OUTCOMES OF EARLY POST TRAUMATIC SEIZURES IN HEAD INJURY PATIENTS AT PARIRENYATWA HOSPITAL.

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SUBMITTED IN PARTIAL FULFILMENT OF THE MASTER OF MEDICINE IN NEUROSURGERY

30/06/2015

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Abstract

Primary Objective; To compare the outcome of Traumatic Brain Injury (TBI) patients who develop early post traumatic seizures with the outcome of patients with post traumatic seizures who do not develop early post traumatic seizures.

Secondary Objectives; To estimate the incidence and risk factors of early post traumatic seizures in traumatic brain injured patients at Parirenyatwa Hospital.

Study factors; Early post traumatic seizures were the main study factor. Other various clinical and radiological factors were also considered.

Study outcomes; The Glasgow outcome score was used to assess outcome. Patients with a GOS of 1,2 or 3 were considered to have a poor outcome whereas patients with GOS of 4 or 5 were considered to have a good outcome.

Subjects; 252 consecutive patients, regardless of age who were admitted at Parirenyatwa Hospital for traumatic brain injury from 01/10/2014 to 15/05/2015.

Methods; A prospective observational study. A data sheet was created which listed all study and outcome factors.

Statistics; Contingency tables and Chi-square statistics were used to compare the outcomes. Both univariate and multivariate analysis was carried out.

Results; 252 patients have been recruited so far. 200 were males and 63 females. 31 patients developed early post traumatic seizures during the course of the study, giving an incidence of 12.3%. 35 patients died giving a case fatality rate of 13.8%. 52 patients (20.6%) had poor outcome. Of the patients who fitted, 64.5% had bad outcome compared to 14.5% of those who did not fit. The
association between fits and poor outcome was found to be statistically significant. The relative risk of poor outcome on univariate analysis in patients with early post traumatic seizures was 10.7 (CI 4.7-24.5) with a p-value of 0.000. Factors which were statistically significantly associated with poor outcome on univariate analysis were; fits, low Glasgow coma scale, age, male sex, anisocoria, alcohol ingestion, retained foreign body, acute epidural haematoma, intracerebral haematoma, multiple cerebral contusions and subarachnoid haematoma. Risk factors found to be associated with fits were; GCS, hemiparesis, retained foreign body, intracerebral haemorrhage, multiple contusions and subarachnoid haemorrhage.

Conclusion: The study demonstrated that early post traumatic seizures are strongly associated with poor outcome. It also showed that several risk factors may be associated with the development of seizures. Reducing the incidence of early post traumatic seizures should reduce the number of TBI patients with poor outcome. This can be done by giving seizure prophylaxis to TBI patients with risk factors for early post traumatic seizures on admission.
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OVERVIEW

There is lack of information on the frequency of occurrence of post traumatic seizures in Zimbabwe. To date no study has looked at the impact of early post traumatic seizures on mortality and morbidity in patients with head injuries. Such information is vital for the creation of local guidelines on the treatment and prophylaxis of early post traumatic seizures.

This study attempted to define the extent of the problem and to assess its impact on outcome in head injured patients. All head injured patients who met the inclusion criteria and were admitted during the study period were assessed. The incidence of those who develop early post traumatic seizures was calculated from this group. It was possible to compare risk factors and outcome between the group of patients who developed early post traumatic seizures and those who did not.
JUSTIFICATION FOR THE STUDY

At present, there is no information on both early and late post traumatic seizures in Zimbabwe. The incidence and outcome of patients with PTS is unknown. This study attempted to establish an initial data base of information on PTS. Prophylaxis is not routinely given at Parirenyatwa hospital. There is need to determine the incidence of PTS in our patients and compare the figures with those of other centres. There is also need to identify the group of traumatic brain injury patients who are at higher risk of developing PTS. We know that the pathophysiological mechanisms underlying early PTS worsen traumatic brain injury. It is important to determine whether early PTS patients have poor outcome compared to other traumatic brain injury patients. This will, hopefully assist in formulating our own policy and guidelines on pharmacoprophylaxis of PTS at Parirenyatwa Hospital.
LITERATURE REVIEW

Introduction

Traumatic Brain Injury (TBI) is a known cause of Post Traumatic Seizures (PTS). In the 1970s, Bryant Jennet classified PTS into early and late seizures. Early seizures occur within 7 days of TBI and late seizures occur after 7 days of injury\(^1\). Although these definitions were arbitrary, they are still widely accepted today. Seizures occurring within a few minutes after injury are classified as immediate seizures\(^2\).

Epidemiology

Traumatic brain injury (TBI) represents a huge burden on the resources of most countries. Worldwide, approximately 10 million people are affected by TBI every year. Population studies in the USA places the incidence of TBI between 180 and 250/100 000\(^3\). Unfortunately, there is lack of data on TBI from most countries in Africa. This is mainly due to poor surveillance systems. Studies have shown that the overall incidence of PTS is 4-53%\(^4\). The incidence of early PTS is between 4% and 16% of TBI patients\(^4\). Records from the Parirenyatwa Hospital surgical wards in Zimbabwe show about 40 patients are admitted with head injury every month\(^5\). These records also show that there has been an incidence of about 12.5% of early PTS at Parirenyatwa Hospital in the past year\(^5\). This study attempted to characterise the epidemiological and clinical features of patients who develop Early PTS at Parirenyatwa Hospital. It also tries to compare their outcomes with those of TBI patients who do not develop Early PTS.

Several risk factors are associated with Early PTS. A review of the literature reveals that commonly cited risk factors for Early PTS include intracranial haemorrhage, severe head injury, younger age and chronic alcoholism\(^4,5,6,7,8,9\). There are several other factors which include depressed skull fractures and retained
foreign bodies after penetrating injuries. It behooves the clinician to look for other causes of seizures in the patient with Early PTS. Previous history of seizures, head injury or brain damage should be sought. Early PTS may also occur as a result of hypoxia and brain ischaemia.

Acute intracranial haematoma, particularly acute subdural heamatoma in children is a strong risk factor for developing Early PTS. Penetrating head trauma carries a high risk of both early and late seizures. The risk is increased if there is a retained fragment in the head. Studies have shown that penetrating head injuries carry a 35-50% risk of seizures over 15 years. The Vietnam Head Injury study revealed a high proportion of PTS. 40.9% of head injured patients went on to develop seizures. This is very high compared to figures found in studies on civilians. Annegers et al found that 7.1% of TBI patients had PTS in a study carried out on civilian subjects.

