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Association Between Emergency Hyperglycemia Management Methods and Glucose Reduction Rate and Stay at Emergency Department

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Abstract

In emergency departments (EDs), hyperglycemia is a prevalent condition that affects 1% of patients. Most individuals with hyperglycemia can be discharged from the emergency department (ED) without needing to be admitted to the hospital since they don't have diabetic ketoacidosis or hyperosmolar hyperglycemic condition. Regarding the effect of reducing blood glucose levels on these patients or the best way to manage this population, opinions differ, and recent research has indicated that managing hyperglycemia in the emergency department may not be beneficial. The aim of this study was to determine actual glucose reduction (AGR) and length of stay at emergency department when using different modalities for management emergency hyperglycemia not hyperosmolar hyperglycemic state or diabetic ketoacidosis. This was a prospective cohort study, conducted on four hundred patients (400) with emergency hyperglycemia (not diabetic ketoacidosis or hyperosmolar hyperglycemic state) their blood glucose level≥350 mg /dl attended to Al-Zahraa hospital ED during the period from November 2022 to September 2023. Emergency department length of stay (EDLOS) was significantly lower in insulin and fluid receiving group (IFR group) compared to fluid receiving group (FR) group and insulin receiving group (IR group). AGR was significantly higher in IFR group compared to IR group and FR group. The current study demonstrated that **IV** insulin combined with IV fluid in the IFR group was not effective at reducing the dose of either but was effective in shortening EDLOS and elevating AGR in the current study.

Keywords: Hyperglycemia, Management of hyperglycemia, EDLOS.

1. Introduction

In emergency departments (EDs), hyperglycemia is a prevalent condition that affects 1% of patients. Most individuals with hyperglycemia can be discharged from the emergency department (ED) without needing to be admitted to the hospital since they don't have diabetic ketoacidosis or hyperosmolar hyperglycemic condition [1]. The efficacy of insulin and IV fluids in lowering blood glucose levels in the emergency department has not been extensively researched. Small studies suggest that oral or intravenous hydration treatment can lower blood glucose levels by around 40 mg/dl per liter [1].

Hyperglycemia is associated with increased mortality, increased intensive care unit admission, longer hospital stays and repeated ED visits [2].

Emergency departments exist to care for patients who are physiologically unstable and require ongoing evaluation and treatment as their condition progresses. Most patients admitted to general medical wards first visit the ED. More than 20% of all emergency department visits are diagnosed with diabetes. Thirty to 40% of all patients treated in the emergency department are diabetics. Thus, emergency rooms are a common place to diagnose and treat diabetes [3].

Emergency departments are open 24 hours a day and serve unscheduled patients who are expected to require urgent care. For many patients, they are the "entrance point" for the health care system, accounting for approximately three-fifths of all hospital admissions [4].

Globally, there has been an imbalance between supply and demand in emergency care over the past two decades as the number of annual emergency department visits has grown rapidly with the population growth affecting both emergency care and length of hospital stay [5]. The aim of the work was to determine actual glucose reduction and length of stay at emergency department when using different modalities for management emergency hyperglycemia not hyperosmolar hyperglycemic state or diabetic ketoacidosis.

2. Patients and Methods

This study included a total number of **400** subjects (Males and females). Their age ranged from **(27-65)** years. They were divided according to different modalities of management of emergency hyperglycemia (not diabetic ketoacidosis or hyperosmolar hyperglycemic state) with blood glucose level **≥350 mg /dl** into three groups as following:

Group I insulin receiving group (IR Group):

included **(119)** patients with hyperglycemia received subcutaneous (SC) insulin only in ED.

Group II fluid receiving group (FR Group):

included **(118)** patients' patients with hyperglycemia received intravenous (IV) fluids only in ED.

Group III insulin and fluid receiving group (IFR Group):

included **(163)** patients with hyperglycemia received combined IV insulin and fluids in ED.

2.1 Exclusion criteria:

1. Type 1 Diabetes Miletus **(DM).**
2. Glomerular filtration rate **(GFR)** < 60 ml /min.
3. Liver cell failure.
4. Severe hypertension.
5. Heart failure.
6. Diabetic ketoacidosis **(DKA)**, hyperosmolar hyperglycemic state **(HHS).**
7. Admitted patient.

