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Clinical presentation and prognosis of patients with Road Traffic Accident (RTA) and head trauma in Egypt & effect of Cerebrolysin®

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Abstract

Aim: To evaluate the clinical presentation and outcomes of patients with road traffic accidents (RTA) and head trauma (HT) from other causes upon admission to the hospital in Greater Cairo between November 1, 2021 and January 12, 2023.

Methods: The retrospective observational study analyzed data from patient files. A total of 81 patients were screened, with 59 meeting the inclusion/exclusion criteria. Among these, 10 patients were under 18 years old and 49 were adults. Adults received 30 ml/day of cerebrolysin®, while children were dosed based on physician recommendations. Assessment at admission included Glasgow Coma Scale (GCS) scores and the presence of post-Concussion (PC) or intracranial (IC) hemorrhage. Prognosis was evaluated based on ICU stay duration and patient status at the end of the observation period.

Results: Of the patients, 38 (64.4%) had mild cases, and 21 (35.6%) had moderate to severe cases, with no significant age difference between those under 18 (p = 0.490). and over 18 (p = 0.209). While head trauma and RTA incidents were more frequent among males across all age groups, there was no significant gender difference in the severity of cases for those under 18 (p = 0.524). and over 18 years (p = 0.363). Most patients, 57 (96.6%), fully recovered. One patient(1.7%) died following an RTA with a GCS score of 7, and another (1.7%) remained in the ICU after 14 days, with a GCS score of 11, suffering from brain contusion, and edema.

Conclusion: Head injury, whether from RTA or other trauma, were more prevalent among young adults and males in the Greater Cairo region. Cerebrolysin® administration improved the prognosis for patients with head trauma and RTA.

Keywords: Cerebrolysin®; RTA; Head Trauma; GCS Score; Prognosis

Abbreviations: Adverse Event (AE), Brain Trauma Foundation (BTF), Central Nervous System (CNS), Contract Research Organization (CRO), Diabetic Peripheral Neuropathy (DPN), Glasgow Coma Scale (GCS), Head Injury (HI), Intracranial (IC), Low- and Middle-Income Countries (LMICs), Post-Concussion (PC), Road Traffic Accident (RTA), Statistical Analysis Plan (SAP), Serious Adverse Event (SAE), Standard Deviation (SD), Traumatic Brain Injury (TBI), Traumatic Head Injury (THI).

Introduction

Traumatic injury is a leadingcause of death globally, with approximately 53,000 annual fatalities in the United States alone [1, 2]. In 2016, around 55 million individuals worldwide suffered from traumatic brain injury (TBI); 87% of which occurred in low- and middle-income countries (LMICs) [3]. Falls are the predominant cause of TBI globally; however, in LMICs, road traffic accidents are a significant contributor [3]. The incidence of TBI is expected to rise. [4].

Severe TBI often leads to extended hospital stays and substantial financial burden [5]. Mortality rates among severe TBI patients are notably high [6, 7]. According to recent literature, TBI is one of the most common causes of death and long-term disability,with mortality rate varying by region, from 13 per 100,000 in China [8] to 11 per 100,000 in Europe and 17 per 100,000 in USA [9]. Implementation of treatment algorithms based on the Lund concept and Brain Trauma Foundation (BTF) recommendations has reduced TBI mortality [10, 11].

Head injuries (HI) are significant mortality risk factors across all age groups globally [12]. By 2030, traumatic injuries are

projected to be among the top twenty causes of death worldwide [13]. Underreporting and misdiagnosis in Egypt leads to fewer documented cases than the actual occurrence, despite injuries being the fifth leading cause of death [13, 14].

Globally, head injuries account for nearly 50% of all traumatic injuries, often resulting in long-termneurological issues and requiring prolonged medical treatment. The median prevalence of TBI in the United States was 73.5 per 100,000 [15], while in Latin America and Sub-Saharan Africa, it is higher at 150–170 per 100,000, primarily due to road traffic accidents. [16].

Cerebrolysin® has been used in psychiatry and neurology for over 50 years. It is a non-lipid preparation of free amino acids and low molecular weight neuropeptides administered via IV infusion, also containing magnesium, phosphorus, potassium, and selenium. [17, 18].

Cerebrolysin® has demonstrated neuroprotective properties in vitro and in vivo, including endothelial membrane permeability modulation and anti-inflammatory effects [19–21].