The severity of the TBI is strongly associated with the development of Early PTS. A widely used classification for grading severity of TBI is the Glasgow Coma Scale (GCS). The GCS grades TBI into mild, moderate and severe depending on motor, eye opening and verbal responses. In general, studies on risk of PTS also include amnesia as an indicator of the severity of the injury. Post traumatic amnesia lasting more than 30 minutes is considered significant. Studies have shown that the relative risk of PTS increases with the severity of the head injury. The risk of PTS is more than 10 times greater in severe head injury compared to mild head injury. See figure 1 below.
Age is an important risk factor for PTS. In general risk is higher for the younger patient. Figure 2 below shows that the relative risk of PTS decreases with increasing age.

The fact that in patients with head injuries some develop PTS and others do not has led to the search for a genetic link to PTS. It is not known whether some patients with PTS have a genetic propensity to develop seizures. Researchers have, so far, found no association between family history of epilepsy and development of PTS\textsuperscript{13}.
Investigations should be done in order to detect electrolyte and metabolic conditions which may cause seizures. Conditions like hyponatriaemia, hypoglycaemia, hyperglycaemia and uraemia cause seizures. Central nervous infections may also cause seizures. This may be true for patients with basal skull fractures, particularly those who present late. Alcoholics may suffer from seizures due to withdrawal\textsuperscript{8,11}. Several medications have been found to increase risk of seizures when their blood levels are high. These include antibiotics like quinolones, antidepressants and analgesics\textsuperscript{16}.

**Pathophysiology of PTS**

The pathophysiological mechanisms underlying PTS still remain unclear. Immediate seizures appear to be due to the direct effects of trauma which irritates cells and cause seizures. This is particularly true for those cells with a low threshold for seizures. Early seizures are provoked by several factors caused by the injury. These include brain oedema, raised intracranial pressure, cerebral contusions and lacerations and breakdown of the blood brain barrier. Free iron and haemoglobin in the brain causes inflammatory changes and release of free radicals. There is also increased release of excitatory neurotransmitters like glutamate. All these changes lead to a decreased threshold for seizure activity. Early seizures worsen TBI by causing hypoxia, increasing neuronal cell metabolism and increasing release of excitatory neurotransmitters. Early seizures are also thought to increase cerebral blood flow raising intracranial pressure. For these reasons early seizures have to be treated even though they may not necessarily represent increased risk of developing post traumatic epilepsy. The mechanisms underlying late seizures are also unclear. However, it is believed that deposition of iron from free blood leads to gliosis. There are changes in the membrane conductance of neuronal cells. These pathological changes lead to changes in the neuronal circuitry causing epileptogenesis\textsuperscript{14,15,16,17}. A study carried out using MRI showed features of injury and scarring in the temporal lobes of patients with PTS.
Clinical Features

A seizure is a `paroxysmal usually self-limiting clinical manifestation (motor, sensory, autonomic or psychic) of an abnormal excessive, synchronous discharge of a large population of neurons resulting from diverse aetiologies`\textsuperscript{16}. The International League Against Eilepsy (ILAE) classifies seizures into generalized and partial seizures\textsuperscript{15,16}. This allows standardization of the diagnosis and management of seizures. Partial seizures are those `in which the first clinical and electrographic changes indicate initial activation of a system of neurons in one hemisphere`\textsuperscript{15}. There is no loss of consciousness during partial seizures and the patient remembers the events unlike complex partial seizures. Both simple and complex partial seizures can be secondarily generalized. Generalized seizures are `those in which the first clinical changes indicate initial involvement of both hemispheres`\textsuperscript{15}. Generalized seizures are subclassified into absence, myoclonic, tonic, clonic, atonic and tonic-clonic seizures. It is imperative for the clinician to be able to recognize seizures when they occur because there is need for prompt treatment. 50% of early seizures occur on the first day of trauma. Approximately 80% of these are generalized tonic clonic seizures\textsuperscript{17}. The seizures tend to be focal the longer the duration after trauma. Patients with PTS, especially children may develop status epilepticus\textsuperscript{11}. One study found that 22% of children under 5 years of age developed status epilepticus\textsuperscript{18}. This was much higher than the 11% prevalence of status epilepticus in the general population. Status epilepticus is defined as `a seizure lasting 30 minutes or which is repeated frequently enough not to allow recovery of consciousness for 30 minutes`\textsuperscript{15}.

Investigations

Ideally, CT scan is routinely done for patients with moderate and severe head injuries. The patient with mild head injury and early PTS should also have a CT scan. CT scan usually shows intracranial
haemorrhage in patients with early post traumatic seizures. Electroencephalography (EEG) is usually abnormal in head injury. It is not very useful for diagnosis of Early PTS.

**Treatment**

Various drugs are used to treat early PTS. These are anti-epileptic drugs and include phenytoin, sodium valproate, carbamezepine, benzodiazepines and phenobarbitol. Benzodiazepines like diazepam and midazolam are commonly used for the acute treatment of PTS at Parirenyatwa Hospital.

Benzodiazepines act on GABA (Gamma-aminobutryic acid) receptor/ chloride channel complex. They potentiate the inhibitory effects of the neurotransmitter GABA. Diazepam is given intravenously. 10-20mg can be given as bolus at 5mg/minute. The dose can be repeated every 30-60 minutes for status epilepticus. Diazepam is long acting. Midazolam is short acting and rapidly absorbed. Benzodiazepines cause drowsiness and reduce level of consciousness of the patient.

Phenytoin is also commonly used to treat Early PTS. Phenytoin prevents the propagation of action potentials by binding to closed sodium channels and preventing their opening. Phenytoin is also GABA-nergic. Phenytoin has less sedative effects compared to other anti-convulsants. It is given intravenously to stop a seizure. A loading dose of 15mg/kg is given slowly intravenously at not more than 50mg/minute. This is followed by a maintenance dose of 100mg 8 or 6 hourly. Such a dosage in adults usually achieves adequate serum concentration of the drug (40-80umol/l). Care should be taken in giving phenytoin because there is a non-linear relationship between maintenance doses and steady state concentration. This means that small increases in doses may cause a large increase in the serum levels of the drug. Intravenous administration can cause bradycardia, hypotension and skin necrosis. Using fosphenytoin avoids these problems. Fosphenytoin is a prodrug of phenytoin. Phenytoin can cause ataxia, nystagmus, skin rashes and hypersensitivity reactions. Other side effects like gingival
hypertrophy, hirsitusim, peripheral neuropathy, megaloblastic anaemia and bone demineralization tend to occur with long term use. Phenytoin induces the metabolism of other drugs eg other anticonvulsants, warfarin and contraceptives.

