Research Paper Medical Science

Role of Insulin Aspart in Management of Diabetic Ketoacidosis.

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ABSTRACT

Introduction: Diabetic ketoacidosis (DKA) is an acute, major, life-threatening complication of diabetes. Recently, new analogues of human insulin aspart are used in treatment of mild to moderate diabetic ketoacidosis. AIM: To study the role of subcutaneous insulin aspart in management of diabetic ketoacidosis. **Results:** The mean duration of treatment until glucose concentration was <13.8 mmol/l (<25omg/dl) was not statistically different between patients treated with SC-1h (6.8 + 3h) and SC-2h (6.5+ 3h) or with IV regular insulin (6.9 + 4h). Similarly, the mean duration of treatment until resolution of ketoacidosis was not statistically different among treatment groups 10.3 + 3, 10.8 + 3 and 10.5 + 3 h respectively. **Conclusions:** Treatment with subcutaneous insulin aspart 1 hourly/2hourly represent a safe and effective alternative to intravenous regular insulin in mild to moderate form of diabetic ketoacidosis.

KEYWORDS Diabetic Ketoacidosis, Regular Insulin, Aspart

INTRODUCTION

Worldwide prevalence of type II diabetes in 2010 was estimated about 285 million. India has been labeled as a diabetic capital of the world with an expected 109 million persons with diabetes by 2035. Diabetic ketoacidosis (DKA) is an acute, major, life-threatening complication of diabetes. Type 1 diabetes patients mainly suffer from this complication, but it is also seen in some patients with type 2 diabetes. Most common cause of the DKA is missing insulin. DKA is caused primarily due to severe insulin deficiency associated with elevated level of counter regulatory hormones. Clinical diagnosis based on the findings of dehydration along with high capillary glucose levels, ketones in urine/plasma and is confirmed by blood pH, serum bicarbonate levels and serum osmolarity. Treatment includes correction of dehydration, hyperglycemia, ketoacidosis and electrolyte deficit. The mainstay in treatment of DKA involves the administration of regular insulin via continuous IV infusion or by frequent SC/IM injections. Although several controlled studies in patients with DKA have shown that low-dose insulin therapy is effective regardless of the route of administration, the ideal route of insulin therapy is still a matter of debate. Few studies have reported that patients of DKA treated with IV regular insulin experienced a more rapid fall in plasma glucose and ketone insulin aspart/insulin lispro have come into existence and may represent alternative to the use of regular insulin in the treatment of DKA. Few studies had been carried out with insulin levels than patients treated with IM or SC insulin. Yet the cost of treating DKA with N insulin may be higher. New analogues of human insulin with a rapid onset of action- observe the difference in relation to selective with everlasting regime of regular insulin therapy in these lispro/Insulin aspart (SC route) comparing it with regular insulin (IV route) in mild to moderate diabetic ketoacidosis. The results were equally effective but ICU protocols were more costly as IV regular insulin only can be administered in ICU/ diabetic care unit. This study was planned to variables using typical and aspart insulin in patients of diabetic ketoacidosis admitted in medical wards.

AIMS: To study the role of subcutaneous insulin aspart in management of diabetic ketoacidosis and compare its efficacy and safety with that of continuous intravascular regular insulin in patients with diabetic ketoacidosis.

MATERIAL AND METHODS

Total 45 patients admitted to Medicine Department of Rama Medical College with diabetic ketoacidosis were randomly assigned to receive SC aspart insulin every hour (SC-1h n = 15 patients) or every 2 hours (SC. 2h n = 15 patients), or to receive IV infusion of regular insulin (n = 15 patients). Patients treated with IV regular insulin were admitted to the ICU. Whereas patients treated With SC aspart managed in the general medicine ward. All the laboratory investigation was done according to the need. Inclusion Criteria: Patients of diabetes mellitus in medicine ward With RBS > 25omgldl, Serum bicarbonate < 18mmom, Arterial pH 5 7.30. Urinary ketone present. Exclusion Criteria: Acute myocardial Infarction, End stage renal disease, Hepatic failure and pregnant mother.

RESULTS

The mean age, duration of diabetes, and precipitating cause for DKA were similar among treatment groups. More incidence of hospitalization seen in type- 2 diabetes mellitus (80%) followed by type-1 diabetes mellitus (13%) and newly diagnosed diabetes (7%). infection was the most common precipitating cause of DKA and was recorded in more than half of patients treated with SC Aspart and iv regular Insulin. Infection was the precipitating causes in eight patients (53.3%) those who were on regular insulin. Among infection mainly urinary tract infection in 46% patients, pneumonia in 30% patients, Cellulites / abscess 10% patients. Pelvic inflammatory disease (mainly post partum sepsis) in 9% patients, malaria in 4% patients & others 1%. Poor compliance with insulin in SC 1h six patients (40%). in the SC-2h group five patients (33%) in the IV insulin-treated group six patients (40%). One patient (6.7%) from each groups were newly diagnosed with diabetes on admission. Two patients were from treatment group of malaria (plasmodium vivax positive) and one with lower limb cellulites were diagnosed to be diabetic during hospitalization presented in diabetic ketoacidosis state. The admission biochemical parameters were not significantly different among treatment groups. In patients treated with SC-1h, the mean admission serum glucose was 27.7 $\pm$ 8.3 mmol/l (516 $\pm$150 mg/dl, range 666-366mg/di) serum bicarbonate 10.1 $\pm$ 3 mmol/l (7.1-13.1mmol/l), pH 7.11 $\pm$ 0.09 (7.02-7.20). In patients treated with SC-2h, the mean admission serum glucose was 30.5 $\pm$ 9.4 mmol/l (550$\pm$170) mg/dl, range(720- 380mg/dl), bicarbonate 9.8 $\pm$ 2 mmol/l (7.8-11.8), pH 7.15$\pm$ 0.11 (7.04 -7.26). These values were not statistically different from the mean admission values in patients treated with IV regular insulin glucose 30 $\pm$ 7.2 mmol/l [540 $\pm$ 13omg/dl, range 670-41omg/dl], bicarbonate 10.3 $\pm$ 3mmol/l