Its unique effectiveness in enhancing cognitive and physical performance in TBI patients. Along with its safety profile in hemorrhagic stroke patients, makes it a recommended treatment [22]

This study aims to assess and screen patients with RTA and head trauma in Greater Cairo, focusing on GCS scores, PC and IC Hemorrhage, and the impact of Cerebrolysin® on prognosis through ICU stay duration and discharge status.

Materials and Methods

Study Design: This retrospective observational study analyzed data from patients admitted to the ICU with road traffic accidents (RTA) or head trauma due to other causes between November 1, 2021 and January 12, 2023, at the Italian Hospital in Cairo, Egypt. The objective was to evaluate patients at admission and assess the impact of Cerebrolysin® on their condition.

Objectives: Primary endpoint:

• Assess the clinical presentation of patients with RTA and head trauma from other causes at hospital admission, focusing on GCS Scores, and the presence of Post-Concussion (PC) and/or Intracranial (IC) hemorrhage

Secondary endpoint:

• Evaluate the effect of Cerebrolysin® on patient prognosis, measured by ICU stay duration and status at discharge.

Methods

A comparative analysis was conducted between patients with RTA and those with head trauma from other causes, examining age, gender, presence of PC and/or IC hemorrhage at hospital admission. Prognosis was evaluated by assessing the severity of condition using GCS scores, ICU stay duration, and discharge status.

Head injury severity was classified using the Glasgow Coma Scale (GCS), which assesses verbal, motor, and eye-opening responses. GCS scores were categorized asmild (13-15), moderate (9-12), or severe (<9) [23]. Outcome at discharge were classified as recovered, still in ICU, or deceased.

Patients who met the inclusion/exclusion criteria received a daily Infusion of 30 ml of Cerebrolysin®, with children dosed per physician recommendations.

Inclusion Criteria:

• Egyptian male and female patients, aged ≥ 8 years, were admitted with RTA or head trauma from other causes, who received cerebrolysin®. Adults received 30 ml/day, and children under 18 were dosed as per physician recommendations.

Exclusion Criteria:

• Patients without head trauma or RTA, those with missing prognosis data, patients with a GCS score less than 6, and adults receiving less than 30 ml/day of Cerebrolysin®.

Statistical Analysis

Sample Size:

• The study included 81 patients with RTA or head trauma, providing a confidence level of 95% and a margin error of 10.87%.

Population:

• Data from 81 patient files were screened, with 59 patients meeting the inclusion/exclusion criteria. Of these. 10 were under 18 years old and 49 were over 18 years old.

Statistical methods:

Data were analyzed using IBM SPSS Version 23 for Windows. Descriptive statistics included the number of patients (n), mean, standard deviation (SD), median, and range. Comparative statistics included the Chi^2 test for categorical variables, the student's t-test to for the numerical variables, and Mann-Whitney U-test for non-parametric numerical variables. Significance was set at $P< 0.05$.

Moral Considerations

The research was conducted in accordance withthe Helsinki Declaration, ensuring all ethical duties were fulfilled for the examination of patients under study.

Results

The study enrolled 59 patients, with 10 (17%) under 18 years and 49 (83%) over18 years. The mean age for age group under 18. was 12.1 ± 2.8 years, while for those over 18, it was 50.3 ± 19.6 years.

Demographics:

• 46% of patients were aged 15-45 years, and 30% were over 60 years old.

• Among those under 18, 5 (50%) had head trauma from other

causes, and 5 (50%) had RTA- related trauma.

• Among those over 18, 28 (57.1%) had head trauma from other causes and 21 (42.9%) had RTA- related trauma.

Gender

• No significant gender differences were found between RTA and head trauma cases in patients under 18 (p = 0.524) or over 18 (p = 0.363) as shown in Table 1.

• Similarly, no significant gender differences were observed between age groups in head trauma. (p = 0.149), or RTA, (p = 0.412) as shown in Table 2.

Table 1: Gender, Severity, GCS Score, ICU stay duration, PC and IC Hemorrhage regarding Head Trauma and RTA in patients under and over 18 years old.

