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13. Traumatic Brain Injury and Use of Antiepileptic Drugs

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Figure 13.1: Traumatic Brain injury

Abstract:

Anti-epileptic drug (AED) prophylaxis in the first seven days of post-traumatic brain injury (TBI) is known to reduce seizure frequency acutely. AED efficacy is equivalent; therefore, the choice of AED may rest with its side effects. We hypothesize that AEDs that impair balance will prolong recovery, shown by a longer hospital stay. In our study, we aimed to evaluate the severity of trauma and the frequency of antiepileptic drug use in patients diagnosed with post-traumatic brain injury.138 patients with head trauma presenting for various reasons were included in the study with a retrospective file review. Patients were classified as mild, moderate, and severe according to the Glasgow Coma Scale at the time of admission to the hospital emergency department. It was determined that most of the cases were scored as mild-moderate at the time of admission to the hospital emergency department. it was observed that there was no need for the use of antiepileptic drugs. When the duration of antiepileptic drug use was analyzed, 65.1% (n=58) had 12 months, 16.7% (n=15) one month, 11.1% (n=10) 15 days, 4.9% (n) =4) six months, 2.2% (n=2) three months.

Keywords:

Head trauma, post-traumatic epilepsy, Glasgow coma scale, Anticonvulsants, Antiepileptic

13.1 Introduction:

Head trauma is a frequently observed situation in many countries and, accordingly, its mortality and morbidity are quite high [1]. The incidence of head trauma has extended to about 50 million cases per year worldwide; Therefore, it is foreseen that about half of the world's population will have a head injury in their lifetime [2]. Patients with head trauma constitute a significant part of the hospitalized patients in the emergency department, neurosurgery, general surgery, orthopedics, and pediatric surgery clinics [3].

Cortical lesions that occur secondarily in trauma may cause the occurrence of epileptic activity [4]. Traumatic brain injury in humans is not homogeneous and varies depending on the way the injury occurs, the distribution of damage caused by the injury, and the extent of the injury. The degree of the head injury may depend on the mechanical force applied directly to the head and secondary complications that may occur indirectly (hypoxia, ischemia, edema, and infection) [5].

The severity of head trauma can be measured with the Glasgow Coma Scale (GCS). They are classified into three groups including severe trauma (GCS 3-8), moderate (GCS 9-13), and mild trauma (GCS 14-15), and after trauma, long-term neuropsychological problems, and, in particular, epilepsy may develop. Post-traumatic epilepsy occurs in the form of recurrent epileptic seizures that develop secondarily in head trauma and can also manifest itself with spontaneous and recurrent seizures [5]. These seizures are classified as acute seizures if they occur within the first 24 hours, early-onset seizures within the first week, and late-onset seizures after a week. Acute seizures are caused by brain injury, but late-onset seizures are caused by oxidative stress factors and are more common in young adults [6]. Early-onset seizures after a head injury are commonly recognized as epilepsy [recurrent unprovoked seizures] because they have different mortality and prognosis [7]. Post-traumatic epilepsy is a disorder that develops secondary to traumatic brain injury and is characterized by symptomatic recurring seizures, and medications such as phenytoin, carbamazepine, sodium valproate, and levetiracetam are used to prevent it at an early stage [8-9]. The purpose of this study was to assess the severity of trauma and the frequency of antiepileptic drug usage in individuals with traumatic brain injury caused by head trauma.

13.2 Materials and Methods:

Between April 2013 and April 2021, 138 patients with head trauma were admitted to Gaziantep Medical Park Hospital emergency department and neurosurgery outpatient clinic for the reason of traffic accidents, falling from a height, gunshot injuries, assault, etc., followed up in the neurosurgery clinic and intensive care unit due to a risk factor for posttraumatic epilepsy (PTE), were enrolled in the study. The cases included in the study were retrospectively examined. The patient's age, GCS, gender, presence of chronic disease, cause of trauma, post-traumatic computed tomography scan (CT), magnetic resonance image (MRI), post-traumatic seizure history, frequency of post-traumatic antiepileptic medication use, trauma severity, presence of seizures, other organ injuries along with head trauma, antiepileptic drugs use, and duration of the use were evaluated. Patients with a known history of epilepsy and patients taking antiepileptic drugs, children under 12 years of age, and pregnant patients were not enrolled in the study.

