ORIGINAL RESEARCH PAPER

General Medicine

A RARE CASE MORTALITY OF DIABETIC KETOACIDOSIS- CEREBRAL EDEMA WITH TONSILLAR HERNIATION- A CONTRADICTORY OPINION.IS SODIUM BICARBONATE A REAL CULPRIT?

KEY WORDS:

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INTRODUCTION:

Diabetic ketoacidosis (DKA) is the most common complication seen in uncontrolled diabetes mellitus. DKA is most commonly seen with patients of type 1 diabetes. Depletion of Insulin leads to high blood sugars which in turn leads osmotic diuresis, production of ketone bodies i.e, β-hydroxybutyric acid and acetoacetic acid, dysregulation of sodium hydrogen exchange mechanism[2]. As a consequence to the above stated mechanisms, cerebral edema has been documented as a fatal complication in DKA. Mortality documented due to cerebral edema is 21-25%[4].

CASE REPORT:

A 24year old female with no known past medical history of diabetes mellitus presented with generalised weakness since 15days, chest pain since 3days, breathlessness since 3days and abdominal pain with vomiting for 1 day.

On initial presentation, patient appeared uncomfortable, had dry oral mucosa and was conscious, oriented to time, place and person with GCS-E4V3M5. pulse was 151 beats/min, regular in rhythm and normal volume, blood pressure was 128/88mm hg, respiratory rate was 48cycles/min ,Kussmaul type of breathing, spo2 was 99% on room air, temperature was 97.8°F and random blood glucose was 590mg/dL. On auscultation s1 and s2 heard normally with no murmurs, her lungs were clear without rales, rhonchi or wheeze,abdomen was soft and non-tender, and not distended.

After bedside evaluation patient was significantly dehydrated and arterial blood gas (ABG) analysis was performed on room air,result showed pH of 6.92,po2 47mm hg,pco2 17 mm of hg, hco3- 3.5, lactate of 24mg/dL,glucose >500mg/dl.

Patient was started on iv fluids NS 1lt in 30mins, 1lt in one hr as per the protocol and fluid resuscitation was done and intubated in view of severe metabolic acidosis and impending respiratory failure in emergency room. insulin infusion was started @6 units/hr. sodium bicarbonate was given @44meq in 100ml of NS in one hr, and repeated same dose after 1 hr in view of severe metabolic acidosis. Simultaneously required blood investigations was sent at the time of admission and showed blood ketones of 3.7, RBS-500mg/dl, blood urea-20.5mg/dl, serum creatinine -0.7mg/dl, serum sodium- 131meq/L, serum potassium 4.9meq/L, serum chloride-100meq/L, hemoglobin-14.1 g/dl, total counts- 21,000 with neutrophils of 74.3%, lymphocytes 20.4%, ESR-5mm/hr, platelets 4lakhs,hs-Trop I <1.5, total bilirubin 0.4, AST-11,ALT-8,ALKP-106, urine routine- protein 1+,sugars 2+,rbc-nill, covid RT-PCR negative.

Chest xray was done to rule out other pathology and noted to be normal. ECG performed revealed sinus tachycardia. 1gm of ceftriaxone was given for empirical antibiotic coverage as co-existing sepsis had not yet been ruled out.

Patient was shifted to icu, insulin infusion and iv fluids was continued and sugars were undercontrol, repeat ABG after 4 hrs showed pH 7.23, pco2 9, po2 361, hoc3- 3.8, lactate 10mg/dl, glucose 216mg/dl.

ABG after 6hrs showed pH 7.20, pco2 10, po2 163, hco3- 3.9, lactate 6mg/dl, glucose 154mg/dl, neutralisation drip was started with 5% dextrose with 10 units of regular insulin. patient was on mechanical ventilation and pupils were 2mm reacting equally to light.

ABG after 18hrs showed pH 7.25, pCO2 13,pO2 214, hco3- 5.7, lactate 6mg/dl,glucose 170mg/dl, blood ketones 4.2, serum potassium 2.7 and potassium correction was given. Acidosis was persistent and ketones were increasing, therefore planned for haemodialysis.

After 20hrs of admission patient had an episode of transient bradycardia (50/min) followed by hypotension and drop in GCS (E1VTM1) and pupils were 4mm dilated not reacting to light, hypotonia of all four limbs, areflexia with plantars mute then started on noradrenaline infusion @ 10mcg/kg/min and emergency MRI brain imaging was done- showed small areas of restriction in cerebral hemispheres and basal cisterns, diffuse cerebral edema with tonsillar herniation, non-visualised superior sagittal sinus and posterior portion of right transverse sinus findings suggestive of meningoencephalitis with cerebral venous thrombosis, patient was started on anti-edema measures and low molecular weight heparin and anti-epileptics after discussing with neurologist and neurosurgeon and noradrenaline infusion increased to 25mcg/kg/min. ophthalmology opinion was sought in view of papilledema and reported no evidence of papilledema.

