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Thorough Laboratory Evaluation of Diabetic Patient upon Discharge; Ketosis Might Remain Unresolved

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Abstract: Beside the extensive protocol determined by researchers, laboratory profiles are not given enough importance. We hereby present a case to elaborate significance of these profiles. A 56 years old lady of Indian race was admitted to emergency department with symptoms of cough, vomiting, giddiness and lethargy. Patient had history of diabetes, hypertension and dyslipidemia and was found dehydrated and tachypnoic with acidotic breath. Initial laboratory profiles revealed diabetic ketoacidosis with sepsis and treatment was initiated as per protocol. Antibiotic was given for 3 days to cover sepsis and patient was discharged without taking laboratory profiles. Patient was however readmitted shortly after discharge with much severe acidosis than observed in first admission. Protocol followed was same as last time with exception of close monitoring of laboratory profiles. Patient was finally discharged however, with a stable profile as compared to initial discharge. Laboratory profiles are important to monitor as these are integral part of treatment protocol which should be followed. We also recommend that these profiles should be recorded at time of discharge as well.

Key words: Diabetic ketoacidosis, laboratory profiles, diagnosis, treatment, discharge, guidelines

INTRODUCTION

Diabetes Mellitus (DM) is a chronic complication of metabolic syndrome and to date is incurable. Apart from gestational diabetes, DM is divided in two entities namely type I and type II, and so are the complications which are based upon the micro and macro vascular damage. These complications could further be divided on the basis of time span as acute and chronic complications of diabetes. Chronic complications either being microvascular or macrovascular take a long time to develop and cause a few medically critical events which may be as a result of stroke, retinopathy, nephropathy and the like. Contrarily, acute complications are sudden episodes of hyper or hypo glycemia which are potentially life threatening and possibly end up in death if not managed properly and in time. Diabetic ketoacidosis (DKA) is among the acute complication of diabetes regardless of the type of DM (Holt and Kumar, 2010).

Infection, non-compliance/non-adherence and physiological or psychological stress leads to the development of hyperglycemia (Kitabchi *et al*., 2006). Acute hyperglycemia triggers production of ketone bodies which in turn causes acidosis and these three are basic components of an episode of DKA. Thus guidelines recommend that more efforts should be made to eradicate the underlying cause while managing DKA (Miyan *et al*., 2012). Nevertheless since the discovery of insulin in 1921 (Bliss, 1993) the then known issue of diabetic acidosis has successfully been diagnosed and treated, the prevalence and mortality rates of DKA, which were once dropped, are increasing again (Ko *et al*., 2005). This image is even worrisome in Malaysia as the number of episodes observed during five years in Malaysia (Huri *et al*., 2009) is nearly same to that observed over 20 years in Korea. This may seem opposing to the actuality that there are number of guidelines available and once DKA is diagnosed, following a standard treatment protocol ensures differentiation of DKA form similar diabetic disorders, successful management of DKA, and helps in avoiding development of complications (Savage *et al*., 2011; Kitabchi *et al*., 2006). Some of the diagnostic features such as ketotic breath, tachypnoea and dehydration are specific attributes of DKA and make it easy to separate DKA from alike hyperglycemic complications (Hyperosmolar Hyperglycemic State, Hyperchloremic Acidosis) while others; i.e. complete blood count, serum electrolyte and blood gasses, are helpful to elucidate severity of an episode of DKA, and for differential diagnosis (Alcoholic Ketoacidosis) (Miyan *et al*., 2012). These biochemical profiles are also important marker of patient's condition that whether the

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condition of patient is progressing towards homeostasis or deterioration (Kitabchi *et al*., 2006). Contrary to the fact that aforementioned profiles are exclusive parts of any guideline, and require a very close and constant observation during the course of hospitalization, these profiles are usually followed until acidosis is resolved and electrolytes are balanced, and patient is discharged without final biochemical evaluation. To clarify this picture, hereby we present a case of recurrent hospitalization of a diabetic patient due to DKA which will highlight continuous monitoring of such profiles.

CASE REPORT

A 56 year old Indian lady was admitted to the emergency department of hospital with complaint of; vomiting for 5 days, cough for 3 days and giddiness and lethargy for 1 day after over eating a fruit from *Durio zibethinus* species. Patient had history of type 2 diabetes, hypertension and dyslipidemia and was currently taking; s/c 30/70 insulin 20ii and 1gm metformin, bd; 4mg perindopril oD; 40mg lovastatin oN. Patient was found to be dehydrated, tachypnoic (respiration rate = 44) and had acidotic breath. Patient was afebrile with blood pressure of 108/66 mmHg and pulse rate of 104 bpm.