Seizure development periods after head trauma are divided into six groups; Group 1: Those who do not have seizures after head trauma, Group 2: Seizures observed simultaneously with head trauma or within 15 days, Group 3: Seizures observed within 15-30 days, Group 4: Seizures observed within 30-90 days, Group 5: Seizures observed within 90-180 days, Group 6: Seizures observed within 180-365 days. All data were statistically analyzed using the "SPSS for Windows 16.0" version, and comparisons were made using the Pearson chi-square test. As descriptive statistics, the average standard deviation (SD) values were provided. The results were deemed significant at the P0.05 level and 95% confidence interval. Before the study (01/2021), it received approval from the SANKO University clinical research ethics committee.

13.3 Results and Discussion:

The patients in the study ranged in age from 12 to 84 years old, with an average age of 39 of the 138 patients, 34 of whom were women and 104 of whom were men. The women's average age was 32.6, while the men's average age was 43.4. During the application of the cases to the hospital emergency service, they were scored as mild, moderate, and severe according to GCS. GCS 3-8 denotes mild traumatic brain injury, GCS 9-12 denotes moderate traumatic brain injury, and GCS 13-15 denotes severe traumatic brain injury. During hospital admission, it was established that the majority of the cases were classified as mild to moderate, and the average hospital admission GCS score was 11.8 points. The patient's Glasgow Coma Scales were rated, and the results are shown in Table 1.A. Fifty-two (37.7%) of patients admitted to the emergency room for head injury did not have an accompanied disease, whereas 86 (62.3%) had an associated disease. When the etiologies of the cases involved in the study were examined: Falling from height accounted for the highest rate of patient groups at 53.6% (n = 74), and traffic accidents at 34% (n = 47). It was observed that 5.7% (n=8) of the patients were admitted to the emergency room as a result of the assault, 3 (1.8%) patients had gunshot injuries, and 6 (4.5%) patients were admitted to the emergency room for other reasons. When the radiological images of the patients after head trauma were examined, it was determined that there was subdural hematoma in mostly 66.7% (n=92), and no finding was encountered in 0.7% (n=1). CBT/MRI out comes of the cases are given in detail in Table A.2.

Table A.1: Glasgow coma scales of the patients

Glasgow Coma Scale Rating	Patient	Ratio
1	2	% 1.44
2	14	% 10,14
4	9	% 7.96
5	113	% 81.8

Table A.2: CBT/MRI Outcomes of Patients

CBT/MRI	Patients (n)	Percent (%)
No finding	1	0.7
Epidural Hematoma	14	10.1
Subdural Hematoma	92	66.7
Intraparenchymal Hematoma	10	7.2
Subdural Hematoma + Intraparenchymal Hematoma	5	3.6
Epidural Hematoma + Subdural Hematoma + Intraparenchymal Hematoma	3	2.2
Epidural Hematoma+ Intraparenchymal Hematoma	10	7.2
Epidural Hematoma+ Subdural Hematoma	2	1.4
Total	138	100

Accompanied organ injuries of the patients with head trauma admitted to the emergency department were evaluated and it was observed that % 90,6 (n=125) of patients had only head trauma, 2.9% (n=4) of patients had chest trauma and head trauma, and 1.4% (n=2) of patients had head trauma and abdominal trauma, 1.4% (n=2) of patients had extremity trauma and head trauma, and 1.4% (n=2) of patients had head trauma, 0.7% (n=1) of the patients had head trauma and pelvic trauma, chest trauma, pelvic trauma, and extremity trauma, 0.7% (n=1) of the patients had head trauma, chest trauma, and abdominal trauma, and 0.7% (n=1) patients had head trauma, chest trauma, and extremity trauma (Table:A.2).