Carbamazepine is commonly used for partial and secondarily generalized seizures. It acts by opening K+ channels and prolonging the closure of Na+ channels. The usual starting dose is 100-200mg orally once or twice daily. The dose may have to be increased gradually because serum levels decrease due to enzyme auto- induction. The aim is to reach a blood level of 13-42um/l \(^{15,16,19}\). Carbamazepine is a cytochrome P450 inducer. Adverse effects of carbamazepine include nausea, drowsiness, confusion, transient rashes, blood dyscrasias and Syndrome of inappropriate ADH secretion (SIADH). The carbamazepine is given in divided doses or as slow release formulations in order to reduce toxicity\(^{15,16,19}\).

Sodium valproate potentiates GABA-ergic activity. It increases the sensitivity of the GABA receptors and decreases the enzyme breakdown of GABA. It has minimal sedative effects. It can be given slowly (3-5 minutes) intravenously as a bolus (up to 10mg/kg) followed by intravenous infusion (maximum 2.5g/day). Adverse effects include tremor, transient hair loss, thrombocytopenia, ataxia and increased appetite. Like the other anticonvulsants, valproate causes neural tube defects and other congenital anomalies when taken during pregnancy\(^{15,19}\).

Phenobarbital is cheap. It can be given orally, intramuscularly or intravenously. The usual dose is 2-5mg/kg/day. Phenobarbitone causes central nervous system depression but has very little systemic side effects\(^{15,19}\). There are several newer anticonvulsants. Some clinical trials have been conducted to assess the efficacy of levetiracetum for the prophylaxis of PTS\(^{20,21,22}\).
Prophylaxis

In 1990 Temkin et al carried out a randomized placebo controlled double blind study on the effectiveness of phenytoin in the prevention of PTS. Their results showed an impressive 73% protective effect of phenytoin against early PTS. However, there was no significant difference in the incidence of late PTS between the controls and the patients on phenytoin\(^5\). Previous studies had shown conflicting results. However, these studies had methodological weakness\(^5\). Current information suggests\(^{23}\)

1. Anticonvulsant therapy reduces early PTS in adults.

2. Anticonvulsant therapy does not protect against late seizures.

3. There is no evidence to suggest that anticonvulsant prophylaxis reduces early and late seizures in children.

Phenytoin is the first choice drug for pharmacoprophylaxis of early PTS in severe head injury. It is given for a week. Carbamazepine is also effective in reducing early PTS. Recent studies have shown that levetiracetam is as effective as phenytoin for prophylaxis. It can be used as a second line drug.

Risk of post traumatic epilepsy with early post traumatic seizures

One third of adults with early post traumatic seizures develop late post traumatic seizures. This is much higher than the 3% incidence of late PTS in patients without early PTS\(^{23,24}\). The risk of developing late PTS in children is less than that of adults with early PTS (10-20%). Immediate PTS are believed to be caused by direct force of trauma triggering epileptogenic activity in cells which have a low threshold for seizures. Given such a pathophysiological mechanism, the risk of developing late post traumatic seizures would be unlikely. However, studies have shown that immediate PTS also carries an increased risk of
late PTS. Current guidelines prophylaxis for late post traumatic seizures in certain head injuries based on CT SCAN findings\textsuperscript{23}. These are the risk factors for late PTS;

1. Biparietal contusions.

2. Dural penetration with bone and metal fragments.

3. Multiple intracranial operations.

4. Multiple subcortical contusions.

5. Subdural haematoma with evacuation.

6. Midline shift greater than 5mm.

7. Multiple or bilateral cortical contusions.
The Research Question

Is there an increased risk of poor outcome in head trauma patients who develop early post traumatic seizures compared to those who do not develop early post traumatic seizures?

Hypothesis

Null Hypothesis: In all patients admitted for head injury at a Central Hospital, the proportion of patients with early post traumatic seizures who have a poor outcome, as measured by the Glasgow outcome scale on discharge, will be the same as the proportion of patients who have a poor outcome who do not develop early post traumatic seizures.

Alternative Hypothesis: In all patients admitted for head injury at a Central Hospital, the proportion of patients with early post traumatic seizures who have a poor outcome, as measured by the Glasgow Outcome Scale on discharge, will be two and half times the proportion of patients who have poor outcome who do not develop post traumatic seizures.

Primary Objective

To compare the outcome of TBI who develop early seizures with the outcome of those TBI patients who do not develop early post traumatic seizures at Parirenyatwa Hospital.

Secondary Objectives

1. To measure the incidence of early post traumatic seizures in patients admitted with TBI at Parirenyatwa Hospital.

2. To identify risk factors associated with poor outcome.
3. To identify the risk factors for developing early post traumatic seizures in patients admitted with head injuries at Parirenyatwa Hospital.

**Study type**

A prospective cohort study.

**Study subjects**

252 consecutive patients, regardless of age who were admitted at Parirenyatwa Hospital for traumatic brain injury from 01/10/2014 to 15/05/15. Patients were monitored from admission until discharge or death. Any seizures were observed, treated and recorded by nurses and doctors trained to diagnose seizures. For the purposes of this study, all seizures occurring within 7 days were treated as early post traumatic seizures.

**Exclusion criteria:**

1. All patients who were unwilling to participate.

2. All unconscious patients or patients younger than 18 years whose relatives or guardians were unwilling to allow them to participate in the study.

**Study Setting**

Parirenyatwa Hospital adult (B9) and paedriatic (A2) neurosurgical wards.
**Study factors**

A. Identification data (hospital number, age, sex)

B. Clinical data (History - previous history of head injury, previous history of fits, alcohol intake, family history of epilepsy, Physical examination - Glasgow Coma Scale, anisocoria, hemiparesis, depressed skull fracture, penetrating injury, retained foreign body)

C. CT Scan findings

1. Haematomas - acute subdural, acute epidural, intracerebral.

2. Contusions - frontal lobe, temporal lobe, parietal lobe, occipital lobe, cerebellar/brain stem or multiple lobe contusions

3. Presence and severity of subarachnoid haemorrhage

CT scan findings was used to diagnose intracranial haemorrhage and brain contusions. Mild, moderate and severe head injury were defined by Glasgow Coma Scale of 13-15, 9-12 and 3-8 respectively.

**Outcome Factors**

Glasgow Outcome Scale (GOS). The GOS has 5 grades.

Grade 1 is death.

Grade 2 is a persistent vegetative state.

Grade 3 is severe disability.
Grade 4 is mild disability.

Grade 5 is normal.

Patients in grades 4 and 5 were classified as good outcome patients and patients in grades 1, 2 and 3 were classified as poor outcome patients. In this way the outcome variable was converted into a dichotomous variable.

