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Original Research Article

Preventing post-operative seizures in chronic subdural hematoma surgery: role of antiepileptic drugs

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ABSTRACT

Background: Seizures are a known complication of chronic subdural hematoma (CSDH) and its surgical treatment. While anti-epileptic drugs (AEDs) are often used prophylactically, there is limited evidence of their efficacy in the Bangladeshi population. This study was planned to determine the role of AEDs in preventing postoperative seizures in patients undergoing surgical treatment for CSDH.
Methods: This quasi-experimental study was conducted on 100 patients with CSDH undergoing Burr hole evacuation in the Department of Neuro Surgery at Bangabandhu Sheikh Mujib Medical University (BSMMU) and Dhaka Medical College Hospital (DMCH) from March 2015 to February 2017. Patients were divided into a study group (n=50, no antiepileptics) and a control group (n=50, given Phenobarbitone). Standard postoperative care was provided, with follow-ups on the 1st postoperative day, at discharge (7-10 days), and at 4 weeks. The control group continued Phenobarbitone post-discharge. Seizure occurrence was monitored throughout follow-ups to evaluate the drug's effectiveness in preventing postoperative seizures.
Results: The study population was predominantly male (71.0%), with most participants aged 51-60 years. At baseline, both groups were similar in terms of demography, clinical presentation, and level of consciousness. No preoperative seizure was noted among the study participants. Postoperative seizure incidence was 4.0% among the study group, whereas no one in the control group had developed a seizure. However, no significant difference in postoperative seizure proportion was found between the two groups.
Conclusions: Routine prophylactic use of antiepileptic adds no benefits in postoperative seizure prevention in CSDH patients.

Keywords: Chronic subdural hematoma, Anti-epileptic drugs, Post-operative seizures, Phenobarbitone

INTRODUCTION

Chronic subdural hematoma (CSDH) is a prevalent condition in neurosurgical practices that necessitates neurosurgical intervention.[1,2] The estimated annual incidence of CSDH ranges from 7 to 30 per 100,000 in extensive population-wide surveys and shows an increase with age.[3] The global prevalence of CSDH is increasing due to the aging population, the increasing use of antithrombotic medications, and the availability of cranial imaging.[4-7] The incidence of CSDH in patients over 65 is around 17-18 per 100,000, with an average age of 63; this is expected to double in the next 15 years due to an aging population. CSDH, a significant but reversible cause of dementia and neurological deficits in older adults, often originates from acute subdural hematomas. Blood accumulation in the subdural space triggers inflammation, fibroblast invasion, and neo-membrane formation,

followed by neo-capillary growth, clot liquefaction, and fibrin degradation, which influences clot formation and hemostasis. The progression of CSDH depends on the balance between plasma effusion or rebleeding and fluid reabsorption.[8,9]

The mechanism of epileptogenesis in chronic subdural hematoma is not fully understood but may result from mass-effect-induced cerebral blood flow reduction or structural trauma. Haemoglobin breakdown products, which are highly epileptogenic, increase seizure risk, particularly in patients with mixed-density hematomas on computed tomography (CT) scans.[10] Although the cerebral cortex is typically shielded by a membrane in later stages of hematoma development, membranes and recurring microbleeds from neovasculature can also provoke seizures, as proposed by Markwalder and Reulen.[11] Though postoperative seizures are a frequently occurring (2.3-17%) yet not well-understood complication in patients undergoing surgical treatment of CSDH. The efficacy of prophylactic treatment with anti-epileptic drugs has not fully determined.[12] Antiepileptic drugs (AEDs) are the conventional treatment for late posttraumatic epileptic seizures (lPTS); however, their application in early posttraumatic epileptic seizures (ePTS) is contentious.[13] The use of prophylactic anti-epileptic drugs (AEDs) in a chronic subdural hematoma (CSDH) is debated, with no consensus reached. A 2013 Cochrane review found no conclusive evidence due to limited observational studies and no randomized trials.[14] While one retrospective study showed reduced seizures with AEDs, others found no benefit.[15-18]

A clearer understanding of the role of AEDs in preventing seizures in this specific surgical population would help in the development of more effective treatment protocols. It would also guide clinicians in making informed decisions regarding the routine use of AEDs, balancing the potential benefits with the risks and side effects of prolonged medication use. However, no such study was conducted in Bangladesh. The aim of the study was to determine the role of anti-epileptic drugs in preventing seizures in patients undergoing surgical treatment for chronic subdural hematoma.