		Head Trauma	RTA	Total	*p*-value
< 18 Yrs.	Female N (%)	3 (60%)	1 (20%)	4 (40%)	0.524 *
	Male N (%)	2 (40%)	4 (80%)	6 (60%)	
> 18 Yrs.	Female N (%)	7 (25%)	8 (38.1%)	15 (30.6%)	0.363 *
	Male N (%)	21 (75%)	13 (61.9%)	34 (69.4%)	
< 18 Yrs.	Mild N (%)	4 (80%)	3 (60%)	7 (70%)	0.490 *
	Moderate to severe N (%)	1 (20%)	2 (40%)	3 (30%)	
> 18 Yrs.	Mild N (%)	19 (67.9%)	12 (57.1%)	31 (63.3%)	0.209 *
	Moderate to severe N (%)	9 (32.1%)	9 (42.9%)	18 (36.7%)	
< 18 Yrs.	GCS Score (mean ± SD)	13.4 ± 1.1	12.4 ± 1.1	12.9 ± 2.0	0.468 **
> 18 Yrs.	GCS Score (mean ± SD)	12.8 ± 1.6	12.0 ± 2.6	12.5 ± 2.1	0.914 **
< 18 Yrs.	ICU stay duration Median (Q1-Q3)	2 (1-4.5)	2 (1.5 - 3)	2 (1-3.5)	0.247 ***
> 18 Yrs.	ICU stay duration Median (Q1-Q3)	3.5 (2-5.8)	4 (2-10)	4 (2-7)	0.494 ***
< 18 Yrs.	PC N (%)	2 (40%)	2 (40%)	4 (40%)	0.738 *
	IC Hemorrhage N (%)	0 (0%)	1 (20%)	1 (10%)	NA *
> 18 Yrs.	PC N (%)	9 (32.1%)	5 (23.8%)	14 (28.6%)	0.377 *
	IC Hemorrhage N (%)	7 (25%)	5 (23.8%)	12 (24.5%)	NA *
< 18 Yrs.	Discharge N (%)	5 (100%)	5 (100%)	10 (100%)	NA *
> 18 Yrs.	Died N (%)	0 (0%)	1 (4.8%)	1 (2%)	0.249 *
	Discharge N (%)	28 (100%)	19 (90.5%)	47 (95.9%)	
	Still in ICU N (%)	0 (0%)	1 (4.8%)	1 (2%)	

* Chi-square test used to find a statistical difference in categorical variables
** Un-paired t-test test used to find a statistical difference in numerical variables
*** Mann-Whitney U test used to find a statistical difference in numerical variables

Table 2: Comparison between age groups and RTA & HT, Gender and severity

		< 18 Yrs.	> 18 Yrs.	*p*-value *
Head Trauma	Female (N=10), N (%)	3 (30%)	7 (70%)	0.149
	Male (N=23), N (%)	2 (8.7%)	21 (91.3%)	
RTA	Female (N=9), N (%)	1 (11.1%)	8 (88.9%)	0.412
	Male (N=17), N (%)	4 (23.5%)	13 (76.5%)	
Overall	Mild (N=38), N (%)	7 (8.4%)	31 (81.6%)	0.685
	Moderate to severe (N=21), N (%)	3 (14.3%)	18 (85.7%)	
Head Trauma	Mild (N=14), N (%)	2 (14.3%))	12 (85.7%)	0.766
	Moderate to severe (N=19), N (%)	3 (15.8%)	16 (84.2%)	
RTA	Mild (N=13), N (%)	2 (15.4%)	11 (84.6%)	0.543
	Moderate to severe (N=13), N (%)	3 (23.1%)	10 (76.9%)	

* Chi-square test used to find a statistical difference in categorical variables

Severity:

• Of all cases, 38 (64.4%) were mild, 16 (27.1%) were moderate, and 5 (8.5%) were severe.

• Among patients under 18, 7 (8.4%) had mild, and 3 (14.3%) had moderate to severe cases

• Among patients over 18, 31 (81.6%) had mild, and 18 (85.7%) had moderate to severe cases, with no significant differences between age groups (p = 0.685) as shown in Table 2.

• No significant differences between RTA and head trauma in patients under18 (p = 0.490) and over 18 (p = 0.209), as per Table 1.

• Also, no significant differences between aged groups in head trauma. (p = 0.766), or RTA, (p-value = 0.543) as shown in Table 2.

GCS Scores:

• The mean GCS score for patients under 18 was 13.4 ± 1.1 for head trauma and 12.4 ± 1.1 for RTA.

• For patients over18, the mean GCS score was 12.8 ± 1.6 for head trauma and 12.0 ± 2.6 for RTA, with no significant differences between groups (p = 0.468 and p = 0.914; respectively), as per Table 1.

ICU Stay:

• For patients under 18, the median ICU stay was 2 days for both head trauma and RTA.

• For patients over 18, the median ICU stay was 3.5 days for head trauma patients and 4 days for RTA, with no significant differences in ICU stay duration between RTA and head trauma in patients under 18 years (p = 0.247) and over 18 years (p = 0.494) as shown in Table 1.

Post-Concussion and IC Hemorrhage:

• In patients under 18, 4 (40%) had PC and 1 (10%) IC Hemorrhage.

