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Original Article

Surgery Section

Association between Hyperglycaemia with Neurological Outcomes Following Severe Head Trauma

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ABSTRACT

Introduction: Head Trauma (HT) is a major cause of death, disability and important public health problem. HT is also the main cause of hyperglycaemia that can increase mortality.

Aim: The aim of this study was to assess the correlation between hyperglycaemia with neurological outcomes following severe Traumatic Brain Injury (TBI).

Materials and Methods: This is a descriptive and correlation study that was carried out at the Imam Khomeini Hospital affiliated with Ilam University of Medical Sciences, Ilam, IR, during March 2014–March 2015 on patients with severe TBI. Data were collected from the patient records on mortality, Intensive Care Unit (ICU) length of stay, hospital length of stay, admission GCS score, Injury Severity Score (ISS), mechanical ventilation, Ventilation Associated Pneumonia (VAP) and Acute Respiratory Distress Syndrome (ARDS). Random Blood Sugar (RBS) level on admission was recorded. Patients with diabetes mellitus (to minimize the overlap between acute stress hyperglycaemia and diabetic hyperglycaemia) were excluded.

Results: About 34(40%) of patients were admitted with hyperglycaemia (RBS ≥ 200 mg/dl) over the study period. The mortality rate, length of ICU stay, hospital stay, ISS and VAP & ARDS in patients with RBS levels ≥ 200 mg was significantly higher than patients with RBS levels below ≤ 200mg ($p<0.05$, $p<0.001$). A significant correlation was found between RBS with GCS arrival, length of ICU stay, length of hospital stay, ISS, mechanical ventilation and VAP & ARDS ($p<0.05$, $p< 0.001$). RBS is a predicate factor for ISS ($p <0.05$, OR : 1.36), GCS ($p <0.001$, OR : 1.69), mechanical ventilation ($p< 0.05$, OR : 1.27), VAP & ARDS ($p <0.001$, OR : 1.68), length of ICU stay ($p <0.001$, OR : 1.87) and length of hospital stay ($p <0.05$, OR : 1.24).

Conclusion: Hyperglycaemia after severe TBI (RBS ≥ 200) is associated with poor outcome. It can be a predictive factor for mortality rate, ICU stay, GCS arrival, VAP & RDS, hospital stay and ISS. Management of hyperglycaemia with insulin protocol in cases with value >200mg/dl, is critical in improving the outcome of patients with TBI.

Keywords: Critical Care, Head injury, Icu, Serum glucose, Traumatic brain injury

INTRODUCTION

Head Trauma (HT) is a major source of death, disability and important public health problem in the world [1-6]. More than 2.4 million referred to hospitals or deaths annually are related to TBI [7]. In the USA, HT causes 290,000 hospital admissions, 51,000 deaths, and 80,000 permanently disabled survivors [8]. The mortality rate of head trauma is up to 20-35% [9] and the costs due to TBI annually are $76.5 billion in the USA [10]. However, injuries related to HT are the main cause of early deaths, conditions such as hypotension, hypoxia, increased intracranial pressure, and hyperglycaemia, can increase mortality. Thus, prevention and early treatment of these parameters that could lead to secondary injuries are considered to improve outcomes [11,12]. After severe TBI, stress due to catecholamine release can lead to increasing blood glucose levels. Hyperglycaemia is a stress response and a metabolic reflection in patients with TBI that in animal research has been associated with increased ischemic brain damage, oedema, septic complications, cell death and high mortality [13-18]. The decrease in blood glucose after intracerebral haemorrhage is associated with reduced risk of tissue oedema and cell death, which predict best results. High level of blood glucose is a predictor of early mortality and worse outcome in patients who have suffered a TBI [14]. Studies show that blood glucose levels more than 300 mg/dl is associated with death [9].

The association between hyperglycaemia and worse outcome in TBI patients are controversial. Some researchers believe that critically ill patients with hyperglycaemia generally have a low Glasgow Coma Scale (GCS) score, increased complications and poor outcome [15,17,19]. On the other hand, some authors disagree on the association of hyperglycaemia and poor outcome in TBI and believe that high blood glucose levels are transient and generally reflect a metabolic response after injury [19]. The aim of this study was to assess the association between hyperglycaemia with outcomes following severe head trauma.

MATERIAL AND METHODS

Study Design

This is a descriptive and correlation study that was carried out at the Imam Khomeini Hospital affiliated with Ilam University of Medical Sciences, Ilam, IR, during March 2014- March 2015. The statically population included all patients that due to severe head trauma, admitted in the ICU ward from March 2014 to March 2015. In this study we assessed the outcome of the neurological function after severe head trauma.