METHODS

This Quasi-experimental study was conducted in the Department of Neurosurgery at Bangabandhu Sheikh Mujib Medical University (BSMMU), and Dhaka Medical College Hospital (DMCH) from March 2015 to February 2017. Before the study, ethical approval was obtained from the institutional review board (IRB) of BSMMU.

Selection of the study participants

Patients with chronic subdural hematoma (CSDH), who were admitted to BSMMU, DMCH were included in this study. Patients with pre-existing seizures, major head injuries with brain contusions or other intracranial lesions, presence of ventriculoperitoneal (VP) shunt, prior craniotomy for hematoma evacuation, and recurrent chronic subdural hematoma were excluded. Following sample size calculation, 105 patients were initially approached, with 5 excluded for not meeting inclusion criteria, leaving 100 patients for the study. Informed written consent was taken from the study participant's guardian.

Allocation of treatment/intervention

Participants were purposively divided into a study group (without antiepileptic drugs) and a control group (with antiepileptic drugs) to assess the effect of prophylactic antiepileptic drugs on postoperative seizures. The control group received Phenobarbitone 100 mg every 12 hours, while the study group did not receive antiepileptic drugs during the study period. Burr hole evacuation of hematoma was performed as per standard practice, avoiding craniotomy to reduce the risk of seizures. Postoperative care was standard in both groups, with immediate management of convulsions if they occurred. Follow-up was done on 1st postoperative day (POD), at discharge (7-10 days) and at 4 weeks of POD. Upon discharge, control group patients were prescribed Phenobarbitone 60 mg, with instructions for emergency intervention in the event of seizures. After discharge the subsequent monitoring was done via outpatient visits and phone calls. During follow up the occurrence or presence of seizure was noted. A flow diagram of the subject recruitment process for the study is provided in Figure 1.

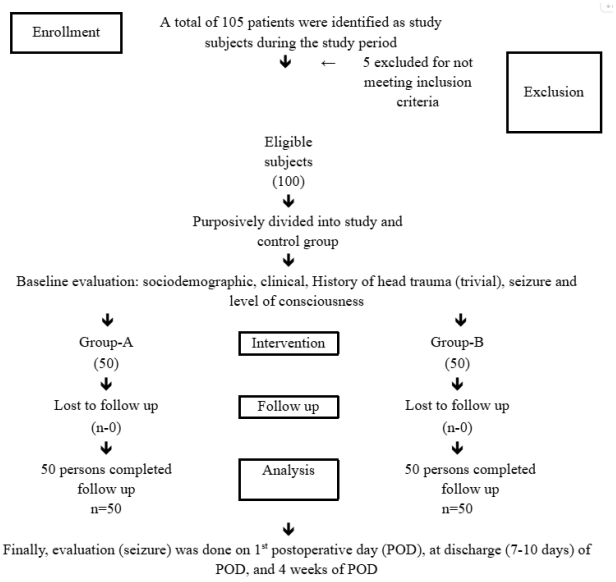

Figure 1: Study flow chart.

Statistical analysis

Data were analyzed using SPSS version 25, with categorical data expressed as frequencies and percentages and continuous data as mean and standard deviation. Differences in baseline characteristics, clinical features,

level of consciousness, and presence of seizure at follow-up between the study and control group were assessed by Chi-square tests or Fisher's exact test, with a significance level set at $p<0.05$.

