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Search details

Incidence of fits in adults with severe traumatic brain injury compared to incidence of fits in adults with a history of epilepsy.

Management of patients with severe traumatic brain injury with or without a prior history of fits.

Resources searched

NICE Evidence; TRIP Database; Cochrane Library; CINAHL; EMBASE; MEDLINE; PsychINFO; Google Scholar

**Database search terms:** "severe traumatic brain injur*"; severe adj1 (trauma* OR injur*) adj2 brain; "severe TBI"; exp CRANIOCEREBRAL TRAUMA; fit*; seizure*; convulsion*; paroxysm*; exp SEIZURES; incidence; INCIDENCE; treatment*; intervention*; therap*; manag*; exp THERAPEUTICS; adult* OR older* OR geriatric* OR seniors* OR aged OR "older people" OR "older person*"; exp ADULT

**Evidence / Google Scholar search string(s):** ("severe traumatic brain injury" OR "severe TBI" OR "craniocerebral trauma") (fit OR seizure OR convulsion OR paroxysm) incidence / ("severe traumatic brain injury" OR "severe TBI" OR "craniocerebral trauma") (fit OR seizure OR convulsion OR paroxysm)

Summary

Quite a lot of research in this area. I have divided it into those studies dealing with incidence and those dealing with treatment. Inevitably there are some studies dealing with
Guidelines and Policy

Royal College of Surgeons
Head Injury: Triage, assessment, investigation and early management of head injury in infants, children and adults 2007

NICE
Head injury: Triage, assessment, investigation and early management of head injury in children, young people and adults 2014

NICE Pathways
Head injury 2015

NICE Quality Standards
Head injury - quality standard (QS74) 2014

Royal College of Radiologists
Head injury 2012

SIGN
Guideline 130 Brain injury rehabilitation in adults 2013
Guideline 110: Early management of patients with a head injury 2009

Evidence Reviews

AHRQ
Multidisciplinary Postacute Rehabilitation for Moderate to Severe Traumatic Brain Injury in Adults 2012

Cochrane Database of Systematic Reviews
Hyperbaric oxygen therapy for the adjunctive treatment of traumatic brain injury 2012

In people with traumatic brain injury, while the addition of HBOT may reduce the risk of death and improve the final GCS, there is little evidence that the survivors have a good outcome. The improvement of 2.68 points in GCS is difficult to interpret. This scale runs from three (deeply comatose and unresponsive) to 15 (fully conscious), and the clinical importance of an improvement of approximately three points will vary dramatically with the starting value (for example an improvement from 12 to 15 would represent an important clinical benefit, but an improvement from three to six would leave the patient with severe and highly dependent impairment). The routine application of HBOT to these patients cannot be justified from this review. Given the modest number of patients, methodological shortcomings of included trials and poor reporting, the results should be interpreted cautiously. An appropriately powered trial of high methodological rigour is required to define which patients, if any, can be expected to benefit most from HBOT.
We found a larger number of studies than expected but few RCTs of confirmable quality and none that allowed us to determine if head cooling improves functional outcome. The review has shown that some methods of head cooling can reduce intracranial temperature, which is an important first step in determining effectiveness, but the evidence is not robust.

### Published Research – Databases

**Incidence**

1. Anti-epileptic prophylaxis in traumatic brain injury: A retrospective analysis of patients undergoing craniotomy versus decompressive craniectomy

**Author(s)** Ramakrishnan V., Dahlin R., Hariri O., Quadri S.A., Farr S., Miulli D., Siddiqi J.

**Citation:** Surgical Neurology International, January 2015, vol./is. 6/1, 2152-7806 (01 Jan 2015)

**Publication Date:** January 2015

**Abstract:** Background: Seizures account for significant morbidity and mortality early in the course of traumatic brain injury (TBI). Although there is sufficient literature suggesting short-term benefits of antiepileptic drugs (AEDs) in post-TBI patients, there has been no study to suggest a timeframe for continuing AEDs in patients who have undergone a decompressive craniectomy for more severe TBI. We examined trends in a level-II trauma center in southern California that may provide guidelines for AED treatment in craniectomy patients. Methods: A retrospective analysis was performed evaluating patients who underwent decompressive craniectomy and those who underwent a standard craniotomy from 2008 to 2012. Results: Out of the 153 patients reviewed, 85 were included in the study with 52 (61%) craniotomy and 33 (39%) craniectomy patients. A total of 78.8% of the craniotomy group used phenytoin (Dilantin), 9.6% used levetiracetam (Keppra), 5.8% used a combination of both, and 3.8% used topiramate (Topamax). The craniectomy group used phenytoin 84.8% and levetiracetam 15.2% of the time without any significant difference between the procedural groups. Craniotomy patients had a 30-day seizure rate of 13.5% compared with 21.2% in craniectomy patients (P = 0.35). Seizure onset averaged on postoperative day 5.86 for the craniotomy group and 8.14 for the craniectomy group. There was no significant difference in the average day of seizure onset between the groups P = 0.642. Conclusion: Our study shows a trend toward increased seizure incidence in craniectomy group, which does not reach significance, but suggests they are at higher risk. Whether this higher risk translates into a benefit of being on AEDs for a longer duration than the current standard of 7 days cannot be concluded as there is no significant difference or trend on the onset date for seizures in either group. Moreover, a prospective study will be necessary to more profoundly evaluate the duration of AED prophylaxis for each one of the stated groups.

**Source:** EMBASE

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Available in fulltext from Surgical Neurology International at ProQuest
2. Enteral administration of antiepileptic agents could have efficacy for prevention of post-traumatic seizures in severe traumatic brain injury

**Author(s)** Mocjiduki K., Suzuki H., Kawasaki A., Hotta M., Namiki M., Harada T., Takeda M., Yaguchi A.

**Citation:** Critical Care, March 2014, vol./is. 18/(S174-S175), 1364-8535 (17 Mar 2014)

**Publication Date:** March 2014

**Abstract:** Introduction Antiseizure prophylaxis is recommended for preventing only early post-traumatic seizures (PTS) in the guidelines for the management of severe traumatic brain injury (TBI) by the Brain Trauma Foundation. Phenytoin is recommended to reduce the incidence of early PTS prophylaxis. Early enteral nutrition has recently shown theoretical advantages for prevention of bacterial translocation to maintain normal turnover of gut mucosa and is commonly used for TBI patients. Our hypothesis is that the enteral administration of antiepileptic agents is also useful for early PTS. Methods This retrospective observational study included all adult patients admitted to our tertiary academic medico-surgical ICU due to TBI from September 2011 to August 2012. Patients who have epilepsy as a past history were excluded. Clinical data were collected from electrical medical archives. The baseline characteristics collected were age, gender, diagnosis, antiepileptic agents, timing of start and adverse effects of those agents, and methods of administration. Results Of 65 patients with TBI, 25 patients (18 men, seven women; mean age 56.7 +/- 20.1) who were administered antiepileptic agents for PTS prophylaxis were studied. Fifteen cerebral contusions, 10 acute subdural hematomas, nine traumatic subarachnoid hemorrhages, two cerebral infarctions, two pneumocephalus and one traumatic intracerebral hemorrhage were shown in 25 patients. All patients were alive 28 days after the injury. Fourteen patients (56%) were intravenously administered (13 phenytoin and one phenobarbital), while 11 patients (44%) were administered with enteral feeding (four valproates, four carbamazepine and three zonisamides) as PTS prophylaxis. The average start day of PTS prophylaxis was 2.6 days after the injury by intravenous administration, and 2.2 days by enteral administration, respectively. Two patients with phenytoin showed hepatic dysfunction as an adverse effect and no patient showed early PTS both by intravenous and by enteral administrations. Conclusion The present study has some limitations because it is a single-center retrospective analysis. However, enteral administration of antiepileptic agents could be useful for PTS prophylaxis. Considering cost, adverse effects and serum monitoring, there is a possibility of enteral administration of antiepileptic agents as an alternative to intravenous phenytoin.

**Source:** EMBASE

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3. The use of hyperbaric oxygen therapy as an adjuvant therapy to phenytoin in the control of late post traumatic non convulsive epilepsy in patients with severe traumatic brain injury

**Author(s)** Tahon S.A., Abd Elkader A.A., Fayed A.M., Abd Elmonem S.A.

**Citation:** Neurocritical Care, September 2013, vol./is. 19/1 SUPPL. 1(S226), 1541-6933 (September 2013)

**Publication Date:** September 2013

**Abstract:** Introduction Traumatic Brain Injury (TBI) is one of the leading cause of death and disabilities worldwide. Seizures are common complications after severe TBI and can precipitate secondary brain injury. Several studies detected high incidence of non
convulsive seizures and non convulsive status epilepticus after TBI Methods We conducted a cross sectional study on 50 adult patients with severe TBI admitted to Alexandria main University Hospital. They were all under phenytoin therapy and underwent EEG 7days after admission to detect Non convulsive seizures. Then received 20 sessions of hyperbaric oxygen (5sessions per week) with pressure 1.5ATA. Results statistically significant improvement in the GCS was detected along the first 2 weeks of therapy with the hyperbaric oxygen (the mean GCS in the first week was 6.7 +/-1.1 improved during the second week to reach 9.1 +/-1.5 ) associated with significant improvement in the EEG background. There were no statistically significant differences between the median rates of sharp waves discharge in the first EEG and the second one that was done 2 weeks after hyperbaric therapy (median rate of sharp waves in EEG1 was 30 and in EEG2 was 29, p = 0.161) also there was no statistically significant difference between rate of discharge of spikes and slow wave complexes between the first EEG and the second one done after starting hyperbaric oxygen therapy (median rate of spikes and wave in EEG1 were 30 and in EEG2 was 28, p= 0.524). Conclusions Hyperbaric oxygen therapy may have good effect on the EEG background and reactivity but has no effect on the control of non convulsive late post traumatic epilepsy.

Source: EMBASE

4. Updates on epidemiology & management of epilepsy

Author(s) Beghi E.

Citation: Neuroepidemiology, October 2012, vol./is. 39/3-4(186), 0251-5350 (October 2012)

Publication Date: October 2012

Abstract: Epilepsy is a chronic clinical disorder characterized by repeated unprovoked seizures affecting both sexes and all ages with worldwide distribution. Epidemiological studies on epilepsy must be interpreted in the light of methodological differences and the quality of the reports. Methodological constraints and inconsistencies are mostly prevalent in reports from developing countries, which face problems with case ascertainment and study conduct. The incidence of unprovoked seizures is 33-198 per 100, 000 and the incidence of epilepsy is 23-190 per 100, 000. The rates in Europe and North America ranges from 24 and 53 per 100, 000 per year. The incidence varies with age (younger children and the elderly being at highest risk), etiology, seizure type, and epilepsy syndrome. The overall prevalence of epilepsy ranges from 2.7 to 41 per 1, 000 population, but the rate for active epilepsy varies from 4 to 8 per 1, 000. The prevalence of active epilepsy is generally lower in industrialized countries than in developing countries, which may reflect a lower prevalence of selected risk factors (mostly infections and traumas), a more stringent case verification, and the exclusion of provoked and unprovoked isolated seizures. As with incidence, the prevalence of epilepsy varies with age, etiology, seizure type, epilepsy syndrome, and socio-economic class. At least in part, the risk of epilepsy is accounted for by genetic factors. Genetic or chromosomal syndromes associated with epilepsy account for 2-3% of all epilepsies, while syndromes characterized by simple mendelian inheritance or cytogenetic abnormalities are about 1%. Epilepsies with complex inheritance include the majority of the epileptic syndromes reflecting a gene-environment interactions. Prenatal and perinatal factors are established environmental risk factors but with inconsistent findings, which indicate, at best, a moderate association. Mental retardation and cerebral palsy are the strongest risk factors for epilepsy. CNS infections are worldwide risk factors involving all ages. In developing countries, where infections diseases are commoner than in industrialized countries, epilepsy due to infections has higher prevalence in rural compared to urban areas. In these countries, mostly in South America, neurocysticercosis is a major cause of epilepsy, followed by cerebral malaria, tuberculosis and toxoplasmosis. Alzheimer’s disease carries a sixfold risk of unprovoked seizures and other types of dementia an eightfold risk. Stroke and traumatic brain injury (TBI) are also implicated, with a direct correlation with disease/injury severity. Compared to ischemic stroke, hemorrhagic stroke (primarily subarachnoid hemorrhage) is followed by a higher risk of seizures. Traumatic events provoking concussion with no evidence of tissue disruption usually are not followed by epilepsy. In severe TBI the risk is highest during the first year and diminishes during the ensuing years. After 10 years, only severe injuries still exhibit an increased risk of seizures. Antiepileptic drugs (AED) and, in selected instances, resective surgery are the main therapeutic options. Despite the increasing number of drugs
in the market, there is no evidence that AED modify the natural history of the disease. The number of drug-resistant epilepsies may be reduced by surgery but the long-term effects of surgery are still scarcely understood.

**Source:** EMBASE

Available in fulltext from *Neuroepidemiology* at *ProQuest*

5. Incidence and Risk Factors of Early Post-traumatic Seizures in Nigerians.

**Author(s)** Oluwile, O.S.A.

**Citation:** Brain Injury, 01 September 2011, vol./is. 25/10(980-988), 02699052

**Publication Date:** 01 September 2011

**Abstract:** Objectives: To determine the incidence and risk factors of early post-traumatic seizures (PTS) in Nigerian subjects. Methods: Subjects were recruited consecutively, classified as mild, moderate or severe traumatic brain injury (TBI), and followed for 168 hrs for development of seizures. Results: There were 266 subjects, 213 (80%) males and 53 (20%) females, with mean age 31 years (sd 18, range 1--80, median 30). Causes of TBI were motor traffic accident (MTA) related in 217 (82%), falls in 25 (9%), struck by objects in 15 (5%), firearms in 4 (2%), sports and recreation in 3 (1%), and failed suicide in 2 (1%). Cumulative incidence of early PTS was 119‰‰ (95% CI 80--156). Risk factors were age ≤≤12 years, severity of TBI, history of seizures, and TBI at weekend, but gender and GCS were not. Skeletomotor palsy was independently associated with early PTS. Conclusions: Incidence of early PTS is high in this population, probably due to the relatively high proportion of severe TBI. Risk factors are TBI severity, young age, history of seizures, and TBI at weekends. The best preventive strategy is reduction of MTA, which causes over 80% of TBI. Prophylactic anticonvulsants may benefit subjects with severe TBI and skeletomotor deficits.

