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Research Article

Study of the Neuroprotective Effects of Propofol in Acute Traumatic Cerebral Injury

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Abstract

Introduction: Traumatic brain injury (TBI) is a common presentation in the ED, and one of the important leading causes of death and disability in our communities [1]. Currently the routine use of what known as neuroprotective agents (agents that mainly decrease cerebral metabolic rate for oxygen or decrease cerebral blood flow like intravenous anesthetic barbiturates, inhalation anesthetic isoflurane and intravenous short acting anesthetic etomidate, etc.) have a wide acceptance in daily practice, the most commonly used one is the short acting barbiturate thiopental [2,3]. This study is aimed to study the neuroprotective inspect of propofol in the treatment of patients with severe acute traumatic brain injury on their outcome [4].

Methods: After approval of the medical ethics committee of Alexandria faculty of Medicine this study was carried out on 60 consecutive patients, who will be admitted to the units of Critical Care Medicine department in Alexandria Main University Department and diagnosed as sever traumatic brain injury (GCS of ≤ 8). GCS measured on admission and discharge, GOS measured at 3 months, ICU and hospital stay measured and mortality at the end of the study measured.

Results: The results of the current study yield that, patient with sever traumatic brain injury who received propofol infusion has a better GCS on discharge in comparison with that of admission, shorter ICU stay and shorter hospital stay.

Conclusions: Propofol has a neuroprotective effects in acute traumatic brain injury patients regarding their outcome.

Keywords: *Traumatic Brain Injury (TBI); Glasgow Coma Scale (GCS); Neuroprotection, Propofol*

Introduction

Traumatic brain injury (TBI) is a common presentation in the ED, and one of the important leading causes of death and disability in our communities [1]. Currently the routine use of what known as neuroprotective agents (agents that mainly decrease cerebral metabolic rate for oxygen or decrease cerebral blood flow like intravenous anesthetic barbiturates, inhalation anesthetic isoflurane and intravenous short acting anesthetic etomidate, etc.) have a wide acceptance in daily practice, the most commonly used one is the short acting barbiturate thiopental [2,3]. This study is aimed to study the neuroprotective inspect of propofol in the treatment of patients with severe acute traumatic brain injury on their outcome [4].

Methods

Study population

The study will be carried out on 60 consecutive patients, who will be admitted to the units of Critical Care Medicine in Alexandria Main University Department. The patients were randomly categorized into two groups Group I patients Including 30 patients who will

undergo medical treatment using methods that optimize cerebral perfusion and oxygenation, and Group II Including 30 patients who undergo propofol infusion for two days. Patients of both sexes. Any patient presented with TBI for the first time, All patients had a non-operable brain injury. Pregnant females, post cardiac arrest patients, patients with history of previous brain insult (TBI or CVA), patients with associated any other organ trauma, and Any patient who had a contraindication for propofol infusion (e.g.: shocked, history of I.V. aesthetics anaphylaxis, any co-morbid condition) was excluded from the study.

Treatment

In the first group of patients who were candidates for medical treatment to optimize cerebral perfusion and oxygenation. The other group undergone medical treatment and propofol infusion. The remaining medications for both groups was in line with the international guidelines for treatment of TBI [5].

Statistical analysis

Data were fed to the computer using the Predictive Analytics Software (PASW Statistics 18). Qualitative data were described using number and percent. Association between categorical variables was tested using Chi-square test. When more than 20% of the cells have expected count less than 5, correction for chi-square was conducted using Firsher's Exact test or Monte Carlo correction. Quantitative data were described using median, minimum and maximum as well as mean and standard deviation. The distributions of quantitative variables were tested for normality using Kolmogorov-Smirnov test, Shapiro-Wilk test. D'Agstino test was used if there was a conflict between the two previous tests. If it reveals normal data distribution, parametric tests was applied. If the data were abnormally distributed, non-parametric tests were used. For abnormally distributed data, Mann-Whitney Test (for data distribution that was significantly deviated from normal) were used to analyze two independent population. Wilcoxon signed ranks test was used to compare between the different periods. Significance test results are quoted as two-tailed probabilities. Significance of the obtained results was judged at the 5% level.

