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Original Research Article

INTRAVENOUS AND SUBCUTANEOUS PLAIN INSULIN IN DIABETIC KETOACIDOSIS- A PROSPECTIVE STUDY

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Abstract

Background: The prevalence of diabetes in India has risen from 2.3% in 1970 to 12%-19% in urban areas and from 1.5% to 4%-9% in rural areas in recent years. Diabetes can lead to Diabetic ketoacidosis (DKA) which is one of the most dangerous complications. The present study was undertaken with the objective to evaluate the effect of Subcutaneous Plain Insulin in mild-moderate DKA and Intravenous Plain Insulin in severe DKA.

Methods: The present prospective observational study was conducted in a Tertiary Care Hospital in South Gujarat on total 60 patients having mild-moderate and severe DKA with 30 patients in each group. Patients with mild -moderate DKA were treated with Subcutaneous Plain Insulin and the patients with severe DKA were treated with Intravenous Plain Insulin.

Results: In the present study, 62% of the patients were male and 38% were female and mean age was 40.3±15.98 years. Majority patients having mild-moderate DKA had DM since 6-15 years while majority patients who developed severe DKA had DM since more than 15 years. About three-fourth patients of type 1 DM developed severe DKA while two-third patients of type 2 DM had mild to moderate type of DKA. There was significant improvement in serum glucose level, ketoacidosis and bicarbonate level after treatment in all DKA patients irrespective of the type of treatment received.

Conclusion: Treatment of patients with mild and moderate DKA with SC insulin is as effective as treatment with IV insulin in severe DKA.

Keywords: diabetes, diabetic ketoacidosis, insulin, treatment

Introduction

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Diabetes is a disease resulting from defects in insulin secretion, insulin action, or both characterized by hyperglycemia. Diabetes-related chronic hyperglycemia is linked to long-term damage and dysfunction of various organs, including the eyes, kidneys, nerves, heart, and blood vessels.[1] Diabetes can lead to Diabetic ketoacidosis (DKA) and Hyperosmolar hyperglycemia state (HHS), which are two dangerous and deadly complications.
Ketoacidosis affects 4.6–8.0 per 1000 persons with diabetes each year and those with a persistent risk factor, such as an eating disorder, and those who cannot afford insulin are at higher risk. After a DKA episode, about 30% of children with type 1 diabetes obtain their diagnosis. In persons with diabetes mellitus type 1, lower socioeconomic position and greater area deprivation are linked to an increased risk of diabetic ketoacidosis. According to the multi-centric study, the prevalence of diabetes in India in the 1970s was 2.3 percent in urban areas and 1.5 percent in rural areas. The prevalence has risen to 12% to 19% in urban areas and to 4% to 9% in rural areas in recent years.[2] Cerebral Edema is a complication that affects up to 1% of children with DKA. Previously thought to be uniformly lethal, the probability of death with competent and prompt treatment is now estimated to be between 1% and 5%.[3,4]

Using Subcutaneous Plain Insulin in Mild and Moderate DKA has many benefits than Intravenous Plain Insulin. According to new guidelines in DKA, if patient is alert and able to take oral fluid, patients can be easily managed with Subcutaneous Plain Insulin, without intravenous infusion and continuous monitoring. An alternative to Intravenous Plain Insulin therapy for acute management of mild-moderate DKA is with the use of Subcutaneous Plain Insulin. Thus the present study was done with the objectives to evaluate the effect of Subcutaneous Plain Insulin in mild and moderate DKA and Intravenous Plain Insulin in severe DKA.

Materials and Methods

This prospective, observational study was conducted in the Tertiary Care Hospital in South Gujarat over a period of 2 years after obtaining approval from the institutional ethics committee with ref no GMCS/STU/ETHICS/Approval/9516/20. The study included total 60 patients (30 patients with Mild Diabetic Ketoacidosis for Subcutaneous Plain Insulin and 30 patients with Severe Diabetic Ketoacidosis for Intravenous Plain Insulin) having plasma glucose level >250 mg/dl and fulfilling inclusion criteria. Written informed consent was taken from all the patients who were included in the study.