**Source:** CINAHL

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6. Adenosine A1 receptor gene variants associated with post-traumatic seizures after severe TBI.

**Author(s)** Wagner, Amy K, Miller, Megan A, Scanlon, Joelle, Ren, Dianxu, Kochanek, Patrick M, Conley, Yvette P

**Citation:** Epilepsy research, Aug 2010, vol. 90, no. 3, p. 259-272 (August 2010)

**Publication Date:** August 2010

**Abstract:** Post-traumatic seizures (PTS) are a significant complication from traumatic brain injury (TBI). Adenosine, a major neuroprotective and neuroinhibitory molecule, is important in experimental epilepsy models. Thus, we investigated the adenosine A1 receptor (A1AR) gene and linked it with clinical data extracted for 206 subjects with severe TBI. Tagging SNPs rs3766553, rs903361, rs10920573, rs6701725, and rs17511192 were genotyped, and variant and haplotype associations with PTS were explored. We investigated further genotype, grouped genotype, and allelic associations with PTS for rs3766553 and rs10920573. Multivariate analysis of rs3766553 demonstrated an association between the AA genotype and increased early PTS incidence. In contrast, the GG genotype was associated with increased late and delayed-onset PTS rates. Multivariate analysis of rs10920573 revealed an association between the CT genotype and increased late PTS. Multiple risk genotype analysis showed subjects with both risk genotypes had a 46.7% chance of late PTS. To our knowledge, this is the first report implicating genetic variability in the A1AR with PTS, or any type of seizure disorder. These results provide a rationale for further studies investigating how adenosine neurotransmission impacts PTS, evaluating anticonvulsants in preventing and treating PTS, and developing and testing targeted adenosinergic therapies aimed at reducing PTS.

**Source:** Medline

**Author(s)** Young, G. Bryan, Claassen, Jan

**Citation:** Neurology, Aug 2010, vol. 75, no. 9, p. 760-761, 0028-3878 (Aug 31, 2010)

**Publication Date:** August 2010

**Abstract:** Comments on an article by P. M. Vespa et al. (see record 2010-19255-008). This article studied a subset of 6 patients with traumatic brain injury (TBI) and seizures (the incidence of nonconvulsive seizures (NCS) was over 20%). Four of these had nonconvulsive status epilepticus (NCSE). They were matched with a group of 10 patients with traumatic brain injury (TBI) who did not have seizures on continuous EEG (cEEG), matched for age, sex, and Glasgow Coma Scale scores. The authors found that the study group developed hippocampal atrophy over time on serial MRI scans, with the atrophy being most marked on the same side as the seizures. When brain insults are followed by NCSE, etiology will figure prominently in patient morbidity and mortality. At the same time, there is increasing evidence that NCSE contributes to additional brain injury, at least in the hippocampal region, and may prolong coma, ICU length of stay, and health care costs. The ultimate practical question, therefore, is whether cEEG monitoring and prompt control of NSCE in this situation make a difference in outcomes. Is NCSE merely an epiphenomenon of severe brain injury or does it warrant detection and treatment in itself? A randomized, controlled trial seems justified and necessary, especially since cEEG monitoring in intensive care unit (ICUs) is not currently a general standard of care. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

**Source:** PsycINFO

Available in fulltext from Neurology at the ULHT Library and Knowledge Services' eJournal collection

8. A population-based study of risk of epilepsy after hospitalization for traumatic brain injury

**Author(s)** Ferguson P.L., Smith G.M., Wannamaker B.B., Thurman D.J., Pickelsimer E., Selassie A.W.

**Citation:** Epilepsia, May 2010, vol./is. 51/5(891-898), 0013-9580;1528-1167 (May 2010)

**Publication Date:** May 2010

**Abstract:** Purpose: This study was undertaken to determine the risk of developing posttraumatic epilepsy (PTE) within 3 years after discharge among a population-based sample of older adolescents and adults hospitalized with traumatic brain injury (TBI) in South Carolina. It also identifies characteristics related to development of PTE within this population. Methods: A stratified random sample of persons aged 15 and older with TBI was selected from the South Carolina nonfederal hospital discharge dataset for four consecutive years. Medical records of recruits were reviewed, and they participated in up to three yearly follow-up telephone interviews. Results: The cumulative incidence of PTE in the first 3 years after discharge, after adjusting for loss to follow-up, was 4.4 per 100 persons over 3 years for hospitalized mild TBI, 7.6 for moderate, and 13.6 for severe. Those with severe TBI, posttraumatic seizures prior to discharge, and a history of depression were most at risk for PTE. This higher risk group also included persons with three or more chronic medical conditions at discharge. Discussion: These results raise the possibility that although some of the characteristics related to development of PTE are nonmodifiable, other factors, such as depression, might be altered with intervention. Further research into factors associated with developing PTE could lead to risk-reducing treatments. © 2009 International League Against Epilepsy.

**Source:** EMBASE

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Available in fulltext from Epilepsia (Series 4) at EBSCOhost

Available in fulltext from Epilepsia at Wiley

Author(s) Yablon SA, Dostrow VG

Citation: Physical Medicine & Rehabilitation, 01 June 2001, vol./is. 15/2(301-326), 08887357

Publication Date: 01 June 2001

Abstract: Post-traumatic seizures (PTSs) are an important complication of traumatic brain injury (TBI), and their management is frequently a central pharmacologic consideration among patients recovering from these injuries. A comprehensive review of the literature regarding PTS and epilepsy is presented, addressing incidence, natural history, risk factors for occurrence and recurrence, and influence on neurologic and functional outcome. Treatment issues regarding antiepileptic drug (AED) prophylaxis and symptomatic management are also discussed, and recently published clinical practice guidelines regarding pharmacologic management of PTS are specifically highlighted. Issues related to management of the patient with severe TBI and PTS are emphasized, particularly those encountered in the neurorehabilitation setting.

Source: CINAHL


Author(s)

Citation: Drugs & Therapy Perspectives, 07 May 2001, vol./is. 17/9(12-15), 11720360

Publication Date: 07 May 2001

Abstract: The occurrence of seizures in the first week after traumatic brain injury is a well known phenomenon, and prophylactic administration of anticonvulsants for the initial week after brain injury is considered standard treatment. The incidence of these seizures can have devastating effects on metabolic processes (e.g. glucose utilisation) within the brain. The actual frequency of early post-traumatic seizures may be as high as 20% and may not be detectable except by electroencephalogram (EEG). The main clinical risk factors for seizures are younger age, greater severity of brain injury and subdural haematoma, and penetrating wounds.

Source: CINAHL

Available in fulltext at Drugs & Therapy Perspectives; Collection notes: Academic-License. Please when asked to pick an institution please pick NHS


Author(s) Singer, R B

Citation: Journal of insurance medicine (New York, N.Y.), Jan 2001, vol. 33, no. 1, p. 42-45, 0743-6661 (2001)

Publication Date: January 2001

Abstract: Records of the Rochester Epidemiological Project were used to determine the incidence of secondary seizures after traumatic brain injury (TBI) in all cases treated for this condition in the population of Olmsted County, Minn, from 1935 to 1984. Medical records of the Mayo Clinic and all other medical facilities in Olmsted County, Minn, are in the database of this Project. Incidence rates after TBI were compared with incidence rates of idiopathic epilepsy previously determined for Olmsted County. TBI cases were divided into 3 defined severity categories: mild, moderate, and severe. Out of 4541 cases of TBI accumulated in 50 years only 97 cases developed 1 or more seizures (46 cases of seizure secondary to other definite causes were excluded). Incidence rates were highest in the first year after the head injury. The overall excess incidence rate was very low in mild TBI, only 0.3 per 1000 per year, but was higher in severe TBI, with an excess rate of 10 per 1000 per year. Only 7.2% of the TBI cases were classified as severe (loss of consciousness or
amnesia for more than 24 hours, subdural hematoma, or brain contusion). The long-term incidence of seizures beyond the incidence rate of idiopathic epilepsy is low after mild or moderate TBI, but is at the rate of 10 excess cases per 1000 per year in the minority of cases with severe TBI.

**Source:** Medline

**Treatment**

1. Preliminary guidelines for safe and effective use of repetitive transcranial magnetic stimulation in moderate to severe traumatic brain injury

**Author(s)**: Nielson D.M., McKnight C.A., Patel R.N., Kalnin A.J., Mysiw W.J.

**Citation:** Archives of Physical Medicine and Rehabilitation, April 2015, vol./iss. 96/4(S138-S144), 0003-9993;1532-821X (01 Apr 2015)

**Publication Date:** April 2015

**Abstract:** Transcranial magnetic stimulation has generated extensive interest within the traumatic brain injury (TBI) rehabilitation community, but little work has been done with repetitive protocols, which can produce prolonged changes in behavior. This is partly because of concerns about the safety of repetitive transcranial magnetic stimulation (rTMS) in subjects with TBI, particularly the risk of seizures. These risks can be minimized by careful selection of the rTMS protocol and exclusion criteria. In this article, we identify guidelines for safe use of rTMS in subjects with TBI based on a review of the literature and illustrate their application with a case study. Our subject is a 48-year-old man who sustained a severe TBI 5 years prior to beginning rTMS for the treatment of post-TBI depression. After a 4-week baseline period, we administered daily sessions of low-frequency stimulation to the right dorsolateral prefrontal cortex for 6 weeks. After stimulation, we performed monthly assessments for 3 months. The Hamilton Depression Rating Scale (HAMD) was our primary outcome measure. The stimulation was well tolerated and the patient reported no side effects. After 6 weeks of stimulation, the patient's depression was slightly improved, and these improvements continued through follow-up. At the end of follow-up, the patient's HAMD score was 49% of the average baseline score.

**Source:** EMBASE

2. Anti-epileptic prophylaxis in traumatic brain injury: A retrospective analysis of patients undergoing craniotomy versus decompressive craniectomy

**Author(s)**: Ramakrishnan V., Dahlin R., Hariri O., Quadri S.A., Farr S., Miulli D., Siddiqi J.

**Citation:** Surgical Neurology International, January 2015, vol./iss. 6/1, 2152-7806 (01 Jan 2015)

**Publication Date:** January 2015

**Abstract:** Background: Seizures account for significant morbidity and mortality early in the course of traumatic brain injury (TBI). Although there is sufficient literature suggesting short-term benefits of antiepileptic drugs (AEDs) in post-TBI patients, there has been no study to suggest a time frame for continuing AEDs in patients who have undergone a decompressive craniectomy for more severe TBI. We examined trends in a level-II trauma center in southern California that may provide guidelines for AED treatment in craniectomy patients. Methods: A retrospective analysis was performed evaluating patients who underwent decompressive craniectomy and those who underwent a standard craniotomy from 2008 to 2012. Results: Out of the 153 patients reviewed, 85 were included in the study with 52 (61%) craniotomy and 33 (39%) craniectomy patients. A total of 78.8% of the craniotomy group used phenytoin (Dilantin), 9.6% used levetiracetam (Keppra), 5.8% used a combination of both, and 3.8% used topiramate (Topamax). The craniectomy group used phenytoin 84.8% and levetiracetam 15.2% of the time without any significant difference between the procedural groups. Craniotomy patients had a 30-day seizure rate of 13.5% compared with 21.2% in craniectomy patients (P = 0.35). Seizure onset averaged on postoperative day 5.86 for the craniotomy group and 8.14 for the craniectomy group. There was no significant difference in the average day of seizure onset between the groups P = 0.642. Conclusion: Our study shows a trend toward increased seizure incidence in craniectomy group, which does not reach significance, but suggests they are at higher risk. Whether this higher risk translates into a benefit on being on AEDs for a longer duration than the current standard of 7 days cannot be concluded as there is no significant difference or trend on the onset date for seizures in either group. Moreover, a prospective study will be necessary to more profoundly evaluate the duration of AED prophylaxis for each one of the stated groups.

**Source:** EMBASE

Available in fulltext from Surgical Neurology International at National Library of Medicine
Abstract: Emerging evidence suggests that hypertonic saline (HTS) is efficient in decreasing intracranial pressure (ICP). However there is no consensus about its interaction with brain hemodynamics and oxygenation. In this study, we investigated brain response to HTS bolus with multimodal monitoring after severe traumatic brain injury (TBI). We included 18 consecutive TBI patients during 10 days after neurocritical care unit admission. Continuous brain monitoring applied included ICP, tissue oxygenation (PtO2) and cerebral blood flow (CBF). Cerebral perfusion pressure (CPP), cerebrovascular resistance (CVR), and reactivity indices related to pressure (PRx) and flow (CBFx) were calculated. ICM + software was used to collect and analyze monitoring data. Eleven of 18 (61%) patients developed 99 episodes of intracranial hypertension (IHT) greater than 20 mm Hg that were managed with 20% HTS bolus. Analysis over time was performed with linear mixed-effects regression modelling. After HTS bolus, ICP and CPP improved over time (p < 0.001) following a quadratic model. From baseline to 120 min, ICP had a mean decrease of 6.2 mm Hg and CPP a mean increase of 3.1 mmHg. Mean increase in CBF was 7.8 mL/min/100 g (p < 0.001) and mean decrease in CVR reached 0.4 mmHg. Both changes preceded pressures improvement. PtO2 exhibited a marginal increase and no significant models for time behaviour could be fitted. PRx and CBFx were best described by a linear decreasing model showing autoregulation recover after HTS (p = 0.01 and p = 0.04 respectively). During evaluation, CO2 remained constant and sodium level did not exhibit significant variation. In conclusion, management of IHT with 20% HTS significantly improves cerebral hemodynamics and cerebrovascular reactivity with recovery of CBF appearing before rise in CPP and decrease in ICP. In spite of cerebral hemodynamic improvement, no significant changes in brain oxygenation were identified. (PsycINFO Database Record (c) 2014 APA, all rights reserved)(journal abstract)

Source: PsycINFO


Citation: Journal of Neurotrauma, November 2014, vol./is. 31/22(1872-1880), 0897-7151;1557 (Nov 15, 2014)

Publication Date: November 2014

Abstract: Emerging evidence suggests that hypertonic saline (HTS) is efficient in decreasing intracranial pressure (ICP). However there is no consensus about its interaction with brain hemodynamics and oxygenation. In this study, we investigated brain response to HTS bolus with multimodal monitoring after severe traumatic brain injury (TBI). We included 18 consecutive TBI patients during 10 days after neurocritical care unit admission. Continuous brain monitoring applied included ICP, tissue oxygenation (PtO2) and cerebral blood flow (CBF). Cerebral perfusion pressure (CPP), cerebrovascular resistance (CVR), and reactivity indices related to pressure (PRx) and flow (CBFx) were calculated. ICM + software was used to collect and analyze monitoring data. Eleven of 18 (61%) patients developed 99 episodes of intracranial hypertension (IHT) greater than 20 mm Hg that were managed with 20% HTS bolus. Analysis over time was performed with linear mixed-effects regression modelling. After HTS bolus, ICP and CPP improved over time (p < 0.001) following a quadratic model. From baseline to 120 min, ICP had a mean decrease of 6.2 mm Hg and CPP a mean increase of 3.1 mmHg. Mean increase in CBF was 7.8 mL/min/100 g (p < 0.001) and mean decrease in CVR reached 0.4 mmHg. Both changes preceded pressures improvement.

