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The Utility of Serum Copeptin Levels for the Determination of Injury Severity and Prognosis in Adult Patients with Multiple Blunt Trauma

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Abstract

Objective: This study investigates the role of serum copeptin levels measured in the early post-traumatic period (first 24 hours) in adult patients with multiple blunt trauma (MBT) in determining trauma severity and the predicting prognosis.

Materials and Methods: This prospective cross-sectional study was enrolled 78 consecutive adult patients with MBT and 72 age- and sex-matched healthy controls with no acute traumatic injuries. The serum level of copeptin was assessed in all individuals were included in the study.

Results: No significant difference was observed between the patients with MBT and the control group in serum copeptin levels (3.13±6.10 vs. 3.90±6.82 and p=0.468). In addition, no statistically significant correlation was found between serum copeptin levels and age, revised trauma score (RTS), injury severity score (ISS), and Glasgow Coma scale values in patients with MBT. Additionally, no significant was observed difference between the hospitalized and discharged patients from the emergency department (ED) in terms of serum copeptin levels (1.72±3.05 vs. 1.95±3.50 and p=0.783).

Conclusion: In our study, trauma scores such as high RTS and low ISS values help determine the discharge from the ED in patients with multitrauma. However, we concluded that the serum copeptin level in these patients was not valuable in predicting trauma severity and prognosis in the early post-trauma period (in the first 24 hours).

Keywords: Multiple blunt trauma revised trauma score, injury severity score, prognosis, copeptin

Introduction

Biomarkers such as amyloid A, oxidative stress parameters, and atrial natriuretic peptides are an alternative to trauma scoring, and imaging methods are increasingly being used to evaluate the severity of injury in patients with multiple blunt trauma (MBT) [1]. Various scoring systems exist to evaluate trauma severity and prognosis in patients with MBT. Injury severity score (ISS) is the most predictive and reliable scoring for clinical development and prognosis, a scaled measurement indexed to anatomical injury: By scoring the damage done by trauma on each organ (with abbreviated injury score), the squares of the three highest-scoring values which is most severely injured body regions are added, and ISS is obtained [2], an ISS is greater than 15 represents major trauma. Bolorunduro et al. [3] categorized the ISS as follows. Bolorunduro et al. [3] categorized the ISS as follows. Less than 9 ISS is mild, 9-15 moderate, 16-24 severe, and above 24 profound. Copeptin, the precursor of arginine-vasopressin, is a glycopeptide consisting of 39 amino acids synthesized in the hypothalamus and is secreted from the neurohypophysis. The physiological function of circulating copeptin is still unclear [4,5]. Physiological stimuli such as pain or stress and pathological stimuli such as hypoglycemia, hypoxemia, stroke, infection, and shock cause copeptin release. Studies indicate that increased serum copeptin levels are associated with poor prognosis in many illnesses such as pneumonia, myocardial infarction, diabetes mellitus, heart failure, and stroke [6].

Therefore, we investigate the role of serum copeptin levels, a current marker of inflammation, measured in the early post-traumatic period (first 24 hours) in adult patients with MBT in determining trauma severity and the predicting prognosis.

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Materials and Methods

This prospective cross-sectional study was conducted in accordance with the 1989 Declaration of Helsinki and was approved by the Ethics Committee of University of Health Sciences Turkey, Istanbul Haseki Training and Research and Hospital (trial registration no: 1472). This study was funded by the Health Sciences University Board of Scientific Research Projects (funding no: 2018/078). We study collected venous blood samples from consecutive patients with MBT who were admitted to our tertiary care university hospital emergency department (ED), within 24 h of trauma onset, between October 2018 and January 2019. Seventy-eight consecutive adult patients with MBT (16 females and 62 males, age range 17-92 years) due to various causes (vehicle accidents, vehicle-pedestrian accidents, falling from a height, or assault) as the primary injury, and 72 age- and sex-matched healthy controls with no acute traumatic injuries, were included in the study. Adults exposed to multitrauma were first hemodynamically stabilized and a standard advanced trauma life support (ATLS) protocol was applied to each patient as suggested in the current 2018 ATLS-10 guidelines [7].

