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Original Contribution

Blood sugar changes and hospital mortality in multiple trauma

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ABSTRACT

Objectives: Hyperglycemia with unknown mechanism plays a predictive role in determining the prognosis of multiple trauma patients. The exact time of blood sugar measurement and the role of blood sugar changes in the monitoring of these patients have not been well established.
Methods: This follow-up study was done on multiple trauma patients (>18 years) with an Injury Severity Scores (ISS) > 16. These patients didn't have any history of diabetes, underlying disease, or drug or alcohol use. Data collection was done by the questionnaire (checklist), and the patients were followed by the medical records. Cox regression was used to measure the effect of independent variables on the patients' hospital mortality.
Results: Of a total of 963 patients, 280 patients were enrolled. Of those, 202 were male (72.1%) and 78 were female (27.9%). Hospital mortality was 18 (6.4%). Cox regression analysis suggested that those who had high blood sugar 3 h after admission had higher hospital mortality ($P = 0.04$). Changes in blood sugar, ΔBS (BS 3 h after admission – BS on admission), in these patients was also significantly correlated with hospital mortality ($P < 0.001$). The multivariate model using the backward conditional method showed that ΔBS ($P < 0.001$), international normalized ratio (INR) ($P < 0.001$), and heart rate ($P = 0.036$) were significantly correlated with hospital mortality.
Conclusions: In multiple trauma patients, blood sugar changes in the early hours of admission to the emergency department may help predict hospital mortality, but further studies are needed. Blood sugar monitoring in these patients during this time frame may be helpful in predicting these patients' outcomes. In addition, coagulopathy and tachycardia were significantly associated with hospital mortality.

1. Introduction

Multiple trauma refers to life-threatening injuries in single or multiple organ(s), defined as the severity of injury >16 in the Injury Severity Score (ISS). Multiple trauma is one of the major and common causes of death each year, leading to the deaths of 8.5 million people in the world. This issue has become a serious health problem in developing countries [1-3]. Given that about 80% of deaths occur in the first four hours, rapid diagnosis and proper management of these patients are very important. Hence, the outcome determination for these patients is considered an important part of trauma care [2,3]. Trauma scoring systems, anatomically or physiologically or combined, have been designed to predict multiple trauma patients' outcomes [4-7]; however, given the complexity of these systems, laboratory tests may provide a proper predictor for mortality [3].

Hyperglycemia after trauma (stress-induced hyperglycemia) is one of these laboratory abnormalities. Patients who refer after trauma with hyperglycemia, or critically ill patients, have a poor prognosis. This hyperglycemia can even be a predictor of hemorrhagic shock in these patients. However, in various studies, paradoxical results for the prognostic effect of admission hyperglycemia have been reported. The timing of measurement of blood sugar seems to play an important role in determining its prognostic effect in these patients [8-14].

The aim of this study was to investigate blood sugar (BS) levels in multiple trauma patients on admission, 3 h after admission (BS 3), and the difference between them (ΔBS), and their relationship with hospital mortality. Also, this study investigates the role of international normalized ratio (INR), serum lactate level, base excess (BE), *the ISS,* and *revised trauma score (RTS)* for the prediction of hospital mortality in these patients.

2. Methods

This follow-up study was carried out on patients with multiple trauma that were referred to Bahonar academic Hospital, *Level II Trauma*

Abbreviations: BE, base excess; BS, blood sugar; BS 0, blood sugar on admission; BS 3, blood sugar 3 h after admission; ΔBS, BS 3 h after admission – BS on admission; DBP, diastolic blood pressure; HR, heart rate; Hb, hemoglobin; HCT, hematocrit; INR, international normalized ratio; SBP, systolic blood pressure; ISS, injury severity score; RTS, revised trauma score.

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Center, in southeastern Iran. Multiple trauma patients with ISS > 16 and older than 18 years from 1 September 2015 to 1 September 2016 were enrolled in this study. Patients referred after an hour with a history of chronic lung, kidney, heart, or liver diseases or diabetes, anticoagulant medication consumption, drug or alcohol intoxication, or shock (except hemorrhagic shock) were excluded from the study. After evaluating patients in accordance with advanced trauma life support (ATLS) guidelines, up to 20 min after arrival blood samples were sent to the lab. BS on admission, BS 3 h after admission, ΔBS, INR, serum lactate, and arterial blood gas (ABG) for evaluating base excess (BE) were measured. Also, according to the pre-set questionnaire, age, sex, vital signs, *ISS*, and *RTS* were calculated and recorded for all patients. Before completing the questionnaire, informed consent was taken orally from patients or their relatives. Finally, hospital mortality rate as an outcome for these patients was investigated by using medical records. Cox regression was used to analyze the effect of independent variables on the patients' outcomes. To assess the Proportional Hazard (PH) assumption, the time interaction test was applied. We selected variables with univariate *P*-value < 0.05 to offer them to the multifactorial model. However, because of the low number of mortality events and multicollinearity between independent variables, we only constructed the multifactorial model using expert knowledge. One of the aims of this study was to explore the predictive ability of ΔBS in our multifactorial model; we only adjusted the effect of four established risk factors including heart rate, hematocrit, INR, and BE. Statistical analysis was performed by SPSS 20 software and using survival analysis.