Source: PsycINFO

4. Post-traumatic multimodal brain monitoring: Response to hypertonic saline


Citation: Journal of Neurotrauma, November 2014, vol./is. 31/22(1872-1880), 0897-7151;1557-9042 (15 Nov 2014)

Publication Date: November 2014

Abstract: Emerging evidence suggests that hypertonic saline (HTS) is efficient in decreasing intracranial pressure (ICP). However there is no consensus about its interaction with brain hemodynamics and oxygenation. In this study, we investigated brain response to HTS bolus with multimodal monitoring after severe traumatic brain injury (TBI). We included 18 consecutive TBI patients during 10 days after neurocritical care unit admission. Continuous brain monitoring applied included ICP, tissue oxygenation (PtO2) and cerebral blood flow (CBF). Cerebral perfusion pressure (CPP), cerebrovascular resistance (CVR), and reactivity indices related to pressure (PRx) and flow (CBFx) were calculated. ICM + software was used to collect and analyze monitoring data. Eleven of 18 (61%) patients developed 99 episodes of intracranial hypertension (IHT) greater than 20 mm Hg that were managed with 20% HTS bolus. Analysis over time was performed with linear mixed-effects regression modelling. After HTS bolus, ICP and CPP improved over time (p < 0.001) following a quadratic model. From baseline to 120 min, ICP had a mean decrease of 6.2 mm Hg and CPP a mean increase of 3.1 mmHg. Mean increase in CBF was 7.8 mL/min/100 g (p < 0.001) and mean decrease in CVR reached 0.4 mmHg. Both changes preceded pressures improvement.
PtO$_2$ exhibited a marginal increase and no significant models for time behaviour could be fitted. PRx and CBFx were best described by a linear decreasing model showing autoregulation recover after HTS ($p = 0.01$ and $p = 0.04$ respectively). During evaluation, CO$_2$ remained constant and sodium level did not exhibit significant variation. In conclusion, management of IHT with 20% HTS significantly improves cerebral hemodynamics and cerebrovascular reactivity with recovery of CBF appearing before rise in CPP and decrease in ICP. In spite of cerebral hemodynamic improvement, no significant changes in brain oxygenation were identified.

Source: EMBASE

5. Long-term comparison of GOS-E scores in patients treated with phenytoin or levetiracetam for posttraumatic seizure prophylaxis after traumatic brain injury.

**Author(s)** Gabriel, Wendy M, Rowe, A Shaun

**Citation:** The Annals of pharmacotherapy, Nov 2014, vol. 48, no. 11, p. 1440-1444 (November 2014)

**Publication Date:** November 2014

**Abstract:** Much debate exists on the optimal medication for posttraumatic seizure prophylaxis after traumatic brain injury (TBI). There is some evidence that levetiracetam (LEV) could be neuroprotective and provide long-term benefits in this patient population. The primary objective was to compare the Glasgow Outcome Scale-Extended (GOS-E) 6 months or more after severe TBI. Secondary end points were presence of early seizures (0 to 7 days post-TBI) or late seizures (8 days post-TBI to phone interview), use of anticonvulsant medication when interviewed, medication-related hospital complications, and a summary of phenytoin (PHT) and LEV dosing regimens. This was an IRB-approved, single-center, prospective cohort analysis. Patients were identified by cross-referencing a list of patients receiving LEV or PHT, with a list of patients with ICD-9 code consistent with TBI. After study inclusion, patients were contacted by telephone, and the GOS-E was administered. Data for secondary end points were gathered by retrospective chart review. In all, 19 patients were included in the final analysis. There was no difference in the GOS-E score assessed ≥6 months after injury (5.07±1.69 vs 5.60±2.07, $P=0.58$). There was no difference in the secondary end points of early seizures ($P=0.53$) or late seizures ($P=0.53$). However, the PHT group experienced a higher rate of hospital days with recorded fever (0.20±0.22 vs 0±0; $P=0.014$). Long-term functional outcome in patients who experienced a TBI was not affected by treatment with PHT or LEV; however, patients treated with PHT had a higher incidence of fever during hospitalization. © The Author(s) 2014.

Source: Medline


**Author(s)** Honeybul S., Ho K.M.

**Citation:** Injury, September 2014, vol./is. 45/9(1332-1339), 0020-1383;1879-0267 (September 2014)

**Publication Date:** September 2014

**Abstract:** Object To assess the impact that injury severity has on complications in patients who have had a decompressive craniectomy for severe traumatic brain injury (TBI). Methods This prospective observational cohort study included all patients who underwent a decompressive craniectomy following severe TBI at the two major trauma hospitals in Western Australia from 2004 to 2012. All complications were recorded during this period. The clinical and radiological data of the patients on initial presentation were entered into a web-based model prognostic model, the CRASH (Corticosteroid Randomization After Significant Head injury) collaborators prediction model, to obtain the predicted risk of an unfavourable outcome which was used as a measure of injury severity. Results Complications after decompressive craniectomy for severe TBI were common. The predicted risk of unfavourable outcome was strongly associated with the development of neurological complications such as herniation of the brain outside the skull bone defects (median predicted risk of unfavourable outcome for herniation 72% vs. 57% without herniation, $p = 0.001$), subdural effusion (median predicted risk of unfavourable outcome 67% with an effusion vs. 57% for those without an effusion, $p = 0.03$), hydrocephalus requiring ventriculo-peritoneal shunt (median predicted risk of unfavourable outcome 86% for those with hydrocephalus vs. 59% for those without hydrocephalus, $p = 0.001$), but not infection ($p = 0.251$) or resorption of bone flap ($p = 0.697$) and seizures (0.987). We did not observe any associations between timing of cranioplasty and risk of infection or resorption of bone flap after cranioplasty. Conclusions Mechanical complications after decompressive
cranietomy including herniation of the brain outside the skull bone defects, subdural effusion, and hydrocephalus requiring ventriculo-peritoneal shunt were more common in patients with a more severe form of TBI when quantified by the CRASH predicted risk of unfavoursable outcome. The CRASH predicted risk of unfavoursable outcome represents a useful baseline characteristic of patients in observational and intervention trials involving patients with severe TBI requiring decompressive cranietomy. &quot; 2014 Elsevier Ltd.

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7. Subtypes of post-traumatic epilepsy: Clinical, electrophysiological, and imaging features.

Author(s) Gupta, Puneet K., Sayed, Nasreen, Ding, Kan, Agostini, Mark A., Van Ness, Paul C., Yablon, Stuart, Madden, Christopher, Mickey, Bruce, D’Ambrosio, Raimondo, Diaz-Arrastia, Ramon

Citation: Journal of Neurotrauma, Aug 2014, vol. 31, no. 16, p. 1439-1443, 0897-7151 (Aug 15, 2014)

Publication Date: August 2014

Abstract: Post-traumatic epilepsy (PTE) is a consequence of traumatic brain injury (TBI), occurring in 10–25% of patients with moderate to severe injuries. The development of animal models for testing antiepileptogenic therapies and validation of biomarkers to follow epileptogenesis in humans necessitates sophisticated understanding of the subtypes of PTE, which is the objective of this study. In this study, retrospective review was performed of patients with moderate to severe TBI with subsequent development of medically refractory epilepsy referred for video-electroencephalography (EEG) monitoring at a single center over a 10-year period. Information regarding details of injury, neuroimaging studies, seizures, video-EEG, and surgery outcomes were collected and analyzed. There were 123 patients with PTE identified, representing 4.3% of all patients evaluated in the epilepsy monitoring unit. Most of them had localization-related epilepsy, of which 57% had temporal lobe epilepsy (TLE), 35% had frontal lobe epilepsy (FLE), and 3% each had parietal and occipital lobe epilepsy. Of patients with TLE, 44% had mesial temporal sclerosis (MTS), 26% had temporal neocortical lesions, and 30% were nonlesional. There was no difference in age at injury between the different PTE subtypes. Twenty-two patients, 13 of whom had MTS, proceeded to surgical resection. At a mean follow-up of 2.5 years, Engel Class I outcomes were seen in 69% of those with TLE and 33% of those with FLE. Our findings suggest PTE is a heterogeneous condition, and careful evaluation with video-EEG monitoring and high resolution MRI can identify distinct syndromes. These results have implications for the design of clinical trials of antiepileptogenic therapies for PTE.

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Source: PsycINFO

8. IL-1beta associations with posttraumatic epilepsy development: A genetics and biomarker cohort study

Author(s) Diamond M.L., Ritter A.C., Failla M.D., Boles J.A., Conley Y.P., Kochanek P.M., Wagner A.K.

Citation: Epilepsia, July 2014, vol./is. 55/7(1109-1119), 0013-9580;1528-1167 (July 2014)

Publication Date: July 2014

Abstract: Objective Posttraumatic epilepsy (PTE) is a significant complication following traumatic brain injury (TBI), yet the role of genetic variation in modulating PTE onset is unclear. We hypothesized that TBI-induced inflammation likely contributes to seizure development. We assessed whether genetic variation in the interleukin-1beta (IL-1beta) gene, IL-1beta levels in cerebrospinal fluid (CSF) and serum, and CSF/serum IL-1beta ratios would predict PTE development post-TBI. Methods We investigated PTE development in 256 Caucasian adults with moderate-to-severe TBI. IL-1beta tagging and functional single nucleotide polymorphisms (SNPs) were genotyped. Genetic variance and PTE development were assessed. Serum and CSF IL-1beta levels were collected from a subset of subjects (n = 59) during the first week postinjury and evaluated for their associations with IL-1beta gene variants, and also PTE. Temporally matched CSF/serum IL-1beta ratios were also generated to reflect the relative contribution of serum IL-1beta to CSF IL-1beta. Results Multivariate analysis showed that higher CSF/serum IL-1beta ratios were associated with increased risk for PTE over time (p = 0.008). Multivariate analysis for rs1143634 revealed an association between the CT genotype and increased PTE risk over time (p = 0.005). The CT genotype group also had lower serum IL-1beta levels (p = 0.014) and higher IL-1beta CSF/serum ratios (p = 0.093). Significance This is the first report
implicating IL-1beta gene variability in PTE risk and linking (1) IL-1beta gene variation with serum IL-1beta levels observed after TBI and (2) IL-1beta ratios with PTE risk. Given these findings, we propose that genetic and IL-1beta ratio associations with PTE may be attributable to biologic variability with blood-brain barrier integrity during TBI recovery. These results provide a rationale for further studies (1) validating the impact of genetic variability on IL-1beta production after TBI, (2) assessing genetically mediated signaling mechanisms that contribute to IL-1beta CSF/serum associations with PTE, and (3) evaluating targeted IL-1beta therapies that reduce PTE. A PowerPoint slide summarizing this article is available for download in the Supporting Information section here. &xA9; Wiley Periodicals, Inc. &xA9; 2014 International League Against Epilepsy.

Source: EMBASE


Author(s): Vaaramo, Kalle, Puljula, Jussi, Tetri, Sami, Juvela, Seppo, Hillbom, Matti

Citation: Journal of Neurology, Neurosurgery & Psychiatry, Jun 2014, vol. 85, no. 6, p. 598-602, 0022-3050 (Jun 2014)

Publication Date: June 2014

Abstract: Background: It is not known whether alcohol-related head trauma predicts the new-onset seizures, particularly alcohol-related seizures. Objective: We investigated risk factors for new-onset seizures in a cohort of 739 head trauma subjects. Methods: All subjects with head trauma attending Oulu University Hospital during 1999, including children and very old people but excluding persons with previous seizures and/or neurological diseases, were enrolled and followed up until the end of 2009. The Finnish National Hospital Discharge Register was used to identify all visits due to seizures during the 10-year follow-up. Dates of death were obtained from the official Cause-of-Death Statistics. Cox proportional hazard regression models and Kaplan-Meier survival curves were used to identify predictors of new-onset seizures. Results: New-onset seizures were observed in 42 out of the 739 subjects (5.7%). An alcohol-related index injury (adjusted HR 2.50, 95% CI 1.30 to 4.82, p = 0.006), moderate-to-severe traumatic brain injury (TBI) as the index trauma (3.13, 1.46 to 6.71, p = 0.003) and preceding psychiatric disease (3.23, 1.23 to 9.21, p = 0.028) were significant predictors of new-onset seizures during the follow-up after adjustment for age and sex. An alcohol-related index injury was the only independent predictor of the occurrence of an alcohol-related new-onset seizure (adjusted HR 12.13, 95% CI 2.70 to 54.50, p = 0.001), and these seizures (n = 19) developed more frequently among subjects without (n = 14) than with (n = 5) TBI. Conclusions: We conclude that alcohol-related head trauma predicts new-onset seizures, particularly alcohol-related seizures. A brief intervention is needed in order to prevent the development of alcohol-related seizures. (PsycINFO Database Record (c) 2015 APA, all rights reserved)(journal abstract)

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10. Pressure autoregulation monitoring and cerebral perfusion pressure target recommendation in patients with severe traumatic brain injury based on minute-by-minute monitoring data: Clinical article

Author(s): Depreitere B., Guiza F., Van Den Berghe G., Schuhmann M.U., Maier G., Piper I., Meyfroidt G.