Also, 64.5% (n=89) of the patients had a history of posttraumatic seizures, and 65.2% (n=90) had seizures depending on the severity of the trauma. However, 64.5% (n=89) of the patients with a history of seizures after head trauma began taking antiepileptic drugs. Since 35.5% (n=49) of the patients had no history of posttraumatic epilepsy, antiepileptic drug use was not required. Antiepileptic drug use duration was examined, 65.1% of 89 patients (n=58) needed the use of anticonvulsant drugs over 12 months, 16.7% (n=15) needed one month, 11.1% (n=10) needed 15 days, 4.9% (n=4) needed six months, 2.2% (n=2) needed three months. When the posttraumatic antiepileptic drug use periods of 89 patients were examined, it was determined that 80.8% (n=72) used Phenytoin, 14.6% (n=13) used Levetiracetam, 2.2% (n=2) used Carbamazepine and 2.2% (n=2) used Valproic Acid.

The International League Against Epilepsy (ILAE) and the International Bureau of Epilepsy (IBE) define epilepsy as a brain disorder marked by a chronic proclivity to generate epileptic episodes. Epilepsy is a non-infectious chronic brain illness that affects people of all ages. Epilepsy affects roughly 50 million people globally and is one of the most frequent neurological illnesses [10]. The global incidence of brain injuries is 939 incidents per

100,000 persons per year, affecting approximately 69 million people [11]. Individuals with head injuries who develop posttraumatic epilepsy are reported to have a higher mortality rate compared to head injury patients who do not develop posttraumatic epilepsy. In addition, posttraumatic epilepsy is associated with worse chronic consequences, including neurological, intellectual, and psychological activities [12].

A large-scale study conducted annually in the United States in 2002-2006 included falling from height (35.2%), traffic accidents (17.3%), gunshot injuries (16.5%), assault (10%), and other causes (21%) in the etiologies of head injuries [13]. When the etiologies of our cases were examined, it was seen that falling from height constituted the highest patient group and traffic accidents rank the second. Assault and gunshot injury and other causes were also other factors involved in the etiology, 74 (53.6%) patients fell from a height, 47 (34%) patients had a traffic accident, 8 (5.7%) patients had an injury, 3 (1.8%) patients had a gunshot injury, and 6 (4.5%) patients had other causes to apply to the emergency service. Accordingly, the frequency of causes of head trauma is similar to the studies conducted on this subject.

According to a prior study, the causes of damage are directly associated with age. Head injuries from motor vehicle accidents and attacks, for example, peak in adolescence and early adulthood, and the incidence and mortality associated with head injuries are higher in men in this age range [13]. When the etiologies of our cases were investigated, it was discovered that falling from a great height comprised the largest patient group, with 20 female and 54 male patients, and average ages of 24 and 47.3, respectively. The second most common cause was traffic accidents, with 10 female patients and 37 male patients, with an average age of 48.2 and 47.8 years, respectively. Then there are assaults, gunshot wounds, and other causes. Two of the assault instances were females, six included males, and the average ages were 61 and 62, respectively. The average age of the six male patients with gunshot wounds was 30 years old. Patients who went to the emergency room for various reasons included those who had been involved in occurrences such as work accidents, being trapped beneath rubble, and large things falling on their heads; additionally, two of them were female patients and four were male patients. Children (particularly newborns till the age of four), young people (15- to 24-year-olds), adults over the age of 60, and men of all ages are at the highest risk of traumatic brain damage [14].