Blood sample were taken which revealed severe ketosis (Ketones = 6.4 mmol L^{-1}) and metabolic decomposition (pH = 7.149, Actual HCO_3 = 9.2 mmol L^{-1}). Complete blood count was within limits except for white blood cell count (WBC = 15.5×10^3 μL^{-1}). Renal profile rendered patient having hyponatremia and hyperkalemia (Na = 128 mmol L^{-1}, K^+ = 5.5 mmol L^{-1}). Comparison among the recorded values is much evident in Table 1. Impression was made of "Diabetic ketoacidosis secondary to sepsis" and treatment was initiated. Patent was started with continuous insulin infusion, fluid replacement and IV 1.5 g ampicillin/salbactum td for 3 days followed by oral 375 mg bd for 2 more days. As per the protocol followed, which is given in Table 2, Blood Glucose Level (BGL) was taken as standard with hourly monitoring, while insulin and fluid replacement were adjusted accordingly. Insulin was attuned between 1 unit h^{-1} to a maximum of 10 unit h^{-1} with respect to BGL below 5 mmol L^{-1} and above 25 mmol L^{-1} respectively. Similarly, fluid replacement was also switched between 5% dextrose and 0.9% saline on hourly basis. 5% dextrose was used to overcome hypoglycemia without disrupting continuous infusion of insulin if BGL was lower than 15 mmol L^{-1} while 0.9% normal saline was used otherwise. Potassium was added to intravenous drip from 2 g KCl per intravenous drip to 0.5 g depending on potassium level which ranged from 3 mmol L^{-1} to 5 mmol L^{-1}, respectively. However 100 g KCl in 100 mL of 0.9% normal saline was recommended to be used over 1 h if level of potassium dropped below 3 mmol L^{-1} (fast correct). Last biochemical evaluation performed on 4th day showed relatively stable (though all values were at lower limit threshold) venous blood gasses (pH = 7.395, Actual HCO_3 = 20.6 mmol L^{-1}) and renal profile (Na^+ = 135 mmol L^{-1}, K^+ = 3.5 mmol L^{-1}) while patient was discharged on the night of 6th day from admission with discharge report of resolved DKA, alert and conscious and tolerating well orally contrary to the

Table 1: Important laboratory profiles at different time intervals

Parameter	Day 1	Day 4	Day 7	Day 12
pH*	7.149	7.395	6.793	7.398
Actual HCO_3*	9.2 mmol L^{-1}	20.6 mmol L^{-1}	2.6 mmol L^{-1}	24.4 mmol L^{-1}
Serum Na^+	128 mmol L^{-1}	135 mmol L^{-1}	131 mmol L^{-1}	137 mmol L^{-1}
Serum K^+	5.5 mmol L^{-1}	3.5 mmol L^{-1}	5.2 mmol L^{-1}	3.4 mmol L^{-1}
Ketone**	6.4 mmol L^{-1}	-	4.3 mmol L^{-1}	Nill
White blood cells	16.5×10^3 μL^{-1}	-	19.1×10^3 μL^{-1}	5.6×10^3 μL^{-1}
Hematocrit	43.5%	-	35.9%	33.2%
Heamoglobin	14.3 g dL^{-1}	-	11.6 g dL^{-1}	11.4 g dL^{-1}
Platelet	356×10^3 μL^{-1}	-	296×10^3 μL^{-1}	261×10^3 μL^{-1}
Average BGL***	24 mmol L^{-1}	22.1 mmol L^{-1}	24.9 mmol L^{-1}	12.5 mmol L^{-1}

*pH and Actual HCO_3 are recorded form Venous Blood Gasses. **Ketones on day 4 were not checked. Ketones on day 10 were 2.2 mmol L^{-1}. ***Average Blood Glucose Level on day 6 i.e. day of 1st discharge was 20.4 mmol L^{-1}

Table 2: General protocol followed for solving hyperglycemia and acidosis

Blood glucose level	Units of Insulin	Fluid replacement*, **	Potassium replacement
≤ 5 mmol L^{-1}	1ii/h	5% dextrose	≤ 3 mmol L^{-1} = Fast correct***
5.1-10 mmol L^{-1}	2ii/h	5% dextrose	3-3.5 mmol L^{-1} = 2 g $pint^{-1}$
10.1-15 mmol L^{-1}	4ii/h	5% dextrose	3.6-4 mmol L^{-1} = 1.5 g $pint^{-1}$
15.1-20 mmol L^{-1}	6ii/h	Normal saline	4.1-4.5 mmol L^{-1} = 1.0 g $pint^{-1}$
20.1-25 mmol L^{-1}	8ii/h	Normal saline	4.6-5 mmol L^{-1} = 0.5 g $pint^{-1}$
≥ 25 mmol L^{-1}	10ii/h	Normal saline	≥ 5 mmol L^{-1} = Omit

*Day 1-3 = 1 pint/3 h, Day 4 = 1 pint/4.5 h, Day 5 = 1 pint/12 h, Day 6 = Off. **Day 7-9 = 1 pint/4 h, Day 10 = 1 pint/6 h, Day 11-12 = 1 pint/12h. ***Fast correct = 1 g Potassium chloride in 100cc Normal saline over 1 h

fact that patient was feeling nausea for last 2 days. Medication upon discharge was same as patient was taking prior to the hospital admission.