RESULTS

The study population was predominantly male (71.0%), with most participants aged 51-60 years, accounting for 26.0% of the total participants. The mean age was 60.0±12.8 years. Common symptoms included visual disturbances (91.0%), headaches (82.0%), vomiting (77.0%), and memory disturbances (70.0%), with hemiparesis/paralysis affecting 50% and altered consciousness seen in 66.0%. A history of trivial head trauma was present in 50% of participants. The participants of the study and control group were demographically similar. There were no reported cases of seizures, and clinical characteristics were similar across both study and control groups (Table 1).

The majority of participants had mild impairment, comprising 42.0% of the total, while 34.0% were fully conscious. Moderate impairment was observed in 20% of participants, with more cases in the control group than in the study group. Severe impairment was rare, occurring in only 4.0% of participants, equally distributed between the groups (Table 2).

Table 1: Baseline characteristics of the study participants (n=100).

Variables	Groups N (%)		Total	
	Study group	Control group		
Age (in years)				
31-40	8 (16.0)	10 (20.0)	18 (18.0)	0.948
41-50	6 (12.0)	4 (8.0)	10 (10.0)	
51-60	14 (28.0)	12 (24.0)	26 (26.0)	
61-70	12 (24.0)	12 (24.0)	24 (24.0)	
71-80	9 (18.0)	10 (20.0)	19 (19.0)	
81-90	1 (2.0)	2 (4.0)	3 (3.0)	
Mean±SD	58.9±10.7	61.1±14.6	60.0±12.8	
Gender				
Male	34 (68.0)	37 (74.0)	71 (71.0)	0.509^{ns}
Female	16 (32.0)	13 (26.0)	29 (29.0)	
Clinical findings				
Headache	40 (80.0)	42 (84.0)	82 (82.0)	0.603
Vomiting	40 (80.0)	37 (74.0)	77 (77.0)	0.476
Seizure	0 (0.0)	0 (0.0)	0 (0.0)	
Visual disturbance	46 (92.0)	45 (90.0)	91 (91.0)	0.727
Hemiparesis/paralysis	24 (48.0)	26 (52.0)	50 (50.0)	0.689
Memory disturbance	37 (74.0)	33 (66.0)	70 (70.0)	0.383
Gait disturbance	23 (46.0)	20 (40.0)	43 (43.0)	0.545
Altered level of consciousness (GCS <15)	32 (64.0)	34 (68.0)	66 (66.0)	0.673
History of head trauma (trivial)				
Present	26 (52.0)	23 (46.0)	49 (49.0)	0.548
Absent	24 (48.0)	27 (54.0)	51 (51.0)	

Note: Chi-square test was done; data were presented as frequency (%), mean±SD, ns: non significant.

Table 2: Consciousness level of the study participants.

Variables	Group N (%)		Total	
	Study group	Control group		
Consciousness level (GCS)				
<9	2 (4.0)	2 (4.0)	4 (4.0)	
9-11	8 (16.0)	12 (24.0)	20 (20.0)	0.798
12-14	22 (44.0)	20 (40.0)	42 (42.0)	
15	18 (36.0)	16 (32.0)	34 (34.0)	

Note: A Chi-square test was done, data were presented as frequency N (%).

In the first follow-up, 4.0% of patients in the study group experienced seizures, while no seizures were reported in the control group; however, this difference was not statistically significant (p=0.495). In the second and third follow-ups, no seizures were observed in either group, with 100% of patients in both groups remaining seizure-free (Table 3).

Table 3: Distribution of patients according to post-operative seizure in groups.

Variables		Groups N (%)		P value
		Study group	Control group	
1st follow-up	Yes	2 (4.0)	0	0.495
	No	48 (96.0)	50 (100.0)	
2nd follow-up	Yes	0 (0.0)	0 (0.0)	
	No	50 (100.0)	50 (100.0)	
3rd follow-up	Yes	0 (0.0)	0 (0.0)	
	No	50 (100.0)	50 (100.0)	

Note: Data were presented as frequency (%), Fisher's exact test was done.

