Glucose Monitoring in Critically Ill: Is Absence of "Stress Hyperglycemia" a Cause for Concern?

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Abstract

Aim: To study variations in glucose levels over 48 hours in critically ill patients by capillary blood glucose done on glucometer and compare the same in different categories of patients based on various diseases, as well as their correlation with sepsis and diabetes mellitus.

To compare the same results in a subset of patients with the readings of continuous glucose monitoring.

Material and Methods: We studied 50 critically-ill patients (Age≥18 years), admitted in medical ICU (on mechanical ventilation/ionotropic supports/in sepsis) in a teaching hospital in semi-urban Maharashtra.

Critical illness was defined as any physiological instability leading to disability or death within minutes or hours, based on neurological assessment, respiratory system involvement and cardiovascular involvement.

Capillary blood sugar levels were done 4 hourly using 'NIPRO' glucometer. Site was rotated. 5 patients had simultaneous continuous glucose monitoring, using I-Pro bio-sensor.

Results: Total 50 patients were included in the study. The data was collected and tabulated. Analysis showed that all critically ill patients showed some higher than normal recordings of blood sugar, which till now has been attributed to 'stress-hyperglycaemia'. This may be absent or blunted in sepsis. In the critically-ill patients with primary involvement of gastrointestinal tract, meal-unrelated fluctuations were seen. In critically-ill patients with CNS and CVS involvement, lowest BSL recordings were seen (meal unrelated) at 2 am.

Conclusion: We concluded that that patients who develop hypoglycaemia may have an equally bad prognosis or even worse than those who develop hyperglycaemia during the period of critical illness. CGM devices record tissue glucose levels continuously, and may be useful as a 'tissue hypoglycaemia' alert.

Introduction

The critically ill patient is extensively monitored. Heart rate, blood pressure, SpO_2 and ECG is routine in level 1 ICU. ABG and electrolytes are monitored for patients on ventilator. Blood glucose however is monitored only in diabetics, especially in DKA. Mild hyperglycaemia encountered in non-diabetic patients is labelled as "stress hyperglycaemia" and left alone, which often comes to normal in 24-48 hours. Studies on treatment of "stress hyperglycaemia" with short acting insulins did not show any additional benefits. The most common complication of critical illness is sepsis, leading to multi-organ failure and death. Glucose is the most important carbohydrate fuel in the body. In the fed state, the majority of circulating glucose comes from the diet; in the fasting state, gluconeogenesis and glycogenolysis maintain glucose concentrations.[1] The latter is true in most of the critically ill

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Received: 09.01.2018; Accepted: 11.01.2019

Table 1: Glucose monitoring

Day	Time		Average BSL	
		N	Mean	SD
1	6 am	50	153.14	84.521
1	10 am	50	153.70	71.435
2	2 pm	50	160.22	86. 226
1	6 pm	50	150.92	55.676
1	10 pm	50	159.50	78.247
1	2 am	50	150.30	65.272
2	6 am	50	153.52	70.471
2	10 am	50	155.24	75.287
2	2 pm	50	161.78	76.927
2	6 pm	50	154.82	65.178
2	10 pm	50	163.32	70.524
2	2 am	50	158.06	74.253

F value: 0. 295; P value: 0.983

patients. Glucose can be monitored as venous blood glucose, capillary blood glucose by glucometer, and continuous tissue glucose monitoring. While venous blood glucose and capillary blood glucose are comparable, a lag period of approximately 1-2 hours is seen with tissue glucose. But it is tissue glucose levels which form the internal milieu of organs, where cellular metabolism takes place. In Mammalian cells, glucose provides primary source of energy for brain as well as renal medulla, and is the sole provider of energy for red blood cells and retina. Total consumption of glucose in a 70 kg person is 160g, the brain uses 120g out of this.[2] In the critically ill patient, "stress hyperglycaemia" may be the body's safeguard against 'hypoglycaemia' and a blunted response should be an indication to monitor glucose levels.

Aims and Objectives

To study variations in glucose levels over 48 hours in critically ill patients by capillary blood glucose done on glucometer.

