Research Article

Simvastatin's effects on outcome in TBI

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Abstract
Background/aim: Mortality and morbidity still remain high in patients with traumatic brain injuries. Understanding the role of new treatments in these patients is critical. The aim of this study was to determine the effect of simvastatin on survival and outcome in traumatic brain injury patients**.**
Materials and methods: Forty patients were assigned to receive either simvastatin or a placebo. All data, including the Glasgow Coma Scale score, intensive care unit mortality (ICU), length of ICU stay, and duration of mechanical ventilation, were collected. The effect of simvastatin on the collected data was then investigated.
Results: The Glasgow Coma Scale level was significantly higher in the simvastatin group. The overall mortality rate, duration of mechanical ventilation, and length of intensive care unit stay were similar between the ٢ groups.
Conclusion: Simvastatin could be suggested as an adjunctive therapy in traumatic brain injury patients.
Key words: Simvastatin, traumatic brain injury, outcome

Introduction
Traumatic brain injuries (TBIs) are a leading cause of morbidity and mortality. Recent evidence suggests that TBIs accounted for the majority of trauma deaths in Europe. This situation is comparable in the United States and is even worse in developing countries[١]. Despite recent improvements in the management of patients with TBI in intensive care, mortality and morbidity in these patients still remain high[٢]. Therefore, understanding the role of new treatments in TBI outcome and mortality is critical. An acute inflammatory response occurs within the central nervous system (CNS) after severe TBI. This response leads to brain damage following traumatic injury[٣]. Statins are characterized as reductase inhibitors and have ٣-hydroxy-٣-methylglutaryl coenzyme activity. A wide variety of advantages of statins has been proven through recent research. Antiinflammatory actions, the direct activation of heme oxygenase, direct interference in leukocyte-endothelial interactions, and direct inhibition of major histocompatibility complex class II are the effects of statins that are independent of their lipid-lowering ability[٤].

Materials and methods
Study design
After approval by the local ethics committee of Minia university, ٤٠ patients were enrolled in this placebo-control clinical trial. Valid informed written consent was obtained from all patients or their relatives.

Study participants
Between May ٢٠١٥ to May ٢٠١٦, ٤٠ patients their ages ranged from ١٨ to ٦٠ years with acute TBI (GCS ٩-١٢) admitted to ICU within ٢٤ hours, were screened for eligibility for enrollment in the trial.
Exclusion criteria were allergy to statins, myopathies, major organ dysfunction (renal, liver, cardiovascular) and life threatening multiple trauma.

Randomization
Patients who met the inclusion criteria were randomly assigned to receive either simvastatin (Zocor, ٤٠ mg, tablet) at a dose

of ٨٠ mg on the first day followed by ٤٠ mg daily, or a placebo. The patients were allocated to ١ of the ٢ groups according to a randomization code list in a randomly permuted block design generated using a computer program.

Data extraction

Including, age, sex, Glasgow Coma Scale score on admission and discharge, intensive care unit (ICU) mortality, length of ICU stay and duration of mechanical ventilation were recorded.

Statistical analysis

The collected data were coded, tabulated, and statistically analyzed using SPSS program (Statistical Package for Social Sciences) software version ٢٠.

Descriptive statistics were done for numerical data by mean, standard deviation and minimum& maximum of the range, while they were done for categorical data by number and percentage.

Analyses were done for parametric quantitative data between the two groups using independent sample t test and for non- parametric quantitative data using Mann Whitney test.

Analyses were done for qualitative data between the two groups using Fisher Exact test.

The level of significance was taken at (P value < ٠.٠٥).

Results

Patient characteristics

Forty patients were enrolled in this prospective, randomized study. ٢٠ patients received simvastatin and ٢٠ patients received a placebo. patient characteristics were comparable in terms of age, sex and GCS score upon admission.

Outcome

The overall ICU mortality rate, and the length of ICU stay were similar between the groups. When the GCS score at discharge was compared with GCS at admission, there was an increase in both groups; however, the GCS score at discharge was significantly higher in the simvastatin group (Table ١).

Variables	Statin group (n = ٢٠)	Placebo group (n=٢٠)	P value
ICU stay (days): Range. Mean ± SD	(٢-٨) ٤.٣±١.٣٠	(٢-٨) ٥.٩٠±١.٨١	٠.١٧٠
ICU mortality (no., %) No Yes	١٨ (٨٥٪) ٢ (١٥٪)	١٩ (٩٥٪) ١ (٥٪)	٠.٧٠١
GCS at discharge Median IQR	١١ (١٠-١٢)	١٣ (١١-١٣)	< ٠.٠٠١*

*Statistically significant difference between groups (P < ٠.٠٥).

SD: Standard deviation, GCS: Glasgow Coma Scale, ICU: intensive care unit, (no.) and (%): number and percentage, IQR: interquartile range.

Discussion

The beneficial effect of statin treatment after TBI is probably true in humans as well as in animals[٥]. Our study presents preliminary data that are in agreement with this theory. In this study, TBI patients treated with simvastatin showed higher GCS scores at discharge compared with the control group. The reason for this finding can be related to the antiinflammatory effect of statins on secondary injury mechanisms after TBI. Antiinflammatory and neuroprotective effects of statins have been proven by several preclinical studies[٦].

In this study, patients in the study and control groups did not have significantly

different lengths of ICU stay and the duration of mechanical ventilation. A similar finding was noted by Makris et al., ٢٠١١.

In our study, we failed to find significant difference between both groups as regard to reduction of hospital mortality with statin therapy during ICU stay. Our results were in agreement with Naghibi et al., ٢٠١٦.

The main limitation of this study was that it was carried out in a single institute and only on patients of the same race. Furthermore, the sample size was small.

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