3. Results

A total of 963 trauma patients were admitted within one year. Of them, 683 patients were excluded from the study and 280 were enrolled (Fig. 1). A total of 18 patients (6.4%) died during hospitalization (Table 1). No departure from the PH assumption was seen. Using the Cox proportional hazard regression model, subjects who had high blood sugar levels on admission did not have higher mortality than patients with normal glucose at baseline, but blood sugar 3 h after admission and ΔBS (BS 3 h after admission – BS on admission) was significantly correlated with hospital mortality. In particular, an increase of one unit in ΔBS was associated with a 7% increase in the hazard of mortality. In addition, one unit increase in blood sugar 3 h after admission corresponded to a 5% increase in the risk of death. In the univariate model, increased heart rate, INR, lactate, and ISS had aggressive effects, and high systolic and diastolic blood pressure, hematocrit, BE, and RTS had a protective effect on hospital mortality (Table 2). In the final model and multivariate analysis by using the backward conditional method, only the variables ΔBS ($P < 0.001$), INR ($P < 0.001$), and heart rate ($P = 0.036$) had a significant relationship with hospital mortality (Table 3).

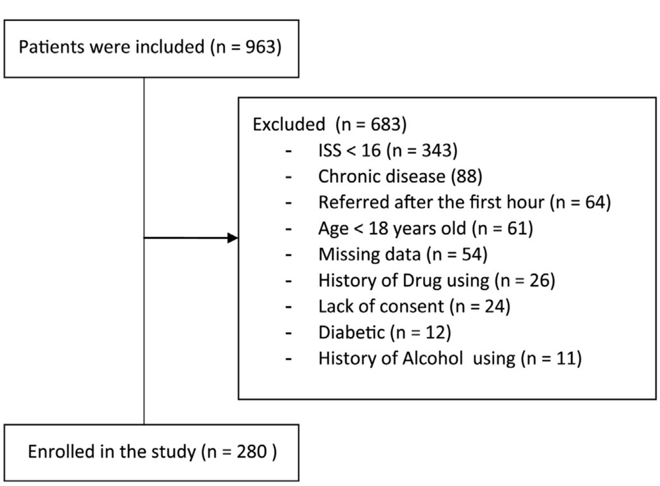

Fig. 1. Flow chart showing enrollment of patients.

Table 1
Patients' characteristics

Variables	Number (%)
Gender	
Male	202 (72.1)
Female	78 (27.9)
Age(y),Mean ± SD	33.93 ± 12.54
ISS,Mean ± SD	26.47 ± 8.49
RTS,Mean ± SD	7.42 ± 0.95
Hospital Mortality	18 (6.4)

As a complementary analysis, a decision tree was constructed. Here, all independent variables were offered to the tree. These models are attractive as they provide pictorial evidence that assists patient management. The decision tree demonstrated that for patients with a ΔBS higher than 32.5, 93.8% had hospital mortality (15 out of 16). Among patients with a ΔBS lower than 32.5, only 3 out of 264 cases experienced death, corresponded to mortality rate of 1%.

3.1. Limitations

There are several limitations in this study. One of the limitations is the fact that it is a unicenter study. Some patients or their relatives did not consent to enrollment, or some patients were referred with delay. Unfortunately, in some cases, there is missing data. Also, some tests—including lactate—were not measured during some hours of the day. This study was limited to patients with multiple trauma >18 years with an ISS > 16 and without any history of diabetes, underlying disease, or drug or alcohol use, which made it impossible to investigate the other patients.

4. Discussion

In this follow-up study on multiple trauma patients admitted to the emergency department, patients with higher difference between blood sugar 3 h after admission and on admission (ΔBS) were found to have higher hospital mortality. Thus, blood sugar levels on admission may not play a predictive role in the mortality of patients, but delay in measurement of blood sugar or blood sugar changes may play a predictive role. Also, other parameters such as prolonged INR and tachycardia can be helpful in predicting hospital mortality in multiple trauma patients.

In multiple trauma patients, stress-induced hyperglycemia could be helpful as an independent predictive of mortality. Hyperglycemia can result from the release of catecholamines and the physiological stress response to trauma [8]. Also, hepatic gluconeogenesis is activated after trauma and glucose metabolism is under the influence of counter-regulatory hormonal responses and signals from the nervous system.

