Correlation Between Serum Homocysteine Levels and Outcome of Patients with Severe Traumatic Brain Injury

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OBJECTIVE: **To examine the relationship between homocysteine (Hcy) plasma levels and the outcome of patients with traumatic brain injury (TBI).**

METHODS: **In a prospective case-control study, demographic, clinical, and Glasgow Coma Scale score data were collected. Outcome was evaluated according to the Glasgow Outcome Scale score at the time of discharge from the hospital and 6 months after hospitalization. Plasma levels of Hcy were measured using high-performance liquid chromatography. Computed tomography scan of the brain was performed within the first 24 hours of hospitalization.**

RESULTS: **The case group comprised 150 patients with TBI (men, 54.7%; mean age, 55.90 years ± 12.31), and a control group comprised 150 healthy individuals (men, 52%; mean age, 49.56 years ± 15.64) were studied. The mean ± SD plasma Hcy level in the TBI group (20.91 μmol/L ± 15.56) was significantly higher than plasma Hcy level in the control group (7.45 μmol/L ± 13.54, $P = 0.000$). There was a significant relationship between Hcy plasma levels and Glasgow Coma Scale score and computed tomography findings classified by the Marshall score. ($P = 0.001$ and $P = 0.028$, respectively). Also, there was a significant difference in mean Hcy plasma between patients who died as a result of TBI and patients who were still alive at the end of the study period according to Glasgow Outcome Scale score ($P = 0.000$ and $P = 0.054$, respectively).**

CONCLUSIONS: **There was a significant correlation in this study between plasma Hcy levels and severity of trauma and prognosis in patients with TBI.**

INTRODUCTION

Traumatic brain injury (TBI) is a major cause of mortality and morbidity resulting from trauma.[1-3] An exact determination of brain damage in the early stages of injury is a necessary factor to determine neurologic prognosis and appropriate treatment.[4] At the present time, the Glasgow Coma Scale (GCS) is the best scale to predict the severity of damage in patients with TBI.[5] Predicting the outcomes of patients with TBI is challenging because analgesics, sedatives, and muscle relaxants administered to these patients affects the neurologic assessment.[6] Imaging studies such as computed tomography (CT) have limitations in patients with TBI and can miss diffuse axonal injury and increase intracranial pressure in some patients.[7] CT also has limitations in determining prognosis of patients and showing brain microscopic changes.[8] In addition, CT scan has limitations after diagnosis and treatment of TBI because of secondary cell damage and central nervous system (CNS) depression.[9,10] Secondary damage after TBI includes oxidative stress, inflammatory damage, and production of metabolites that cause vascular and structural damage in the brain.[11,12]

Homocysteine (Hcy) is a marker of oxidative stress that can lead to lipid peroxidation and reactive oxygen species.[13,14] High levels

Key words
- CT scan
- Glasgow Coma Scale
- Homocysteine
- Outcome
- Prognosis
- Traumatic brain injury

Abbreviations and Acronyms
CNS: Central nervous system
CT: Computed tomography
GCS: Glasgow Coma Scale
GOS: Glasgow Outcome Scale
Hcy: Homocysteine
TBI: Traumatic brain injury

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Table 1. Demographic and Clinical Characteristics of Patients with Traumatic Brain Injury

	TBI Patients, $n = 150$	Control Subjects, $n = 150$	*P* Value
Sex			
Male	82 (54.7)	78 (52)	0.545
Female	68 (45.3)	72 (48)	
Age (years)	55.90 ± 12.31	49.56 ± 15.64	0.657
BMI (kg/m^2)	23.45 ± 12.67	24.23 ± 21.65	0.342
BP (mm Hg)	110.12 ± 25.43	145.44 ± 37.65	0.076
Injury mechanism			
Motor vehicle accident	49 (32.7)	—	
Motorcycle accident	18 (12.0)	—	
Gunshot wound	12 (8.0)	—	
Fall	39 (26.0)	—	
Assault	18 (12.0)	—	
Other	14 (9.3)	—	
GCS score, median (range)	5 (2—8)	15	0.000
Marshall score			
Diffuse I	25 (16.7)	—	
Diffuse II	31 (20.7)	—	
Diffuse III	10 (6.7)	—	
Diffuse IV	14 (9.3)	—	
Evacuated focal mass lesion V	11 (7.3)	—	
Focal mass lesion VI	59 (39.3)	—	
Days in hospital	12.04 ± 6.71	—	
Days in ICU	4.55 ± 1.88	—	
Outcome in hospital			
Deceased (GOS 1)	47 (31.3)	—	
Alive (GOS 2—5)	103 (68.7)	—	
Outcome in 6 months			
Deceased (GOS 1)	28 (18.5)	—	
Alive (GOS 2—5)	75 (72.81)	—	
Homocysteine (μmol/L)	20.91 ± 15.65	7.45 ± 13.54	0.001

Values are presented as number (%) for Alive (GOS 2-5) or mean ± SD for Homocysteine unless otherwise noted.
TBI, traumatic brain injury; BMI, body mass index; BP, blood pressure; GCS, Glasgow Coma Scale; ICU, intensive care unit; GOS, Glasgow Outcome Scale.

of Hcy are associated with an increased risk of subclinical stroke, Alzheimer disease and other forms of dementia, and other neuropsychotic disorders.[4] Also, an elevated level of Hcy is associated with magnetic resonance imaging findings such as brain atrophy, silent brain infarcts, and white matter hyperintensity.[15-18] The Hcy level can change in patients with TBI. Because there is no specific study to assess Hcy level in patients with TBI, the present study aimed to examine the relationship between this marker and clinical trends and the outcome of such patients. The objectives of our study were to examine the relationship between Hcy level and outcome at hospital discharge or 6 months after discharge in patients with TBI.

MATERIALS AND METHODS

Patients

The present study was approved by the ethics committee of Ilam University of Medical Science, Ilam, Iran. Written informed consent was obtained from all patients. This prospective case-control study comprised 150 patients with TBI admitted to Imam Khomeini Hospital in Ilam City in the west of Iran during the period February 2014 to February 2015. This medical center is a trauma and referral center in the west of Iran that treats 700,000 patients. Demographic data including sex, age, body mass index, and medical history were collected from study patients. TBI was confirmed by CT scan. All patients underwent CT based on the protocol of Marshall et al.,[6] and CT scan was repeated in the event of any clinical deterioration, such as rapidly disturbed consciousness, acute focal neurologic deficit, seizure, or status epilepticus. The age range of patients was 20—70 years. To be included in the study, patients had a GCS score of ≤8 on admission. Exclusion criteria included an Injury Severity Score >15; multiple trauma; pregnancy; use of oral contraceptives or hormone therapy; bleeding disorders; endocrine disorders; anticoagulant treatment; alcoholism; drug abuse; systematic diseases including end-stage renal disease, cirrhosis, chronic heart failure, and diabetes; and age <20 years. Patients were assessed based on guidelines for the management of brain trauma, including GCS score, blood pressure, pulses, temperature, electrocardiogram, liquid equality, and laboratory parameters. Also, ventricular drain placement, monitoring of intracranial pressure, placement of a central venous pressure catheter, and surgical intervention were performed for decompression of the mass. Outcome of patients with TBI was divided according to mortality during hospitalization, duration of hospitalization, and GOS score after 6 months.[19] To analyze the