Citation: Journal of Neurosurgery, June 2014, vol./is. 120/6(1451-1457), 0022-3085;1933-0693 (June 2014)

Publication Date: June 2014

Abstract: Object. In severe traumatic brain injury, a universal target for cerebral perfusion pressure (CPP) has been abandoned. Attempts to identify a dynamic CPP target based on the patient's cerebrovascular autoregulatory capacity have been promising so far. Bedside monitoring of pressure autoregulatory capacity has become possible by a number of methods, Czosnyka's pressure reactivity index (PRx) being the most frequently used. The PRx is calculated as the moving correlation coefficient between 40 consecutive 5-second averages of intracranial pressure (ICP) and mean arterial blood pressure (MABP) values. Plotting PRx against CPP produces a U-shaped curve in roughly two-thirds of monitoring
time, with the bottom of this curve representing a CPP range corresponding with optimal autoregulatory capacity (CPPopt). In retrospective series, keeping CPP close to CPPopt corresponded with better outcomes. Monitoring of PRx requires high-frequency signal processing. The aim of the present study is to investigate how the processing of the information on cerebrovascular pressure reactivity that can be obtained from routine minute-by-minute ICP and MABP data can be enhanced to enable CPPopt recommendations that do not differ from those obtained by the PRx method, show the same associations with outcome, and can be generated in more than two-thirds of monitoring time. Methods. The low-frequency autoregulation index (LAX) was defined as the moving minute-by-minute ICP/MABP correlation coefficient calculated over time intervals varying from 3 to 120 minutes. The CPPopt calculation was based on LAX-CPP plots and done for time windows between 1 and 24 hours and for each LAX type. The resulting matrix of CPPopts were then averaged in a weighted manner, with the weight based on the goodness of fit of a U-shape and the lower value of the LAX corresponding to the U-bottom, to result in a final CPPopt recommendation. The association between actual CPP/CPPopt and outcome was assessed in the multicenter Brain Monitoring with Information Technology Research Group (BrainIT) database (n = 180). In the Leuven-Tubingen database (60-Hz waveform data, n = 21), LAX- and PRx-based CPPopts were compared. Results. In the BrainIT database, CPPopt recommendations were generated in 95% of monitoring time. Actual CPP being close to LAX-based CPPopt was associated with increased survival. In a multivariate model using the Corticosteroid Randomization After Significant Head Injury (CRASH) model as covariates, the average absolute difference between actual CPP and CPPopt was independent of increased mortality. In the high-frequency data set no significant difference was observed between PRx-based and LAX-based CPPopts. The new method issued a CPPopt recommendation in 97% of monitoring time, as opposed to 44% for PRx-based CPPopt. Conclusions. Minute-by-minute ICP/MABP data contain relevant information for autoregulation monitoring. In this study, the authors' new method based on minute-by-minute data resolution allowed for CPPopt calculation in nearly the entire monitoring time. This will facilitate the use of pressure reactivity monitoring in all ICUs.

Source: EMBASE


Author(s): Wilson, Dulaney A., Selassie, Anbesaw W.

Citation: Epilepsy & Behavior, Mar 2014, vol. 32, p. 42-48, 1525-5050 (Mar 2014)

Publication Date: March 2014

Abstract: Background: While traumatic brain injury (TBI) can lead to epilepsy, individuals with preexisting epilepsy or seizure disorder (ESD), depending on the type of epilepsy and the degree of seizure control, may have a greater risk of TBI from seizure activity or medication side effects. The joint occurrence of ESD and TBI can complicate recovery as signs and symptoms of TBI may be mistaken for postictal effects. Those with ESD are predicted to experience more deleterious outcomes either because of having a more severe TBI or because of the cumulative effects of repetitive TBI. Methods: We conducted a case–control study of all emergency department visits and hospital discharges for TBI from 1998 through 2011 in a statewide population. The severity of TBI, repetitive TBI, and other demographic and clinical characteristics were compared between persons with TBI with preexisting ESD (cases) and those without (controls). Significant differences in proportions were evaluated with confidence intervals. Logistic regression was used to examine the association of the independent variables with ESD. Results: During the study period, 236,164 individuals sustained TBI, 5646 (2.4%) of which had preexisting ESD. After adjustment for demographic and clinical characteristics, cases were more likely to have sustained a severe TBI (OR = 1.49; 95% CI = 1.38–1.60) and have had repetitive TBI (OR = 1.54; 95% CI = 1.41–1.69). Conclusion: The consequences of TBI are greater in individuals with ESD owing to the potential for a more severe or repetitive TBI. Seizure control is paramount, and aggressive management of comorbid conditions among persons with ESD and increased awareness of the hazard of repetitive TBI is warranted. Furthermore, future studies are needed to examine the long-term outcomes of cases in comparison with controls to determine if the higher risk of severe or repetitive TBI translates into permanent deficits. (PsycINFO Database Record (c) 2014 APA, all rights reserved)(journal abstract)

Source: PsycINFO

Author(s) Lamar, Cory D., Hurley, Robin A., Rowland, Jared A., Taber, Katherine H.

Citation: The Journal of Neuropsychiatry and Clinical Neurosciences, Mar 2014, vol. 26, no. 2, p. 108-113, 0895-0172 (Spr 2014)

Publication Date: March 2014

Abstract: This article presents a review of risks, pathophysiology, potential biomarkers in post-traumatic epilepsy. Traumatic brain injury is a heterogeneous disorder involving several different mechanisms including concussive forces, acceleration-deceleration forces, blast injury, and projectile missiles. Each of these mechanisms can result in numerous clinical sequelae including but not limited to post-traumatic epilepsy (PTE). Numerous studies have documented the risks associated with the development of PTE with moderate to severe brain injuries conferring the greatest risk. The characteristics of the seizure itself will also reflect the anatomic heterogeneity of traumatic brain injuries (TBI), with the majority of the seizure foci occurring in the temporal and frontal lobes. The process of epileptogenesis that occurs as a result of a brain injury is still not fully understood but it remains a prime target for the study and application of antiepileptogenic therapy. A large number of clinical trials have aimed at the prevention of PET. All failed to either prevent or alter the period of epileptogenesis associated with TBI. (PsycINFO Database Record (c) 2014 APA, all rights reserved)

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13. Enteral administration of antiepileptic agents could have efficacy for prevention of post-traumatic seizures in severe traumatic brain injury

Author(s) Mocjiduki K., Suzuki H., Kawasaki A., Hotta M., Namiki M., Harada T., Takeda M., Yaguchi A.

Citation: Critical Care, March 2014, vol./is. 18/(S174-S175), 1364-8535 (17 Mar 2014)

Publication Date: March 2014

Abstract: Introduction Antiseizure prophylaxis is recommended for preventing only early post-traumatic seizures (PTS) in the guidelines for the management of severe traumatic brain injury (TBI) by the Brain Trauma Foundation. Phenytoin is recommended to reduce the incidence of early PTS prophylaxis. Early enteral nutrition has recently shown theoretical advantages for prevention of bacterial translocation to maintain normal turnover of gut mucosa and is commonly used for TBI patients. Our hypothesis is that the enteral administration of antiepileptic agents is also useful for early PTS. Methods This retrospective observational study included all adult patients admitted to our tertiary academic medico-surgical ICU due to TBI from September 2011 to August 2012. Patients who have epilepsy as a past history were excluded. Clinical data were collected from electrical medical archives. The baseline characteristics collected were age, gender, diagnosis, antiepileptic agents, timing of start and adverse effects of those agents, and methods of administration. Results Of 65 patients with TBI, 25 patients (18 men, seven women; mean age 56.7 +/- 20.1) who were administered antiepileptic agents for PTS prophylaxis were studied. Fifteen cerebral contusions, 10 acute subdural hematomas, nine traumatic subarachnoid hemorrhages, two cerebral infarctions, two pneumocephalus and one traumatic intracerebral hemorrhage were shown in 25 patients. All patients were alive 28 days after the injury. Fourteen patients (56%) were intravenously administered (13 phenytoin and one phenobarbital), while 11 patients (44%) were administered with enteral feeding (four valproates, four carbamazepine and three zonisamides) as PTS prophylaxis. The average start day of PTS prophylaxis was 2.6 days after the injury by intravenous administration, and 2.2 days by enteral administration, respectively. Two patients with phenytoin showed hepatic dysfunction as an adverse effect and no patient showed early PTS both by intravenous and by enteral administrations. Conclusion The present study has some limitations because it is a single-center retrospective analysis. However, enteral administration of antiepileptic agents could be useful for PTS prophylaxis. Considering cost, adverse effects and serum monitoring, there is a possibility of enteral administration of antiepileptic agents as an alternative to intravenous phenytoin.

Source: EMBASE

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14. More harm than good: Antiseizure prophylaxis after traumatic brain injury does not decrease seizure rates but may inhibit functional recovery

**Author(s)** Bhullar I.S., Johnson D., Paul J.P., Kerwin A.J., Tepas III J.J., Frykberg E.R.

**Citation:** Journal of Trauma and Acute Care Surgery, January 2014, vol./is. 76/1(54-61), 2163-0755;2163-0763 (January 2014)

**Publication Date:** January 2014

**Abstract:** BACKGROUND: The purposes of this study were to examine the current Brain Trauma Foundation recommendation for antiseizure prophylaxis with phenytoin during the first 7 days after traumatic brain injury (TBI) in preventing seizures and to determine if this medication affects functional recovery at discharge. METHODS: The records of adult (age Q 18 years) patients with blunt severe TBI who remained in the hospital at least 7 days after injury were retrospectively reviewed from January 2008 to January 2010. Clinical seizure rates during the first 7 days after injury and functional outcome at discharge were compared for the two groups based on antiseizure prophylaxis, no prophylaxis (NP) versus phenytoin prophylaxis (PP). Statistical analysis was performed using W2. RESULTS: A total of 93 adult patients who met the previously mentioned criteria were identified (43 [46%] NP group vs. 50 [54%] PP group). The two groups were well matched. Contrary to expectation, more seizures occurred in the PP group as compared with the NP group; however, this did not reach significance (PP vs. NP, 2 [4%] vs. 1 [2.3%], p = 1). There was no significant difference in the two groups (PP vs. NP) as far as disposition are concerned, mortality caused by head injury (4 [8%] vs. 3 [7%], p = 1), discharge home (16 [32%] vs. 17 [34%], p = 0.7), and discharge to rehabilitation (30 [60%] vs. 23 [46%], p = 0.9). However, with PP, there was a significantly longer hospital stay (PP vs.NP, 36 vs. 25 days, p = 0.04) and significantly worse functional outcome at discharge based on Glasgow Outcome Scale (GOS) score (PP vs.NP, 2.9 vs. 3.4, p > 0.01) and modified Rankin Scale score (2.3 T 1.7 vs. 3.1 T 1.5, p = 0.02). CONCLUSION: PP may not decrease early posttraumatic seizure and may suppress functional outcome after blunt TBI. These results need to be verified with randomized studies before recommending changes in clinical practice and do not apply to penetrating trauma. (J Trauma Acute Care Surg. 2014;76: 54Y61. Copyright © 2013 Lippincott Williams and Wilkins.

**Source:** EMBASE

15. In silico model of cerebral oxygen flux after traumatic brain injury

**Author(s)** Kohler K., Nallapareddy S.R., Ercole A.

**Citation:** Journal of the Intensive Care Society, January 2014, vol./is. 15/1 SUPPL. 1(S95), 1751-1437 (January 2014)

**Publication Date:** January 2014

**Abstract:** Traumatic brain injury (TBI) is a major cause of death and serious disability in young adults. Intensive care of patients with severe TBI is predicated on the assessment and optimisation of cerebral oxygen delivery in the face of acutely evolving pathological processes. Impaired oxygen diffusion is implicated in secondary neuronal injury.1 A number of bedside methods exist for the assessment of oxygen delivery but these are, to some extent, indirect measures of the underlying pathophysiology and are correlated in a complex way. Measured parenchymal brain oxygen tension (PbtO2) has been shown to be associated with impaired oxygen diffusion.2 However, the quantitative assessment of the contribution of deranged diffusion to dysoxia at the bedside is lacking, as the precise determinants of PbtO2 are poorly characterised and difficult to separate. We have modelled cerebral oxygen flux as a modified Krogh tube geometry. We numerically solve the diffusion equation with a spatially distributed sink term representing cerebral metabolism in cylindrical polar coordinates. The solutions give the local oxygen tension as a function of distance from the capillary (Figure 1), which may subsequently be spatially integrated to yield predictions for PbtO2. We are able to model the behaviour of PbtO2 as a function of clinically relevant parameters. Furthermore, we have performed measurements of PbtO2 against surrogate model input parameters in severe TBI patients on our neurosciences critical care unit. (Table Presented) We demonstrate that PbtO2 varies with cerebral blood flow, metabolic rate and diffusion geometry. We show that, ceteris paribus, the PbtO2/PaO2 relationship is sensitive to diffusion geometry and that in vivo PbtO2
behaviour can be well fitted to our in silico model. In summary, our model of cerebral oxygen flux enables metabolic, oxygen delivery and diffusion contributions to PbtO2 to be separated. Fitting the model to in vivo data may allow diffusion impairment to be characterised clinically, and this may be useful in guiding therapy. Mathematical models of cerebral oxygen delivery offer a way to 'unify' our understanding of the various monitoring modalities used in neurocritical care and may provide the basis for improved understanding of cerebral dysxia clinically.

Source: EMBASE

16. Acute traumatic brain injury in persons with epilepsy and seizure disorders

Author(s) Wilson D.A., Selassie A.W.
Citation: Epilepsy Currents, January 2014, vol./is. 14/(276), 1535-7597 (January-February 2014)
Publication Date: January 2014
Abstract: Rationale: Traumatic brain injury (TBI), affecting almost 2 million Americans annually, can lead to chronic and long-term disability including epilepsy. In persons with epilepsy, seizure activity or medication side effects may result in TBI depending on the epilepsy characteristics and the degree of seizure control. A major concern, especially in persons with epilepsy with poorly controlled seizures, is the cumulative effect of repetitive TBI in a short period of time resulting in insufficient recovery time between TBIs. Persons with epilepsy may be at higher risk of functional deficits and worsening of seizures owing to cumulative effects of repetitive TBI because signs and symptoms of TBI, especially mild TBI, may be confused with seizure effects. We hypothesize that those with pre-existing epilepsy or seizure disorder (ESD) are more likely to sustain repetitive TBI and higher severity than those without ESD. 277 Methods: This is a retrospective cohort study of all TBI encounters in South Carolina non-federal emergency departments and hospitals from 1998 through 2011. Multiple admissions and late effects of the same TBI were excluded and the index TBI for each individual was identified. The presence of preexisting comorbidity conditions, such as heart disease, hypertension and diabetes, was determined. Cases were persons with preexisting ESD at the time of index TBI and controls were persons with TBI without evidence of ESD. Demographic and clinical characteristics were compared between cases and controls using t-test for continuous variables and chi-square tests of association for categorical variables. Logistic regression was used to examine the association of the independent variables with ESD. Further, cases and controls were compared regarding the proportion of selected comorbidities; significant differences in proportions were evaluated with confidence intervals. Results: From 1998 to 2001, 235,797 individuals sustained TBI and 5,637 (2.4%) had preexisting ESD. Higher proportions of cases were black, aged 25 years or older, covered by Medicare or Medicaid, have more than one comorbid condition, hospitalized, died in hospital, have repetitive TBI and have sustained TBI because of a fall. All chronic conditions occurred more often in the cases than in controls. After adjustment for these demographic and clinical characteristics, cases were more likely to have repetitive TBI (Odds Ratio=1.54; 95% Confidence Interval 1.41-1.69) and severe TBI (Odds Ratio=1.49; 95% Confidence Interval 1.38-1.60). Cases were twice as likely to have at least one comorbid condition compared with controls (Odds Ratio=2.09; 95% Confidence Interval 1.95-2.25). Conclusions: The findings underscore the risk of sustaining severe and repetitive TBI in persons with preexisting ESD. Adequate control of seizures and use of protective equipment in those with intractable and atonic seizures and a propensity for falls are crucial to avoiding TBI. Future studies examining the long term cumulative effects of TBI in persons with ESD are needed to fully inform clinical decision making.