All participants were subjected to the Chi-squared tests; were used to compare groups that had with qualitative data ; independent t-tests ; were used to compare two groups that had quantitative data and a parametric distribution ;Mann-Whitney tests; were used to compare two groups that had quantitative data and a non-parametric distribution; One Way ANOVA tests were used to compare more than two groups that had quantitative data and a parametric distribution. Two quantitative parameters in the same group were correlated using Spearman correlation coefficient.
Probability:

- $P > 0.05$: Non-significant
- $P < 0.05$: Significant
- $P < 0.01$: Highly significant.

3. Results

As show in table 2 the most common causes of emergency hyperglycemia were missed dose, stress, and UTI in this study. As shown in table 3 there was not statistically significant between IR group and IFR group regarding insulin dose. There was no statistically significant difference between FR group and IFR group regarding fluid dose.
As shown in table 4 EDLOS was significantly lower in IFR group compared to FR group and IR group. EDLOS was significantly lower in FR group compared to IR group. AGR was significantly higher in IFR group compared to IR group and FR group. AGR was significantly higher in IR compared to FR group.
As shown in table 5, there is a significant positive correlation between EDLOS & insulin dose and a significant negative correlation with AGR. There was a positive correlation between EDLOS & duration of DM and a negative correlation with age in IR group.
There was a significant negative correlation between AGR & insulin dose, duration of DM and EDLOS. There was a positive correlation between AGR & age in IR group.
As shown in table 6 the most common causes of hyperglycemia; EDLOS was a significantly lower time in patients with stress as a cause of emergency hyperglycemia in comparison to other common causes in IR group.
As shown in table 7 there is a significant positive correlation between ED LOS & fluid dose and a significant negative correlation with AGR. There was a positive correlation between ED LOS & duration of DM and a negative correlation with age in FR group. There was a significant negative correlation between AGR & insulin dose and EDLOS. There was a positive correlation between AGR & age and duration of DM in FR group.
As shown in table 8 a significant positive correlation between EDLOS and insulin dose & fluid dose. There was a significant negative correlation with AGR. There was a negative correlation between EDLOS & duration of DM and a positive correlation with age in IFR group. There was a significant negative correlation between AGR & fluid dose and EDLOD. There was a positive correlation between AGR & duration of DM and a negative correlation with insulin dose & age in IFR group

Table 1: Descriptive data of the study groups.

		Total no.=400
Sex	Female	249 (62.2%)
	Male	151 (37.8%)
Age	Mean ± SD	52.70 ± 9.66
	Range	27 – 89
Home Treatment	Insulin	232 (58.0%)
	OHD	158 (39.5%)
	Insulin +OHD	8(2.0%)
	Not yet	2(0.5 %)
Duration of DM (Years)	Median (IQR)	8 (5 - 15)
	Range	0 – 35
Causes of hyperglycemia		
Missed dose	No. (%)	140 (35.0%)
Stress		108 (27.0%)
UTI		73 (18.2%)
Chest Infection		16 (4.0)
Not complaint		14 (3.5%)
Skin Abscess		13 (3.2%)
Uncontrolled diet		7 (1.8%)
Diabetic Foot		5 (1.2%)
Renal Colic		5 (1.2%)
Gluteal abscess		4 (1.0%)
Common cold		3 (0.8%)
Stopped treatment		3 (0.8%)
Others		9 (2.2%)

OHD: Oral hypoglycemic drugs & UTI: Urinary tract infection.

Table 2: Distribution of patients regarding causes of emergency hyperglycemia among the study groups.

Cause Of hyperglycemia	IR group No.=119	FR group No.=118	IFR group No.=163
Missed dose	75(63%)	17 (14.4%)	48 (29.4%)
Stress	12 (10.1%)	75(63.5%)	21 (12.9%)
UTI	14 (11.8%)	12(10.2%)	47 (28.8%)
Chest Infection	5 (4.2%)	4 (3.4%)	7 (4.3%)
Not complaint	5(4.2%)	3 (2.5%)	6 (3.7%)
Skin Abscess	2(1.7%)	2 (1.7%)	9 (5.5%)
Un controlled diet	0(0%)	3 (2.5%)	4 (2.5%)
Diabetic Foot	0 (0%)	0 (0%)	5 (3.1/%)
Renal coli	3(2.5%)	1(0.8%)	1(0.6%)
Gluteal abscess	0(0%)	0 (0%)	4 (2.5%)
Common cold	0 (0%)	1 (0.8%)	2(1.2%)
Stopped treatment	0 (0%)	0 (0%)	3 (1.8%)
Others	3 (2.5%)	0 (0%)	6 (3.7%)

UTI: Urinary tract infection.