**Methods:**

252 consecutive patients, regardless of age who were admitted at Parirenyatwa Hospital for traumatic brain injury from 01/10/2014 to 15/05/15. Patients were monitored from admission until discharge or death. Data was collected as soon as the patient was seen by the doctor in the ward. Any seizures occurring thereafter were observed, treated and recorded by nurses and doctors trained to diagnose seizures. A data collection sheet was created which was available to all doctors in the neurosurgical wards at Parirenyatwa Hospital (see appendix). The data collection sheet captured the relevant information regarding the study and outcome factors. The usual treatment and prophylaxis protocols and regimens for post traumatic seizures at the hospital were followed.
Statistics:

Contingency tables were created in order to compare the outcome (GOS) and the exposure. TBI patients with early post traumatic seizures represented the exposed group and those without early post traumatic seizures were the non-exposed. The Chi-square statistic was used to look for the presence of significant association between the study factors and the outcome. Relative risk was be used to assess the strength of association between the independent variables and the outcome since this was a prospective study. Multivariate analysis was performed to assess confounding. The STATA version 12 statistical software package was used for ease of calculations.

Sample size

The sample size was calculated using Pocock’s formula. The following assumptions were made; the level of significance was set at 5% and the required power was 80%. Chiarreti et al demonstrated that poor outcome occurs in about 19.1% of patients without early post traumatic seizures. A study conducted in Nigeria had almost similar figures (19.2%). For this study, it was assumed that 20% of the non-exposed patients would have a poor outcome. These studies also showed that outcome was worse in TBI patients with early PTS. 53% of patients with early PTS had poor outcome in the Chiarreti study. It was assumed that 50% of the exposed would have a poor outcome. Therefore, it was assumed that 20% of the non-exposed and 50% of the exposed would have a poor outcome. The proportion of exposed patients with poor outcome is expected to be two and half times the proportion of non-exposed patients with poor outcome. Based on these figures a sample size of at least 36 in each group was required in order to detect the important size difference. Parirenyatwa ward records show that there has been an incidence of 12.5% for early post traumatic seizures in the past one year. This meant that a minimum of 288 patients was required in order to detect at least 36 patients with early PTS.
**Ethics:**

This study involves a very important subject in Neurosurgery. TBI constitutes the bulk of neurosurgical admissions at Parirenyatwa Hospital. Extensive research on PTS has been done in the developed world but very few studies have been done in the developing world. Unfortunately, it is difficult to extrapolate findings from the developed world to our own circumstances because of differences in availability of technology and expertise. This study should provide relevant information for use in the poorly resourced environment.

Most of the study subjects were not expected to be able to accept or decline participation in the study because of the severity of their illness. However, informed consent was sought from close relatives or guardians.

**Results**

A total of 252 eligible patients have been recruited into the study so far. 2 patients were excluded because they remained unconscious until they died with no relatives to give consent. There were 200 males (79.5%) and 52 females (20.5%). Only 35 (14%) of these patients were 12 years old or younger. 31 (12.3%) patients had early post traumatic seizures during the course of the study. This is consistent with findings from previous studies (4-16%)\(^25\). 35 patients died giving a case fatality ratio of 13.8%. 11 (31.4%) of the 35 patients who died had early post traumatic seizures. Only 187 (74%) out of the 252 patients had head CT scan done leaving 65 patients with missing radiological data.
**Graph 1.** Comparing numbers of patients younger than 12 and older patients.

**Graph 2.** The incidence of early post traumatic seizures at Parirenyatwa hospital was found to be 12.3% in this study.
14% of the study group were children 12 years old or younger. Of these 35 children, 7 (20%) developed seizures. 24 of the 217 adults (11.1%) who participated in the study developed seizures. The proportion of children who developed seizures was higher than for adults. This fact has been confirmed by other studies in the past. However, on statistical analysis there was no significant difference between the proportion of fits in children compared to adults for our study. Univariate analysis showed a p-value of 0.141 with a relative risk of 2.0 and confidence interval of 0.8-5.1. The null hypothesis could therefore, not be rejected and we accepted that they may be no difference between the two groups.

13% (33) of the patients had severe head injury based on the Glasgow Coma Scale. 24 of these 33 patients died during the course of the study. This represents a case fatality rate of 73% amongst the patients with severe head injury. This is shocking but hardly surprising given the limited facilities at the hospital. There are only 6 ICU beds available for all medical and surgical specialties for the whole hospital. Patients with severe head injury often have to be nursed in a general ward. Theatre time is also limited. This results in delays in performing emergency neurosurgical operations. The mortality rates for severe head injuries from specialized trauma centres in the developed countries are approximately 20%. These figures have improved from high mortality rates of 80% in the 1950s in developed countries. Other developing countries have quoted mortality rates of 35-46%. As expected, the mortality rates for moderate head injury was much lower with 17 out of 73 (23.3%) patients dying. This is much higher than figures from the developed world were 4-8% of moderate head injury patients die.
Graph 3. Showing frequency according to GOS. The number of patients in GOS 1 i.e. 36 (14.2%) gives the case fatality rate for the duration of the study. 1=patients who die, 3=severe neurological deficits, 4=mild neurological deficits and 5=normal.

Table 1. STATA table comparing age and outcome

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</table>
No patients were discharged with a GOS of 2 during the course of the study. Patients who are classified GOS 2 are in a vegetative state. They are unconscious and entirely dependant. Such patients were kept in the hospital until they improved and were discharged or until they died.

**Graph 4.** Outcome dichotomized into good outcome (79% of patients) and bad outcome (21%).
Graph 5. Proportion of patients based on Glasgow Coma Scale.

Fits compared to outcome

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. tab fits Outcome
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Table 2. Fits compared to outcome. 1=patients who die, 3=severe neurological deficits, 4=mild neurological deficits and 5=normal.
For the sake of simplicity and to allow easier comparison with previous studies, the outcome variable was divided into two categories namely; poor outcome and good outcome. Other investigators have used a similar dichotomization\textsuperscript{25,26}. Patients with Glasgow Outcome Scale of 1, 2 or 3 represent the poor outcome patients. Those whose GOS is 4 or 5 are the good outcome patients. Dichotomizing the outcome variable in this manner represents a practical and clinically useful way of assessing the patients. The good outcome patients become independent and less of a burden to society. The bad outcome patients are either dead or heavily dependent on others. Previous studies have used this method to classify their patients \textsuperscript{25,26}.