Results

In this study there was neither significant difference between the two groups as regards demographic data (Table 1). The age of the studied patients ranged from 2.5 to 67.0 years with a mean of 28.42 ± 17.58 year in group I and ranged from 3.5 to 70.0 years with a mean of 28.48 ± 19.39 year in group II. There was no statistically significant difference between the two groups. There were 8 females (26.7%) in group I, and 6 females (20%) in group II. It was obviously observed that the highest percentage of TBI in the two studied groups was among young adult males.

	Control (n = 30)		Propofol (n = 30)		Test of sig.
	No.	%	No.	%	
Sex					
Male	22	73.3	24	80.0	p = 0.542
Female	8	26.7	6	20.0	
Age					
Min. – Max.	2.50 - 67.0		3.50 - 70.0		MW_p = 0.918
Mean ± SD	28.42 ± 17.58		28.48 ± 19.39		
Median	27.50		27.50		

Table 1: *Comparison between the two groups according to demographic data.*

p: p value for Chi Square test; ^{MW}p: p value for Mann Whitney test.

In this study the mechanism of trauma in group I was RTA in 22 (77.3%) patients and FFH in 8 (26.7%) patients; while in group II it was RTA in 19 (63.3%) patients and FFH in 11 (36.7%) patients.

As regard GCS; in group I; GCS ranged from 3.0 - 8.0 on admission with a mean of 6.03 ± 1.54 and ranged from 3.0 - 14.5 at discharge with a significant increase in the mean value to 9.30 ± 3.90 ($p < 0.001$). In group II; GCS ranged from 3.0 - 8.0 on admission with a mean of 5.60 ± 1.43 and ranged from 3.0-13.5 at discharge with a significant increase in the mean value to 9.28 ± 3.93 ($p < 0.001$). The percentage of change in GCS in the two studied groups during the study by comparing GCS on admission and discharge in both groups, the comparison showed that the percentage of change in the median value was 54.51% in group I while it was 67.24% in group II with a higher percentage of improvement in GCS in group II although this change was statistically not significant MWP (0.505).

	Control (n = 30)	Propofol (n = 30)	MW_p
Admission			
Min. - Max.	3.0 - 8.0	3.0 - 8.0	
Mean ± SD	6.03 ± 1.54	5.60 ± 1.43	0.195
Median	6.50	6.0	
Discharge			
Min. - Max.	3.0 - 14.50	3.0 - 13.50	
Mean ± SD	9.30 ± 3.90	9.28 ± 3.93	0.917
Median	10.50	11.0	
P	< 0.001*	< 0.001*	
% of Chg.	54.51	67.24	0.505

Table 2: *Comparison between the two groups according to GCS.*

*^{MW}p: p value for Mann Whitney test; p: p value for Wilcoxon signed ranks test; *: Statistically significant at p ≤0.05*

In this study we found regarding the CT findings; in group I, the most frequent lesion was BE in 14 (46.7%) patients followed with SAH in 12 (40.0%) patients. in group II; also the most frequent lesion was BE in 19 (63.3%) patients followed by SAH in 13 (43.3%) patients. Most patients showed a combination between 2 lesions (sometimes more) except in 2 patients; 1 in each group whom CT was UR through all the study period. In group I; 5 (16.7%) patients developed new lesions plus the initial lesions in follow-up CT, 10 (33.3%) patients developed new lesions after disappearance of the initial lesions in follow-up CT, 1 (3.3%) patient showed disappearance of some of the initial lesions without developing of new lesions in follow-up CT, 1 (3.3%) patient showed the same initial lesion through all the study in follow-up CT, while 13 (43.3%) patients showed UR follow-up CT. In group II; 7 (23.3%) patients developed new lesions plus the initial lesions in follow-up CT, 7 (23.3%) patients developed new lesions after disappearance of the initial lesions in follow-up CT, 2 (6.7%) patient showed disappearance of some of the initial lesions without developing of new lesions in follow-up CT, 1 (3.3%) patient showed the same initial lesion through all the study in follow-up CT, while 13 (43.3%) patients showed UR follow-up CT.

