The Professional Medical Journal
www.theprofesional.com

https://doi.org/10.29309/TPMJ/2021.28.12.6494

ORIGINAL PROF-0-6494

To determine the effectiveness of antiepileptic drugs in treatment of acute traumatic brain injury for preventing seizure.

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Article received on:
24/03/2021
Accepted for publication:
02/06/2021

ABSTRACT… Objectives: To determine the effectiveness of antiepileptic drugs in treatment of acute traumatic brain injury for preventing seizure. **Study Design:** Cross Sectional Study. **Setting:** Ziauddin Hospital, North Campus, Karachi. **Period:** 2014 to 2016. **Material & Methods:** Eighty diagnosed cases of traumatic brain injury were included in this study. Patients were examined physically and neurological assessment, with mental status was assessed by Glasgow Coma scoring. A blood sample was taken and Computed tomography was performed. Antiepileptic therapy was given for a period of one week minimally or 10 days maximally and patients were assessed clinically for seizures. All information was collected in the predesign proforma. **Results:** The patients median age was 25[16-43]. There were 70% male and 30% female**.** Rate of seizure was 6.3% (5/80) cases mortality was observed 5% (4/80) cases. Rate of seizure was significantly high in patients who had moderate TBI as compare to mild TBI (p=0.016). It was also significantly high in those cases who had diabetes and IHD. Rate of mortality was significantly high in seizure cases (p=0.0005). **Conclusion:** Prophylactic antiepileptic drugs are effective in decreasing the risk of early post-traumatic seizures in acute traumatic brain injury. These drug may provide an important and alternative treatment option for seizure prevention in acute TBI patients and prevent further brain damage.

Key words: Antiepileptic Drugs, Seizures, Traumatic Brain Injury.

Article Citation: Nasir S, Shehbaz L, Usmani MS, Saad A, Khan N. To determine the effectiveness of antiepileptic drugs in treatment of acute traumatic brain injury for preventing seizure. Professional Med J 2021; 28(12):1737-1741. https://doi.org/10.29309/TPMJ/2021.28.12.6494

INTRODUCTION

Traumatic brain injury (TBI) accounts for a major cause of death and disability worldwide. Every year two million population suffers from traumatic brain injury (TBI).[1] In U.S. According to WHO estimates, mild TBIs accounts for 70-90% of cases while the rest 10%-30% constitutes the moderate to severe injuries leading to disabilities and contributing to mortality.[2,3] TBI is classified as mild, moderate, severe according to Glasgow Coma Score and pathological classification is intracranial hemorrhage. (EDH, SDH, SAH, ICH, diffuse axonal injury and contusion hemorrhage).[8]

Post traumatic seizures complicate a wide range of patients with TBI, if they are not given the early prophylactic antiepileptic therapy. Post traumatic epilepsy (PTE) constitutes 5% of all the seizures and 20% of symptomatic epilepsy.[4,5] It complicates 1.9 to more than 30% of traumatic brain injuries which varies with the type and duration of TBI.[6] The treatment of early posttraumatic seizures is important as seizures will already compromise the damaged brain. The American college of Neurology also recommends use of early prophylactic antiepileptic therapy for seizures.[7] A 2001 the data from 10 randomized control trials, Cochrane review via using meta-analysis found early use of prophylactic antiepileptic therapy to be useful for the seizures prevention.[6] The Anti-epileptic drugs available for treatment are phenytoin, sodium valproate, levetiracetam, carbamazepine and some few other drugs are under randomized controlled trial, but no randomized controlled trials have been done to show usefulness of one over the other.

To manifest the advantage of prophylactic treatment in mild and moderate types of acute traumatic brain injury[9], Our Goal of the study was

to evaluate the efficacy of antiepileptic therapy in management of mild and moderate types of acute traumatic brain injury to see its outcome.