• In patients over 18, 14 (28.6%) had PC and 12 (24.5%) IC Hemorrhage, with no significant differences between groups, as shown in Table 1.

Prognosis:

• All patients under 18 were discharged.

• Among patients over 18, 1 (4.8%) died, 1 (4.8%) remained in ICU and 19 (90.5%) were discharged, with no significant differences in prognosis between RTA and head trauma cases (p = 0.249), as shown in Table 1.

Safety:

• One 34-years-old male patient with RTA and IC Hemorrhage, GCS score of 7, died after 10 days of receiving Cerbrolycin® (30 ml/day), Citicoline, Brain Stimulants, chest care, and multivitamins. The cause of death was IC hemorrhage deterioration.

• One 25-years-old female patient with RTA and a GCS score of 11 remained in the ICU for more than 14 days due to brain contusion and edema. She received Cerbrolycin® (30 ml/day), brain stimulants, dehydrating measures, and multivitamin

Discussion

In our study; 17% of enrolled patients were under 18 years old, while 83% were over 18 years old, reflecting the demographic of head trauma cases in Greater Cairo. Nearly half (46%) of the patients with head trauma were between 15 and 45 years old, with only 30% being over 60 years old, which aligns with findings by Sivakumar et al. (2018). In India and various studies from South

Africa, England, and Belgium, indicating that younger, active age groups are most effective by head injury. [24, 25]. Similar trends were observed in Egyptian studies, such as a cross-sectional study of 423 traumatic head injury cases at Menoufia University Hospital, where RTA was more common among the middle-aged (45 – 60 years). [26], and in Upper Egypt. [27]

Males in our study were approximately three times more likely to suffer had head trauma than female, consistent with an Egyptian study of 2,124 patients [28]. and a study in Pakistan with 1,338 patients [29]. A cross-sectional study in Ethiopia with 260 participants also highlighted those males, who are more likely towork outdoors, face higher risks of road accidents, assaults, and injuries, often in more stressful situations [30, 31]. This increased exposure explains the higher incidence of head trauma among younger males, impacting their life and work abilities. [32].

Road traffic accidents are a leading cause of head injuries in Egypt, attributed tointense traffic, high vehicles numbers, non-compliance with traffic laws, poo road planning, and lack of awareness regarding protective measures [33, 34]. Similar findings were reported by Pate et al in India and across five European countries and Taiwan [33, 34]

In terms of severity, 64.4% of cases in our study were mild, 27.1% were moderate, and 8.5% were severe, consistent with other studies [35, 36] and another Egyptian study. [37]. Research on Cerebolysin's therapeutic effects in brain injuries suggests its potential in improving patient prognosis [38, 39]. Our study found that 96.6% of patients were discharged, 1.7% died and 1.7% remained in the ICU, similar to outcomes observed in Egypt and Pakistan, where complete recovery was common. [37, 40] . Higher mortality rates were noted in studies of conservatively managed severe TBI patients [33].

A significant relationship between GCS scores and outcome was evident, with 100% of recovered cases having mild GCS scores, while the deceased patient had a severe score. This corroborates the GCS as a reliable predictor of traumatic case prognosis. Studies have shown that lower GCS score correlate with higher risks of infection and complication. [36, 41]

A 2020 study demonstrated significant efficacy of Cerebrolysin® in improving multidimensional outcome, with superior results compared to placebo across multiple outcome measurements. [42]. The CAPTAIN meta-analysis also found normalization of HADS score in 70.5% of Cerebrolysin® treated patients compared to 39.5% in the placebo group. [43]

Cerebrolysin's positive effects have been validated in vitro and in vivo, showing reduced microglial activity, decreased excitotoxicity, lowered free radicals' production, and increased neuronal survival. [20, 44]. Clinical studies confirm its neuroprotective properties, beneficial at all stages post-TBI, from the initial 24 hours up to 20 months after injury. Its efficacy appears dose- and time-dependent, suggesting similar trends in human studies [20, 35].

Conclusions

Head injury whether due to trauma or RTA, were more prevalent among young males in Greater Cairo, with most cases being mild. Prognosis for both head trauma and RTA were similar. Cerebrolysin® improved patients outcomes compared to conservative treatment.

Limitations

The study had a small sample size and short duration GCS Scores at follow-up visits were missing, and the absence of a control group receiving conservative management limited the assessment of Cerebrolysin® efficacy.

Recommendations

Future studies should include larger sample size, and compare Cerebrolysin® with conservative treatment, assessing data at baseline and study conclusion.

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