Table 3: Insulin dose and fluid dose of the study groups.

		IR group No. = 119	FR group No. = 118	IFR group No. = 163	
Insulin dose (SC)	Mean ± SD	13.74 ± 5.18		11.69 ± 6.00	P2=0.1
	Range	5 – 25		5 – 30	
Fluids dose (cc)	Mean ± SD		1076.92 ± 407.98	842.94 ± 383.01	P3=0.5
	Range		500 – 2000	150 – 2000	

P-value >0.05: Non-significant; P-value <0.05: Significant (*); P-value< 0.01: highly significant (**)
P2=IR group VS IFR group, P3=FR group VS IFR group.

Table 4: ED length of stay (EDLOS) and actual glucose reduction (AGR) among the study groups.

ED LOS (hrs.)	Mean ±SD	2.52 ± 0.82	1.98 ± 0.94	1.61 ± 0.70	P 0.000 ** P1 0.000 ** P2 0.000 ** P3 0.000 **
	Range	0.75 – 4.5	0.5 – 7	0.33 – 4	
AGR (mg/dl)	Mean ±SD	135.61 ± 57.95	115.14 ± 55.40	232.87± 86.27	P 0.000 ** P1 0.026 * P2 0.000 ** P3 0.000 **
	Range	-350 – -36	-323 – 43	-467 – -41	

P-value >0.05: Non-significant; P-value <0.05: Significant (*); P-value< 0.01: highly significant (**).
One Way ANOVA test followed by post hoc test
P1=IR group VS FR group, P2=IR group VS IFR group, P3= FR group VS IFR group.

Table 5: Correlation between EDLOS & actual glucose reduction (AGR) and other parameters in IR group.

	r	P-value	r	P-value
Insulin dose (unit)	0.365	0.000 **	-0.488	0.000**
Age	-0.171	0.063	0.009	0.925
Duration of DM (Years)	0.079	0.392	-0.188	0.040*
ED LOS (hrs)	-	-	-0.517	0.000**
AGR (mg/dl)	-0.517	0.000**	-	-

P-value >0.05: Non-significant; P-value <0.05: Significant (*); P-value< 0.01: highly significant (**). DM: Diabetes Miletus, EDLOS: Emergency department length of stay, AGR: Actual glucose reduction.

Table 6: Relation between EDLOS & the most common causes of hyperglycemia in IR group.

	Mean ±S D	Range		
Missed dose	2.56 ± 0.8	0.75 – 4	-0.586	0.559
Stress	1.78 ± 0.65	1 – 3	3.467	0.001**
UTI	2.61 ± 0.97	1 – 4.5	-0.403	0.687

P-value >0.05: Non-significant; P-value <0.05: Significant (*); P-value< 0.01: highly significant (**). Independent T-test
EDLOS: Emergency department length of stay, UTI: urinary tract infection.

Table 7: Correlation between EDLOS & AGR and other parameters in FR group.

	EDLOS (hrs)		AGR (mg/dl)	
	r	P-value	r	P-value
Fluid dose (cc)	0.644	0.000**	-0.342	0.000**
Age	-0.100	0.282	*0.213*	**0.020*
Duration of DM (Years)	0.018	0.846	0.118	0.204
EDLOS (hrs)	--	--	-0.435	0.000**
AGR (mg/dl)	-0.435	0.000**	--	--

P-value >0.05: Non-significant; P-value <0.05: Significant (*); P-value< 0.01: highly significant (**).
EDLOS: Emergency department length of stay, AGR: Actual glucose reduction.

Table 8: Correlation between EDLOS, AGR and other parameters in IFR group.