MATERIAL & METHODS

It was a cross-sectional study conducted at Ziauddin Hospital, Karachi from 2014 to 2016. Data was collected from patients of acute traumatic brain injury admitted through emergency in Neurosurgery Department at Ziauddin Hospital North Nazimabad meeting inclusion criteria. Informed and written consent was taken from the patient or the patient's attendant. Patients underwent detailed physical and neurological assessment, with particular note being made of their mental status assessed by Glasgow Coma scale. A venous blood sample was taken for complete blood count, Urea, Creatinine, Electrolytes and Computed tomography was performed. Patients were given treatment; first loading dose 15-20 mg/kg then maintenance dose 5 mg/kg. Treatment was administered for a minimum of one week or for a maximum of 10 days and patient will be assess clinically for seizures. Any adverse event was recorded specifying the time of onset, the duration, the severity and the relationship to the test medication. Data was analyzed by statistical software package SPSS version 20.0. Statistical analysis was expressed as frequencies and percentages. Descriptive statistics including patient's age, gender, and admission number was entered. Differences in drugs between groups were tested with chi-squared test. Mean ± SD and median (IQR) were calculated for quantitative variables and analyzed by Non-parametric Mann Whitney u test applied. P value ≤0.05 was considered significant.

RESULTS

Total 80 diagnosed cases of traumatic brain injury were included in this study. The patient's median age was 25(25^{th} -75^{th} percentile 16-43). There were 70% were male and 30% female**.** Out of 80 patients, 14(17.5%) had co-morbid, in which 14 were hypertensive, 8 diabetic mellitus, 3 IHD and one had CVA (Table-I). There were 44(55%) mild and 36(45%) moderate traumatic brain injury. Rate of seizure was 6.3% (5/80) cases, mortality was observed 5% (4/80) cases as presented in Figure-1. Rate of seizure was significantly high in patients who had moderate TBI as compare to mild TBI (p=0.016). It was also significantly high in those cases who had diabetes and IHD. Rate of mortality was significantly high seizure cases (p=0.0005) as shown in Table-II. Effectiveness of antiepileptic drugs treatment in term of prevention of seizure in acute traumatic brain injury patients was observed in 93.8% (75/80) cases while there were no side effects of the treatment.

Variables	Point Estimate
Age (Years)	25[16-43]
Systolic BP (mmHg)	130[110-140]
Diastolic BP (mmHg)	74[68-80]
Hear Rate (beat/Minutes)	90[70-110]
Gender	
Male	56(70%)
Female	24(30%)
Comorbid	
Hypertensive	14(17.5%)
Diabetic Mellitus	8(10%)
IHD	3(3.8%)
CVA	1(1.3%)

Table-I. Baseline characterstics of patietns (n=80).

Variables	n	Seizure		P-Values
		Positive (n=5)	Negative (n=75)	
Age (Years) †	80	25[16-42]	37[12-56]	0.588
Gender				
Male	56	4(7.1%)	52(92.9%)	0.614
Female	24	1(4.2%)	23(95.8%)	
TBI				
Mild	44	0(0%)	44(100%)	0.016*
Moderate	36	5(13.9%)	31(86.1%)	
Hypertensive				
Yes	14	2(14.3%)	12(85.7%)	0.171
No	66	3(4.5%)	63(95.5%)	
Diabetes mellitus				
Yes	8	2(25%)	6(75%)	0.02*
No	72	3(4.2%)	69(95.8%)	
IHD				
Yes	3	1(33.3%)	2(66.7%)	0.05*
No	77	4(5.5%)	73(94.8%)	
Mortality				
Yes	4	4(100%)	0(0%)	0.0005**
No	76	1(1.3)	75(98.7%)	

Table-II. Comparison of characteristics of patients with and without seizure.

Data are presented as †median [25th – 75th percentile], n (%).
Mann Whitney U test and chi-square test or fisher exact test used.
*P≤0.05
**p≤0.01

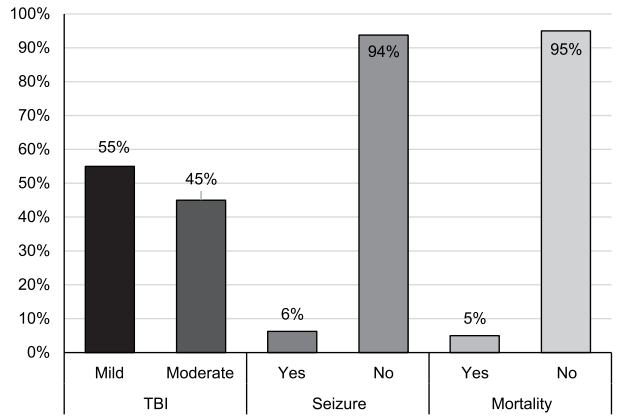

Figure-1. Severity TBI, seizure and mortality of patients.

