

## Diabetic Ketoacidosis: Update on Treatment and its Complications

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### ABSTRACT

Diabetic ketoacidosis is a quite common ailment in hospitals, despite its preventability. A large population of our country is facing diabetic ketoacidosis during their stay in the hospitals. There are many people who are facing challenges with the treatment of this common disease. The disease is easily managed by professionals nowadays. The management of this disease has been improved with a new era and new technologies. The national policies have been introduced which aid in the provision of the standard to the patients, expanding best services and decreasing the rate of deaths and disabilities in the patients with diabetic ketoacidosis. The management of diabetic ketoacidosis includes metabolic targets and leveling the electrolytes and decreasing the harmful effects of this complication.

**Key words:** Diabetes, Diabetic ketoacidosis, Treatment of DKA

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### INTRODUCTION

Diabetic ketoacidosis is quite common in hospitals. It is a preventable disease and can be treated with time management. The patients having diabetes face this complication in their life if the sugar levels are not controlled well. The controlling and management of diabetic ketoacidosis is not much complicated and can lead to positive outcomes. The ailment "diabetic Ketoacidosis" is a potentially life-threatening condition and can lead to morbidity and mortality in the patients. Patients with DKA can live their normal life if the disease is managed accordingly. The reason behind DKA is the unequal distribution of insulin in the blood of the patient. If the levels of insulin are decreased, then the levels of antagonistic hormones like glucagon will be enhanced. The DKA in type 1 diabetes, if not managed well will result in increased disability and hospital stays. The rate of mortality has been reduced in the previous decade by 1 percent [1]. The advancement in inpatient care by near-patient testing technology has been reported. This includes helping in the

fast diagnosis and close monitoring of medication response. The National Diabetes Inpatient Audits showed that the diabetic patients develop DKA while staying in the hospital [2].

Before proceeding forward, we will continue with the understanding of diabetic ketoacidosis and its treatments and managements. The symptoms and causes of diabetes ketoacidosis along with risk factors are also discussed in this article. Diabetic ketoacidosis is abbreviated as DKA. It is the presence of excess acid in the blood of the patient. It occurs due to the excessive sugar levels continuously in the blood of the patient. Diabetes ketoacidosis can be mortal if not treated timely. It is not that acute as it takes hours to become serious so it can be manageable and treatable. Diabetic ketoacidosis is an imbalance in the concentration of acid in the plasma of the human body.

The symptoms of diabetic ketoacidosis vary from person to person, but the majority of the symptoms include:

- ✓ Dry and rough skin.
- ✓ Dry mouth leading to thirst.
- ✓ Increased urination.
- ✓ Vomiting.

- ✓ Nausea.
- ✓ Fatigue.
- ✓ Pink face.
- ✓ Loss of attention.
- ✓ Muscular pain.
- ✓ Pain in abdomen.
- ✓ Tightness.
- ✓ Headache.
- ✓ Weakness.

If such symptoms appear in a person with diabetes, it shows that the person requires emergency care. So, it is recommended to provide the patient hospital services for the prevention of mortality. If a person has more than one following symptom, it means he requires emergency care. The symptoms include:

- ✓ The fruity smell in the breath.
- ✓ Tired and confused personality.
- ✓ Hurting belly.
- ✓ Queasy feeling.
- ✓ Difficulty or shortness of breath.

### **Causes and risk factors for diabetic ketoacidosis**

The disease Diabetic Ketoacidosis occurs due to an imbalance of insulin in the body of a person. The cells of the body cannot use insulin properly for energy, so they use fat as a source of energy. The burning of fats makes a byproduct which is the called ketones. If the process carries on, the ketones accumulate in the body of the person and resulting in high concentrations of ketones in the body. This accumulated fat can disturb the chemical reactions in the body resulting in the throw off the entire human system. The metabolic reactions have a severe body effect on the body of the patient.

The other reasons for ketone development are as following:

- ✓ Missing a meal.
- ✓ Stressed or sick.
- ✓ Reaction due to insulin.
- ✓ Not take appropriate insulin.
- ✓ Poor coherence with the treatment of insulin.

- ✓ Insufficient insulin treatment within the hospital.
- ✓ Infections: mostly chest, skin, or urinary tract.
- ✓ Acute vascular/coronary event.

DKA can occur due to the presence of type 2 diabetes. The occurrence of diabetic ketoacidosis due to type 2 diabetes is exceedingly rare. There is another problem with the patients with type 2 diabetes which is called Hyperosmolar Hyperglycemic Non-ketotic Syndrome (HHNS). This disease can lead to severe dehydration. The dehydration further causes several issues.