Source: EMBASE

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17. Neuroactive steroids ganaxolone and allopregnanolone in the treatment of epilepsy, traumatic brain injury, and neurobehavioral disorders

Author(s) Rogawski M.A.
Citation: Neuropsychopharmacology, December 2013, vol./is. 38/(S37), 0893-133X (December 2013)
Abstract: Background: I will discuss recent studies on the development of the neuroactive steroids for the treatment of epilepsy, traumatic brain injury (TBI), and other neurological and psychiatric conditions. Methods: Studies in animal epilepsy and seizure models. Pharmacokinetic studies in animal models. Controlled (randomized and blinded) and open label clinical trials in various patient populations. Results: I begin with a discussion of the synthetic neuroactive steroid ganaxolone, which has been administered to over 900 patients. I will report the results of a 147 subject double-blind, placebo-controlled clinical trial of orally administered ganaxolone in the treatment of partial onset seizures in adults. This study met a predefined statistical criterion for efficacy. Ganaxolone was found to be safe and well tolerated. There was no increase in the frequency of discontinuations or treatment emergent adverse events in the ganaxolone treatment group compared to the placebo group. Results of the 1-year open label extension study, which demonstrated increasing efficacy over time, will also be presented. I will also provide an update on ongoing studies with ganaxolone in the treatment of anxiety in fragile X and posttraumatic stress disorder (PTSD). Recently, we have begun clinical studies of the natural neurosteroid allopregnanolone. We have developed an intravenous formulation, which is being studied for the treatment of moderate and severe traumatic brain injury. We have developed extensive evidence in animal models supporting the utility of allopregnanolone in the treatment of status epilepticus, when administered intravenously and also intramuscularly. We are embarking on a program to develop allopregnanolone for use in acute status epilepticus and also for the treatment of in hospital nonconvulsive status epilepticus. Conclusions: Neuroactive steroids have potential utility in the treatment of epilepsy, TBI, and several neurobehavioral conditions including fragile X and PTSD.

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18. The use of hyperbaric oxygen therapy as an adjuvant therapy to phenytoin in the control of late post traumatic nonconvulsive epilepsy in patients with severe traumatic brain injury

Author(s) Tahon S.A., Abd Elkader A.A., Fayed A.M., Abd Elmonem S.A.
Citation: Neurocritical Care, September 2013, vol./is. 19/1 SUPPL. 1(S226), 1541-6933 (September 2013)
Publication Date: September 2013
Abstract: Introduction Traumatic Brain Injury (TBI) is one of the leading cause of death and disabilities worldwide. Seizures are common complications after severe TBI and can precipitate secondary brain injury. Several studies detected high incidence of non convulsive seizures and non convulsive status epilepticus after TBI Methods We conducted a cross sectional study on 50 adult patients with severe TBI admitted to Alexandria main University Hospital. They were all under phenytoin therapy and underwent EEG 7days after admission to detect Non convulsive seizures. Then received 20 sessions of hyperbaric oxygen (5sessions per week) with pressure 1.5ATA. Results statistically significant improvement in the GCS was detected along the first 2 weeks of therapy with the hyperbaric oxygen therapy. There were no statistically significant differences between the median rates of sharp waves discharge in the first EEG and the second one that was done 2 weeks after hyperbaric therapy (median rate of sharp waves in EEG1 was 30 and in EEG2 was 29, p = 0.161) also there was no statistically significant difference between rate of discharge of spikes and slow wave complexes between the first EEG and the second one after starting hyperbaric oxygen therapy (median rate of spikes and wave in EEG1 were 30 and in EEG2 was 28, p= 0.524). Conclusions Hyperbaric oxygen therapy may have good effect on the EEG background and reactivity but has no effect on the control of nonconvulsive late post traumatic epilepsy.
Source: EMBASE
19. Effect of rosuvastatin on cytokines after traumatic head injury
Citation: Journal of Neurosurgery, March 2013, vol./is. 118/3(669-675), 0022-3085;1933-0693 (March 2013)
Publication Date: March 2013
Abstract: Object. The favorable effect of statin treatment after traumatic brain injury (TBI) has been shown in animal studies and is probably true in humans as well. The objective of this study was to determine whether acute statin treatment following TBI could reduce inflammatory cytokines and improve functional outcomes in humans. Methods. The authors performed a double-blind randomized clinical trial in patients with moderate to severe TBI. Exclusion criteria were as follows: prior severe disability; use of modifiers of statin metabolism; multisystem trauma; prior use of mannitol, barbiturates, corticosteroids, or calcium channel blockers; isolated brainstem lesions; allergy to statins; previous hepatopathy or myopathy; previous treatment at another clinic; and pregnancy. Patients were randomly selected to receive 20 mg of rosuvastatin or placebo for 10 days. The main goal was to determine the effect of rosuvastatin on plasma levels of tumor necrosis factor-a, interleukin (IL)-1b, IL-6, and IL-10 after 72 hours of TBI. Amnesia, disorientation, and disability were assessed 3 and 6 months after TBI. Results.Thirty-six patients were analyzed according to intention-to-treat analysis; 19 patients received rosuvastatin and 17 received placebo. The best-fit mixed model showed a significant effect of rosuvastatin on the reduction of tumor necrosis factor-a levels (p = 0.004). Rosuvastatin treatment did not appear to affect the levels of IL-1b, IL-6, and IL-10. The treatment was associated with a reduction in disability scores (p = 0.03), indicating a favorable functional outcome. Life-threatening adverse effects were not observed. Conclusions. The authors' data suggest that statins may induce an antiinflammatory effect and may promote recovery after TBI. The role of statins in TBI therapy should be confirmed in larger clinical trials. Clinical trial registration no.: NCT00990028. &#xa9; AANS, 2013.
Source: EMBASE

20. Barbiturates use and its effects in patients with severe traumatic brain injury in five European countries
Author(s) Majdan M., Mauritz W., Wilbacher I., Brazinova A., Rusnak M., Leitgeb J.
Citation: Journal of Neurotrauma, January 2013, vol./is. 30/1(23-29), 0897-7151;1557-9042 (01 Jan 2013)
Publication Date: January 2013
Abstract: The guidelines for management of traumatic brain injury (TBI) recommend that high-dose barbiturate therapy may be considered to lower intracranial pressure (ICP) that is refractory to other therapeutic options. Lower doses of barbiturates may be used for sedation of patients with TBI, although there is no mention of this in the published guidelines. The goal of this study was to analyze the use of barbiturates in patients with severe TBI in the European centers where the International Neurotrauma Research Organization introduced guideline-based TBI management and to analyze the effects of barbiturates on ICP, use of vasopressors, and short-and long-term outcome of these patients. Data on 1172 patients with severe TBI were collected in 13 centers located in five European countries. Patients were categorized into three groups based on doses of barbiturates administered during treatment. Univariate and multivariate statistical methods were used to analyze the effects of barbiturates on the outcome of patients. Fewer than 20% of all patients with severe TBI were given barbiturates overall, and only 6% was given high doses. High-dose barbiturate treatment caused a decrease in ICP in 69% of patients but also caused hemodynamic instability leading to longer periods of mean arterial pressure <70 mm Hg despite increased use of high doses of vasopressors. The adjusted analysis showed no significant effect on outcome on any stage after injury. Thiopental and methohexital were equally effective. Low doses of thiopental and methohexital were used for sedation of patients without side effects. Phenobarbital was probably used for prophylaxis of post-traumatic seizures. &#xa9; 2013, Mary Ann Liebert, Inc.
Source: EMBASE
Available in fulltext from Journal of Neurotrauma at ProQuest

21. Vagus nerve stimulation to augment recovery from severe traumatic brain injury impeding consciousness: A prospective pilot clinical trial
Author(s) Shi C., Flanagan S.R., Samadani U.
Objectives: Traumatic brain injury (TBI) has high morbidity and mortality in both civilian and military populations. Blast and other mechanisms of TBI damage the brain by causing neurons to disconnect and atrophy. Such traumatic axonal injury can lead to persistent vegetative and minimally conscious states (VS and MCS), for which limited treatment options exist, including physical, occupational, speech, and cognitive therapies. More than 60,000 patients have received vagus nerve stimulation (VNS) for epilepsy and depression. In addition to decreased seizure frequency and severity, patients report enhanced mood, reduced daytime sleepiness independent of seizure control, increased slow wave sleep, and improved cognition, memory, and quality of life. Early stimulation of the vagus nerve accelerates the rate and extent of behavioral and cognitive recovery after fluid percussion brain injury in rats. Methods: We recently obtained Food and Drug Administration (FDA) approval for a pilot prospective randomized crossover trial to demonstrate objective improvement in clinical outcome by placement of a vagus nerve stimulator in patients who are recovering from severe TBI. Our hypothesis is that stimulation of the vagus nerve results in increased cerebral blood flow and metabolism in the forebrain, thalamus, and reticular formation, which promotes arousal and improved consciousness, thereby improving outcome after TBI resulting in MCS or VS. Discussion: If this study demonstrates that VNS can safely and positively impact outcome, then a larger randomized prospective crossover trial will be proposed. © W. S. Maney & Son Ltd 2013.

Source: EMBASE
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22. How does dysautonomia influence the outcome of traumatic brain injured patients admitted in a neurorehabilitation unit?

Author(s) Laxe, Sara, Terré, Rosa, León, Daniel, Bernabeu, Montserrat

Citation: Brain injury, Jan 2013, vol. 27, no. 12, p. 1383-1387 (2013)

Publication Date: January 2013

Abstract: Patients surviving severe traumatic brain injury (TBI) may suffer from symptoms presumed to be related to an excessive sympathetic production known as paroxysmal sympathetic hyperactivity (PSH). While this condition is more common in the acute phase, prognosis is less clear in rehabilitation settings. The goal of this study is to describe the functional status of patients with PSH admitted in a rehabilitation hospital and to determine its prognostic influence during rehabilitation. A cohort study was undertaken of all the patients admitted in a neurorehabilitation hospital suffering from PSH. Functional outcomes were reported according to the Glasgow outcome scale-extended (GOSE), the Disability Rating Scale (DRS) and the Functional Independence Measure (FIM). Thirteen out of 39 patients suffered symptoms compatible with PSH. Neuroimaging of PSH patients showed more diffuse lesions. The FIM at admission was lower in the PSH group who was transferred for rehabilitation at an earlier stage. At discharge no differences were seen using the FIM, DRS and GOS-E. Functional status is similar and PSH does not appear to influence recovery during the rehabilitation, although PSH patients are more likely to undergo psychoactive medications and special care is needed to approach their caregivers that perceive PSH as a complication for rehabilitation.

Source: Medline
Available in fulltext from Brain Injury at EBSCOhost

23. Comparison of long-term outcomes of patients with severe traumatic or hypoxic brain injuries treated with intrathecal baclofen therapy for dysautonomia

Author(s) Hoarau X., Richer E., Dehail P., Curyn E.

Citation: Brain Injury, November 2012, vol./is. 26/12(1451-1463), 0269-9052;1362-301X (November 2012)

Publication Date: November 2012

Abstract: Primary objective: To compare the long-term outcome of patients with severe traumatic brain injury and patients with hypoxic brain injury with dysautonomia and hypertonia treated with intrathecal baclofen therapy. Methods and procedures: Fifty-three patients with severe traumatic (n=43/53) or hypoxic (n=10/53) brain injuries treated by intrathecal baclofen therapy were included to be evaluated with the Coma Recovery ScaleRevised, the Barthel Index, the Glasgow Outcome Scale, the Ashworth scale, the
scores of hypertonic attacks, of sweating episode and of voluntary motor responses. A retrospective analysis highlighted patients’ characteristics at admission and before surgery and their complications. Main outcomes and results: After a mean follow-up time of 9.6 years, 13/53 (24.5) patients had died. Alive patients with traumatic brain injury had a higher level of consciousness recovery (p<0.02) and more abilities in daily living (p<0.008) in the long-term. Their dysautonomia and limb hypertonia also significantly improved, contrary to patients with hypoxic brain injury who needed higher doses of baclofen (p<0.03). Conclusions: At long-term follow-up, patients with hypoxic brain injury had a poorer functional outcome than patients with traumatic brain injury with persistent symptoms of dysautonomia associated with uncontrolled hypertonia, despite the use of intrathecal baclofen. © 2012 Informa UK Ltd All rights reserved. Source: EMBASE Available in fulltext from Brain Injury at EBSCOhost Available in fulltext from Brain Injury at EBSCOhost