Inclusion criteria:

1. All patients of type 1 and type 2 Diabetes mellitus with DKA (Diabetic Ketoacidosis) willing to participate in study and those who gave consent and in patients having stuporous & unconscious mental status patient‘s relatives consent was taken for the study.
2. Patients above 18 years of age (Male and Female) of type 1 and 2 Diabetes Mellitus.
3. To find out the other conditions in which Subcutaneous Plain Insulin will not respond & shifting those patients to intravenous insulin.

Exclusion criteria:

1. Pregnant females

A pre-tested semi structured proforma was used for data collection. The Criteria for diagnosis of potential candidate of Mild, Moderate and Severe Diabetic Ketoacidosis are as follows:
Mild and Moderate DKA: Plasma glucose concentration >250; pH – 7.25 – 7.30; HCO3- >10; Urine – positive aceto acetate; Mental status - ALERT

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Severe DKA: Plasma glucose concentration >250; pH – 7.00 – 7.24; HCO3- <10; Urine-positive aceto acetate; Mental status – DROWSY STUPOR COMA
Following dosage of the drug was used for the treatment:

Mild and Moderate DKA: Initial Bolus Dose of 0.3 units/kg Subcutaneous Plain Insulin, followed by a Maintenance Dose of 0.2 units/kg every 2 hours. When blood glucose level was <250 mg/dl; administer 0.1 units/kg every 2 hourly till urine acetoacetate is negative.
Severe DKA: Fix Weight Based Dosage of 0.1 units/kg/hr following 0.1 units/kg bolus Intravenous Plain Insulin

Results
In the present study, 62% of the patients were male and 38% were female with a mean age of 40.3±15.98 years. In mild-moderate DKA, majority male patients were from 51-60 years of age group while female were from 41-50 years of age group. Whereas in severe DKA, most of male patients belong to 31-40 years of age group followed by 13-30 years of group while female patients were from 21-30 years of age group. (Table 1)

Table 1: Distribution of patients according to age group, gender and type of DKA

Age group in years	Mild moderate DKA		Severe DKA	
	Male	Female	Male	Female
13-20	0	0	5	3
21-30	0	1	5	6
31-40	2	1	7	2
41-50	4	5	1	0
51-60	8	2	1	0
>61	4	3	0	0
Total	18	12	19	11
Chi-square (P value)	4.15 (0.386)		3.48 (0.48)	

In the present study, majority of the patients having mild-moderate DKA had DM since 6-15 years while majority patients who developed severe DKA had DM since more than 15 years but still there is no significant association found between type of DKA and duration of having DM. (Chi-square=6.07, P value=0.109) (Table 2)

Table 2: Association between duration of DM and development of DKA

Duration of DM in years	Type of DKA			p value
	Mild- Moderate DKA	Severe DKA	Total	0.109
0-5	3	4	7	
6-10	11	7	18	
11-15	11	6	17	
>15	5	13	18	
Chi-square=6.07, df=4				

There is significant difference found in serum glucose level after treatment in all DKA patients which shows better sugar control in mild-moderate DKA group of patients with subcutaneous insulin and in severe DKA group of patients with intravenous insulin.(Table 3)

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Table 3: Paired t-test between serum glucose on admission and after treatment

Mean	Standard Deviation	Standard Error of mean	95% confidence interval of mean		t-test	df	p-value
			Lower	Upper			
241.03	44.11	8.05	224.56	257.5	29.92	29	0.000

There is significant control in DKA after treatment. Also there was significant improvement in bicarbonate level after treatment in all patients which shows good efficacy of mode of treatment. In mild-moderate type of DKA, more than half patients had high potassium level (56.7%) while it was high in almost all patients in severe DKA. (96.67%) (Table 4-6)

Table 4: Paired t-test between Arterial pH on admission and after treatment

Mean	Standard Deviation	Standard Error of mean	95% confidence interval of mean Lower Upper		t-test	df	p-value
-0.085	0.075	0.014	-0.112	-0.057	-6.23	29	0.000

Table 5: Paired t-test between Bicarbonate on admission and after treatment

Mean	Standard Deviation	Standard Error of mean	95% confidence interval of mean Lower Upper		t-test	df	p-value
-11.01	4.045	0.739	-12.521	-9.499	-14.9	29	0.000

Table 6: Distribution of patients according to level of K in both type of DKA

K level	Mild-moderate DKA	Severe DKA
<3.5	13(43.3)	1(3.33)
>3.5	17(56.7)	29(96.67)
Chi-square with Yate‘s correction=11.27, p value=<0.001		

In the present study, out of 30 patients of mid-moderate DKA it was positive in 4 patients while only 2 patients showed positive findings in severe DKA after treatment. Majority of the patients had better outcome in severe DKA group of patients while 2 patients died in this group during treatment. (Table 7,8)

Table7: Distribution of patients according to urine ketone findings after Rx.