DISCUSSION

Head injury is surveyed as a "Silent epidemic of the post industrialization era" and the concussion being the characteristic of TBI.[10] The diagnosis for the severity of disease is, by consciousness level and amnesia after trauma (PTA), it precisely been assorted on GCS at presentation mild[11,12], moderate and severe. However recently it has been argued that GCS of 13 should be categorized as moderate TBI, studies indicate that they had a greater risk of abnormal CT findings.[13,14]

Age related incidence has been approximated as bimodal with one peak seen at 15-24 years of age and another after 65 years of age.[15] Presently it was observed in patients between 11 to 30 years of age. Likewise in two separate studies.[16,17] second and fourth decade are most affected age groups respectively from the same region.

In this study out of 80 cases, 70% were male and 30% were female. Despite the fact that male gender is considered a predisposing factor for TBI[18,19] but the impact on the outcome is ambiguous, which found lower achievement in females after mild TBI.[20]

There were 55% mild traumatic brain injury cases and 45% were moderate traumatic brain injury. While in another study[8] admissions were offered to every patient with moderate to severe TBI.

In present study SDH, EDH and Frontal contusional bleed were the common CT findings. In Umerant et al study[8] acute SDH in 94(7.6%), brain contusion were in 175(14.1%) patients, EDH in 72(5.8%), SAH in 88(7.1%), depressed skull fracture in 57(4.6%) while pnuemocephlous were the dominant finding on 63(5.1%).

It complicates 1.9 to more than30% of traumatic brain injuries which varies with the type and duration of TBI.[6] The treatment of early post traumatic seizures is important as seizures will already compromise the damaged brain. The American college of neurology also recommends use of early prophylactic antiepileptic therapy for seizures.[7] A 2001 The data from 10 randomized control trials, Cochrane review via using meta-analysis found early use of prophylactic antiepileptic therapy but has no any effect in preventing seizures, death or neurological disability.[8]

In this study rate of seizure was a 6.3% (5/80) case so effectiveness of antiepileptic drugs treatment in term of prevention of seizure in acute traumatic brain injury patients was observed in 93.8% (75/80) cases while there was no side effect of the treatment. In all studies treatment effects were indistinguishable with the exception[21-23], which showed no treatment effect. It was estimated that pooled relative risk for early seizure prevention was 0.34 (95% CI 0.21–0.54; p=0.000). On this ground, In acute phase, 1 patient didn't have seizure out of 10. Alternatively, in acute phase 100 patients were managed with prophylactic antiepileptic drugs, 10 patients didn't have seizure. There were marked heterogeneity noticed between studies (÷2=16.44; df=5; p=0.005) for late seizures, hence for a summary relative risk was not calculated. The lack of blinding in the report and different drug type in that may account for some of the heterogeneity in the findings.[24,25] The relative risk was 1.28 (95% CI 0.90–1.81; p=0.046), with ÷2=0.14 (df=3; p=0.990) in the remaining four studies summary.

Mortality rate was 5 % (4/80) cases and hypotension was reported in one case in this study. SDH Occurrence increased approximately upto 5%[26] and 1 has a high mortality out of 5 cases.[27] The interval between trauma, surgery and prior GCS is directly related with the mortality.[27]

In latest analysis of randomized controlled trials of the prophylactically antiepileptic drugs uses for effectiveness in TBI, on bases of seizures end points, it is suggested, prophylactically antiepileptic drugs can used in first week after injury in high risk patients.[28]

CONCLUSION

Prophylactic antiepileptic drugs are effective in mild and moderate acute traumatic brain injury to decrease the risk of early post-traumatic seizures. These drugs may provide an important and alternative treatment option for seizure prevention in acute TBI patients and prevent further brain damage.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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3	M. Saad Usmani	Did write up, manuscript preparation, final layout.	
4	Alvia Saad	Data entry & Final layout.	
5	Naveed Khan	Manuscript preparation, final layout.