To compare the blood glucose levels over 48 hours in

Disease wise classification of patients

Patients with and without sepsis

Diabetics and non-diabetics

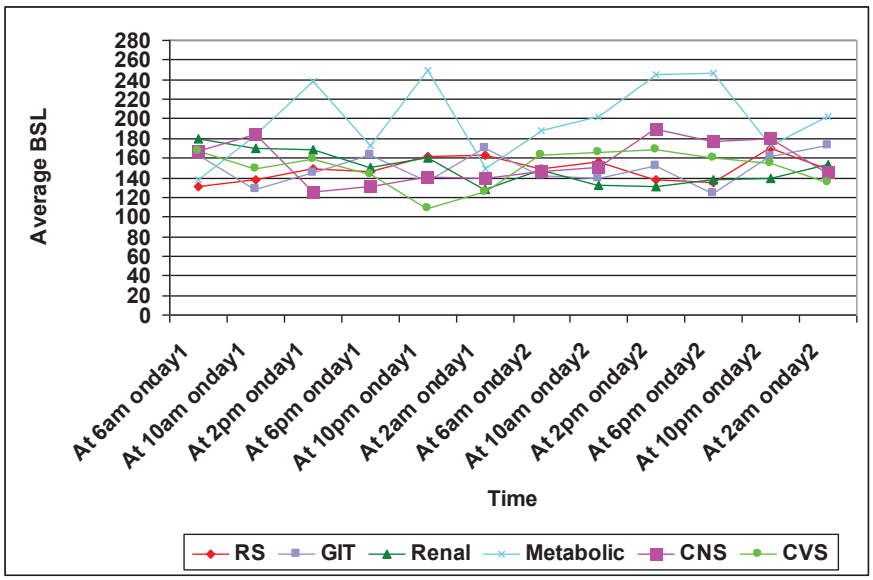
Compare glucometer evaluation and continuous glucose monitoring graphs in a small subset of patients

Materials and Methods

50 critically ill patients on admission to Medical intensive care unit of a teaching hospital in semi-urban Maharashtra were serially included in the study. Capillary blood glucose was measured 4 hourly for a duration of 48 hours using NIPRO glucometer. 5 patients had simultaneous continuous glucose monitoring, using I-Pro bio-sensor.

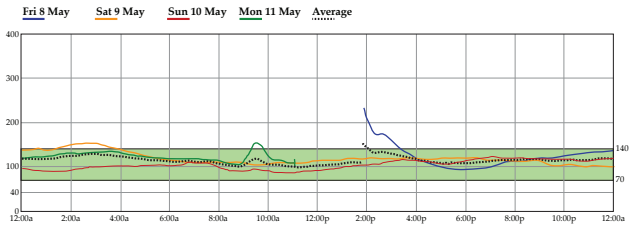
Data was recorded in proforma.

Statistical analysis was done using Microsoft excel and Epi-info software. The frequency distribution and graph were prepared for the variables. The categorical variables were assessed using Pearson chi-square. Mantel Hanzel Odds Ratio (OR) and corresponding 95% Confidence Interval (CI) were calculated for dichotomous variables.



BSL readings on CGM with those by finger-prick method in a case of fulminant hepatitis

Patient 4 –**Non Diabetic** ::Fulminant Hepatitis



BLOOD GLUCOSE LEVELS (Finger – Prick Method)

DAY TIME	Day 1	Day 2	Day 3	Day 4
12am		150	133	140
6am		107	105	104
12pm		100	100	132
6pm	100	110	92	

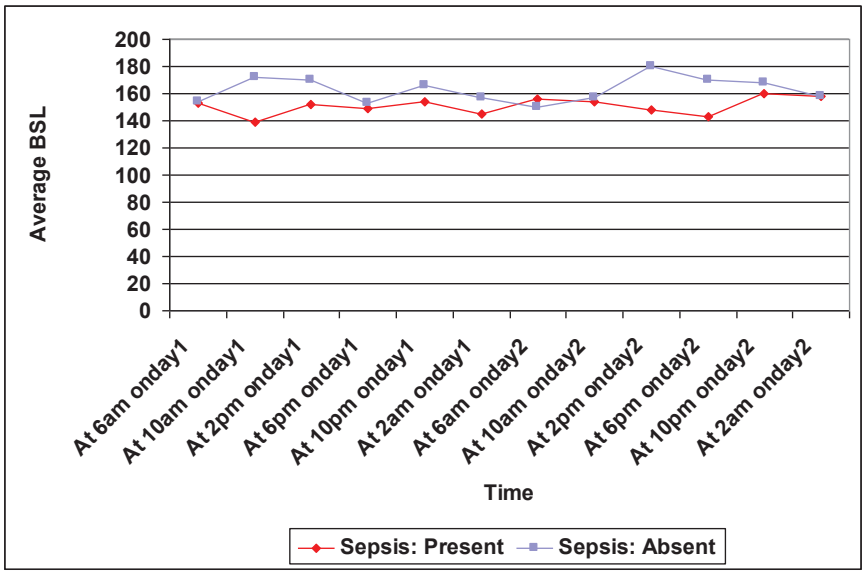
Fig. 1: Line diagram comparing average BSL over 48 hours according to type of diseases in study group

Results

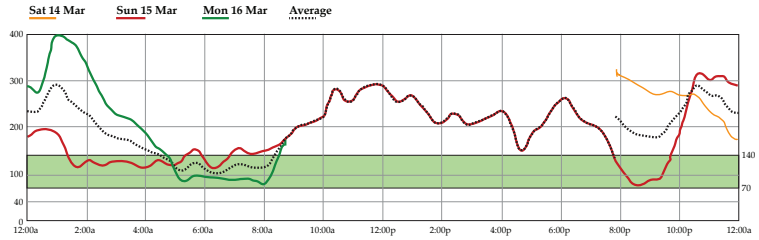
Our study included critically ill patients aged above 18 years, maximum being in 40-60 years age group. 56% were males, 44% females. In our study, average capillary BSL of critically - ill patients (time and day matched) ranged between 150 - 163 mg/dl, a variation of only 13 mg%, suggestive of 'stress-hyperglycaemia'. On graphic representation, the highest readings were at 2 pm and 10 pm, corresponding to post prandial blood sugar.