### **Tests and diagnosis of diabetic ketoacidosis**

Analyze the presence of ketones in the body when the sugar level of the body is greater than 259mg/dL or if the patient has any of the above symptoms, for example, thirsty feeling, frequent urination, and dry mouth.

The sugar levels can be checked by the urine test strip. There is the presence of ketone measurement options in some glucometers too. If the level of sugar in the body is high, one must try to reduce the levels of glucose and check the ketones after half an hour.

Some tests to find out the DKA are as follows:

- ✓ Bloodwork, consisting of electrolytes and metabolic panel.
- ✓ Urine analysis.
- ✓ Blood gas in the arteries.
- ✓ Tests for finding out infection.
- ✓ Blood Pressure.
- ✓ X-ray of the Chest.
- ✓ ECG.

### **Treatment of diabetic ketoacidosis**

If DKA is not treated at its first, then the person may go to a comma. He can die too if the therapy is not provided to the patient. The therapies if DKA includes the following managements:

- ✓ IV insulin to reduce ketones in the body.
- ✓ Fluids for hydration and for bringing blood metabolism into normal balance.
- ✓ Replacement of electrolytes by an IV to replace vital electrolytes like sodium, chloride or potassium, to keep the muscles, heart, and nerves functioning.

### Complications of diabetic ketoacidosis

DKA severities are possible if the patient does not get emergency therapy as soon as possible like insulin or electrolyte replacement. These complications include:

- ✓ Hypoglycemia/ low blood glucose levels.
- ✓ Hypokalemia or low blood potassium levels.
- ✓ Cerebral edema if the blood glucose levels are managed quickly.
- ✓ Unconsciousness.
- ✓ Mortality.

When it comes to the most common complication of diabetic ketoacidosis, hypoglycemia is the one that pops up with the maximum ratio with about 5 to 25% of patients with DKA. Cardiovascular disorders, seizures, and arrhythmias are most observed severe outcomes of hypoglycemia. For such patients, blood sugar monitoring every hour is required for the treatment in acute phase of disease.

Hypolemia is also common, and it comes up with issues like cardiac arrhythmias, muscle weakness, and cardiac arrest. For this complication monitoring and management is continuously required. Other complications associated with electrolyte imbalance in DKA patients involve hyperchloremia, which is found in every 1 out of 3 patients, and hyponatremia and hypomagnesemia.

In children, cerebral edema is found. It is found less in adults. Its risk attributes encapsulate new-onset diabetes, younger age, lower carbon dioxide's partial pressure, existence of symptoms for long period, low bicarbonate ratio, severe acidosis, excessive glucose level, declined sodium level, rapid hydration, and withheld fluid in stomach. When it comes to rhabdomyolysis, it has been found in DKA patients too, even though it is more common with HHS. So, acute phase of disease hypophosphatemia along with DKA can cause rhabdomyolysis. Moreover, DKA can also cause serious respiratory failure, pneumonia, pulmonary edema, and ARDS. Elevated pulmonary venous pressure and increased pulmonary capillary permeability was found the reason behind the development of pulmonary edema in DKA patients.

### Novel findings of Diabetes along with DKA: T1DM

It is luckily becoming less obvious to look for DKA as the primary presentation of type-1 diabetes mellitus; however, it is one of the most common presentations in children [3]. Mostly, if the cause of Diabetic Ketoacidosis is diabetes, the direction of thoughts set on type-1 diabetes. This is most common in the case of young people having an accurate body mass index. Some patients with type-2 diabetes mellitus also develop DKA, so that is called "Flatbush diabetes" or Ketosis prone type 2. The "Flatbush diabetes" is due to the ethnicity for example African-Caribbean ethnicity. The main cause of this problem is due to genetic factors along with some metabolic stress or any illness.

The lack of specific autoantibodies along with the diagnosis of Type-1 Diabetes Mellitus (zinc transporter 8, glutamic acid decarboxylase, and insulin autoantibody 2) increases the suspicion of Type 2 diabetes mellitus. The management of the discussed ketoacidosis is difficult to treat and takes more than 1 week for its management. Any person with complaints of DKA should be supposed to have type -1 diabetes mellitus and managed accordingly.

### Management of diabetes ketoacidosis

In 2013, a national guideline was published by the "Joint British Diabetes Societies" for the management of diabetic ketoacidosis in the hospitals to improve the standard of care in health care units [4].

