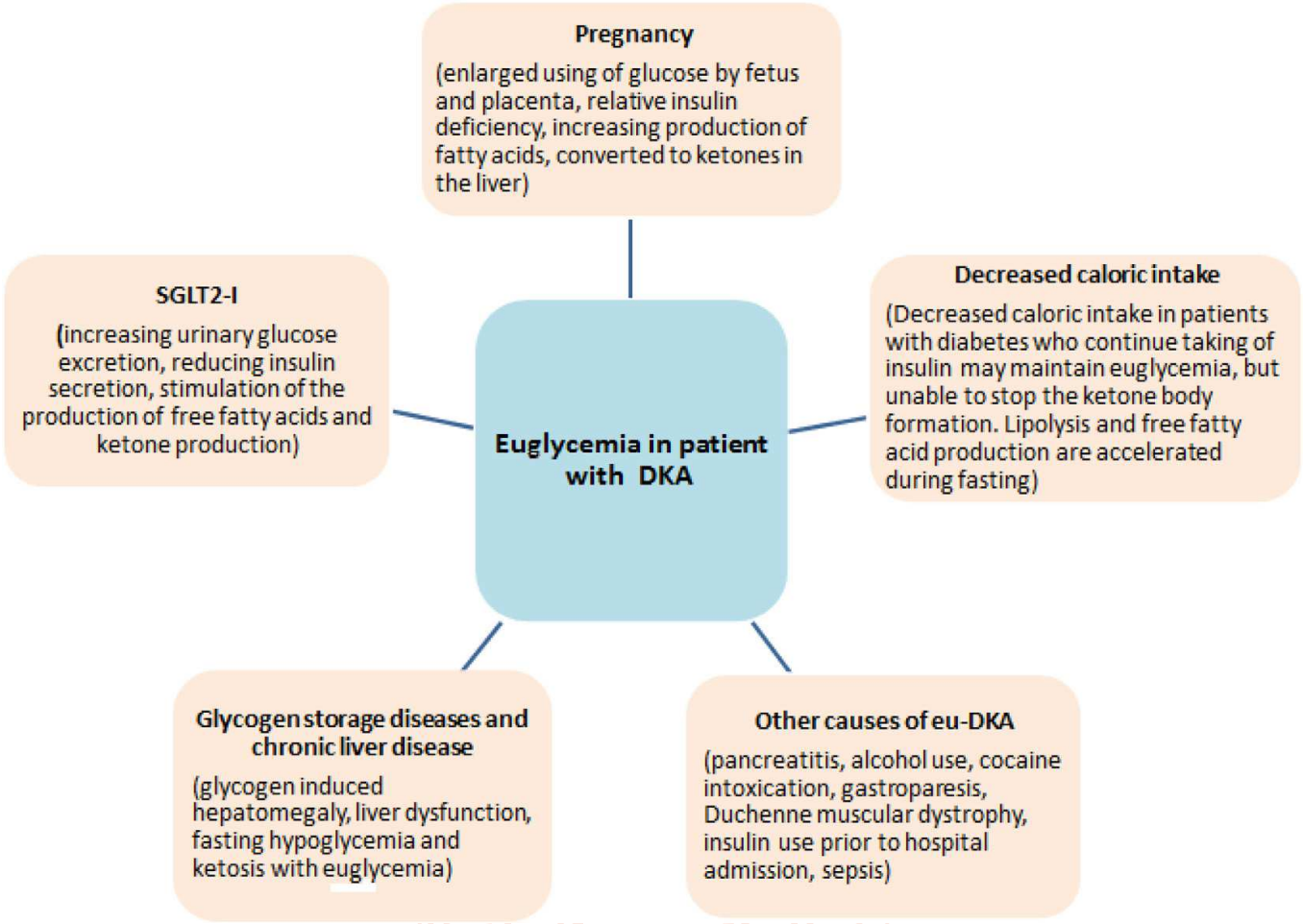

Figure 3: Possible etiopathogenetic mechanisms of Euglycemic diabetic ketoacidosis.(2)

DIAGNOSIS:

Diabetic ketoacidosis with euglycemia is a life-threatening medical emergency. The absence of hyperglycemia delays the diagnosis of Euglycemic diabetic ketoacidosis in the emergency room or intensive care unit.(1,2) However, Euglycemic diabetic ketoacidosis is a diagnosis of exclusion, requiring the exclusion of alternative causes of high anion gap metabolic acidosis.(1) Patients with prolonged alcoholism may develop alcoholic ketoacidosis.(1,10)