On segregating patients according to their primary system involvement, different patterns emerged. Gastro-intestinal patients showed maximum (meal-unrelated) fluctuations, while in patients with primarily renal involvement, lowest average was 128 (at 2 am) and highest 180 (at 6 am).

Patients with CNS critical-illness, mostly strokes, showed a low of 125 (at 2 pm, day 1) and a high of 190 (at 2 pm on day 2), indicating a time



Patient 5 –**Non Diabetic** : Sepsis



BLOOD GLUCOSE LEVELS (Finger – Prick Method)

DAY TIME	Day 1	Day 2	Day 3	Day 4
12 am		377	90	112
6 am		70	110	100
12 pm		106	116	118
6 pm	84	100	94	

Fig. 2 : Line diagram showing comparison of average BSL over 48 hours in sepsis/no sepsis patients in study group, followed by comparison of graph showing BSL readings on CGM with those by finger-prick method in a case of sepsis

delay for development of 'stress-hyperglycaemia), and low sugars in acute phase.

Patients with CVS critical illness also showed a low sugar level of 125 (at 2 am), and a high sugar level of 170 (at 2 pm). The dip at night may be significant.

In the Sepsis versus non-sepsis analysis, patients with sepsis had BSL ranging between 140-160 mg/dL, while the non-sepsis group had BSL between 150-180 mg/dL. This may point towards a 'blunted stress-hyperglycaemia' response in sepsis, and 'tissue hypoglycaemia' as a possibility.

Continuous glucose monitoring done in only 5 patients simultaneously, due to cost restraints, showed marked hyperglycaemia in 3 patients who were diabetic, but showed lower sugars in patient of fulminant hepatitis and erratic high and low in patient with sepsis; However, the low and high sugar levels did correspond in the 2 methods of estimation, albeit with a lag period in CGM.

Discussion

In studies by C. Dana, et al[3] and Xu Li, Ma Y, Chen, et al[4] bedside capillary glucose monitoring in intensive care was comparable with laboratory venous blood glucose.

Krinsley JS,[5] Falciglia M, et al,[6] Umpierrez GE,[7] Freire AX, et al[7] studied hyperglycaemia in heterogenous population of critically ill, and found "admission diagnosis" and "admission hyperglycaemia" to be risk factors.

Egi M, Bellomo R, et al[8] and Christiansen C, Toft P, et al[9] studied hyperglycaemia, both acute and chronic in diabetics and non-diabetics, while Paul E. Merik, Rilando Bellomo[10] felt "stress hyperglycemia is an essential survival response".

In a study by Suleiman M, Hammerman H et al,[11,12] impaired glucose metabolism and fasting glucose emerged an independent risk factor in patients with acute Myocardial Infarction.

Waeschle RM, et al,[13] Ellger Bet, et al,[14] Hiroyuki Hirasawa et al[15] studied glucose metabolism in sepsis and associated uncontrolled hyperglycaemia with increased mortality. However Tiruvoipati R, et al[16] felt "stress hyperglycaemia may not be harmful in critically ill patients with sepsis."

The Metabolic group, mostly diabetics, showed hyperglycaemia as expected, and were on treatment with insulin. Stegenga ME, et al[17] felt "Diabetes does not alter mortality or homeostatic and inflammatory responses in patients with severe sepsis."

Significant hypoglycaemia was not seen in any of our patients.

Egi M, Bellomo R, et al,[18] The NICE –SUGAR study,[19] Hermanides J, et al[20] studying effect of Hypoglycaemia, concluded that hypoglycaemia does increase mortality in Critically ill.

Roosmarijn TM, Jan Hendrik Leopold et al,[21] Wedong ZHU, et al,[22] in their studies with Continuous Glucose monitoring, had mixed opinions regarding efficacy.

Whereas Carol Lorencio, Yenny Leaf et al[23] felt there is better accuracy in real-time Continuous Glucose Monitoring in patients with Septic Shock.

Conclusions

A majority of our patients showed borderline hyperglycaemia, probably 'stress-hyperglycaemia'.

On segregating patients according to primary system affected, fluctuating and 'meal-unrelated' hyperglycaemia emerged in patients with gastro-intestinal disease, most marked in CGM records of patient with fulminant hepatitis. Sepsis patients showed overall lower average glucose levels than in those without sepsis, as also seen in CGM graph.

Limitations of Study

Small sample size, CGM could not be done in every patient due to costs.

Clinical Implications

Critically ill patients may have fluctuating glucose levels, depending upon the primary system or organ involvement. In sepsis, there may be 'blunting of the stress-hyperglycaemia' response, making patients prone to 'hypoglycaemia' and increased mortality. Continuous Glucose monitoring in sepsis gives an idea of overall glucose trend, and can act as a 'hypoglycaemia alert'.

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