However, patient was readmitted on the very next day just at 7th hour from discharge with severe shortness of breath, Kussmaul breathing and Glasgow Coma Scale score of 11/15 ($E_3V_4M_4$). Patient was found to be dehydrated and ECG revealed sinus tachycardia. Serum ketones were immediately checked and found to be positive (Ketones = 4.3 mmol L^{-1}). Arterial blood gasses analysis and complete blood count showed severe metabolic acidosis (pH = 6.793, Actual HCO_3 = 2.6 mmol L^{-1}) and infection (WBC = 19.1×10^3 μL^{-1}). Same impression as last time was made and patient was again started on the protocol mentioned in Table 2. However, patient this time was given 4.5 g piperacillin/tazobactam td for 5 days to cover for sepsis. Patient this time however was discharged with very stable blood profiles (WBC = 5.6×10^3 μL^{-1}, Na^+ = 137 mmol L^{-1}, K^+ = 3.4 mmol L^{-1}, pH = 7.398, Actual HCO_3 = 24.4 mmol L^{-1}) and nil ketones (Table 1) on 30/70 insulin 20ii and 500 mg metformin, bd; 4 mg prindopril oD; 40 mg lovastatin oN; and 1.2 g slow potassium td for 3 days.

DISCUSSION

Diabetic ketoacidosis is an acute complication of diabetes and is most common among the hospital admissions due to hyperglycemia. DKA takes around a week from initiation up to its complete resolution. Infection is the most common event which leads to DKA followed by non-compliance and trauma (Umpierrez and Kitabchi, 2003). Under stressful condition, either lack of sufficient insulin or inability of insulin, to perform normal physiological function triggers production of keto-acids (ketosis) which in turn cause loss of serum bicarbonate (Kitabchi *et al*., 2006). Loss of bicarbonate causes a moderate to severe drop in blood pH (acidosis). As per guidelines, patient is initially given normal saline drip and intravenous insulin during the course of hospitalization (Savage *et al*., 2011; Kitabchi *et al*., 2006). Acidosis is resolved partially by initiation of fluid resuscitation. The leftover is done by continuous administration of insulin which ceases the production of keto-acids. However, ketones take more time to dissipate, remain present in the circulation and get excreted via urine and expiration. Time taken by ketones to disappear from blood is directly related to glucose control since insulin puts a lock on production of ketones. In the reported case, it is clearly observed that BGL of the patient during the first admission was not controlled and was 15.8 mmol L^{-1} at time of 1st discharge. This hyperglycemia may be the result of underlying infection (Butler *et al*., 2005) which apparently was not resolved as number of WBC was still higher at the time of 2nd admission. It is also notable that after initial tests performed at the time of admission, no test was performed to get insight of CBC and ketones during the course of hospitalization and the tests, which even performed, were 2 days prior to discharge. Moreover, patient did register complaint of nausea and had an episode of vomiting one day prior of 1st discharge. Hyperkalemia on 2nd admission clarifies the reason of nausea and vomiting (Seifter, 2011). It also render a notion that 2nd episode was in fact continuation of 1st one rather than recurrence of DKA. Then, it was presumed that with normalization of pH, DKA has been resolved and infection eradicated. However, due to hyperglycemia, the production of ketone bodies was not shut down completely (Miyan *et al*., 2012) and hence, DKA was again observed just after seven hours from initial discharge. This point should be clear that upon 2nd admission, patient received utterly same treatment protocol which was followed on 1st admission, which is given in Table 2, with a minute modification that infection was taken more critically and patient received a full course of IV antibiotic. Once infection was eradicated, glycemic level automatically tapered to a lower category hyperglycemia and condition of patient stabilized over a period of time. Furthermore, a thorough evaluation was carried out in order to sketch a clear picture of patient's biochemical profile prior to discharge.

CONCLUSION

Diabetic ketoacidosis is an acute complication of diabetes. With passage of time, its management has been modified in positive direction. Adherence to any published protocol not only saves life but avoids complications as well. Published guidelines clearly indicate that improvement in condition of patient should be judged by biochemical profiles from time to time. With presentation of this case, we strongly emphasize that treatment protocol should be followed religiously and this undeniably includes biochemical profiles as well. Furthermore, we suggest that a thorough evaluation of patient via laboratory profiles should be performed prior to discharge in order to avoid recurrence or continuation of episode of DKA.

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