The inclusion criteria included: more than 18 years of age, Glasgow Coma Scale (GCS) score ≤ 8 within the first 48 hour of admission, not having other trauma such as internal haemorrhage (in the chest and abdominal), orthopaedic trauma or trauma to the chest. Patients with diabetes mellitus (to minimize the overlap between acute stress hyperglycaemia and diabetic hyperglycaemia) and absence of samples information were excluded. Diagnosis of diabetes mellitus was confirmed according to laboratory test include RBS and Hb A1c level.

We collected data on mortality, ICU length of stay, hospital length of stay, admission GCS score, ISS, age, requirement of mechanical ventilation and VAP & ARDS. RBS on admission was recorded. RBS levels were determined by laboratory test on the first 24 hour of admission. The patients were divided according to their admission RBS: ≤ 200 mg/dl or ≥ 200 mg/dl. Significant

hyperglycaemia was defined as a serum glucose concentration ≥200 mg/dl. Severity of injury was measured with the ISS which is an anatomic description of injury. It is a score from 0 to 75 where 75 are lethal, and a score above 15 indicates severe trauma [20].

This study is the result of clinical findings. After getting written permission (grant no: 2200/94/6909) in addition to coordinating with the hospital managers, all information was considered confidential and written informed consent was optioned from all patients or relative.

STATISTICAL ANALYSIS

All statistical analyses were performed using SPSS, version 16 (SPSS Inc, Chicago, IL, USA). Categorical data were expressed as percentages. Values were presented as mean ± SD. Independent t-test, Pearson correlation coefficient or Spearman rank order correlation test and logistic regression analyses were performed when appropriate. The p<0.05 was considered significant.

RESULTS

A total of 83 patients were included in the study. The mortality rate of the patients was 54.2%. About 34 (40 %) of patients were admitted with hyperglycaemia (RBS ≥ 200 mg/dl) over the study period. The baseline characteristic of patients are shown in [Table/Fig-1,2]. The mortality rate of 88.2% among patients with RBS levels ≥ 200 mg/dl was significantly higher than those patients with levels below 200mg/dl. The length of ICU stay (16.7 ± 11.8), hospital stay (22.5± 11.1), ISS (29.28± 3.52) and VAP & ARDS (19, 55.8%) in patients with RBS levels ≥ 200 mg was significantly higher than patients with RBS levels ≤ 200mg (p<0.05, p<0.001). The admission GCS in patients with RBS levels ≥ 200 mg/dl was significantly lower than other patients (p< 0.05) [Table/Fig-2]. According to univariate analysis, a significant correlation was found between RBS level with GCS arrival, length of ICU stay, length of hospital stay, ISS, mechanical ventilation and VAP & ARDS (p<0.05, p< 0.001) [Table/Fig-3].

The logistic regression analysis show that RBS is a predicate factor for ISS (p <0.05, OR: 1.36), GCS (p <0.001, OR: 1.69), mechanical ventilation (p< 0.05, OR : 1.27), VAP & ARDS (p <0.001, OR: 1.68), length of ICU stay (p <0.001, OR : 1.87) and, length of hospital stay (p <0.05, OR: 1.24). The Wald test shows that ICU stay, GCS arrival, VAP & RDS, mechanical ventilation, hospital stay ISS are the most important variables in prediction [Table/Fig-4].

DISCUSSION

Severe TBI defined as head injury associated with a GCS score of 3 to 8 at 6 h after injury or deterioration of GCS to 8 or less within 48 hour of injury and lasting for at least 6 hour is a leading cause of death and disability worldwide [21]. Studies indicate annually due to TBI about 1.5 million affected people die and millions receive emergency treatment [22-24]. Hyperglycaemia is more frequently observed in severe head trauma and in patients that suffered multiple traumas [19].

We have found that hyperglycaemia after severe TBI is associated with poor outcome. Several studies have demonstrated that admission hyperglycaemia were associated with adverse outcome [25-27]. Miller et al., found the impact of severity of brain trauma on blood sugar increasing rate [28]. Study with Laird et al., confirmed this result [29]. Studies showed that hyperglycaemia in admission were associated with severity of trauma and leads to increased mortality, hospital and ICU length of stay [25,30-33]. Some studies have shown that insulin in severely TBI patients lead to decreased mortality rate and ICU length of stay [34]. Young et al., found an association between admission hyperglycaemia and poor outcome at 18 day; 3 month and 1 year follow up of 59 adults after TBI. Lam et al., showed an association between admission glucose and initial GCS in 169 adults with severe TBI

Parameter	Survivors [n=45 (54.2%)]	Non Survivors [n=38 (45.8%)]
Age (year) (Mean ±SD)	33.7± 14.2	37.2± 16.7
Length of ICU stay (day) (Mean ±SD)	23.3± 15.9	11.7 ± 13.8
Length of hospital stay(day) (Mean ±SD)	29.4 ± 17.7	12.5± 14.1
Admission GCS, (Mean ±SD)	6 ± 2	4± 2
ISS (Mean ±SD)	25.43± 6.38	29.28± 7.52
Serum glucose (Mean ±SD)	137.38± 61.46	280. 57± 75.49
Mechanical ventilation (n %)	41 (91.1%)	38 (100%)
VAP & ARDS (n %)	16 (35.5%)	7 (18.4%)