	ED LOS ()		AGR(mg/dl)	
	r	P-value	r	P-value
Insulin dose (I.U)	0.332	0.000**	- 0.044	0.579
Fluid dose (cc)	0.481	0.000**	-0.319	0.008**
Age	0.012	0.878	-0.047	0.547
Duration of DM (Years)	-0.062	0.430	0.108	0.170
ED LOS (hrs)	--	--	-0.578	0.000**
AGR (mg/dl)	-0578	0.000**	--	--

P-value >0.05: Non-significant; P-value <0.05: Significant (*); P-value< 0.01: highly significant (**).
AGR: Actual glucose reduction, EDLOS: Emergency department length of stay.
DM: Diabetes Milletus.

4. Discussion

Hyperglycemia accounts for up to 20% of patients visiting the emergency department (ED) [6.]
The aim of the study was to determine the association between different modalities of management emergency hyperglycemia with length of stay at emergency department (ED LOS) and actual glucose reduction (AGR).
The most common causes of emergency hyperglycemia in our study were missed dose (35%), stress (27%), and UTI (18.2%).
[2] in a multicenter retrospective study to identify risk factors predicting unplanned recurrent ED visits due to hyperglycemia, reported that the most common precipitating causes of hyperglycemia were lack of medication or insulin adherence (35.8%), persistent poor control or underdosing of medication or insulin (28.9%), and infections from various sources (21.7%).

Poor medication adherence in T2D is well documented, highly prevalent and is linked to insufficient glycemic control, increased morbidity and mortality and higher outpatient and emergency department expenses. Poor drug adherence is associated with non-patient factors (e.g., absence of integrated treatment in many health care systems and clinical inertia among medical staff), demographics (e.g., younger, lower education level , lower income level), critical perception of medical institutions, patient's perception of their medications (e.g., perceived ineffectiveness of treatment), and the burden patients feel in receiving and taking their medications (e.g., complexity of treatment, copayments , hypoglycemia) [7].

Insulin therapy reduces the hepatic glucose production, increases peripheral glucose utilization and inhibits lipolysis, ketogenesis and glucagon secretion, resulting in lower plasma glucose levels and reduced ketoacidosis [8].

Intravenous (IV) fluid therapy expands intravascular volume, improves renal perfusion and reduces peripheral insulin resistance by reducing levels of counter-regulatory hormones; the end result is a lower blood glucose level [8].

Regarding EDLOS (the duration from the time of arrival to the emergency department to the time of discharge from it) and AGR (attendance blood glucose level –discharging blood glucose level) among three groups with different modalities of management of emergency hyperglycemia:

The current study shows that EDLOS was significantly lower in IFR group (1.61 ± 0.70 hr) compared to FR group (1.98 ± 0.94 hr) and IR group (2.52 ± 0.82 hr). EDLOS was significantly lower in FR group compared to IR group.

IR group was significantly more effective for glucose reduction than FR group with higher EDLOS that can be reduced through discharge stable patient early before reach target blood glucose.

Regarding insulin and fluid doses used in the current study, there was no statistically significant difference between IR group, and IFR group regarding insulin dose & there was no statistically significant difference between FR group and IFR group regarding fluid dose.

IV insulin combined with IV fluid in the IFR group was not effective at reducing the dose of either but was effective in shortening EDLOS and elevating AGR in the current study.

Although no studies have specifically looked at the comparison between different modalities for emergency hyperglycemia regarding ED length of stay and AGR and treatment approaches for hyperglycemia in the ED vary from study to study, previous studies have investigated the effect on lowering blood glucose levels and length of stay the ED.

[1] retrospectively conducted a chart review analysis to identify the relationship between insulin and intravenous fluids and ED glucose reduction & ED LOS and found that mean EDLOS was approximately 4.7 hr & mean AGR was approximately 196 mg /dl in IR group and mean EDLOS was approximately 4.6 hr & mean AGR was approximately 180 mg /dl in FR group. The study provides evidence that insulin and intravenous fluids are moderately effective and prolong ED LOS, it is possible that efforts to reduce blood glucose levels in the ED in otherwise healthy patients are not worth it as well as demonstrating that glucose reduction is a function of insulin and intravenous fluid will vary significantly among patients.

[9] found that 10 units of SC insulin were associated with a mean glucose reduction of 33 mg / dl and no change of time that blood glucose was associated with an emergency department stay. The researchers used SC insulin as part every 2 hours to lower blood glucose levels to levels achieved at discharge from the emergency department. Although this literature is limited, it appears to indicate that the emergent use of insulin in the emergency department for managing non-urgent hyperglycemia provides a little clinical benefit. Nevertheless, none of these studies have investigated the use of

intravenous regular insulin to evaluate whether a fast-acting treatment approach provides benefit or harm.