In alcoholic ketoacidosis, the ketone molecules are mostly β-hydroxybutyrate (instead of acetoacetate), which is undetectable by urine strip testing.(40) It's important to distinguish between euglycemic ketoacidosis and starving ketosis, which can occur as a result of fasting or any other disease that causes a reduction in calorie intake.(2,39)

Sepsis, with or without lactic acidosis, is a common emergency presentation that might mask Euglycemic diabetic ketoacidosis. The presence of serum ketones in the absence of high lactate levels aids in the diagnosis of sepsis.(16,17)

Serum and urine ketones, electrolytes (including calcium and magnesium), glucose, renal function (creatinine, blood urea nitrogen), blood gas analysis (venous or arterial), lactic acid, chest radiograph, and electrocardiogram (EKG) are among the laboratory tests available. Toxic alcohol consumption is diagnosed by a large osmolar gap (the difference between measured and computed serum osmolarity), inebriate state and multiorgan involvement. Sepsis and septic shock are diagnosed using a combination of symptoms and laboratory tests that demonstrate leukocytosis, procalcitonin, organ failure, and lactate. (22)

Laboratory Values for DKA and EDKA

Measurement	Reference	DKA	EDKA
Blood glucose[a]	80-130 mg/dL	>250 mg/dL	<250 mg/dL
Arterial pH	7.35-7.45	<7.3	<7.3
Serum bicarbonate	22-26 mEq/L	<18 mEq/L	<18 mEq/L
Urine ketones	None present	Present	Present
Serum ketones	None present	Present	Present
Anion gap	0 mEq/L	10-12 mEq/L	10-12 mEq/L

Table 3: Even though hyperglycemia is a key criterion in the diagnosis of diabetic ketoacidosis, about 2.6 % to 3.2 % of diabetic ketoacidosis admissions are cases of Euglycemic diabetic ketoacidosis, which includes metabolic acidosis and ketoacidosis as well as euglycemia.(54)

DIFFERENTAL DIAGNOSIS:

Ketoacidosis with normal glucose must be evaluated as a differential diagnosis. It's critical to have the right diagnosis of the underlying illness that's causing the ketoacidosis so that proper treatment can begin. Ketoacidosis caused by hunger and alcoholic ketoacidosis are two more prevalent causes.(1) Infections such as pneumonia, genitourinary infection, and bacteraemia should be ruled out as soon as possible. Consider intra abdominal infection and pancreatitis in patients who arrive with abdominal pain. In the right clinical scenario, consider toxic alcohol (methanol, ethylene glycol) or paraldehyde ingestion, salicylate overdose, lactic acidosis, starving ketosis, and pregnancy.(20) With a low or normal glucose (mean of 118 mg/dL in one small research) and a history of continuous alcohol consumption with poor nutritional intake, alcoholic ketoacidosis can appear with severe metabolic acidosis, nausea, and vomiting.(40,41) As a result, distinguishing between Euglycemic diabetic ketoacidosis and Alcoholic ketoacidosis(AKA) in patients who have been drinking for a long time might be difficult.(6)

COMPLICATION:

Persistent vomiting, dehydration, hypoglycemia, hypovolemic shock, respiratory failure, cerebral edoema, coma, seizures, infection, thrombosis, myocardial infarction, and death are all potential complications of Euglycemic diabetic ketoacidosis.(42) Maternal Euglycemic diabetic ketoacidosis has been shown to increase foetal (up to 9%) and maternal mortality.(43,44)

TREATMENT:

Stepwise Treatment Approach for Managing EDKA

Step 1—Stop inciting agent, if applicable (e.g., SGLT2i)
Step 2—Start fluid replacement with monitoring of electrolytes and ketones
Step 3—Start continuous insulin infusion
Step 4—Start dextrose administration

Table 4: stepwise approach to the management of Euglycemic diabetic ketoacidosis.(54)

STEP 1: Stop Inciting Agent, if Applicable: The inciting agent(s) must be stopped as soon as Euglycemic diabetic ketoacidosis is diagnosed in the event of Euglycemic diabetic ketoacidosis caused by sodium-glucose co-transporter-2 inhibitors or drug intoxication.(20,25) A proper medication reconciliation is necessary for establishing differential diagnoses, such as Euglycemic diabetic ketoacidosis, as well as determining the best course of treatment.

