

Case Report

**SEVERE DIABETIC KETOACIDOSIS TREATED WITH
TRIS HYDROXYMETHYL AMINOMETHANE**

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We present a case of severe diabetic ketoacidosis complicated by pancreatitis, which developed insulin resistance, persistent acidosis and hypernatremia, and was successfully treated with Tris Hydroxymethyl Aminomethane.

In recent years it has become a common practice to treat patients with diabetic ketoacidosis (DKA) with low dose insulin therapy¹⁻³ and rehydration. Occasionally these patients become persistently acidotic and develop severe insulin resistance⁴ and may require active correction of the metabolic acidosis with infusion of large amounts of sodium bicarbonate⁵. This may lead to hypernatremia and worsening of the acidosis⁶⁻⁸. The use of an alternative sodium-free alkalinising agent like Tris Hydroxymethyl Aminomethane (THAM)⁹, may correct the acidosis and reduce sodium loading.

We report a case of severe DKA complicated by pancreatitis, who developed insulin resistance, persistent acidosis and hypernatremia and was successfully treated with THAM.

THE CASE

A known diabetic 40 year old Yemeni female presented with a two week history of polydipsia, polyuria, nocturia and vomiting. On examination she was obese, fully conscious, afebrile and had mild epigastric tenderness. Her blood pressure was 110/70 mmHg and the pulse rate 70 per minute, without postural change. The initial laboratory investigations showed plasma glucose 28.1 mmol/L and bicarbonate (HCO₃) level of 20 mEq/L. Serum sodium (Na⁺) was 135 mEq/L, potassium (K⁺) 4.4 mEq/L, chloride (Cl⁻) 106 mEq/L and calcium (Ca⁺⁺) 2.2 mmol/L. Serum osmolality, BUN and creatinine were normal. Serum albumin was 38 gm/L and complete blood count showed a haematocrit of 42%. Serum acetone was negative. She was admitted as a case of uncontrolled diabetes.

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She started deteriorating rapidly the following day. She had nausea and vomited several times, became drowsy and irritable with severe epigastric pain and tenderness. Laboratory investigations showed deterioration with the following findings: plasma glucose 32.6 mmol/L, BUN 10.4 mmol/L, creatinine 239 umol/L, Na⁺ 130, K⁺ 7.1, Cl⁻ 107 and HCO₃ 5.1 mEq/L. Her arterial blood gas (ABG) revealed pH 6.92, PCO₂ 2.0 KPa, PO₂ 16.7 KPa (FiO₂ 50%) and HCO₃ 2 mEq/L. Serum acetone was large, in 1:1 dilution, and lactic acid level was not available. Serum amylase was 289 iu/L and lipase more than 1000 u/L. The haematocrit, serum albumin and calcium dropped from initial normal values to 29%, 18 gm/L and 1.6 mmol/L respectively. Serum triglycerides and liver function tests were normal. Chest x-ray showed left pleural effusion. CT scan and ultrasound of the abdomen were normal.

The diagnosis was changed to DKA complicated by severe idiopathic pancreatitis. She remained haemodynamically stable but showed severe insulin resistance with persistent acidosis, despite adequate hydration, progressive increases in insulin and bicarbonate therapy. After 72 hours the patient started developing hypernatremia; remained acidotic; became severely bradycardic and unresponsive, and was resuscitated and mechanically ventilated. Her ABG at that time showed the following result: pH 7.01, PCO₂ 1.5 KPa, PO₂ 18.5 KPa (on FiO₂ 50%) and HCO₃ 3 mEq/L (Table 1). She also had serum sodium of 168 mEq/L and bicarbonate infusion was discontinued. A total of 1025 mEq of sodium bicarbonate had been given over the last 36 hours.

Table 1: Laboratory data and insulin therapy prior to THAM infusion

-----Days								
Electrolytes	Arterial blood gases			Daily				
in Na+	K+	HCO ₃	pH	PCO ₂	PO ₂	FiO ₂	insulin	
admi- mEq/L	mEq/L	mEq/L		KPa	KPa	%	given	
ssion								(units)
Day 1	135	4.4	20					60
Day 2	130	7.1	3	6.92	2	16.7	40	120
Day 3	140	4.3	3.2	7.04	1.6	16.9	40	385
Day 4a*	161	2.7	11	7.29	3	9.3	21	460
Day 4b*	168	3	3	7.01	1.5	18	50	

* a and b refer to before and after bradycardia and resuscitation, respectively.

She was given 180 mmol of THAM, half the calculated dose, in 100 ml of 50% dextrose, over two hours and there was resolution of the acidemia with the following result: PH 7.49, PCO₂ 3.4 KPa, PO₂ 13.1 KPa (FiO₂ of 40%) and HCO₃ 19 mEq. Serum potassium dropped to 2.4 mEq/L. Her acid/base status remained on the alkalotic side without further THAM for the next 48 hours (Table 2) and normalised by the third day. Her serum Na⁺ returned to normal level but her insulin requirements remained high for another ten days. She made full recovery.

Table 2: Laboratory data and insulin therapy after THAM infusion

-----Days								
Electrolytes	Arterial blood gases			Daily				
in Na+	K+	HCO ₃	pH	PCO ₂	PO ₂	FiO ₂	insulin	
admi- mEq/L	mEq/L	mEq/L		KPa	KPa	%	given	
ssion								(units)
Day 4	162	2.4	19	7.49	3.4	12.1	40	460
Day 5	163	5.2	26	7.50	4.5	18.5	40	550
Day 6	147	4.5	24	7.43	4.6	20.1	40	740
Day 7	139	5.6	23	7.39	5.3	13.6	35	710

DISCUSSION

Insulin resistance exists in varying degrees in patients with DKA and may be severe enough to require very large doses of insulin⁴. Unresponsiveness to insulin may be due to failure to correct acidemia¹⁰, hypovolaemia with hyperosmolality¹¹, hyperketonemia^{12,13}, phosphorous deficiency¹⁴ and elevated levels of stress-induced-insulin counterregulatory hormones^{15,16}. The insulin resistance seen in this case could have resulted from a combination of factors

including the acidemia, hyperketonemia, hyperosmolality, co-existing pancreatitis and probably persistent hypovolaemia. This may account for the continued high insulin requirement for up to ten days post-THAM. It is known that adequate fluid replacement alone reduces the blood glucose concentration by 10 to 90 mg/dl/hr¹⁵. Assessment of fluid status was done on clinical grounds without any objective invasive monitoring.

The use of bicarbonate in DKA is controversial^{5,7,8} and it has been suggested that bicarbonate therapy worsens the acidemia of DKA^{7,8}. Our patient received large quantities of sodium bicarbonate in an attempt to correct the acidosis and this resulted in severe hypernatremia and probably contributed to persistence of acidemia.

In view of the persistent acidemia and hypernatremia, THAM was substituted for sodium bicarbonate⁹. THAM promotes reduction of plasma glucose, sodium and potassium levels. An earlier effective use of THAM in DKA was in decompensated acidotic diabetic patients with end stage renal disease¹⁷. THAM effectively buffered intracellular acidosis and facilitated both net cellular dextrose utilisation and potassium accumulation before extracellular or arterial pH normalised¹⁷. It has been suggested that addition of THAM to conservative therapy can provide a more rapid reversal of cellular acidosis in DKA¹⁷.

Our patient demonstrated that the use of bicarbonate in severe diabetic ketoacidosis may worsen acidemia and lead to hypernatremia. In such potentially serious situations tris hydroxyl methyl aminomethane may be beneficial.

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