DISCUSSION

CSDH is a significant neurosurgical problem that primarily impacts the elderly, sometimes resulting from mild head trauma or spontaneous haemorrhage in vulnerable individuals. Surgical intervention, such as burr hole evacuation, is the standard treatment to alleviate symptoms and reduce hematoma volume. Patients undergoing this treatment are susceptible to seizures, which may hinder recovery, extend rehabilitation, and negatively impact outcomes. AEDs are frequently employed prophylactically to prevent seizures. The effectiveness of AEDs in preventing seizures in patients having surgery for CSDH remains contentious.

In our study, the majority of patients in both the study and control groups were older than 50 years, with a mean age of 58.9±10.7 years in the study group and 61.1±14.6 years in the control group. Most patients (26%) were aged 51-60, followed by 24% in the 61-70 age range. These findings are consistent with Soleman et al who reported an average age of 63 years, and Rubin et al. who found a mean age of 67 years.[16,19] Similarly, Babatola et al. reported that the majority of the patients were between 61-70 years.[20] In terms of gender distribution, males predominated in both groups, with a male-to-female ratio of 2.1:1 in the study group and 2.8:1 in the control group. These findings align with Soleman et al where males comprised 64% of the sample, and Rubin et al, Ohno et al, and Honda et al reported male percentages between 66% and 75%, which is similar to our study.[16,19,21,22]

Clinically, the most common findings among patients were visual disturbances, headaches, vomiting, and memory disturbances, with rates of 91%, 82%, 77%, and 70%, respectively. These results are comparable to previous studies, such as Babatola et al where headache prevalence was 89.6%, and Fogelhelm et al, which reported headache rates between 72% and 82%.[20,23] Hemiparesis and gait disturbance were observed in 50% and 43% of patients, while 66% exhibited an altered level of consciousness (GCS<15), a finding similar to Sucu et al who reported altered consciousness in 60% of patients.[24]

Additionally, we observed that half of the patients had a history of head trauma, with 52% in the study group and 46% in the control group, aligning with previous studies by Drapkin et al and Luxon et al which reported head trauma rates of 51% and 48%, respectively.[8,25] Notably, Iliescu et al reported a higher rate of trauma history at 77%.[9]

Epileptic seizures are a well-documented manifestation that may occur following surgical intervention for chronic subdural hematoma. Literature indicates that the incidence of epileptic episodes in a CSDH ranges from 2.3% to 5.3% postoperatively, dramatically elevating morbidity and mortality rates.[13,26,27] A 2013 Cochrane systematic review of trials investigating the efficacy of ASP in the CSDH population.[14] No recommendation was provided after the review due to the insufficient quality of evidence in the literature. Among the studies that were considered, there were a few authors who stated that the incidence of postoperative seizures was not high enough to warrant the utilization of preventive antiepileptic prescriptions.[16,21]

In this study, there was no history of seizures in either study group. However, the study group with no prophylactic antiepileptic exhibited seizure in 4.0% of patients, while none did in the control group. By the second and third follow-ups, no seizures were observed in any group, mirroring the findings of Rubin et al where postoperative seizures occurred in 1.8% of patients, and Ohno et al where seizure incidence remained low.[16,21] However, this difference was not significant enough to justify the use of antiepileptic drugs prophylactically to control seizures.

Limitations

The study was conducted in Dhaka city only, thus limiting generalizability. No side effect or complications following using antiepileptic drug was noted.

CONCLUSION

In conclusion, this study elucidated the demographic and clinical characteristics of patients with chronic subdural hematoma, predominantly comprising older males. No preoperative seizures were observed among the study subjects; nevertheless, the occurrence of postoperative seizures is exceedingly rare. The low incidence level restricts the capacity to ascertain the necessity of preventive antiepileptic medication administration. However, it can be concluded that postoperative

antiepileptic prophylaxis offers no advantage for individuals undergoing surgical treatment for chronic subdural hematoma. These findings align with the current literature and underscore the necessity for additional thorough research into optimum seizure prevention measures for this population.

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