Table 2
Univariate Cox regression analysis and their association with mortality

Variables	Mortality (Mean ± SD)		OR (95% CI)	*P* value
	NO	Yes		
HR(counts/min)	90.7 ± 16.88	132.8 ± 15.07	1.03 (1,1.05)	0.05
SBP(mm Hg)	121.02 ± 14.99	97.22 ± 18.23	0.97 (0.94, 0.99)	0.02
DBP(mm Hg)	72.78 ± 11.14	59.89 ± 14.03	0.96 (0.92, 0.99)	0.02
Hb(g/dl)	12.91 ± 1.72	10.25 ± 2.02	0.77 (0.61, 0.97)	0.03
HCT(%)	38.84 ± 4.76	32.69 ± 4.70	0.88 (0.78, 0.97)	0.02
BS 0 (mg/dl)	101.4 ± 21.67	145.3 ± 17.02	0.99 (0.96, 1.03)	0.81
BS 3 (mg/dl)	108.86 ± 23.48	183.83 ± 11.67	1.05 (1.02, 1.09)	0.04
ΔBS	7.44 ± 6.51	38.50 ± 11.39	1.07 (1.03, 1.11)	0.00
INR	1.09 ± 0.20	1.80 ± 1.55	2.24 (1.48, 3.38)	0.00
Lactate (mmol/lit)	22.63 ± 4.02	35.61 ± 6.7	1.12 (1.03, 1.21)	0.01
BE (mmol/lit)	−1.79 ± 3.38	−11.48 ± 4.37	0.87 (0.77, 0.99)	0.04
ISS	25.04 ± 6.60	47.22 ± 5.16	1.07 (0.99, 1.14)	0.06
RTS	7.61 ± 0.58	4.65 ± 1.03	0.38 (0.22, 0.61)	0.00

Table 3
Multivariate Cox regression analysis

Variable	Mortality	
	OR (95% CI)	*P* value
ΔBS	1.09 (1.03, 1.11)	0.001
INR	3.17 (1.48, 3.38)	0.001
HR	1.04 (1, 1.05)	0.036

Following this, an impaired glucose uptake in heart and skeletal muscles occurs, which is called "diabetes of injury" [15]. But there is controversy in estimating when blood sugar levels should be measured as a prognostic factor. One study has shown that blood sugar on admission is ineffective in prediction of mortality in emergency patients [14]. However, some studies have shown that the measurement of blood sugar on admission has been effective not only in determining mortality [16], but also in prediction of morbidity in trauma patients [17]. Even blood suger control is recommended to improve outcomes of these patients [11]. Laird et al. showed that early measurement of blood sugar during the first 24 to 48 h of admission was effective in determining mortality of trauma patients [18]. Wahl et al. showed that more severe hyperglycemia causes higher hospital mortality in these patients [13]. Egi et al. reported that mean blood sugar is effective in predicting mortality in critically ill patients [19]. Hence, there is controversy about the timing of blood sugar measurement to determine outcomes. Blood sugar measurement is a convenient, available, and cheap test, and monitoring changes in critically ill trauma patients can be helpful in determining hospital mortality. Therefore, blood sugar monitoring could be considered for patients with multiple trauma [16]. Given that most deaths occur in the early hours of admission, our study examines blood sugar changes on admission and 3 h after admission. It showed that measurement of blood sugar 3 h after admission and also ΔBS (the difference between blood sugar 3 h after admission and on admission) have a predictive effect on hospital mortality and introduce it as an independent risk factor.

Coaglupathy is common immediately after trauma. There is a relationship between impaired coagulation tests and mortality in these patients [20,21] due to adrenalin release in blood which increases endothelial damage and activates fibrinolysis [22]. Also the activation of protein c pathway appears to be involved in its release. Therefore, coagulopathy immediately after trauma may indicate critical conditions such as shock or need for blood transfusion, and can be helpful in determining these patients' outcomes [23]. Our study demonstrated a significant relationship between prolonged INR on admission and hospital mortality.

In multiple trauma patients, tachycardia may be an ominous sign. Tachycardia plays a considerable role in determining trauma patients' outcomes [24]. However, the absence of tachycardia cannot rule out a critical condition [25]. Viewing tachycardia in combination with the physiologic trauma score is helpful in determining trauma patients' outcomes [26]. This study indicates that patients with increased heart rate on admission have higher hospital mortality.

This study found a significant relationship in the univariate model between hypotension, decreased hematocrit, increased lactate, decreased BE, RTS, and increased ISS and hospital mortality, but this relationship was not significant in the multivariate model. Several reasons may account for these findings: according to this study sample size, the event was low and the correlation between variables was high, suggesting that the role of these variables in determining the mortality of patients may be very faint. In the other words, the role of ΔBS may be significant, and may diminish the role of other variables with which they have strong correlation. Therefore, another study is required with a larger sample size and the proper event in this respect.

5. Conclusions

Blood sugar measurement on admission in multiple trauma patients may be helpful in predicting their outcomes, but our study did not confirm this. ΔBS (difference between blood sugar 3 h after admission and on admission) can be a better indicator in determining outcomes for multiple trauma patients referred to the emergency department. We also found that coagulopathy and tachycardia are helpful in predicting hospital mortality. Further studies with larger sample sizes in this field are required.

Conflict of interest

None declared.

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