24. Decompressive craniectomy or not: Intraoperative experience in 41 patients with severe traumatic brain injury

Author(s) Yang C.-H., Li Q., Wu C., Ma J.-P., You C.
Citation: Chinese Journal of Traumatology - English Edition, June 2012, vol./is. 15/3(158-161), 1008-1275 (June 2012)
Publication Date: June 2012
Abstract: Objective: To present our experience in using decompressive craniectomy (DC) among severe traumatic brain injury (TBI) patients during operation and to discuss its indication. Methods: From October 2008 to May 2009, 41 patients aged between 18 and 75 years with severe TBI were included in this study. They underwent DC or non-DC (NDC) according to their intraoperative findings. Postoperative intracranial pressure (ICP), complications, requiring second operation or not and outcomes were observed. Results: Fifteen patients underwent DC and 26 patients did not. The average postoperative ICP of each patient was lower than 20 mm Hg. For patients received DC, 2 had seizures after operation and 1 developed cerebrocele in the follow-up period; only 1 NDC patient had post-traumatic seizures, but none of them had delayed haematoma, cerebrospinal fluid fistula, cerebrocele or infections. At the end of follow-up, 10 patients died, 6 had the GOS of 2, 2 of 3, 9 of 4 and 14 of 5. Conclusions: DC is necessary to manage fulminant intracranial hypertension or intraoperative brain swelling. If there was not brain swelling after removal of the haematoma and necrotized neural tissues, it is safe to replace skull flap. The intraoperative finding is an important factor to decide whether to perform DC or not.
Source: EMBASE

25. Placebo-controlled trial of amantadine for severe traumatic brain injury

Citation: New England Journal of Medicine, March 2012, vol./is. 366/9(819-826), 0028-4793;1533-4406 (01 Mar 2012)
Publication Date: March 2012
Abstract: BACKGROUND: Amantadine hydrochloride is one of the most commonly prescribed medications for patients with prolonged disorders of consciousness after traumatic brain injury. Preliminary studies have suggested that amantadine may promote functional recovery. METHODS: We enrolled 184 patients who were in a vegetative or minimally conscious state 4 to 16 weeks after traumatic brain injury and who were receiving inpatient rehabilitation. Patients were randomly assigned to receive amantadine or placebo for 4 weeks and were followed for 2 weeks after the treatment was discontinued. The rate of functional recovery on the Disability Rating Scale (DRS; range, 0 to 29, with higher scores indicating greater disability) was compared over the 4 weeks of treatment (primary outcome) and during the 2-week washout period with the use of mixed-effects regression models. RESULTS: During the 4-week treatment period, recovery was significantly faster in the amantadine group than in the placebo group, as measured by the DRS score (difference in slope, 0.24 points per week; P = 0.007), indicating a benefit with respect to the primary outcome measure. In a prespecified subgroup analysis, the treatment effect was similar for patients in a vegetative state and those in a minimally conscious state. The rate of improvement in the amantadine group slowed during the 2 weeks after treatment (weeks 5 and 6) and was significantly slower than the rate in the placebo group (difference
in slope, 0.30 points per week; P = 0.02). The overall improvement in DRS scores between baseline and week 6 (2 weeks after treatment was discontinued) was similar in the two groups. There were no significant differences in the incidence of serious adverse events.

**CONCLUSIONS:** Amantadine accelerated the pace of functional recovery during active treatment in patients with post-traumatic disorders of consciousness. (Funded by the National Institute on Disability and Rehabilitation Research; ClinicalTrials.gov number, NCT00970944.) Copyright © 2012 Massachusetts Medical Society.

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Available in fulltext from *New England Journal of Medicine* at the ULHT Library and Knowledge Services' eJournal collection

### 26. Antiseizure prophylaxis

**Author(s)**

**Citation:** Pediatric Critical Care Medicine, January 2012, vol./is. 13/1 SUPPL,(S72-S82), 1529-7535;1947-3893 (January 2012)

**Publication Date:** January 2012

**Abstract:** The incidence of early PTS in pediatric patients with TBI is approximately 10% given the limitations of the available data. Based on a single class III study (4), prophylactic anticonvulsant therapy with phenytoin may be considered to reduce the incidence of early posttraumatic seizures in pediatric patients with severe TBI. Concomitant monitoring of drug levels is appropriate given the potential alterations in drug metabolism described in the context of TBI. Stronger class II evidence is available supporting the use of prophylactic anticonvulsant treatment to reduce the risk of early PTS in adults. There are no compelling data in the pediatric TBI literature to show that such treatment reduces the long-term risk of PTS or improves long-term neurologic outcome. Copyright © 2012 Brain Trauma Foundation.

**Source:** EMBASE
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**Author(s)** Haddad, Samir H, Arabi, Yaseen M

**Citation:** Scandinavian journal of trauma, resuscitation and emergency medicine, Jan 2012, vol. 20, p. 12. (2012)

**Publication Date:** January 2012

**Abstract:** Traumatic brain injury (TBI) is a major medical and socio-economic problem, and is the leading cause of death in children and young adults. The critical care management of severe TBI is largely derived from the "Guidelines for the Management of Severe Traumatic Brain Injury" that have been published by the Brain Trauma Foundation. The main objectives are prevention and treatment of intracranial hypertension and secondary brain insults, preservation of cerebral perfusion pressure (CPP), and optimization of cerebral oxygenation. In this review, the critical care management of severe TBI will be discussed with focus on monitoring, avoidance and minimization of secondary brain insults, and optimization of cerebral oxygenation and CPP.

**Source:** Medline
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Available in fulltext from *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine* at National Library of Medicine
Author(s) Debenham, Sierra, Sabit, Behzad, Saluja, Rajeet S, Lamoureux, Julie, Bajsarowicz, Paul, Maleki, Mohammad, Marcoux, Judith
Citation: The Canadian journal of neurological sciences. Le journal canadien des sciences neurologiques, Nov 2011, vol. 38, no. 6, p. 896-901, 0317-1671 (November 2011)
Publication Date: November 2011
Abstract: The American Academy of Neurology recommended using phenytoin or carbamazepine to prevent early post-traumatic seizures (PTS) in severe traumatic brain injuries (TBI). In this study, we examined the effects of using phenytoin prophylaxis on mild, moderate, and severe TBIs. There have been no studies looking at compliance rate and side effects of systematic use of phenytoin at a large population scale. The goal of this study is to determine 1) the proportion of TBI patients receiving phenytoin prophylaxis; 2) which parameters decided when to decide administer phenytoin; 3) prophylaxis efficacy and complication rate. We retrospectively studied all patients admitted with a TBI over a two year-period and collected the following information: age, GCS score, CT-scan Marshall grade, incidence of early PTS, incidence of phenytoin use and time delay, side effects, and incidence of over-dosage or under-dosage. 1008 patients were included. 5.4% had early PTS, 2.3% while on prophylaxis and 3.1% while not on prophylaxis, 1.9% before reaching the hospital and 1.2% prior to phenytoin administration while in hospital. Delay of administration was 5 hours. 64.8% received prophylaxis and physicians used positive CT scan as the primary decision-making parameter (p
Source: Medline
Available in fulltext from Canadian Journal of Neurological Sciences at EBSCOhost
Available in fulltext from Canadian Journal of Neurological Sciences at EBSCOhost

Author(s) Oluw?le, O.S.A.
Citation: Brain Injury, 01 September 2011, vol./is. 25/10(980-988), 02699052
Publication Date: 01 September 2011
Abstract: Objectives: To determine the incidence and risk factors of early post-traumatic seizures (PTS) in Nigerian subjects. Methods: Subjects were recruited consecutively, classified as mild, moderate or severe traumatic brain injury (TBI), and followed for 168 hrs for development of seizures. Results: There were 266 subjects, 213 (80%) males and 53 (20%) females, with mean age 31 years (sd 18, range 1--80, median 30). Causes of TBI were motor traffic accident (MTA) related in 217 (82%), falls in 25 (9%), struck by objects in 15 (5%), firearms in 4 (2%), sports and recreation in 3 (1%), and failed suicide in 2 (1%). Cumulative incidence of early PTS was 119‰‰ (95% CI 80--156). Risk factors were age ≤≤12 years, severity of TBI, history of seizures, and TBI at weekend, but gender and GCS were not. Skeletomotor palsy was independently associated with early PTS. Conclusions: Incidence of early PTS is high in this population, probably due to the relatively high proportion of severe TBI. Risk factors are TBI severity, young age, history of seizures, and TBI at weekends. The best preventive strategy is reduction of MTA, which causes over 80% of TBI. Prophylactic anti-seizure therapy may benefit subjects with severe TBI and skeletomotor deficits.
Source: CINAHL
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Author(s) Lv, Li-Quan, Hou, Li-Jun, Yu, Ming-Kun, Ding, Xue-Hua, Qi, Xiang-Qian, Lu, Yi-Cheng
Citation: Archives of physical medicine and rehabilitation, Sep 2011, vol. 92, no. 9, p. 1515-1518 (September 2011)
Publication Date: September 2011
Abstract: Paroxysmal sympathetic hyperactivity (PSH) after severe brain injury is detrimental to the recovery of patients. Pharmacologic management of PSH is difficult and efficacy is unpredictable or incomplete. This report presents 8 cases of PSH after extremely
severe traumatic brain injury in which hyperbaric oxygen therapy (HBOT) controlled paroxysmal autonomic changes and posturing in the early subacute phase after limited success with conventional medication regimens. Thus, HBOT may present an option for the management of PSH in addition to pharmacologic therapy. Potential mechanisms for these effects are discussed. Copyright © 2011 American Congress of Rehabilitation Medicine. Published by Elsevier Inc. All rights reserved.


**Author(s)** De Reuck, Jacques

**Citation:** Clinical neurology and neurosurgery, Jul 2011, vol. 113, no. 6, p. 469-471 (July 2011)

**Publication Date:** July 2011

**Abstract:** This prospective study compares the characteristics of patients with a moderately severe traumatic brain injury (TBI) and cerebral contusions who develop late-onset seizures to those who do not. Thirty-nine adult TBI patients with cerebral contusions, who did not need a neurosurgical treatment, could be followed up for more than 3 years. Fourteen patients developed seizures during that period and 25 did not. The Glasgow Coma Scale (GCS) score on admission and the modified Rankin (mR) score on discharge from the hospital, the computed tomography (CT) and/or magnetic resonance imaging (MRI) findings, the electroencephalogram (EEG) patterns as well as the vascular and habit risk factors were compared between both groups. The mean GCS and mR scores were moderately severe and comparable between both groups. Early-onset seizures represented 21.4%. The overall seizure recurrence was 85.7% after treatment with carbamazepine or valproate sodium. Still 3 patients did not remain seizure-free after addition of another antiepileptic drug. The average number of brain contusions on CT/MRI was approximately the same. Vascular risk factors and alcohol abuse were more observed in the seizure patients. Abnormal EEG findings on discharge from the hospital were significantly more frequent in the patients who developed late-onset seizures afterward (P Source: Medline

Available in fulltext from Clinical Neurology and Neurosurgery at ProQuest


**Author(s)** Pinder, Colin, Young, Carolyn

**Citation:** Brain injury, Jan 2011, vol. 25, no. 6, p. 634-637 (2011)

**Publication Date:** January 2011

**Abstract:** The use of prophylactic anticonvulsants following brain injury is controversial. When used for this reason or for treatment of early seizures, anticonvulsants, particularly phenytoin, can cause severe cognitive side-effects. This study presents a case of a woman with a severe brain injury with severe cognitive impairment who improved dramatically following withdrawal of phenytoin. The literature regarding such cognitive side-effects is contradictory with no consistent indication of choice of anticonvulsants to use in this situation. As a result of the dramatic improvement in this case, one should now routinely withdraw or change phenytoin treatment in all brain injury patients with significant cognitive impairment.

Source: Medline

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33. Sodium valproate for prevention of early posttraumatic seizures.

**Author(s)** Ma, Chi-yuan, Xue, Ya-jun, Li, Ming, Zhang, Yang, Li, Guang-zhao

**Citation:** Chinese journal of traumatology = Zhonghua chuang shang za zhi / Chinese Medical Association, Oct 2010, vol. 13, no. 5, p. 293-296, 1008-1275 (October 1, 2010)

**Publication Date:** October 2010

**Abstract:** To assess the preventive effect of sodium valproate on early posttraumatic seizures in traumatic brain injury (TBI) patients. The retrospective study was based on 159 patients with TBI treated at Department of Neurosurgery, Nanjing General Hospital of Nanjing Command enrolled between January 1, 2008 and December 31, 2009. The in-hospital section of the retrospectively collected database includes information on age, sex, initial Glasgow Coma Score (GCS), results of CT scanning, operation, usage of sodium valproate, seizures in the first week after injury and outcome. Seven patients (4.4%) showed early posttraumatic seizures. Although the incidence was zero in patients who
received sodium valproate treatment, the difference between the treatment and control
groups was not statistically significant. Of the 87 severe TBI patients (GCS 3-8), 6 patients
in the control group (6.9%) suffered from early seizures during the first week after TBI and
no patient who received preventive therapy suffered from seizures. The difference between
the treatment and the control groups was still not statistically significant. Of the 72 mild and
moderate TBI patients (GCS 9-15), only 1 patient in the control group suffered from
seizures and no patient in the treatment group suffered. Although the results suggest that
the study is not sufficiently powerful to detect a clinically important difference in the seizure
rates between the treatment and control groups, sodium valproate is effective in decreasing
the risk of early posttraumatic seizures in severe TBI patients. Further prospective studies
are recommended.

Source: Medline

34. Adenosine A1 receptor gene variants associated with post-traumatic seizures after
severe TBI.
Author(s) Wagner, Amy K, Miller, Megan A, Scanlon, Joelle, Ren, Dianxu, Kochanek,
Patrick M, Conley, Yvette P
Citation: Epilepsy Research, Aug 2010, vol. 90, no. 3, p. 259-272 (August 2010)
Publication Date: August 2010
Abstract: Post-traumatic seizures (PTS) are a significant complication from traumatic brain
injury (TBI). Adenosine, a major neuroprotective and neuroinhibitory molecule, is important
in experimental epilepsy models. Thus, we investigated the adenosine A1 receptor (A1AR)
gene and linked it with clinical data extracted for 206 subjects with severe TBI. Tagging
SNPs rs3766553, rs903361, rs10920573, rs6701725, and rs17511192 were genotyped,
and variant and haplotype associations with PTS were explored. We investigated further
genotype, grouped genotype, and allelic associations with PTS for rs3766553 and
rs10920573. Multivariate analysis of rs3766553 demonstrated an association between the
AA genotype and increased early PTS incidence. In contrast, the GG genotype was
associated with increased late and delayed-onset PTS rates. Multivariate analysis of
rs10920573 revealed an association between the CT genotype and increased late PTS.
Multiple risk genotype analysis showed subjects with both risk genotypes had a 46.7% chance of late PTS. To our knowledge, this is the first report implicating genetic variability
in the A1AR with PTS, or any type of seizure disorder. These results provide a rationale for
further studies investigating how adenosine neurotransmission impacts PTS, evaluating
anticonvulsants in preventing and treating PTS, and developing and testing targeted
adenosinergic therapies aimed at reducing PTS.