[Table /Fig-1]: Clinical outcome according to patient's mortality

Parameter	Glucose ≤ 200mg/dl (n= 49)	Glucose ≥ 200mg/dl (n=34)	p-value
Age (year) (Mean ±SD)	31.4± 11.2	32.2± 11.4	0.25*
Length of ICU stay (day) (Mean ±SD)	11.3± 13.9	16.7 ± 11.8	0.00***
Length of hospital stay(day) (Mean ±SD)	16.4 ± 13.7	22.5± 11.1	0.00***
Admission GCS, (Mean ±SD)	7 ± 1	5± 3	0.03**
ISS (Mean ±SD)	21.43± 4.38	29.28± 3.52	0.01**
Mechanical ventilation (n %)	47 (95.9%)	34 (100%)	0.08*
VAP & ARDS (n %)	7 (14.2%)	19 (55.8%)	0.00***
Mortality Rate	15 (30.6%)	30 (88.2%)	0.00***

[Table/ Fig-2]: Clinical outcome according to glucose level.
*p> 0.05, **p<0.05, ***p<0.001

Parameter	Admission GCS	ISS	ICU stay	Hospital Stay	Mechanical Ventilation	VAP& ARDS
Serum glucose (RBS≥ 200mg/dl)	r= - 0.75 p=0.00	r=0.47 p=0.03	r= 0.52 p=0.00	r= 0.34 p=0.00	r= 0.41 p=0.01	r= 0.37 p=0.04

[Table/Fig 3]: Correlation between serum glucose with different variables.
*p> 0.05, **p<0.05, ***p<0.001/

Parameter	Serum glucose(RBS≥ 200mg/dl)				
	B	SE	Wald	p	Odds Ratio
ISS	1.75	0.15	11.32	0.03	1.36
GCS	-1.54	0.12	21.17	0.00	1.69
Mechanical ventilation	1.68	0.13	14.47	0.04	1.27
VAP & ARDS	1.79	0.8	18.43	0.00	1.68
ICU stay	1.94	0.23	23.17	0.00	1.87
Hospital stay	1.27	0.17	13.18	0.03	1.24

[Table/Fig 4]: Logistic regression analysis between serum glucose with different variables
*p> 0.05, **p<0.05, ***p<0.001

[27]. Marton in children found that hyperglycaemia within the first 24 hour of TBI was highly associated with poor outcome [35]. Rovlias et al., in the study on 267 patients with moderate or severe TBI demonstrated that the levels of hyperglycaemia were reliable predictors of severity and neurological damage [36].

Normalization of blood glucose using an intensive insulin protocol improved clinical outcomes, and, decreased mortality by 42% [32]. Our results showed association between hyperglycaemia and VAP & ARDS. Sung found that admission hyperglycaemia is an independent predictor of infection in trauma patients [32] that is consistent with our study. On the other hand, Parish reported that admission hyperglycaemia was not associated with poor outcome in a small series of children [37].

In general, critical illness-induced hyperglycaemia can lead to increased prevalence of infections, increased inflammation; produce adverse effects via changes in immune function, changes in endothelium integrity, and threatening mitochondrial function

[27]. By inducing neurohormonal reactions, acute trauma leads to changes in carbohydrate, protein, and fat metabolism. With releasing special cytokines and body defense regulating hormones, trauma results in increased blood sugar level (hyperglycaemia), which significantly affects body function and treatment process. It seems that activation of the sympathoadrenal system (by hypothalamus and pituitary) is the major factor of increased blood sugar levels [30]. Systemic hyperglycaemia is harmful because it contributes to anaerobic metabolism in the brain following acute injury, resulting in brain tissue lactic acidosis and secondary neuronal injury [13].

Management of hyperglycaemia with insulin protocol is critical in the outcome of patients with TBI. In this study for management to control blood sugar level in cases with value >200mg/dl, Regular insulin protocol was administered subcutaneously. Treatment for controlling hyperglycaemia needs to be initiated within the first 24 hour of admission [13]. Further studies are needed for determine the exact level of serum glucose that is harmful for patients with TBI. Management of hyperglycaemia with insulin protocol in cases with value >200mg/dl, is critical in improving the outcome of patients with TBI. In this study a large group of ICU trauma patients were evaluated. On the other hand, data were collected from Level 1 trauma center that provide the highest level of surgical care which this strength point of this study.

LIMITATION

We recognize some limitations of the study including low of sample size.

CONCLUSION

To conclude, hyperglycaemia includes blood glucose cut off value too as used in this study after severe TBI is associated with poor outcome. It can be a predictive factor for mortality rate, ICU stay, GCS arrival, VAP & RDS, mechanical ventilation, hospital stay and ISS.

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