[17.3-13.3], pH 7.12 ± 0.14 [6.98 - 7.26]. The rate of decline of blood glucose concentration and changes in acid-based parameters during treatment were not significantly different among treatment groups. The mean duration of treatment until glucose concentration was <13.8 mmol/l (<25omg/dl) and was not statistically different between patients treated with SC-1h (6.8 ± 3h) and SC-2h (6.5± 3h) or with IV regular insulin (6.9 ± 4h). Similarly, the mean duration of treatment until resolution of ketoacidosis was not statistically different among treatment groups 10.3 ± 3, 10.8 ± 3 and 10.5 ± 3 h respectively.

TABLE1: BIOCHEMICAL PROFILE ON ADMISSION

	SC- 1 Hr	SC- 2Hr	IV REGULAR
n (Number Of Patient)	15	15	15
Age (Years)	36 ± 10	34 ± 11	38±11
Sex (Male/Female)	8/7	9/6	10/5
BMI (Kg/M^2)	28±9	29±7	29±7
DKA Precipitating Cause 1. Infection	8 (53.3%)	9(60%)	8 (53.3%)
2. Poor Compliance	6(40%)	5(33.3%)	6(40%)
3. New Onset Diabetes	1 (6.7%)	1 (6.7%)	1 (6.7%)
Glucose (Mmol/L)	27.7±8.3	30.5±9.4	30±7.2
Bicarbonate (Mmol/L)	10.1±3	9.8±2	10.3±3
Arterial Ph	7.11±0.09	7.15±0.11	7.12±0.14
Anion Gap (Mmol/L)	18 ± 2	19 ± 4	19 ± 3
Serum Potassium (Mmol/L)	5.0 ± 0.8	4.9± 1.1	4.8± 1.3
Serum Osmolarity (Mmol/Kg)	309 ± 16	312 ± 20	312 ± 12
Hba_{1c}	11.0 ±1.6	10.8 ± 1.4	10.7± 1.6

TABLE 2: RESPONSE TO MEDICAL TREATMENT

	SC-1h	SC-2h	Regular IV insulin
N	15	15	15
Length of hospital stay (days)	6.2 ± 4	5.9 ± 3	6.8 ± 3
Duration of treatment until glucose <13.8mmol/l in hour	6.8 ± 3	6.5 ± 3	6.9 ±4
Duration no therapy until resolution of DKA in hours (h)	10.3 ±3	10.8 ± 3	10.5 ± 3
Amount of insulin until glucose <13.8 mmol/l (units)	61 ± 33	64± 28	62± 31
Amount of insulin resolution of DKA (units)	89 ± 27	91± 21	87± 33
Episodes of Hypoglycemia	0	0	0

DISCUSSION

Our study reported that most common precipitating factor for DKA was infection recorded in more than half of the patients (55.5%) (mainly caused by urinary tract infection 46%. pneumonia 30%, celiulites/abscess 10%, pelvic inflammatory disease 9%) among treatment groups followed by poor compliance with insulin in 37.7% and 6.7% in newly diagnosed diabetes mellitus. Comparing with the study done in University of Tennessee and Emroy University School of Medicine, Atlanta in 2004 which reported poor compliance with insulin to be the most common cause recorded in 58% of the patients followed by infection in 25% patients than newly diagnosed diabetes mellitus in 18%. Our study reported that rate of decline of blood glucose and change in acid base parameters during treatment was not significantly different among treatment group. Study done with the insulin analogue in University of Tennessee by G. Umpierrez GE et. al. With insulin aspart and manna RD steinmetz L Campos PR, et. al with insulin lispro was having similar result. our study reported that there was no statistical difference in length of hospital stay among treatment groups. The length of hospital stay was more with precipitating cause rather than the type of Insulin treatment. Similar results were also shown in study done by Guillermo Umpierrez et.al. There were no hypoglycemic episodes during the treatment among the treatment group as compared with other study done with Insulin Analogue, there was one hypoglycemic episode in each group reported in study done by Guillermo Umpierrez with Insulin Aspart in 45 patients, and 6 hypoglycemic episode with IV regular and 4 hypoglycemic episode with Insulin Lispro was reported in study done in 60 patients by Ersoz H.O. M. et. al. There were no mortality and recurrence of Ketoacidosis in our study similar results were also from the study done by Guillermo umpierrez et. al. This study can be extrapolated in private set-up for non ICU management thus significantly reducing the financial burden by patient during ICU management.

CONCLUSIONS

Treatment with subcutaneous insulin aspart 1 hourly/2hourly represent a safe and effective alternative to intravenous regular insulin in mild to moderate form of diabetic ketoacidosis. Our study concludes that use of newer insulin (aspart in our study) in management of diabetic ketoacidosis can make the management of diabetic ketoacidosis, easily implemented (subcutaneous mode of therapy), less complicated especially in relation to hypoglycemia and cost effective as it can be performed safely and comfortably in a non ICU set up.

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