### Key elements of the management of diabetic ketoacidosis

The vital primary therapeutic conciliation in DKA is suitable fluid management in the patients along with insulin therapy. The goals of the replacement of fluids are as follows:

- ✓ Removal of ketones.
- ✓ Refurbishment of plasma volume.
- ✓ Stabilization of electrolytes.

The dose adjustment of insulin is done based on the weight of the patient. Insulin is administered in the body by intravenous route. The dose of insulin is 0.1 units per kg per hour. The weight of the patient can be estimated, and treatment can be given without any delay. If there will be a delay in treatment, the patient may suffer from threatening consequences.

Ketogenesis is stopped by insulin infusion at a fixed rate intravenously. This constant rate of insulin also decreases the ratio of glucose in the blood along with electrolyte balance. The whole treatment requires monitoring at regular intervals of time. The monitoring includes serum potassium, venous pH, glucose, and capillary ketones. The utilization of arterial blood is not essentially required as the venous blood can be used in its place. There is not a huge difference between the venous and arterial blood's Ph/HCO<sub>3</sub> for the analysis of DKA.

### Targets of management

- ✓ Reducing the ketone concentration in the blood by approximately 0.5mmol/L/hour.
- ✓ Increasing the bicarbonate levels of blood in veins by approximately 3mmol/L/hour.
- ✓ Reducing the glucose levels of blood in the capillaries by approximately 3mmol/L/hour.
- ✓ Maintaining the levels of potassium in the range of 4-5 mmol/L.

If the given targets are not achievable then the rate of infusion of the insulin should be enhanced. It is recommended to infuse dextrose to avoid the risk of hypoglycemia. This dextrose is infused at a concentration of 10 percent. It is suggested to start dextrose when the concentration of glucose in the blood falls below 14 mmol/L. 0.9% normal saline is also infused to normalize the circulatory volume. The infusion of all these fluids at the same time is essential for the management of DKA.

### DKA resolution

- ✓ Bicarbonate greater than 15.0 mmol/L.
- ✓ pH greater than 7.3 units.
- ✓ Blood ketone levels less than 0.6 mmol/L.

### Restoration

If the treatment is not being successful, and the DKA is not managed well, check for the placement of the cannula along with its patency. Make sure that the rate of insulin is correct. Check for any concomitant disease or disorder like myocardial infarction, intra-abdominal sepsis, etc. find out that if the insulin resistance is a problem like obesity or steroid therapy. Increase the rate of insulin infusion. Again, find out the status of fluid and consider the increasing rate of intravenous fluids.

### Insulin continuous administration by subcutaneous route

It is suggested to continue the long-acting insulin along with the infusion of insulin to reduce the effect of rebound increased blood glucose levels when the intravenous treatment would be stopped. If the patient is showing the symptoms of DKA with an early diagnosis of DKA, the recommendations ask for the start-up of basal insulin as early as possible. Continue intravenous insulin until the basal insulin become ready to administer.

### Intravenous insulin

Mostly all of the patients showing the DKA need to have the initial specialist review. The treatment with IV insulin depends on the cause of DKA. It is suggested to restart the therapy of insulin. If the previous medication is not going well, then the review is necessary to be considered. As the DKA is managed, the patient is capable to eat or drink. The insulin therapy can be reinitiated. However, it is recommended to not stop intravenous insulin until after 1 hour of the subcutaneous insulin taken along with the diet. If the long-acting insulin is stopped for any reason, then the stat dose of Insulatard is recommended to give to the patient at a half dose to that of the regular dose of the patient. If the patient is on BID fixed-mix insulin, for example, Novo Mix 30, reinitiate the normal dose of insulin subcutaneously before taking breakfast or before taking the evening diet. Do not stop the IV infusion of insulin at least for half to one hour of SC insulin.

The recommendations regarding the SC insulin therapy and management should be managed by a diabetic specialist. If the Diabetic Ketoacidosis is resolved while the patient is not able to eat or drink, then manage the fluid status of the patient accordingly by giving insulin infusion and IV fluids.