STEP 2: Start Fluid Replacement With Monitoring of Electrolytes and Ketones: The initial focus of Euglycemic diabetic ketoacidosis(EDKA) therapy should be fluid resuscitation.(3) Fluid loss from Euglycemic diabetic ketoacidosis can vary from 6 to 9 litres, and rehydration is required for appropriate tissue perfusion and metabolic abnormalities to be resolved.(3) During the first 1 to 2 hours of fluid resuscitation, the American Diabetes Association advises 1 L/hour to 1.5 L/hour of normal saline or lactated Ringer's solution.(3) Until the anion gap closes and the acidosis is addressed, IV fluid supplementation should be continued as needed based on patient considerations.(3) Ketones and electrolytes should be checked every hour and every two hours, respectively, until blood ketones are less than 0.6 mmol/L and electrolytes are stabilized.(53)

STEP 3: Start Continuous Insulin Infusion: Despite the lack of hyperglycaemia in Euglycemic diabetic ketoacidosis, insulin plays an important role in the treatment and management of the condition.(25) Insulin

suppresses the formation of ketones by promoting glucose utilisation by decreasing gluconeogenesis and glycogenolysis.(3) Adequate fluid replacement should be followed by continuous insulin infusion, starting at a rate of

0.05 U/kg/hour and increasing to 0.1 U/kg/hour with serum potassium levels >3.3 mEq/L.(54) As a result, if hypokalemia is present, insulin therapy should be postponed until potassium levels return to normal. Potassium levels should be monitored every 2 hours until electrolyte stability is achieved.(53) To regulate blood glucose, the patient may be started on subcutaneous long-acting insulin and pre-meal rapid-acting insulin once the Euglycemic diabetic ketoacidosis has resolved. After subcutaneous insulin is given, the insulin infusion should be sustained for at least 1 hour.(3)

STEP 4: Start Dextrose Administration: Because blood glucose concentrations are less than 250 mg/dL, Euglycemic diabetic ketoacidosis therapy necessitates the addition of dextrose 5 % (D5W) to fluids.(20) Dextrose must be administered to restore normal cellular utilization, leading in increased clearance and decreased ketone body formation.(52) In the presence of insulin, adding D5W to fluids also avoids hypoglycemia by acting as an exogenous source of glucose.(20,52) Dextrose 10% may be used if ketoacidosis persists despite D5W dosing.(54)

- Stop sodium-glucose co-transporter-2 inhibitors immediately and do not restart unless another cause for the ketoacidosis is identified and resolved.
- Ensure volume restoration with the isotonic fluid of sodium chloride 0.9%.
- Ensure potassium levels are above 3.3 mEq/L before insulin administration.
- Start insulin administration with continuous intravenous infusion; change to intensive subcutaneous regime when acid–base balance is restored.
- Consider additional glucose infusion at the initiation of therapy.
- Bicarbonate could be administrated at a higher than the aforementioned pH level (<6.9).
- Ensure proper ventilation is achieved while infusing bicarbonate in order to avoid intracellular acidosis.
- In case of bicarbonate use, consider administration of calcium intravenously to prevent fall in calcium.

Table 5: Therapeutic measures for Euglycemic diabetic ketoacidosis associated with sodium-glucose co-transporter-2 inhibitors use.(55)

PREVENTON:

- Withdraw sodium-glucose co-transporter-2 inhibitors at least 3 days before major surgical procedures.
- Withdraw sodium-glucose co-transporter-2 inhibitors in patients hospitalised for serious illness.
- Use insulin instead of sodium-glucose co-transporter-2 inhibitors in the presence of other predisposing risk factors for diabetic ketoacidosis.(55)

Off-label use of sodium-glucose co-transporter-2 inhibitors in type 1 diabetes should be treated with caution,

- Starting with a low dose and gradually increasing.
- Insulin lowering plan that is unique to you.
- Carbohydrate intake education for patients.
- Excessive alcohol consumption or prolonged exercise, fasting must be avoided. (12,32)

SURGERY: Stopping sodium-glucose co-transporter-2 inhibitors at least 24 hours before a surgery, procedure, or intense physical activity is recommended by the American Association of Clinical Endocrinologists and the American College of Endocrinology (e.g., marathon running).(32) Several case reports, however, imply that the effects of sodium-glucose co-transporter-2 inhibitors last longer than the five half-lives of elimination (2-3 days), with glucosuria and ketonemia being present 8 to 10 days after stopping treatment.(50)

CONCLUSION:

Euglucemic diabetic ketoacidosis is a rare disease with serious risk factors often associated with multifactorial etiology. Sodium-glucose co-transporter-2 inhibitors can cause a variety of issues so they should be administered with caution and may require considerable counselling or constant monitoring. If patients who consume sodium-glucose co-transporter-2 inhibitors is admitted to the hospital, they should be checked for diabetic ketoacidosis. Intravenous fluids and insulin therapy should be given to such patients, and the underlying reason should be investigated and treated carefully so that the patient's quality of life can be improved.

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