As regard the Glasgow outcome score (GOS); in group I; 16 (53.3%) patients showed a good outcome (GOS 4 - 5 at 3 months), while in group II; 17 (56.7%) patients showed a good outcome (GOS 4 - 5 at 3 months). There was no significant difference between the two groups. In comparing between the GOS at 3 month and GCS on admission in the two groups we found that: in group I; patients with bad outcome (14 patients) they had a GCS on admission ranged from 3.0 - 7.0 with a mean of 5.43 ±1 .65; while patients with good outcome (16 patients) they had a GCS on admission ranged from 4.0 - 8.0 with a mean of 6.56 ± 1.26, which is statistically not significant p (0.070), in group II; patients with bad outcome (13 patients) they had a GCS on admission ranged from 3.0 - 7.0 with a mean of 5.0 ± 1.35, while patients with good outcome (17 patients) they had a GCS on admission ranged from 4.0 - 8.0 with a mean of 6.06 ± 1.34, which is statistically significant p (0.046).

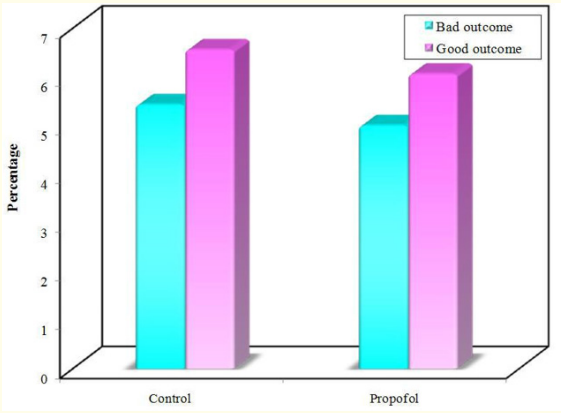

Figure 1: *Relation between GOS at 3 months and GCS admission in each group.*

As regard ICU stay in days; in group I; ICU stay ranged from 5.0 - 39.0 days with a mean of 16.67 ± 10.30, while in group II; ICU stay ranged from 4.0 - 28.0 days with a mean of 12.37 ± 6.51; although this represents the allover ICU stay of all the cases regarding their outcome. So when comparing the ICU stay in days in two groups between patients with good outcome (GOS 4 - 5 at 3 months) we found that: In group I, patients with good outcome (16 patients) had an ICU stay ranged from 5.0 - 39.0 days with a mean of 14.31 ± 10.24; while in group II; patients with good outcome (17 patients) had an ICU stay ranged from 4.0 - 21.0 days with a mean of 10.94 ± 5.06. So, patients with good outcome in group II had an obviously shorter ICU stay than patients with good outcome in group I; although this difference is statistically not significant.

	Control (n = 16)	Propofol (n = 17)	Test of sig.
ICU stay			
Min. - Max.	5.0 - 39.0	4.0 - 21.0	
Mean ± SD	14.31 ± 10.24	10.94 ± 5.06	$MW_{p=}$ 0.481
Median	11.50	11.0	

Table 3: *Comparison between the two groups according to ICU stay in good outcome cases.*

^{MW}p: p value for Mann Whitney test

As regard hospital stay in days; in group I; hospital stay ranged from 5.0 to 62.0 days with a mean of 24.60 ± 16.20 days, while in group II; it ranged from 4.0 to 54.0 days with a mean of 19.37 ± 13.56 days. There was no significant difference between the two groups.

In the current study we found mortality at 6 months; in group I; 11 (36.7%) patients died at 6 months from date of admission, while in group II; 9 (30.0%) patients died at 6 months from date of admission. There was no significant difference between the two groups.

Discussion and Conclusion

The results of the current study yield that TBI is more common in young adult males [6,7]. As regarding GCS mean value during the study period, the two groups show the same difference between the GCS on admission and at discharge ($P < 0.001$), which showed statistically significant increase in the mean value of the GCS in group I from 6.03 ± 1.54 to 9.30 ± 3.90 and in group II from 5.60 ± 1.43 to 9.28 ± 3.93. This improvement in GCS in both groups showed the significance of applying the protocols of conventional management of