### Diabetic ketoacidosis in certain conditions

#### Pregnancy

Ketones are toxic components for the developing fetus, thus DKA is dangerous both for mother and fetus during pregnancy as it brought the threat of fetal demise. Therefore, women should be clinically monitored from time to time, especially near their delivery time, or they should be provided with professional obstetric and medical care with high dependency unit. In pregnant ladies, DKA can be identified with symptoms

like abdominal pain. This condition can appear with awfully specific rise in glucose levels in females. During different stages of pregnancy, it is advised by the doctors to manage a schedule according to DKA protocol along with fetal monitoring and obstetric care to look out for any complications related to diabetes in the mother [5]. With medical advancements and scientific development, the management of DKA during pregnancy has also taken a turn. Therefore, it is required for the doctors to maintain a track book of the pregnant females, keep an eye on weight for FRIII initial dose measurements. However, when it comes to insulin, females are almost resistant to it during pregnancy so to sort this out upward titration may be required for managing insulin infusion rate.

#### **Pump users**

Continuous subcutaneous insulin fusion is therapy for patients who need to maintain normal insulin levels by artificial means, and they use pump therapy. These patients do not rely on long-acting insulin which becomes problematic for them. This is because any interruption in the insulin insertion can cause a delay and as a result hyperglycemia followed by ketoacidosis can build up so quickly that it will become problematic. This interruption can be due to dislodged or blocked cannula and if the problem is sorted out on time, e.g. by setting the cannula, starting another insulin insertion method like intravenous infusion, or changing the tube, then the situation can be handled well. CSII becomes unreliable in patients who develop DKA because it affects and alters the tissue perfusion which ultimately impacts the insulin absorption. In such situations, pump therapy is temporarily left and DKA's standard treatment is opted. However, when the DKA issue is resolved then patient can be put back onto CSII based upon basal rate and intravenous infusion should also be continued until the ingestion of meal.

#### **Sodium glucose cotransporter-2 inhibitors and DKA**

Under the new category of oral therapies for the treatment of type 2 diabetes mellitus, Sodium-glucose cotransporter-2 inhibitors like empaglifozin are in trend. These are licensed in UK since 2013. In the renal proximal convoluted tubule, this sodium glucose cotransporter-2 inhibitor plays its reversible role by declining glucose reabsorption, thus it increases the

glucose excretion through urine. However, by the year 2015, some cases were identified by post marketing surveillance of fatal DKA cases of those patients who were using SGLT2 inhibitor. Some of the cases were of those patients who were wrongly diagnosed as T2DM, but in actual they were patients of T1DM [6]. Patients with euglycaemia might have presentation atypical with DKA as moderate rise in blood glucose levels marked acidosis or ketonaemia. It is advised that the treatment with SGLT2i should be stopped as soon as possible if DKA is diagnosed in the patient and should not be restarted until the DKA issue has completely resolved. Moreover, patients scheduled for major surgery or are diagnosed with acute serious illnesses should stop administering SGLT2i until they have recovered.

#### **Preventing Re-occurring of DKA: Enhancement of healthcare outcomes**

Only a small portion of patients among a huge proportion of DKA patients, have Type 1 diabetes mellitus. These patients are often young and found to have poor psychosocial status, more challenges and bad compliance with the insulin therapy schedule. In such scenarios, the focus is basically upon management and education of these patients instead of changing the insulin regimen. By providing psychological services to these patients with T1DM, it has been found that positive results are obtained and chances of DKA development reduces. It is imperative to refer T1DM patients to diabetes specialists within 24 hours of admittance with DKA for review before they are discharged [7].

DKA is a complication of diabetes and becomes life threatening for the patient. If it isn't treated properly and on time, then it can even cause death. This disorder affects multiple organs of the body and it comes with different symptoms and signs. Therefore, its management heavily relies on a team of interprofessionals that take care of diabetes mellitus. Majority of the patients usually show up to the emergency health care unit when their conditions drastically decline, and here the treatment of DKA usually begins after diagnosis.

In order to diagnose it appropriately, the doctor or nurse should be well aware of the signs and symptoms related to DKA and must immediately admit the patient to the unit. Endocrinologist

should also be consulted when the patient is under monitoring, resuscitated and their blood is drawn. Immediate tests of blood are imperative to know about the condition of DKA and imaging might also be required to keep a check on pneumonia. Moreover, CT scan might also be required if ketoacidosis impacts the mental state of patient, and a radiologist should be immediately consulted for such situations. Monitoring of DKA patient undergoing CT scan is extremely important. If MI as the trigger is suspected or any infection, then cardiologist and infection disease expert must also be consulted. The patient's physicians must be aware of the patient's insulin therapy. After the discharge from the hospital, social healthcare workers should indulge in the care of patients as re-admittance due to DKA is quite common. Multiple factors like education, socio-economic status, insulin therapy and access to this treatment, health care coverage rate, and status of mental health play quite an important role in patient's recovery.

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