In this study, 52 (37.7%) of patients who presented to the emergency room owing to head trauma did not have a chronic condition, whereas 86 (62.3%) patients did. The average age of those who did not have a chronic disease was 26.65 years, while the average age of those who did have a chronic disease was 64.13 years, with 104 men and 34 women participating. As a result, older people and men are more likely to have brain injuries. Tseng et al. found that 96 patients (46.7%) had a skull bone fracture in the emergency room, 28 patients (14.2%) had a midline shift, and 29 patients (14.7%) had head traumas. Head traumas are often accompanied by other system injuries, the other system injuries most commonly associated with cranial cerebral injury are the face, thorax, and abdomen injuries [15]. According to the findings of the study by Bahloul et al, 437 patients with head trauma suffered injuries in areas other than the head. Extracranial pathology was found in 61.6% of the patients, with 31.6% having rib or long bone fracture, 24.9% having facial damage, 23.6% having chest, 10.8% having abdomen, 8.9% having pelvic, and 1.8% having spinal injury [16].

In our study, accompanied organ injuries were evaluated in patients admitted to the emergency department due to head trauma, and 90.6% of patients had isolated head injuries, while 2.9% had chest injuries, 1.4% had abdominal injuries, 1.4% had limb injuries, 0.7% pelvis injuries, 0.7% chest and limb injuries, 1.4% chest, pelvis and limb injuries, 0.7% chest and abdominal injuries, and the results were similar to the reports in the literature.

In a community-based study conducted in the United States, 2.118 patients hospitalized with head injuries were followed up on for three years to establish the cumulative incidence of posttraumatic epilepsy. After accounting for a large decline in posttraumatic epilepsy (55% in 3 years), a risk of 4.4 was discovered per person. Post-traumatic epilepsy is more likely in people who have a history of psychiatric illnesses and depression [17]. Due to the severity of the stress, posttraumatic epilepsy seizures emerged in 64.5% of patients in our study.

A study assessing the risk of long-term epilepsy in children and young people following traumatic brain injury followed over 1.6 million children and young adults for up to 30 years after head trauma. The risk of epilepsy persists for more than ten years following mild brain injury, severe brain injury, and skull fracture, according to research. The relative risk of epilepsy increased with age in mild and severe injuries and was found to be higher, particularly in those over the age of 15 with mild and severe injuries. Women were found to be at somewhat higher risk than men. After mild and severe brain injury, the likelihood of epilepsy increased in patients with a family history of epilepsy [18]. The level of brain damage associated with traumatic brain injury increases the likelihood of epilepsy. Although traumatic brain damage is one of the few potentially preventable causes of epilepsy, it accounts for less than 10% of all cases [19]. Posttraumatic epilepsy is responsible for 20% of symptomatic seizures in the general community and 5% of all epilepsy patients sent to specialized epilepsy centers, according to another study [20].Seizures that occur within the first 24 hours after head trauma is referred to as acute seizures, those that occur between 24 hours and the first 7 days (early post-traumatic epilepsy) are referred to as provocative seizures and seizures that occur after 7 days (late post-traumatic epilepsy) are referred to as unprovoked seizures [21].

Temkin et al. evaluated the risk factors for early-onset seizures and found that a depressed skull fracture and subdural hematoma are related to approximately 25% of the risk of acute or early posttraumatic seizures. However, acute and early post-traumatic seizures are also indicators of the severity of brain injury and may account for the observed link between late-onset seizures [22]. The incidence of acute posttraumatic seizures is 1-4%, early-onset seizures are 4-25%, and late-onset seizures are 9-42%, according to Agrawal et al. [1].

In our study, it was found that 50 (36.2%) patients had a posttraumatic epilepsy seizure similar to the studies in the literature, and 88 (63.8%) patients had no epileptic seizure depending on the severity of the trauma. Seizures were observed within the first 24 hours in 1.6% of cases, within a week in 10.2% of cases, and began after the first week in 24.4% of the cases. According to a study, the risk of developing late-onset epilepsy is higher in patients who have an early-onset seizure after a head injury, and the recurrence rate of seizures was also found to be higher in such patients[23].A study, which deciphers the risk factors in a 2-year cohort of all patients aged 18 years and over with head trauma through the US National Trauma Data Bank, expanded the knowledge of the frequency of early-onset seizures, and it was shown that more than 80% of seizures are tonic-clonic rather than focal. This number is relatively low compared to other studies such as smoking, obesity, hypertension, or vascular disease were more common in those with seizures [24]. Although prophylactic seizure treatment is effective in preventing early posttraumatic seizures, it does not reduce the risks of long-term seizures, death, or neurological deficits [25].