After 3hrs of above mentioned event,in view of persistent hypotension second inotrope was added (adrenaline@ 5mcg/kg/min) . Third inotrope support was started (vasopressin @2units/hr) 4hrs after the initiation of second inotrope support.

Repeat ABG showed PH 7.15, pco2-20, po2-193,hco3-7, lactate -15mg/dl,glucose 292mg/dl. Emergency dialysis started in

view of persistent severe metabolic acidosis. Vitals during haemodialysis pre-HD, pulse 112/min, BP 110/80 mm hg. Post-HD pulse 116/min, BP-110/74mm hg.

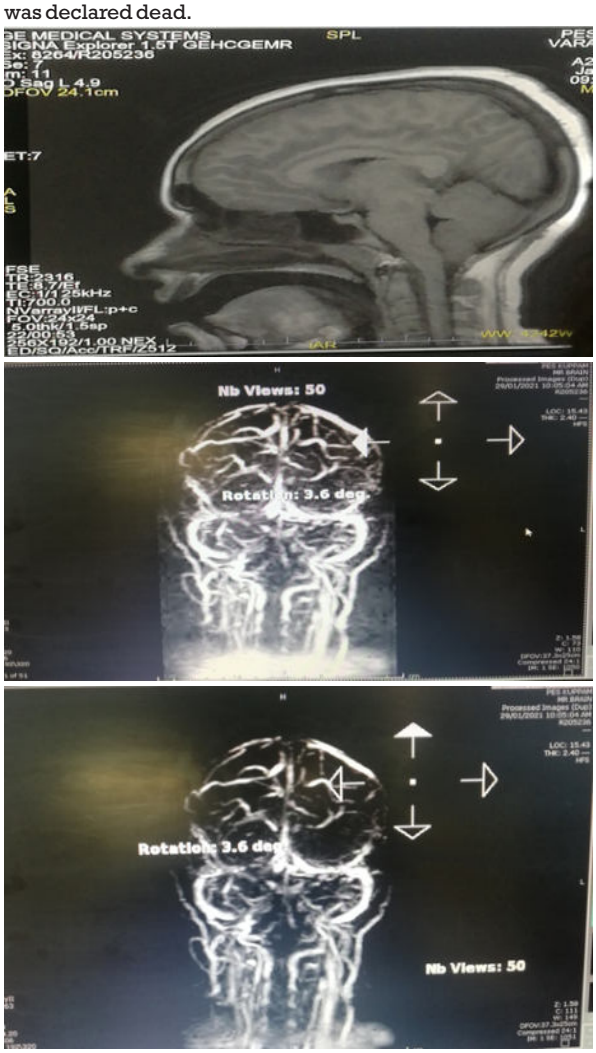
Blood sugars increased and were persistently high (>300mg/dl) despite increasing insulin infusion dose(30 units/hr).

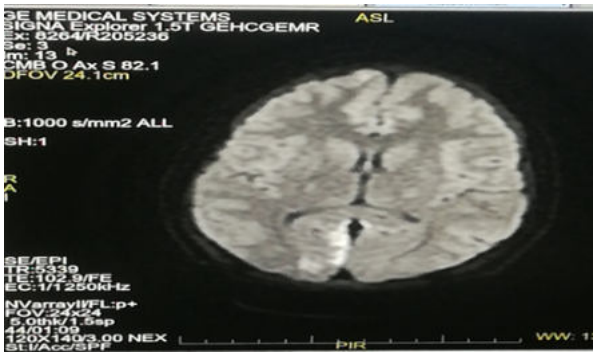
Patient had refractory hypotension despite triple inotrope support.

Repeat ABG after 36hrs showed pH 7.27, pco2- 10, po2-160, hco3- 4.6, lactate-37mg/dl, glucose-372 mg/dl. started on sodium bicarbonate infusion in view of persistent metabolic acidosis and planned for haemodialysis.

ECG showed ventricular tachycardia and synchronised shock of 150 joules was delivered following which sinus rhythm restored and planned for emergency haemodialysis during this preparation patient again had ventricular tachycardia and was given a synchronised shock of 180 joules and amiodarone 300mg slow iv stat followed by infusion @30mg/kg/hr was started. After 1 hr of amiodarone infusion patient again had ventricular tachycardia and was given a synchronised shock of 200 joules following which sinus rhythm restored. Repeat ABG showed pH 7.15, pco2-27,po2-12,hco3- 9.4,lactate -111mg/dl,glucose-149mg/dl.