TBI in both groups. The comparison showed that the percentage of change in the median value of GCS in the two groups was 54.51% in group I while it was 67.24% in group II with a higher percentage of improvement in GCS in group II, although this change was statistically not significant MWP (0.505) [8]. As regard Glasgow outcome score (GOS) at 3 months, in group I (53.3%) of the patients showed a good outcome (GOS 4 - 5 at 3 months), while in group II (56.7%) of the patients showed a good outcome (GOS 4 - 5 at 3 months). There was no significant difference between the two groups. On measuring GOS for the two groups we took in our consideration that no other therapeutic modalities (e.g.: hyperbaric oxygen therapy) were applied to any patient in either groups, to assure the elimination of any other treatment rule in the final outcome of the patients except the conventional treatment of TBI alone in group I and the conventional treatment of TBI plus propofol in group II. In comparing between the GOS at 3 month and GCS on admission in the two groups we found that, in group I; patients with bad outcome had a GCS on admission ranged from 3.0 - 7.0 with a mean of 5.43 ± 1.65; while patients with good outcome had a GCS on admission ranged from 4.0 - 8.0 with a mean of 6.56 ± 1.26, which is statistically not significant p (0.070). On other hand in group II; we found that patients with bad outcome had a GCS on admission ranged from 3.0 - 7.0 with a mean of 5.0 ± 1.35, while patients with good outcome had a GCS on admission ranged from 4.0 - 8.0 with a mean of 6.06 ± 1.34, which is statistically significant p (0.046), which denoting better outcome in group II than group I regarding the GCS on admission of both groups. This statistically significant better outcome in group II patients regarding their GCS of admission denotes that propofol has a neuroprotective properties that deceased the neurological complications of TBI and help to restore the normal or near normal neurological functions after TBI which can be attributed to its unique properties as a reducer of the cerebral metabolic rate of oxygen (CMRO2), an attenuator of glutamate-mediated excitotoxic mechanisms by either decreasing NMDA receptor activation, reducing glutamate release, or recovering the function of transporters responsible for glutamate uptake into neuronal and glial cells, a potentiator of GABAergic neuronal activity, a free radicals scavenger and an antioxidant.

As regard the ICU stay of the good outcome cases in the two groups (after exclusion of the cases with bad outcome as it may showed relatively shorter ICU stay which ended catastrophically with death) we found that, in group I, patients had an ICU stay ranged from 5.0 - 39.0 days with a mean of 14.31 ± 10.24; while in group II; patients had an ICU stay ranged from 4.0 - 21.0 days with a mean of 10.94±5.06. So, patients with good outcome in group II had an obviously shorter ICU stay than patients with good outcome in group I; although this difference is statistically not significant.

As regard the hospital stay in the two groups we found that, in group I, patients had a hospital stay ranged from 5.0 - 62.0 days with a mean of 24.60 ± 16.20 days; while in group II; patients had a hospital stay ranged from 4.0 - 54.0 days with a mean of 19.37 ± 13.56 days. Again, like in ICU stay days we found that patients in group two had a shorter hospital stay than patients in group I; again this difference is statistically not significant.

As regard the mortality after 6 months (time of finishing this study) we found that, in group I; 11 (36.7%) patients died; while in group II; 9 (30.0%) died. The number of patients died in group II was lesser than the number of patients died in group I and this may be contributed to the number of patients with a good outcome (GOS at 3 months of 4 - 5) in group II was more than the number of patients with a good outcome (GOS at 3 months of 4 - 5) in group I; which may affect the style of life and complications in the patients.

The final outcome of this study regarding to the number of patients fulfilling the criteria of success (improved GCS, decreased ICU stay and GOS at 3 months of 4 - 5) in each of the two groups at the end of the study period was improvement in GCS in both groups (increase in the mean value of the GCS in group I from 6.03 ± 1.54 to 9.30 ± 3.90 and in group II from 5.60 ± 1.43 to 9.28 ± 3.93). Seventeen patients (56.7%) out of thirty in group II (who had a good outcome according to GOS) fulfilled the criteria of shorter ICU stay which ranged from 4.0 - 21.0 days with a mean of 10.94 ± 5.06 days than patients with good outcome in group I. There were no significant difference in GOS at 3 month between the two groups, but when we compare between GOS at 3 months and GCS on admission in the two groups we found that the seventeen patients (56.7%) with good outcome (GOS at 3 months 4 - 5) in group II in relation to their GCS on admission had a statistically significant difference not found in the corresponding patients in group I.

Propofol has a neuroprotective effects in acute traumatic brain injury patients regarding their outcome.

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