Source: Medline

35. Adenosine A1 receptor gene variants associated with post-traumatic seizures after
severe TBI
Author(s) Wagner A.K., Miller M.A., Scanlon J., Ren D., Kochanek P.M., Conley Y.P.
Citation: Epilepsy Research, August 2010, vol./is. 90/3(259-272), 0920-1211 (August
2010)
Publication Date: August 2010
Abstract: Post-traumatic seizures (PTS) are a significant complication from traumatic brain
injury (TBI). Adenosine, a major neuroprotective and neuroinhibitory molecule, is important
in experimental epilepsy models. Thus, we investigated the adenosine A1 receptor (A1AR)
gene and linked it with clinical data extracted for 206 subjects with severe TBI. Tagging
SNPs rs3766553, rs903361, rs10920573, rs6701725, and rs17511192 were genotyped,
and variant and haplotype associations with PTS were explored. We investigated further
genotype, grouped genotype, and allelic associations with PTS for rs3766553 and
rs10920573. Multivariate analysis of rs3766553 demonstrated an association between the
AA genotype and increased early PTS incidence. In contrast, the GG genotype was
associated with increased late and delayed-onset PTS rates. Multivariate analysis of
rs10920573 revealed an association between the CT genotype and increased late PTS.
Multiple risk genotype analysis showed subjects with both risk genotypes had a 46.7% chance of late PTS. To our knowledge, this is the first report implicating genetic variability
in the A1AR with PTS, or any type of seizure disorder. These results provide a rationale for
further studies investigating how adenosine neurotransmission impacts PTS, evaluating
anticonvulsants in preventing and treating PTS, and developing and testing targeted
adenosinergic therapies aimed at reducing PTS. © 2010 Elsevier B.V.
Source: EMBASE

**Author(s)** Young, G. Bryan, Claassen, Jan

**Citation:** Neurology, Aug 2010, vol. 75, no. 9, p. 760-761, 0028-3878 (Aug 31, 2010)

**Publication Date:** August 2010

**Abstract:** Comments on an article by P. M. Vespa et al. (see record 2010-19255-008). This article studied a subset of 6 patients with traumatic brain injury (TBI) and seizures (the incidence of nonconvulsive seizures (NCS) was over 20%). Four of these had nonconvulsive status epilepticus (NCSE). They were matched with a group of 10 patients with traumatic brain injury (TBI) who did not have seizures on continuous EEG (cEEG), matched for age, sex, and Glasgow Coma Scale scores. The authors found that the study group developed hippocampal atrophy over time on serial MRI scans, with the atrophy being most marked on the same side as the seizures. When brain insults are followed by NCSE, etiology will figure prominently in patient morbidity and mortality. At the same time, there is increasing evidence that NCSE contributes to additional brain injury, at least in the hippocampal region, and may prolong coma, ICU length of stay, and health care costs. The ultimate practical question, therefore, is whether cEEG monitoring and prompt control of NCSE in this situation make a difference in outcomes. Is NCSE merely an epiphenomenon of severe brain injury or does it warrant detection and treatment in itself? A randomized, controlled trial seems justified and necessary, especially since cEEG monitoring in intensive care unit (ICUs) is not currently a general standard of care. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

**Source:** PsycINFO

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37. Mortality reduction after implementing a clinical practice guidelines-based management protocol for severe traumatic brain injury


**Citation:** Journal of Critical Care, June 2010, vol./is. 25/2(190-195), 0883-9441 (June 2010)

**Publication Date:** June 2010

**Abstract:** Introduction: The objective of this study was to examine the effect of implementing a clinical practice guidelines-based management protocol on the outcome of patients with severe traumatic brain injury (TBI). Methods: We carried out a pre-post guideline implementation study using previously collected data in the Intensive Care Unit (ICU). All patients older than 12 years with severe TBI, defined as a Glasgow Coma Scale score of 8 or less, from March 1999 to January 2001 (control group) and from February 2001 to December 2006 (protocol group) were identified and included in this study. Patients in the protocol group were managed using a clinical practice guidelines-based management protocol, derived from the guidelines published by the Brain Trauma Foundation. Primary outcome was hospital mortality, whereas the secondary outcome was ICU mortality. To assess whether the ICU protocol might have led to an increase in the number of surviving patients with severe disability, we examined the association of the protocol use and the need for tracheostomies, mechanical ventilation duration, and ICU and hospital length of stay (LOS) among survivors. Results: During the study period, a total of 434 patients met the inclusion criteria. After adjustment for several prognostic factors, the use of protocol was independently associated with a significant reduction in hospital and ICU mortality (odds ratio, 0.45; 95% confidence interval, 0.24-0.86; and odds ratio, 0.47; 95% confidence interval, 0.23-0.96, respectively). The use of the protocol was not associated with an increase in the need for tracheostomies, mechanical ventilation duration, ICU LOS, and hospital LOS. Conclusion: The protocol implementation was associated with a reduction in hospital and ICU mortality. This improvement was not associated with an increase in the frequency of tracheostomies and in ICU or hospital LOS, suggesting that the improved survival was not associated with the increased number of surviving patients with severe disability and that the functional status might have also improved. © 2010 Elsevier Inc.

**Source:** EMBASE

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38. A population-based study of risk of epilepsy after hospitalization for traumatic brain injury

**Author(s)** Ferguson P.L., Smith G.M., Wannamaker B.B., Thurman D.J., Pickelsimer E.,
Purpose: This study was undertaken to determine the risk of developing posttraumatic epilepsy (PTE) within 3 years after discharge among a population-based sample of older adolescents and adults hospitalized with traumatic brain injury (TBI) in South Carolina. It also identifies characteristics related to development of PTE within this population.

Methods: A stratified random sample of persons aged 15 and older with TBI was selected from the South Carolina nonfederal hospital discharge dataset for four consecutive years. Medical records of recruits were reviewed, and they participated in up to three yearly follow-up telephone interviews. Results: The cumulative incidence of PTE in the first 3 years after discharge, after adjusting for loss to follow-up, was 4.4 per 100 persons over 3 years for hospitalized mild TBI, 7.6 for moderate, and 13.6 for severe. Those with severe TBI, posttraumatic seizures prior to discharge, and a history of depression were most at risk for PTE. This higher risk group also included persons with three or more chronic medical conditions at discharge. Discussion: These results raise the possibility that although some of the characteristics related to development of PTE are nonmodifiable, other factors, such as depression, might be altered with intervention. Further research into factors associated with developing PTE could lead to risk-reducing treatments.

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Author(s) Stuart, R Morgan, Schmidt, Michael, Kurtz, Pedro, Waziri, Allen, Helbok, Raimund, Mayer, Stephan A, Lee, Kiwon, Badjatia, Neeraj, Hirsch, Lawrence J, Connolly, E Sander, Claassen, Jan

Citation: Neurocritical care, Apr 2010, vol. 12, no. 2, p. 188-198 (April 2010)

Abstract: Critical care management of patients with severe acute brain injury has undergone tremendous advances. Neurosurgeons and neurointensivists have a large armamentarium of invasive monitoring devices available to help detect secondary brain injury and guide therapy. No consensus exists regarding patient specific selection of monitoring devices, the placement of devices in relation to injured brain tissue, or the preferred insertion technique. Here we review our experience in a consecutive series of acutely brain injured patients who underwent multimodality monitoring. Sixty-one patients admitted to the Neurological Intensive Care Unit underwent multimodality intracranial monitoring between January 2005 and October 2008. Patient demographics, hospital length of stay, types of monitoring devices and modalities monitored, insertion techniques, device placement location relative to injury, and complications are reported. Monitored modalities included brain tissue oxygen (PbtO(2)) in 97% (N = 59), microdialysis (MD) in 79% (N = 48), intracranial electroencephalography in 31% (N = 19), brain temperature in 18% (N = 11), and cerebral blood flow in 11% (N = 7). On average, monitoring started within 2 days (0-8) of admission and was continued for 7 days (1-17). The majority of probes (56%; N = 35) were placed into patients with focal brain injuries, while in 43% N = 26 the injury was diffuse. Among those with focal injury, probe placement was categorized as peri-lesional in 46% (N = 16), and within a clot or infarct in 17% (N = 6). The most frequent complication of multimodality brain monitoring was device malfunction or dislodgement (43%; N = 26). Rates of hematoma and infection were 3 and 5%, respectively. Average NICU length of stay was 17 days (3-48) and 26% (N = 16) of patients were dead at discharge. Collaboration among institutions is necessary to establish practice guidelines for the choice and placement of multimodal monitors. Further advancement in device technology is needed to improve insertion techniques, inter-device compatibility, and device durability. Multimodality data needs to be analyzed to determine the preferable device location.

Source: Medline
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40. Prospective, randomized, single-blinded comparative trial of intravenous levetiracetam versus phenytoin for seizure prophylaxis.

**Author(s)** Szafarski, Jerzy P, Sangha, Kiranpal S, Lindsell, Christopher J, Shutter, Lori A

**Citation:** Neurocritical care, Apr 2010, vol. 12, no. 2, p. 165-172 (April 2010)

**Publication Date:** April 2010

**Abstract:** Anti-epileptic drugs are commonly used for seizure prophylaxis after neurological injury. We performed a study comparing intravenous (IV) levetiracetam (LEV) to IV phenytoin (PHT) for seizure prophylaxis after neurological injury. In this prospective, single-center, randomized, single-blinded comparative trial of LEV versus PHT (2:1 ratio) in patients with severe traumatic brain injury (sTBI) or subarachnoid hemorrhage (NCT00618436) patients received IV load with either LEV or fosphenytoin followed by standard IV doses of LEV or PHT. Doses were adjusted to maintain therapeutic serum PHT concentrations or if patients had seizures. Continuous EEG (cEEG) monitoring was performed for the initial 72 h; outcome data were collected. A total of 52 patients were randomized (LEV = 34; PHT = 18); 89% with sTBI. When controlling for baseline severity, LEV patients experienced better long-term outcomes than those on PHT; the Disability Rating Scale score was lower at 6 months (P = 0.042) and the Glasgow Outcomes Scale score was higher at 6 months (P = 0.039). There were no differences between groups in seizure occurrence during cEEG (LEV 5/34 vs. PHT 3/18; P = 1.0) or at 6 months (LEV 1/20 vs. PHT 0/14; P = 1.0), mortality (LEV 14/34 vs. PHT 4/18; P = 0.227). There were no differences in side effects between groups (all P > 0.15) except for a lower frequency of worsened neurological status (P = 0.024), and gastrointestinal problems (P = 0.043) in LEV-treated patients. This study of LEV versus PHT for seizure prevention in the NSICU showed improved long-term outcomes of LEV-treated patients vis-à-vis PHT-treated patients. LEV appears to be an alternative to PHT for seizure prophylaxis in this setting.

**Source:** Medline

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41. Dosing and safety of cyclosporine in patients with severe brain injury.

**Author(s)** Hatton, Jimmi, Rosbolt, Bonnie, Empey, Philip, Kryscio, Richard, Young, Byron

**Citation:** Journal of neurosurgery, Oct 2008, vol. 109, no. 4, p. 699-707, 0022-3085 (October 2008)

**Publication Date:** October 2008

**Abstract:** Cyclosporine neuroprotection has been reported in brain injury models but safety and dosing guidelines have not been determined in humans with severe traumatic brain injury (TBI). The purpose of this investigation was to establish the safety of cyclosporine using 4 clinically relevant dosing schemes. The authors performed a prospective, blinded, placebo-controlled, randomized, dose-escalation trial of cyclosporine administration initiated within 8 hours of TBI (Glasgow Coma Scale score range 4-8; motor score range 2-5). Four dosing cohorts (8 patients treated with cyclosporine and 2 receiving placebo treatment per cohort) received cyclosporine (1.25-5 mg/kg/day) or placebo in 2 divided doses (Cohorts I-III) or continuous infusion (Cohort IV) over 72 hours. Adverse events and outcome were monitored for 6 months. Forty patients were enrolled over 3 years (cyclosporine cohorts, 24 male and 8 female patients; placebo group, 8 male patients). Systemic trough concentrations were below 250 ng/ml during intermittent doses. Higher blood concentrations were observed in Cohorts III and IV. There was no significant difference in immunological effects, adverse events, infection, renal dysfunction, or seizures. Mortality rate was not affected by cyclosporine administration, independent of dose, compared with placebo (6 of 32 patients receiving cyclosporine and 2 of 8 receiving placebo died, P>0.05). At 6 months, a dose-related improvement in favorable outcome was observed in cyclosporine-treated patients (p

**Source:** Medline

42. Levetiracetam versus phenytoin for seizure prophylaxis in severe traumatic brain injury


**Citation:** Neurosurgical focus, October 2008, vol./is. 25/4(E3), 1092-0684 (Oct 2008)

**Publication Date:** October 2008

**Abstract:** OBJECT: Current standard of care for patients with severe traumatic brain injury (TBI) is prophylactic treatment with phenytoin for 7 days to decrease the risk of early posttraumatic seizures. Phenytoin alters drug metabolism, induces fever, and requires
therapeutic-level monitoring. Alternatively, levetiracetam (Keppra) does not require serum monitoring or have significant pharmacokinetic interactions. In the current study, the authors compare the EEG findings in patients receiving phenytoin with those receiving levetiracetam monotherapy for seizure prophylaxis following severe TBI. METHODS: Data were prospectively collected in 32 cases in which patients received levetiracetam for the first 7 days after severe TBI and compared with data from a historical cohort of 41 cases in which patients received phenytoin monotherapy. Patients underwent 1-hour electroencephalographic (EEG) monitoring if they displayed persistent coma, decreased mental status, or clinical signs of seizures. The EEG results were grouped into normal and abnormal findings, with abnormal EEG findings further categorized as seizure activity or seizure tendency. RESULTS: Fifteen of 32 patients in the levetiracetam group warranted EEG monitoring. In 7 of these 15 cases the results were normal and in 8 abnormal; 1 patient had seizure activity, whereas 7 had seizure tendency. Twelve of 41 patients in the phenytoin group received EEG monitoring, with all results being normal. Patients treated with levetiracetam and phenytoin had equivalent incidence of seizure activity (p = 0.556). Patients receiving levetiracetam had a higher incidence of abnormal EEG findings (p = 0.003). CONCLUSIONS: Levetiracetam is as effective as phenytoin in preventing early posttraumatic seizures but is associated with an increased seizure tendency on EEG analysis.