After 1hr patient's central pulses were not felt and CPR was started according ACLS guidelines and one shock of 200 joules were delivered in view of pulseless ventricular tachycardia despite which ROSC could not be achieved and was declared dead.





Above MRI brain images showing small areas of restriction in cerebral hemispheres and basal cisterns, diffuse cerebral edema with tonsillar herniation, non-visualised superior sagittal sinus and posterior portion of right transverse sinus findings suggestive of meningoencephalitis with cerebral venous thrombosis.

DISCUSSION:

Diabetic ketoacidosis is a serious and potentially life threatening complication of diabetes mellitus. Typically associated with insulin dependent states like type 1 diabetes mellitus, it may also occur in type 2 diabetes in conditions like extreme stress[3]. DKA is characterized by hyperglycemia, ketosis and high anion gap metabolic acidosis. DKA can occur in persons of all ages, but nearly 65% of cases occur in persons 50 years of age and below. The cause of death in DKA is cerebral edema/ sepsis/ myocardial infarction (hyperviscosity due to hyperosmolarity). Volume depletion is a hallmark of the disease process. Neurologic manifestations such as cerebral edema, seizures and coma may be seen in DKA[1].

Cerebral edema is a devastating complication of DKA. Factors associated with development of cerebral edema include newly diagnosed diabetes, younger age, first episode of DKA, severity of DKA at presentation, it has been proved that rapid change in osmolarity by means of rapid rehydration by administration of intravascular fluid and by bolus insulin this activate sodium/hydrogen ion exchanger increasing the ICF sodium concentration following which water flows by osmotic gradient into the intravascular compartment[15]. so studies proved that progressive fall in serum sodium and osmolality by means of rapid IV infusion it increases the ICF sodium concentration and also water inside the brain cell and causes brain swelling[7]. Other causes favouring cerebral edema is low paco2 and high urea at the time of presentation but high urea was not present in our case. These factor excluded as a causative factor in cerebral edema. Large amount of hypotonic fluids given inappropriately will also cause cerebral edema. it has been decided by the experimental authorities that bolus insulin and hypotonic solutions will pay for cerebral edema but we hadn't followed this regimen in our case.

The patient discussedin this report received 5.5L of IV fluids in the first 12hrs of presentation to the hospital. Studies have shown that patient developing cerebral edema will have severe DKA and therefore be more dehydrated and should receive larger amounts of fluids. Both hypocapnia (causes cerebral vasoconstriction) and intravascular volume depletion would be expected to cause cerebral hypoperfusion[8].

Severe acidosis causes impaired myocardial contractility and decreased peripheral vascular resistance. However the addition of bicarbonate to correct metabolic acidosis, in DKA has been shown to be unhelpful and in some cases even harmful. Insulin therapy by inhibiting lipolysis will correct the acidosis without the use of bicarbonate[6]. Bicarbonate administration in metabolic acidosis is associated with

adverse effects such as hypokalemia, hypercapneia, and cerebral edema[9,10]. Okuda et al. demonstrated that in DKA, bicarbonate therapy increases hepatic production of ketone levels.

The point of discussion in our case is we had given sodium bicarbonate twice as an infusion to correct acidosis is correct or not. In experimental studies involves sodium bicarbonate given as bolus and increases the perivenular permeability and it crosses the blood brain barrier and causes the cerebral edema but in our case we gave sodium bicarbonate infusion[12]. So the cause of cerebral edema is significantly remains as hypothesis as definite causative factor has not been established. We intensivist and medical team cannot pinpoint the exact cause for the cerebral edema in our case. Normally in DKA the mortality is 0.5-1% but in case of DKA with cerebral edema mortality raises to 35%[14].so even at the onset of cerebral edema we have tried with mannitol and steroids but efforts were futile. Our heroic efforts to save the young lady went in vain so what are the doubts regarding the treatment of this case -1. Is sodium bicarbonate foeor likeable friend. 2. Is the bicarbonate is to be taken of in the treatment of ketoacidosis as bicarbonate is thought to be the causative factor for cerebral edema. 3. In the case of uncontrolled diabetic ketoacidosis, shall we go for haemodialysis initially instead of sodium bicarbonate. This question to be answered by all well qualified physicians all over the world and what is the current status of bicarbonate in the treatment of medical practice.

CONCLUSION:

The best way to treat diabetic patients is not to go for DKA. This is the first thing we will have to keep in mind despite good diabetic diet control and parenteral insulin, some diabetics will go for DKA because of intercurrent infections. In DKA suspicion of benefits will be in use of 1, bolus insulin and 2. Sodium bicarbonate infusion. As certain studies both will pave way for cerebral edema. Ultimate discussion is to be made in DKA whether will go for haemodialysis or persist with sodium bicarbonate.

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