Head trauma is an important risk factor for the development of epilepsy. A fifth of epilepsies are post-traumatic epilepsy, this type of epilepsy is a syndrome with generalized and focal seizures which have a structural cause. Clinical trials of antiepileptic drugs in this group do not distinguish between etiologies, and there are no tests for medicines, especially for patients with posttraumatic epilepsy. Therefore, the considerations to be taken into account are to ensure seizure control if possible and to avoid specific head trauma [26]. Phenytoin and Levetiracetam used to treat early-onset seizures caused by PTE have been revealed to be effective at an early stage but not prevent the occurrence of late-onset epilepsy, however, phenytoin is still the first choice. However, anti-epileptic drugs have narrow therapeutic limits and high toxicity even in neurologically stable patients. A new generation of antiepileptics such as gabapentin, topiramate, and lamotrigine are preferred in patients with PTE who experience post-traumatic stress disorders [27-28]. In a study conducted by Mee et al., it was concluded that prophylactic anti-epileptic drugs were not preferred in 52% of posttraumatic patients, but were used in 38% for a month, but 90% of doctors could not make a joint decision in determining the duration of treatment [29].

When choosing a drug to treat PTE, the patient's pre-traumatic psychological state should be considered. If there is such a problem, lamotrigine, lacosamide, oxcarbazepine or carbamazepine should be preferred by assessing their side effects for long-term treatment. Phenytoin and carbamazepine are effective in preventing early-onset PTE in high-risk patients after head trauma; However, prophylactic use of phenytoin, carbamazepine, or phenobarbital for preventing late-onset post-traumatic seizures is not recommended [30].

When deciding on epilepsy treatment, it should also be questioned whether the patient has drug or alcohol use. Likewise, late mortality was observed at a higher rate in people who had seizures of posttraumatic epilepsy than in patients with similar injuries and who did not have epilepsy [31-32]. It has been discovered that around one-third of epilepsy, cases are drug-resistant, and it has yet to be established whether there is a systematic difference in posttraumatic instances compared to other causes. In some drug-resistant PTEs, epilepsy surgery can be explored, and surgical treatment has been accepted for many years. Modern studies demonstrate that surgery, whether single-focus or multi-focus, can be successful in well-selected situations. This study demonstrates that only one area is epileptogenic and that the patient can deal with the cognitive effects of excision [34].

Antiepileptic medicines were started in 50 (36.2%) of the patients in our research who had a history of seizures following head trauma. We did not need the use of antiepileptic drugs for 88 (63.8%) patients with complaints of head trauma. Of the 50 patients with epilepsy after the head injury, 65.1% needed to use antiepileptic drugs for 12 months and over, 4.9% needed them for 6 months, 2.2% needed them for 3 months, 16.7% needed them for 1 month, and 11.1% needed them for 15 days. In the treatment of such patients, phenytoin was used in 80.8% of the patients, levetiracetam was used in 14.6% of the patients, valproic acid was used in 2.2% of the patients, carbamazepine was used in 2.2% of the patients.

13.4 Conclusion:

Inconclusion, a person carries an increased risk of epilepsy in connection with the severity of brain damage that can occur after a head injury. In our study, the GCS score was found to be 11.8 points (moderate). In addition, the frequency of antiepileptic drug use was also found to be 36.2%. When deciding on PTE treatment, the patient's pre-traumatic psychological status, previously diagnosed psychiatric diseases, and drug or alcohol use should also be questioned. In light of all these results, we think that effective emergency antiepileptic drug treatment, if necessary, is important in preventing secondary brain damage in patients with head trauma.

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