Urine ketone	Type of DKA	
	Mild-moderate DKA	Severe DKA
Positive	4	2
Negative	26	28

Table 8: Distribution of patients according to outcome in severe DKA. (n=30)

Outcome	Frequency	Percent
Discharge	28	93.3

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Death	2	6.7

Discussion:

In the present study, majority (61.7%) of the patients were male. Similar observations were made by Efstathiou SP et al[5] who found 66% male patients in their study. In contrast to this, Afrose et al[6] have found higher incidence of DKA in females as compared to males. Some other studies have also reported a female predominance.[7] In this study, minimum age of the patients with DKA was 14 years and maximum age was 72 years, with the mean age 40.3±15.98 years. In mild-moderate DKA, majority male patients were from 51-60 years of age group while female were from 41-50 years of age group. These results are in accordance with the study by Afrose et al[6] who found minimum age 14 yrs and the maximum age 69 years in their study and the mean age was 42.9±12.9 yrs. Similar observations were made by Efstathiou SP et al[5] and Umpierrez et al[8] in their respective studies.

Present study reported significant association between type of DM and DKA. About three-fourth patients of type 1 DM developed severe DKA while two-third patients of type 2 DM had mild to moderate type of DKA. In a similar study, Newton et al[9] have found 78 patients of type 1 DM and 25 patients of type 2 DM. While in other studies, about one-third of patients who present with DKA were having type 2 diabetes.[10-12]

In the present study, majority patients having mild-moderate DKA had DM since 6-15 years while majority patients who developed severe DKA had DM since more than 15 years. Also, majority (30.0%) of the patients had DM since 6-10 and for more than 16 years each. About 28.3% were having DM since 11-15 years while 11.7% patients had DM since less than 5 years. In a study by Afros et al[6] the duration of diabetes observed varied from 6 months to 17 years, with the maximum number of patients having diabetes of duration of 2-5 yrs constituting 32%. On the other hand, Newton et al[9] found the mean duration of DM to be 12.7±10.0 years in type 1 DM and 5.6±4.4 years in type 2 DM in their study.

In the present study, mean serum glucose was 415.17±39.91 in mild-moderate DKA group and 537.13±64.05 in patients having severe DKA while overall it was 476.15±81.13. Overall mean HbA1c was 11.01±2.28 while overall mean pH, HCO3 and Na were 6.93±0.33, 11.31±4.01 and 136.9±4.397 respectively. Umpierrez et al[8] found that mean S.glucose was 44±21 in mild-moderate DKA group and 40±13 in patients treated with intravenous insulin while mean HbA1c was 11.5±1.6 in SC group and 11.4±2 in IV group. Mean pH and HCO3 were 7.13±0.15 and7.6±4.

The present study found significant control in serum glucose level, ketoacidosis and significant improvement in bicarbonate level after treatment in all patients which shows better efficacy of treatment in mild-moderate DKA group of patients with subcutaneous insulin and in severe DKA group of patients with intravenous insulin. One study reported that treatment of patients with mild and moderate DKA with hourly injections of SC lispro insulin is as effective as treatment with low-dose IV regular insulin.[8] However, most medical centers and authorities recommend the administration of IV infusion because of the delayed onset of action and prolonged half-life of SC regular insulin.[13-17] The present study reported a mortality of 6.7% in severe DKA group of patients. Patients hospitalized for DKA have been found to have mortality rates as high as 10%–30% in studies from various underdeveloped nations.[18]

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Conclusion

The present study concludes that there is a significant association between type of DM and DKA. Patients with type 1 DM are at a higher risk of developing severe DKA while those with type 2 DM are more likely to develop mild to moderate type of DKA. There is significant improvement in serum glucose level, ketoacidosis and bicarbonate level after treatment in all DKA patients suggesting that there is better sugar control in mild-moderate DKA group of patients on treatment with Subcutaneous Insulin and in severe DKA group of patients on treatment with Intravenous Insulin.

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