After vital functions had been monitored, written informed consent was obtained directly from the patient or from their authorized representative. Healthy volunteers were informed about the study protocol, and written consent was obtained from all participants before their participation in the study. The inclusion criteria were adult patients (≥18 years of age) with MBT. The revised trauma score (RTS), Glasgow Coma scale (GCS), and ISS values were calculated for each patient. Patients were divided into two groups: Those with ISS <25 (group 1; mild to severe trauma) and ISS ≥25 (group II; profound trauma).

Blood samples were drawn from the antecubital vein of each subject immediately after presentation to the ED; samples were immediately placed on ice at 4°C without the use of medications or serum infusions and collected in vacuum gel tubes. Plasma was separated from the cells by centrifugation at 2515×g for 10 min using a centrifuge (Electro-mag M615E, Istanbul, Turkey) and immediately stored at -80°C until the analysis of serum copeptin levels. Serum level of copeptin was assessed in MBT patients and healthy controls. It was estimated that at least 78 participants and 72 controls would be required to detect significant differences among the patient groups with a power of 95% and an alpha error of 5%.

Statistical Analysis

The data collected in the study were analyzed using SPSS 15.0 for Windows (IBM Corp., Armonk, NY, USA). Descriptive statistics are expressed in numbers and percentages of categorical variables. Numerical variables are expressed as the mean, standard deviation, and minimum and maximum values. The numerical variables in the two independent groups were compared using the Student independent t-test (comparison of copeptin level) when the data conformed to normal distributions. When the data were not normally distributed, the Mann-Whitney U test was used to compare two independent groups (e.g., age and gender). The ratios in the groups were compared using the chi-square test. Pearson's correlation coefficient was used to evaluate any correlation between ISS or RTS values and data that were normally distributed (serum level of copeptin). The significance level was set at $p<0.05$.

Results

A total of 78 adult patients with MBT, 62 male (79.5%) and 16 female (20.5%), were conducted in the study. The control group included 72 healthy volunteers, 49 (77.8%) were male and 14 (22.2%) female. The mean age of the patients with MBT was 37.10±17.70 (age range; 17-92); the mean RTS value was 7.70±1.10, mean ISS 24.0±13.30, and mean GCS 13.8±3.1.

Table 1 shows the mechanisms of injury in patients with MBT in our study. There were falling from height in 28 patients, motor vehicle accidents in 17 patients, assault in 18 patients, motor vehicle-pedestrian accidents in 9 patients, and motorcycle accidents in 6 patients.

No significant difference was observed between the patients with MBT and the control group in terms of serum copeptin levels (3.13±6.10 vs. 3.90±6.82 and p=0.468). In addition, no statistically significant correlation was found between serum copeptin levels and age, RTS, ISS, and GCS values in patients with MBT (Table 2). Twenty-five patients (32%) were hospitalized, and 53 (68%) were discharged from the ED. Mean

Table 1. Causes of multiple blunt trauma in patients admitted to the emergency department

		n	%
Cause of multiple blunt trauma	Fall from a height	28	36
	Motor vehicle crash	17	22
	Assault	18	23
	Motor vehicle-pedestrian crash	9	12
	Motorcycle crash	6	7

Table 2. Correlation between serum copeptin level and age, RTS, ISS and GCS values

	Copeptin (ng/mL)	
	rho	p*
Age	-0.175	0.125
RTS	0.044	0.700
ISS	-0.065	0.571
GCS	0.127	0.267

*ISS, RTS, GCS, serum copeptin values and age were calculated by Pearson correlation test. RTS: Revised trauma score, ISS: Injury severity score, GCS: Glasgow Coma scale

ISS values were significantly elevated, whereas mean RTS values were significantly decreased in hospitalized patients compared to discharged patients (p=0.025 and p<0.001; Table 3). In addition, the mean age of the hospitalized patients was lower than discharged patients from the ED (30.70±13.00 vs. 38.70±18.10 and p=0.036; Table 3).

However, no significant difference was observed between the hospitalized and discharged patients from the ED in terms of serum copeptin levels (1.72±3.05 vs. 1.95±3.50 and p=0,783; Table 3). When patients were evaluated with ISS scores in terms of trauma severity; there was no statistically significant difference in age, gender, and serum levels of copeptin between patients with ISS <25 and ISS ≥25 (p=0.355, p=0.260, and p=0.595, respectively; Table 4).