Fits compared to outcome- dichotomised

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. tab fits outcome

      | outcome |
      |        | ok | badd | Total |
      | fits   |    |      |      |
      | no     | 189| 32   | 221   |
      | yes    | 11 | 20   | 31    |
      | Total  | 200| 52   | 252   |
```

\textbf{Table 3. Simplied STATA table showing the outcome dichotomized into 1=poor outcome and 2=good outcome. Outcome ok=GOS 4 or5 and bad outcome GOS 1,2 or 3. Patients who had fits represent the exposed and those who did not have fits represent the non-exposed group.}
. logistic outcome  fits

Logistic regression

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<td>0.000</td>
<td>0.0055166</td>
<td>0.0450615</td>
</tr>
</tbody>
</table>

Tab 4. *Stata table showing the relationship between the exposure (fits) and outcome.*

The calculations above show that 20.6% (52 patients) of the patients had a bad outcome compared to 79.3% who had a good outcome fig7. However, of note is the fact that 64.5% (20 out of 31 patients) of patients who developed fits had bad outcome compared to 14.5% (32 from 221) of patients who did not develop fits. This represents a highly significant statistical difference between the two proportions.

Patients with post traumatic seizures were ten times more likely to suffer poor outcome compared to those who did not have fits. The relative risk was 10.7, with a 95% confidence interval of 4.7-24.5 and a p-value=0.00. *We therefore rejected the null hypothesis and accepted the alternative hypothesis that the proportion of patients with head injury who develop seizures with poor outcome is more than the proportion of patients who have poor outcome who do not develop post traumatic seizures.*

On univariate analysis of the independent variables, the following factors were found to be statistically significantly associated with the outcome; male sex, alcohol intake, reduced GCS, anisocoria, hemiparesis, depressed skull fracture, retained foreign body, fits, acute epidural haematoma,
intracerebral haemorrhage, contusions (frontal, temporal, parietal and multiple lobe) and subarachnoid haemorrhage.

**Table 5.**

**Univariate analysis-comparing independent variables with outcome.**

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>Chi 2</th>
<th>p-value</th>
<th>Relative risk</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;12</td>
<td>0.0348</td>
<td>0.065</td>
<td>0.315</td>
<td>0.09-1.07</td>
</tr>
<tr>
<td>&gt;12</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>sex</td>
<td>12.02</td>
<td><em>0.005</em></td>
<td>11.38</td>
<td>1.62-80.02</td>
</tr>
<tr>
<td>Previous head injury</td>
<td>0.16</td>
<td>0.69</td>
<td>0.77</td>
<td>0.21-2.86</td>
</tr>
<tr>
<td>Alcohol intake</td>
<td>16.97</td>
<td><em>0.000</em></td>
<td>4.05</td>
<td>2.1-7.9</td>
</tr>
<tr>
<td>Level of consciousness</td>
<td>57.01</td>
<td><em>0.000</em></td>
<td>5.6</td>
<td>3.2-8.5</td>
</tr>
<tr>
<td>anisocoria</td>
<td>16.4</td>
<td><em>0.000</em></td>
<td>7.2</td>
<td>2.8-18.6</td>
</tr>
<tr>
<td>hemiparesis</td>
<td>20.8</td>
<td><em>0.00</em></td>
<td>6.5</td>
<td>2.9-14.3</td>
</tr>
<tr>
<td>Depressed skull fracture</td>
<td>1.66</td>
<td><em>0.183</em></td>
<td>1.8</td>
<td>0.75-4.5</td>
</tr>
<tr>
<td>Penetrating injury</td>
<td>0.54</td>
<td>0.445</td>
<td>1.96</td>
<td>0.35-11</td>
</tr>
<tr>
<td>Retained foreign</td>
<td>5.55</td>
<td><em>0.032</em></td>
<td>12.2</td>
<td>1.2-119.7</td>
</tr>
<tr>
<td></td>
<td>Value</td>
<td>p-value</td>
<td>CI</td>
<td></td>
</tr>
<tr>
<td>--------------------------</td>
<td>-------</td>
<td>---------</td>
<td>------------</td>
<td>----------</td>
</tr>
<tr>
<td>Fits</td>
<td>33.5</td>
<td><strong>.000</strong></td>
<td>10.7</td>
<td>4.7-24.5</td>
</tr>
<tr>
<td>Acute subdural haematoma</td>
<td>0.91</td>
<td>0.33</td>
<td>2.6</td>
<td>0.62-4.17</td>
</tr>
<tr>
<td>Seizure treatment</td>
<td>31.22</td>
<td><strong>.000</strong></td>
<td>14.44</td>
<td>5.3-39.2</td>
</tr>
<tr>
<td>Acute epidural haematoma</td>
<td>4.32</td>
<td><strong>.031</strong></td>
<td>2.9</td>
<td>1.1-7.65</td>
</tr>
<tr>
<td>Intracerebral haemorrhage</td>
<td>11.98</td>
<td><strong>.002</strong></td>
<td>14.2</td>
<td>2.7-73.8</td>
</tr>
<tr>
<td>Frontal lobe contusions</td>
<td>5.14</td>
<td><strong>.02</strong></td>
<td>7.65</td>
<td>1.17-6.01</td>
</tr>
<tr>
<td>Temporal lobe contusions</td>
<td>1.4</td>
<td><strong>.22</strong></td>
<td>1.82</td>
<td>0.7-4.8</td>
</tr>
<tr>
<td>Parietal lobe contusions</td>
<td>4.3</td>
<td><strong>.03</strong></td>
<td>2.9</td>
<td>1.1-7.65</td>
</tr>
<tr>
<td>Occipital lobe contusions</td>
<td>0.03</td>
<td>0.85</td>
<td>1.17</td>
<td>0.2-5.9</td>
</tr>
<tr>
<td>Cerebellar/brainstem contusions</td>
<td>0.91</td>
<td>0.32</td>
<td>4.1</td>
<td>0.2-67.3</td>
</tr>
</tbody>
</table>
Multivariate analysis was performed using multiple logistic regression. Modelling was done and some of the independent variables had to be dropped. The following variables were found to be significantly related to the outcome after taking into account confounding; fits, level of consciousness, hemiparesis, alcohol, anisocoria, multiple contusions and subarachnoid haemorrhage.