Furthermore, [10] carried out a retrospective observational study to assess the impact of regular insulin on blood glucose reduction and length of stay in the emergency department in 450 patients who received intravenous regular insulin (those who visited the ED with non-urgent hyperglycemia) .They came to the conclusion that patients received more than five units of intravenous regular insulin to treat isolated hyperglycemia in the ED experienced a moderate drop in blood glucose levels and found no difference in ED length of stay when compared to patients who received < or = 5 units. However, the use of intravenous insulin for this reason led to hypokalemia in 7.9 % of cases.

In a randomized controlled trial,[11] compared blood glucose control in patients with hyperglycemia who were discharged from the emergency department (ED) between "loose" (<600 mg/dL) and moderate" (<350 mg/dL).The degree of glycemic control didn't significantly alter the results after 7 days ; however , patients whose blood glucose was reduced to less than 350 mg/dL spent an additional 29 minutes in the emergency department.

Regarding factors affecting EDLOS and AGR among three groups in the current observation study:

EDLOS was significantly correlated positively with insulin dose and negatively with AGR and there was a significant negative correlation between AGR and insulin dose in IR group, so no benefit was taken from stay in ED after SC insulin even with higher doses of insulin in management of emergency hyperglycemia.

Contrary to our observation,[1] reported that administration of insulin was not associated with a change in EDLOS.

A retrospective analysis by [12] of 161 patients receiving SC rapid acting insulin and revealed no differences in the degree of glycemic correction and duration of hospital stay between complete and partial correction.

There was a significant negative correlation between AGR and duration of DM in IR group and this can be related to insulin resistance that developed over time & microvascular complication that decreased the effectiveness of insulin.

In the current study, EDLOS was a significantly lower time in patients with stress as a cause of emergency hyperglycemia in comparison to other common causes in IR group (1.78 ± 0.65) and in FR group (1.84 ± 0.75).

Patients with stress as a cause of emergency hyperglycemia benefit from the use of subcutaneous insulin or IV fluid with lower EDLOS.

There was no significant correlation between AGR and most common causes of emergency hyperglycemia in the three groups, so causes of emergency hyperglycemia have no role in AGR.

EDLOS was significantly correlated positively with fluid dose and negatively with AGR and there was a significant negative correlation between AGR and fluid dose in FR group, therefore administration of intravenous fluids to ED patients with hyperglycemia should probably not be considered critical antihyperglycemic therapy. Instead, it would be prudent to reserve intravenous fluid administration for hypovolemic patients.

Contrary to our observation, [1] reported that administration of IV fluids had a modest glucose reduction (27 mg /dl per liter of fluids) and was associated with 45-min increase in ED LOS.

[13] conducted a prospective non blinded RCT on 48 subjects Comparing the efficacy and safety of oral versus iv fluids for reducing blood glucose in patients with hyperglycemia in the ED and found that both were equal and modest in reducing blood glucose approximately (39 mg /dl per liter of oral or iv fluids).

There was a significant positive correlation between AGR and age in FR group and this can be explained by these old patients who were hypovolemic so IV fluids were effective with them in increasing AGR.

There was a significant positive correlation between EDLOS and insulin dose & fluid dose. There was a significant negative correlation between AGR & fluid dose and EDLOD in IFR group .so no benefit was obtained from administration of higher doses of IV fluids in IFR group and this may be affected by multiple factors related to this group.

5. Conclusion

1. IR group was significantly more effective for glucose reduction than FR group with higher EDLOS that can be reduced through discharge stable patient early before reach target blood glucose.
2. IV insulin combined with IV fluid in the IFR group was not effective at reducing the dose of either but was effective in shortening EDLOS and elevating AGR in the current study.
3. No benefit was taken from stay in ED after SC insulin even with higher doses of insulin in management of emergency hyperglycemia.
4. Patients with stress as a cause of emergency hyperglycemia benefit from the use of subcutaneous insulin or IV fluid with lower EDLOS.
5. Administration of intravenous fluids to ED patients with hyperglycemia should probably not be considered critical antihyperglycemic therapy. Instead, it would be prudent to reserve intravenous fluid administration to hypovolemic patients.

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