Discussion

Molecular studies indicate that copeptin, as a biochemical parameter, plays an important role in the pathogenesis and progression of acute critical diseases [8]. Although many studies investigate serum copeptin levels in several non-traumatic diseases, there are limited clinical studies investigating the serum level of copeptin in acute traumatic situations and predicting trauma severity and prognosis. These studies have been performed in isolated head trauma patients [9]. In a study conducted by Westermann et al. [10], endogenous vasopressin and copeptin levels in patients with MBT were compared with the healthy group. However, no study investigated the role of copeptin levels in predicting trauma severity and prognosis in the early posttraumatic period within 24 hours. Therefore, our study is the first research to analyze the serum copeptin level in MBT patients and the role of copeptin levels in predicting trauma severity and prognosis in the first 24 hours.

İpekci et al. [11] included 82 cases with multiple trauma. They observed that the value of copeptin on admission to ED was significantly higher in multi-trauma cases than in the control group. The level of copeptin decreased significantly after 24 hours. In our study, similar to İpekci et al. [11] , there was no statistically significant difference between the patient with MBT and healthy individuals regarding mean serum copeptin levels. In addition, no significant correlation was observed between serum copeptin level and trauma scores, including RTS, ISS, and GCS values.

In a study that included 105 patients with moderate head trauma, Castello et al. [12] reported no significant correlation between the serum copeptin levels and the age of the patients. Similarly, we observed no significant correlation between copeptin level and age.

In a study that compared plasma copeptin levels of 87 trauma patients with healthy controls, Westermann et al. [10] found that copeptin levels were significantly higher in patients with MBT than the healthy controls. Another study by Dong et al. [9] investigated posttraumatic plasma copeptin levels in patients with head trauma and observed that copeptin increased in the first six hours after trauma and peaked within 2 hours. Unlikely, no statistically significant difference was found between the patient and control groups in terms of mean serum copeptin

Table 3. Comparison of age, gender, and serum copeptin levels between the hospitalized and discharged patient groups

	Hospitalized (n=25, 32%)	Discharge (n=53, 68%)	
Characteristic	**Mean ± SD**	**Mean ± SD**	**p***
Age	30.70±13.00	38.70±18.10	0.036
RTS	7.00±1.80	7.90±0.30	0.025
ISS	35.70±16.30	18.10±1.70	>0.001
Copeptin (ng/mL)	1.72±3.05	1.95±3.50	0.783

Data are expressed in numbers, percentages, and mean ± SD. *The Mann-Whitney U test was used to compare the age and gender distribution between groups, and Student's t-test was used to compare serum copeptin levels between groups. SD: Standard deviation, RTS: Revised trauma score, ISS: Injury severity score

Table 4. Comparison of age, gender, and serum copeptin levels between the ISS <25 and ISS ≥25 patient groups

		ISS <25 (n=61)	ISS ≥25 (n=17)	
Characteristic		**Mean ± SD**	**Mean ± SD**	**p***
Age		38.10±17.90	33.60±16.90	0.355
Gender	**Male**	47 (77%)	15 (88.2%)	0.260
	Female	14 (23%)	2 (11.8%)	
Copeptin (ng/mL)		3.53±6.46	3.31±6.62	0.595

Data are expressed in numbers, percentages, and mean ± SD. *The Mann-Whitney U test was used to compare the age and gender distribution between groups, and Student's t-test was used to compare serum copeptin levels between groups. SD: Standard deviation, ISS: Injury severity score

level in our study. In addition, there was no significant correlation between serum copeptin levels and trauma scores. Copeptin is released simultaneously from the neurohypophysis via osmotic or hemodynamic stimulus. There were few cases with traumatic brain injury and hemodynamically unstable in our study. More studies investigating the role of serum copeptin levels in patients with MBT are needed.

Conclusion

In conclusion, considering the findings obtained in our study, trauma scores such as high RTS and low ISS values are useful in determining the discharge from the ED in patients with multitrauma. However, we concluded that the serum copeptin level in these patients was not valuable in predicting trauma severity and prognosis in the early post-trauma period (in the first 24 h).

Ethics

Ethics Committee Approval: Ethics Committee of University of Health Sciences Turkey, Istanbul Haseki Training and Research and Hospital (trial registration no: 1472).

Informed Consent: Written informed consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: T.A., A.A., T.Ak., Concept: Ö.S., Design: T.A., Ö.S., Data Collection or Processing: T.A., A.A., T.Ak., Analysis or Interpretation: T.A., Ö.S., Literature Search: T.A., A.A., Writing: T.A., A.A., T.Ak., Ö.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

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