```
. logistic outcome1 alcohol1 conscious1 hemi1 anisocoria1 multiple1 sah fits1
```

| outcome          | Odds Ratio | Std. Err. | z     | P>|z| | [95% Conf. Interval] |
|------------------|------------|-----------|-------|-----|---------------------|
| alcohol1         | 3.398656   | 2.011568  | 2.07  | 0.039 | 1.065381             | 10.842 |
| conscious1       | 2.653135   | 0.933794  | 2.77  | 0.006 | 1.330994             | 5.288621 |
| hemi1            | 6.084868   | 3.72624   | 2.95  | 0.003 | 1.832289             | 20.2073 |
| anisocoria1      | 4.723897   | 3.872785  | 1.89  | 0.058 | 0.9472423            | 23.55807 |
| multiple1        | 8.188839   | 7.858994  | 2.19  | 0.028 | 1.248266             | 53.7202 |
| sah              | 20.55312   | 21.94511  | 2.83  | 0.005 | 2.535287             | 166.6205 |
| fits1            | 6.466939   | 3.936023  | 3.07  | 0.002 | 1.961667             | 21.31926 |
| _cons            | 6.43e-08   | 1.86e-07  | -5.73 | 0.000 | 2.22e-10             | 0.000186 |

Table 6. Stata output showing multiple logistic regression after modeling.
After dropping some of the other variables and multiple logistic regression the strength of association between the exposure of interest (seizures) and outcome was still present although somewhat reduced. Patients with early post traumatic seizures were 6.1 more times likely to have a bad outcome than those without early post traumatic seizures.

**Risk for early post traumatic seizures**

Statistical analysis was also done in order to explore the relationship between the occurrence of early post traumatic seizures and the other independent variables. The aim was to identify possible risk factors for early post traumatic seizures. Both univariate analysis and logistic regression were carried out.

**Association between occurrence of fits and risk factors- Univariate analysis**

On univariate analysis, six factors were found to be statistically significantly associated with the development of fits. These variables were; severe head injury (level of consciousness <=8), moderate head injury (LOC 9-12), hemiparesis, retained foreign body, acute intracerebral haemorrhage and subarachnoid haemorrhage. Patients with severe head injuries were found to be 3.5 times more likely to develop early post traumatic seizures compared to patients with mild head injury (relative risk= 3.46 with CI 1.87-6.83 and p=0.0002).
Table 7

Univariate analysis of risk factors for seizures.

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>Chi-2 value</th>
<th>p-value</th>
<th>Relative risk</th>
<th>Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe head injury</td>
<td>14.01</td>
<td><strong>0.0002</strong></td>
<td>3.46</td>
<td>1.87-6.83</td>
</tr>
<tr>
<td>Moderate head injury</td>
<td>6.18</td>
<td><strong>0.012</strong></td>
<td>2.17</td>
<td>1.25-3.77</td>
</tr>
<tr>
<td>Hemiparesis</td>
<td>10.2</td>
<td><strong>0.001</strong></td>
<td>4.5</td>
<td>1.9-10.9</td>
</tr>
<tr>
<td>Foreign body</td>
<td>3.45</td>
<td><strong>0.047</strong></td>
<td>7.6</td>
<td>1-55.7</td>
</tr>
<tr>
<td>Acute intracerebral haemorrhage</td>
<td>15.44</td>
<td><strong>0.000</strong></td>
<td>21.3</td>
<td>4-112</td>
</tr>
<tr>
<td>Subarachnoid haemorrhage</td>
<td>13.13</td>
<td><strong>0.000</strong></td>
<td>10.2</td>
<td>3-35</td>
</tr>
<tr>
<td>Multiple cont</td>
<td>2.73</td>
<td><strong>0.078</strong></td>
<td>3.15</td>
<td>0.88-11.3</td>
</tr>
</tbody>
</table>

Patients with the above conditions are likely to develop post traumatic seizures and should be considered for anti-seizure prophylaxis.
DISCUSSION

By definition, early post traumatic seizures occur within a week of head injury. Previous studies have shown that patients who develop early post traumatic seizures have poor outcomes and are at higher risk of developing late seizures. The negative effect of post traumatic seizures on outcome is biologically plausible given the pathophysiology of seizures (see section on causes and consequences of seizures below page 31). Furthermore, post traumatic seizures may also cause cognitive and behavioural problems later on. To date, no studies have been carried out in Zimbabwe to validate the negative association of early post traumatic seizures and poor outcome. Indeed, the incidence of PTS is not known. This study showed that patients who develop early post traumatic seizures at our institution fare much worse than Traumatic Brain Injury patients who remain seizure free. The incidence of early PTS was also found to be high (12.96%) although it is similar to figures from other previous studies. Several factors were found to be associated with fits. This provides a means of attempting to prevent early PTS by identifying patients with these risk factors and offering them prophylaxis.
The causes and consequences of early post traumatic seizures.

The mechanisms of epileptogenesis in TBI are poorly understood. However, it is postulated that traumatic brain injury causes a disruption in the blood-brain-barrier. This leads to changes in the homeostasis of the central nervous system. These changes in the electrolyte, fluid and
neurotransmitter levels cause increased excitability of neurons resulting in seizures. This pathway is shown on fig 3. Fig 3 also shows the effects of trauma and seizures on the brain. Seizures are due to increased neuronal activity which causes an increase in the energy requirements of the brain. Seizures also cause a decrease in cerebral blood flow and disturbed cellular metabolism. Both these factors result in reduced energy production so that the increased demand cannot be met. This disordered physiology results in cytotoxic oedema. Thus secondary brain injury is worsened. Changes in fluid and electrolytes as a result of seizures cause an increase in brain osmolarity. This is compounded by the development of cytotoxic oedema. The increased brain osmolarity leads to vasogenic oedema. Both cytotoxic and vasogenic oedema worsen secondary brain injury as a result of seizures.

The disruption of the blood-brain-barrier is central to the development of post traumatic seizures. The BBB covers most of the cerebral microvasculature. It is composed of specialized endothelial cells. These endothelial cells are held together by tight junctions, they have a continuous basement membrane, increased mitochondria and are supported by astrocytic processes or podocytes. The BBB provides a means of selecting substances that can enter the brain depending on its requirements. Small lipid soluble molecules can cross by diffusion. Larger molecules (amino acids, glucose) enter by carrier mediated processes. Some proteins enter by pinocytosis.

Disruption of the BBB exposes the brain to unregulated substances which increases the excitability of neurons. These substances include potassium and glutamate. See fig. An elevated potassium level in the brain is associated with an increase in seizures²⁹ PH Ilfland et al.
The concentrations of potassium in the brain are tightly regulated. Gradients are maintained across the cell membrane and across the BBB. These gradients provide a means of enabling rapid repolarisation in the neurons. Control of potassium movement is by sodium/potassium pumps on the neuronal membrane. More importantly, the astrocytes are involved in potassium movement. Astrocytes act as potassium buffers. They mop up excess K+ and they also act as spatial buffers. In this case a syncytium of astrocytes mops K+ from an area of high concentration to another part of the brain with low concentration. Astrocytes are also involved in the control of movement of water in the brain. They have aquaporins on their end feet.

Glutamate is an excitatory neurotransmitter. Normally its concentration is much higher in the plasma compared to the brain. A disruption of the BBB leads to exposure of the brain to excess glutamate concentrations. This results in increased neuronal excitability and seizures.

Free radicals are also believed to be important in the pathogenesis of seizures. Haemoglobin and other blood products are believed to have deleterious effects on tissues when they are outside the vasculature. They cause damage to cells leading to increased epileptogenesis.

In summary, TBI results in disruption of the BBB which, in turn alters central nervous homeostasis leading to seizures. The seizures themselves cause cytotoxic and vasogenic oedema through various mechanisms. This worsens secondary brain injury.
**Fig4.** Quantitative gradients across the BBB and their predicted effect on neuronal excitability after TBI.

The font sizes on the left and rights side of the idealized BBB are roughly proportional to their trans-BBB concentrations under homeostatic conditions\(^{29}\).

### Incidence of seizures

Occurrence of seizures was measured prospectively. This allowed calculation of incidence. It also helps to establish a clear temporal relationship between the occurrence of fits and the outcome. The
incidence of post traumatic seizures in this study was high. This was not surprising given that most patients did not receive seizure prophylaxis. Most of the head injury patients are referred from various centres throughout the country. There are no clear protocols for seizure prophylaxis. It is up to the referring or attending doctors and nurses to institute prophylaxis. This figure is probably an underestimate of the true incidence of early PTS at our institution. There are no video Electroencephlography (EEG) facilities available. Diagnosis of seizures depended on actual observation of fits by attending clinical staff. It is possible that many fits could have been missed during the study. Furthermore, even though the clinical staff attending the traumatic brain trauma patients were all qualified to work in a neurosurgical unit, there was no special training course on diagnosis of seizures before the starting the study. This may have allowed inter-observer error.

Outcome of TBI patients with early post traumatic seizures.

Patients with post traumatic seizures were ten times more likely to suffer a bad outcome compared to those who did not develop fits. This association was statistically significant. This finding is also in keeping with the pathophysiology of post traumatic seizures see fig 3. This is a prospective study. The temporal relationship between fits and the outcome is very clear. However, there is the possibility of confounding. Confounding occurs when there is the mixing of the effects of an exposure with that of another exposure. The other exposure must be associated with the outcome independent of the original exposure. For example, our exposure of interest in this case is seizures. However, we know that fits may be associated with severe head injury. Patients with severe head injury are more likely to develop seizures given what we know of the pathophysiology of both conditions. Patients with severe head injury are likely to have poor outcome independent of seizures. Multiple logistic regression was done and all exposure factors were included in the equation in order to cater for confounding. Seizures were
still found to be statistically significantly associated with poor outcome even after factoring in other exposures. This study confirms that seizures are associated with poor outcome in head injury patients. Some of the weaknesses in the assessment of the exposure factor during the study have already been pointed out. There may have been underestimation of the incidence of fits due to lack of 24-hour monitoring with video EEG and possible inter-observer error because different clinical staff would observe and record the seizures. Outcome was assessed using the Glasgow Outcome Scale. This is a widely accepted method of measuring outcome in head injury patients. Several previous studies have utilized this tool. This allows easier comparison of the results of this study and these earlier studies.

For ease of statistical analysis, outcome was dichotomized into poor outcome and good outcome. This was an arbitrary classification which was used instead of the usual 5 classes of the GOS. Previous studies have utilized the same dichotomization. Poor outcome included patients with GOS of 1, 2 or 3 and good outcome included grades 4 and 5 patients. Apart from allowing easier computations this stratification is also clinically relevant. Patients who were normal or had mild deficits were grouped as having a good outcome. Patients who died, were in a vegetative state or had severe deficits were placed in the bad outcome group. GOS was done on discharge. This was performed by neurosurgical residents in the team who were all conversant with the GOS.

Other factors which were found to be significantly associated with poor outcome on univariate analysis were; male sex, alcohol intake, reduced GCS, anisocoria, hemiparesis, depressed skull fracture, retained foreign body, acute epidural haematoma, intracerebral haemorrhage, contusions (frontal, temporal, parietal and multiple lobe) and subarachnoid haemorrhage. These findings are consistent with results of previous studies. The Brain Trauma Foundation has drawn up a list of 'Early Indicators of Prognosis in Severe Traumatic Brain Injury' in its Guidelines on Management and Prognosis of Severe Head Injury 2000. The other source of information was the IMPACT study. The IMPACT study was a large meta-analysis involving 8 randomised controlled trials and 3 large cohort studies with a sample size of about
9000 patients\textsuperscript{30}. The result of these studies was to come up with ‘building blocks’ of modifiable and non-modifiable risk factors for poor outcome (see page 4, adapted from Youmans Neurological Surgery Vol 4, 2011)\textsuperscript{30}. Most of these ‘building blocks’ were used as independent variables in this study. Analysis of the IMPACT study results revealed that the GCS particularly the motor component had the strongest association with outcome (Univariate Odds Ratio 7.48 and Confidence Interval 5.6-9.8)\textsuperscript{30}. The current study also found a strong association between the GCS and outcome. The very strong association between male sex and poor outcome needs to be interpreted with caution. The confidence interval is very wide. This could reflect the large difference in the number of males to females in the sample. There has been no such strong association between male sex and poor outcome in previous studies. There is also no plausible biological explanation in the literature so far. Some investigators have found some genetic factors to be linked to post traumatic epilepsy\textsuperscript{31}. Ramon Diaz-Arrastia et al found that patients with inheritance of the apolipoprotein E e4 allele were more likely to develop post traumatic seizures. However this allele is not sex linked and moreover, the association was with late seizures\textsuperscript{31}. The rest of the above study factors were expected to be associated with poor outcome given the pathophysiology. This study should also have considered other potential risk factors for poor outcome and development of early post traumatic seizures. These include laboratory parameters. Laboratory results like haemoglobin and serum electrolyte levels should have a bearing on outcome in head injury patients. Serum S-100 levels have also been linked to prognosis in head injury patients\textsuperscript{29}. Serum S-100 levels have been found to closely correlate with breach of the blood brain barrier. It is therefore, a useful biomarker of brain injury. In assessment of the CT scans, diffuse axonal injury was not specifically considered. This is a fairly common pathology in head injury patients and could have been asessed using the Marshall radiological grading system.
Risk factors for early PTS

One of the secondary objectives of this study was to find the study factors which are significantly associated with the development of seizures. The purpose of this line of investigation was to identify those TBI patients who could benefit from prophylaxis. Antiseizure prophylaxis has been found to reduce the occurrence of early post traumatic seizures\(^{21,22,23,24}\). On univariate analysis, the following factors were found to be associated with fits; severe head injury (level of consciousness \(\leq 8\)), moderate head injury (LOC 9-12), hemiparesis, foreign body, acute intracerebral haemorrhage and subarachnoid haemorrhage. The lack of association between some of the variables (eg acute subdural haemorrhage, brain contusions) and fits is surprising. However, it should be noted that diagnosis of these conditions required CT scan imaging. Not all patients were could have CT scans done. This lack of association could be due the fact that these diagnoses may not have been picked up in those patients who did not undergo CT scanning. Therefore, the results for these variables also have to be interpreted with caution.

Validity of the study

Several issues in both the design and analysis were considered in order to improve the validity of the study. The study type was prospective. A prospective study allows a clear temporal relationship between the exposure and the outcome to be established. It is also the best way to directly measure the incidence and relative risk of a study factor. By its nature, a prospective study allows accurate ascertainment of both the exposure and outcome. These events are observed and recorded as they occur rather than in retrospect. The above factors strengthened the internal validity of the study. The external validity of a study refers to the generalisability of its findings to other populations. The results of this study can be easily applicable to all populations with limited resources. In other words, the results of this study can be generalized to all populations in the developing world.
Selection of the exposed group and comparison group.

The exposed group comprised admitted patients with TBI who developed seizures. Selection of admitted patients as a study group allowed easier measurement of the both the exposure and outcome since these patients were already being monitored in the hospital. The study period was limited to the duration of admission only. This allowed easier follow up. In fact, there were no losses to follow up and this helped to strengthen the internal validity of the study. In choosing a comparison group there is need to ensure that \textit{the groups being compared should be as similar as possible with respect to all other factors that may be related to the disease except the determinant under investigation}\footnote{32}. A simple way of meeting these criteria is choose a general cohort and then select a group of patients with the exposure from the general cohort and another group without the exposures. This means that all other variables are randomly distributed and therefore, likely to be similarly distributed between the two groups. This method was employed in the design of this study. A general cohort of traumatic brain injury patients admitted at Parirenyatwa hospital was used. The exposed and non-exposed were selected from the same cohort.

Ascertainment of exposure and outcome

The seizures and outcomes were directly observed and recorded. This greatly enhanced the accuracy of the data. The data sheet provided a Glasgow Outcome Scale to make assessment easier. Furthermore, all patients had an assessment of the GOS done by a neurosurgery registrar on discharge. Parirenyatwa hospital has no facilities for video EEG recording. It is possible that some patients who fitted could have been missed leading to underestimation of the incidence of seizures. It causes misclassification error because some patients who had fits were probably placed in the non-exposed. However, this is a random misclassification error. The lack of Video EEG and other advanced monitoring equipment affects both the exposed and non-exposed groups in a similar manner. This type of misclassification bias cannot
cause the presence of an association between exposure and outcome where there is none. A random misclassification error, unlike a non-random misclassification error is not detrimental to the internal validity of a study.

The presence of missing data was worrying. This applied to patients who were unable to undergo CT scanning. Patients were required to pay for CT scanning. We knew some of them would be unable to afford the CT scan. Unfortunately, the study itself was poorly funded and we could not assist these patients. However, during the course of the study the hospital started paying for emergency CT scans. As a result, the number of participants with missing data was not as high as we had feared. This problem had been anticipated even before the study commenced. This was discussed with the statistician who knew that he had to take this problem into consideration during the analysis stage of the study.

Ascertainment of both exposure and outcome could have been further strengthened by following up all patients including the discharged patients for at least 7 days. However, internal validity of the study could not have affected because both the exposed and non-exposed were equally affected by this bias. It led to a random misclassification error.

In general, the both the internal and external validity of the study were strong. This means that the findings of the study most likely represent the true state of the disease at Parirenyatwa hospital. Furthermore, the results can be readily generalized to other populations in the developing world.

Conclusion

This study has managed to achieve the following;

1. It has shown that there is a strong association between early post traumatic seizures and poor outcome.
2. It has also identified other factors associated with poor outcome.

2. It has provided an incidence of early post traumatic seizures for our institution.

3. It has identified the risk factors for early post traumatic seizures in our head injury patients.

This information is very useful for the management of our head injury patients. It should form the basis of head injury and traumatic brain injury protocols. We should try to reduce the number of patients who have poor outcome by reducing the incidence of fits. This can be done by seizure prophylaxis. The risk factors that have been found to be associated with seizures in this study can be used to identify our head injury patients who are likely to benefit from seizure prophylaxis. Therefore, all TBI patients who have risk factors for developing seizures will receive anti-seizure prophylaxis as part of our head injury protocol. This protocol should be made available to all clinical staff who handle trauma patients including referring hospitals and paramedics.

The study has also highlighted other problems related to management of head injury patients at our institution. The mortality rate of 73% in patients with severe head injury is most alarming. Other countries in the developing world have brought these figures down to less than 50% \(^{28}\). Much has to be done in order to improve our situation. A head injury protocol has to be developed as a matter of urgency. Unfortunately, other factors may be difficult to control since they are related to economic and policy matters. These include increasing the number of available Intensive Care Unit beds and emergency theatres.
DATA COLLECTION SHEET

A. Identification data

1. Patient identity

2. Age

3. Sex

B. Clinical data

4. Previous history of head injury

5. Previous history of fits

6. Family history of epilepsy

7. Alcohol intake

8. Level of consciousness

9. Anisocoria

10. Hemiparesis

11. Depressed skull fracture

12. Penetrating injury

13. Retained foreign body

14. Fits
15. Seizure prophylaxis       YES........       NO........
16. Seizure treatment        YES........       NO........

C. CT Scan findings

16. Acute subdural Haematoma        YES........       NO.............
17. Acute Epidural Haematoma        YES........       NO.............
18. Intracerebral Haemorrhage       YES.....       NO......
19. Frontal lobe brain contusions   YES......       NO......
20. Temporal lobe brain contusions  YES........       NO........
21. Parietal lobe brain contusions  YES........       NO........
22. Occipital lobe brain contusions YES........       NO......
23. Cerebellar/brain stem contusions YES......       NO......
24. Multiple lobe contusions       YES........       NO......
25. Subarachnoid haemorrhage       YES........       NO........
D. Outcome

1. Death

2. Vegetative state

3. Severe disability

4. Mild disability

5. Normal
ABREVIATIONS

BBB  Blood Brain Barrier

CT   Computed Tomography

GABA Gamma-aminobutyric acid

GCS  Glasgow Coma Scale

GOS  Glasgow Outcome Scale

PTS  Post traumatic Seizures

TBI  Traumatic Brain Injuries
REFERENCES


17. Evans WR, Scachter SC. Post traumatic seizures and epilepsy. Review article. Up to Date May 2013.