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43. Nonconvulsive electrographic seizures after traumatic brain injury result in a delayed, prolonged increase in intracranial pressure and metabolic crisis

Author(s): Vespa P.M., Miller C., McArthur D., Eliseo M., Etchepare M., Hirt D., Glenn T.C., Martin N., Hovda D.
Citation: Critical Care Medicine, December 2007, vol./is. 35/12(2830-2836), 0090-3493 (December 2007)
Publication Date: December 2007
Abstract: OBJECTIVE: To determine whether nonconvulsive electrographic post-traumatic seizures result in increases in intracranial pressure and microdialysis lactate/pyruvate ratio. DESIGN: Prospective monitoring with retrospective data analysis. SETTING: Single center academic neurologic intensive care unit. PATIENTS: Twenty moderate to severe traumatic brain injury patients (Glasgow Coma Score 3-13). MEASUREMENTS AND MAIN RESULTS: Continuous electroencephalography and cerebral microdialysis were performed for 7 days after injury. Ten patients had seizures and were compared with a matched cohort of traumatic brain injury patients without seizures. The seizures were repetitive and constituted status epilepticus in seven of ten patients. Using a within-subject design, post-traumatic seizures resulted in episodic increases in intracranial pressure (22.4 +/- 7 vs. 12.8 +/- 4.3 mm Hg; p < .001) and an episodic increase in lactate/pyruvate ratio (49.4 +/- 16 vs. 23.8 +/- 7.6; p < .001) in the seizure group. Using a between-subjects comparison, the seizure group demonstrated a higher mean intracranial pressure (17.6 +/- 6.5 vs. 12.2 +/- 4.2 mm Hg; p < .001), a higher mean lactate/pyruvate ratio (38.6 +/- 18 vs. 27 +/- 9; p < .001) compared with nonseizure patients. The intracranial pressure and lactate/pyruvate ratio remained elevated beyond postinjury hour 100 in the seizure group but not the nonseizure group (p < .02). CONCLUSION: Post-traumatic seizures result in episodic as well as long-lasting increases in intracranial pressure and microdialysis lactate/pyruvate ratio. These data suggest that post-traumatic seizures represent a therapeutic target for patients with traumatic brain injury. © 2007 Lippincott Williams & Wilkins, Inc.
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44. Gabapentin in the management of dysautonomia following severe traumatic brain injury: A case series

Author(s): Baguley I.J., Heriseanu R.E., Gurka J.A., Nordenbo A., Cameron I.D.
Citation: Journal of Neurology, Neurosurgery and Psychiatry, May 2007, vol./is. 78/5(539-541), 0022-3050:1468-330X (May 2007)
Publication Date: May 2007
Abstract: The pharmacological management of dysautonomia, otherwise known as autonomic storms, following acute neurological insults, is problematic and remains poorly researched. This paper presents six subjects with dysautonomia following extremely severe
traumatic brain injury where gabapentin controlled paroxysmal autonomic changes and posturing in the early post-acute phase following limited success with conventional medication regimens. In two subjects, other medications were reduced or ceased without a recurrence of symptoms. It is proposed that medications that can block or minimise abnormal afferent stimuli may represent a better option for dysautonomia management than drugs which increase inhibition of efferent pathways. Potential mechanisms for these effects are discussed.

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45. Magnesium sulfate for neuroprotection after traumatic brain injury: a randomised controlled trial.


Citation: The Lancet. Neurology, Jan 2007, vol. 6, no. 1, p. 29-38, 1474-4422 (January 2007)

Publication Date: January 2007

Abstract: Traumatic brain injuries represent an important and costly health problem. Supplemental magnesium positively affects many of the processes involved in secondary injury after traumatic brain injury and consistently improves outcome in animal models. We aimed to test whether treatment with magnesium favourably affects outcome in head-injured patients. In a double-blind trial, 499 patients aged 14 years or older admitted to a level 1 regional trauma centre between August, 1998, and October, 2004, with moderate or severe traumatic brain injury were randomly assigned one of two doses of magnesium or placebo within 8 h of injury and continuing for 5 days. Magnesium doses were targeted to achieve serum magnesium ranges of 1.0-1.85 mmol/L or 1.25-2.5 mmol/L. The primary outcome was a composite of mortality, seizures, functional measures, and neuropsychological tests assessed up to 6 months after injury. Analyses were done according to the intention-to-treat principle. This trial is registered with , number . Magnesium showed no significant positive effect on the composite primary outcome measure at the higher dose (mean=55 average percentile ranking on magnesium vs 52 on placebo, 95% CI for difference -7 to 14; p=0.70). Those randomly assigned magnesium at the lower dose did significantly worse than those assigned placebo (48 vs 54, 95% CI -10.5 to -2; p=0.007). Furthermore, there was higher mortality with the higher magnesium dose than with placebo. Other major medical complications were similar between groups, except for a slight excess of pulmonary oedema and respiratory failure in the lower magnesium target group. No subgroups were identified in which magnesium had a significantly positive effect. Continuous infusions of magnesium for 5 days given to patients within 8 h of moderate or severe traumatic brain injury were not neuroprotective and might even have a negative effect in the treatment of significant head injury.

Source: Medline
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46. Update on the management of severe head injury in adults

Author(s) Hunningher A., Smith M.

Citation: Care of the Critically Ill, October 2006, vol./is. 22/5(124-129), 0266-0970 (October 2006)

Publication Date: October 2006

Abstract: The effective management of patients with severe traumatic brain injury requires an understanding of the underlying pathological processes and a co-ordinated,
comprehensive and multidisciplinary approach to treatment. Over the last decade there have been major changes in the way in which adults with severe TBI are managed. Improvements in pre-hospital management and resuscitation have reduced the incidence of early secondary ischaemic insults and led to improvements in outcome. More recently the management of patients on the intensive care unit has been guided by better understanding of the pathophysiology of brain injury and by new and improved monitoring techniques. There has been a shift of emphasis from primary control of ICP to a multifaceted approach of maintenance of cerebral perfusion and oxygenation. The evidence base for therapies in head injury is constantly being revised and international consensus guidelines offer up to date advice for clinicians. However, head injury is a heterogeneous pathology and the concept of individualised therapy is gaining ground as evidence suggests that protocol-guided therapy to maintain cerebral perfusion and oxygenation throughout the entire treatment episode can offer improvements in outcome.

Source: EMBASE

47. Severe traumatic brain injury: management and prognosis.
Author(s) Pace, M C, Cicciarella, G, Barbato, E, Maisto, M, Passavanti, M B, Gazzero, G, Barbarisi, M, Aurilio, C
Citation: Minerva anestesioligica, Apr 2006, vol. 72, no. 4, p. 235-242, 0375-9393 (April 2006)
Publication Date: April 2006
Abstract: The aim of the study is to assess the efficacy of early treatment in severe traumatic brain injury by evaluating patients’ survival and functional recovery. We subdivided 184 patients into 2 groups (Group A: patients admitted to hospital within the first hour of injury; Group B: patients admitted after the first hour of injury). In order to maintain the mean arterial pressure (MAP) >90 with cerebral perfusion pressure (CPP) >70 mmHg, we used plasma expanders; in 76 patients with MAP >90 mmHg, we administered dopamine, and in 5 cases noradrenaline. In 157 patients we used mechanical ventilation (MV). For orotracheal intubation and sedation/analgesia, we administered: propofol (a bolus of 2 mg/kg+1 mg/kg/h)+midazolam (0.03 mg/kg/h) + cisatracurium besilate (0.2 mg/kg) in 113 patients, or thiopentone sodium (a bolus of 4 mg/kg + 1-2 mg/kg/h)+cisatracurium besilate (0.2 mg/kg) in 44 patients with endocranial hypertension without bleeding and convulsions. After muscle relaxation we administered remifentanyl (0.075 microg/kg/min). Surgical decompression was performed in 57 cases. Data were analysed with Student's t-test. The number of deaths was significantly lower in Group A (P
Source: Medline
Available in fulltext from Minerva Anestesiologica at Free Access Content

48. Primer on medical management of severe brain injury.
Author(s) Vincent, Jean-Louis, Berré, Jacques
Citation: Critical care medicine, Jun 2005, vol. 33, no. 6, p. 1392-1399, 0090-3493 (June 2005)
Publication Date: June 2005
Abstract: To review the current understanding of the medical management of severe brain injury. The MEDLINE database, bibliographies of selected articles, and current English-language texts on the subject. Studies related to management of intracranial hypertension, traumatic brain injury, and brain edema. All studies relevant to the subject under consideration were considered, with a focus on clinical studies in adults. Basic rules of resuscitation must apply, including adequate ventilation, appropriate fluid administration, and cardiovascular support. The control of intracranial pressure can be considered in three steps. The first step should be initial slight hyperventilation with a target PaCO2 of 35 mm Hg and cerebrospinal fluid drainage for intracranial pressure of >15-20 mm Hg. The second step should be mannitol or hypertonic saline and hyperventilation to target PaCO2 of 28-35 mm Hg. The third step should be barbiturate coma or decompressive craniectomy. Additional management issues, including seizure prophylaxis, sedation, nutritional support, use of hypothermia, and corticosteroids, are also discussed. Brain injury is frequently associated with the development of brain edema and the development of intracranial hypertension. However, with a coordinated, stepwise, and aggressive approach to management, focusing on control of intracranial pressure without adversely affecting cerebral perfusion pressure, outcomes can be good.
Source: Medline
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49. Efficacy of standard trauma craniectomy for refractory intracranial hypertension with severe traumatic brain injury: A multicenter, prospective, randomized controlled study

**Author(s)** Jiang J.-Y., Xu W., Li W.-P., Xu W.-H., Zhang J., Bao Y.-H., Ying Y.-H., Luo Q.-Z.

**Citation:** Journal of Neurotrauma, June 2005, vol./is. 22/6(623-628), 0897-7151 (June 2005)

**Publication Date:** June 2005

**Abstract:** To compare the effect of standard trauma craniectomy (STC) versus limited craniectomy (LC) on the outcome of severe traumatic brain injury (TBI) with refractory intracranial hypertension, we conducted a study at five medical centers of 486 patients with severe TBI (Glasgow Coma Scale score < 8) and refractory intracranial hypertension. In all 486 cases, refractory intracranial hypertension, caused by unilateral massive frontotemporoparietal contusion, intracerebral/subdural hematoma, and brain edema, was confirmed on a CT scan. The patients were randomly divided into two groups, one of which underwent STC (n = 241) with a unilateral frontotemporoparietal bone flap (12 x 15 cm), and the second of which underwent LC (n = 245) with a routine temporoparietal bone flap (6 x 8 cm). At 6-month follow-up, 96 patients (39.8%) in the STC group had a favorable outcome on the basis of the Glasgow Outcome Scale, including 62 patients who had a good recovery and 34 who showed moderate deficits. Another 145 patients (60.2%) in the STC group had an unfavorable outcome, including 73 with severe deficits, nine with persistent vegetative status, and 63 who died. By comparison, only 70 patients (28.6%) in the LC group had a favorable outcome, including 41 who had a good recovery and 29 who had moderate deficits. Another 175 patients (71.4%) in the LC group had an unfavorable outcome, including 82 with severe deficits, seven with persistent vegetative status, and 86 who died (p < 0.05). In addition to these findings, the incidence of delayed intracranial hematoma, incisional hernia, and CSF fistula was lower in the STC group than in the LC group (p < 0.05), although the incidence of acute encephalomyelocele, traumatic seizure, and intracranial infection was not significantly different in the two groups (p > 0.05). The results of the study indicate that STC significantly improves outcome in severe TBI with refractory intracranial hypertension resulting from unilateral frontotemporoparietal contusion with or without intracerebral or subdural hematoma. This suggests that STC, rather than LC, be recommended for such patients. © Mary Ann Liebert, Inc.

**Source:** EMBASE

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50. Prolonged refractory status epilepticus following acute traumatic brain injury: a case report of excellent neurological recovery

**Author(s)** Peets A.D., Berthiaume L.R., Bagshaw S.M., Federico P., Doig C.J., Zygun D.A.

**Citation:** Critical care (London, England), 2005, vol./is. 9/6(R725-728), 1466-609X (2005)

**Publication Date:** 2005

**Abstract:** INTRODUCTION: Refractory status epilepticus (RSE) secondary to traumatic brain injury (TBI) may be under-recognized and is associated with significant morbidity and mortality. METHODS: This case report describes a 20 year old previously healthy woman who suffered a severe TBI as a result of a motor vehicle collision and subsequently developed RSE. Pharmacological coma, physiological support and continuous electroencephalography (cEEG) were undertaken. RESULTS: Following 25 days of pharmacological coma, electrographic and clinical seizures subsided and the patient has made an excellent cognitive recovery. CONCLUSION: With early identification, aggressive physiological support, appropriate monitoring, including cEEG, and an adequate length of treatment, young trauma patients with no previous seizure history and limited structural damage to the brain can have excellent neurological recovery from prolonged RSE.

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51. Does glucocorticoid administration prevent late seizures after head injury?

**Author(s)** Watson, Nathaniel F, Barber, Jason K, Doherty, Michael J, Miller, John W, Temkin, Nancy R

**Citation:** Epilepsia, Jun 2004, vol. 45, no. 6, p. 690-694, 0013-9580 (June 2004)
Publication Date: June 2004
Abstract: Preventing posttraumatic epilepsy has been a difficult challenge. In this study we evaluated the association between glucocorticoid administration after traumatic brain injury (TBI) and posttraumatic seizures. We examined a seizure-prevention trial database of 404 patients with severe TBI for exposure to glucocorticoids in the early (~2 days after their injury) or no association (p = 0.66; hazard ratio = 0.77; 95% CI, 0.23-2.56; p = 0.10 among the three groups). Receiving glucocorticoids within 1 day, or > or =2 days after TBI was not associated with second late seizure development. Glucocorticoid treatment after TBI is not associated with decreased late posttraumatic seizures, and early treatment is associated with increased seizure activity.

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52. Increased risk of late posttraumatic seizures associated with inheritance of APOE epsilon4 allele

Author(s) Diaz-Arrastia R., Gong Y., Fair S., Scott K.D., Garcia M.C., Carlile M.C., Agostini M.A., Van Ness P.C.

Citation: Archives of Neurology, June 2003, vol./is. 60/6(818-822), 0003-9942 (01 Jun 2003)
Publication Date: June 2003
Abstract: Background: Late posttraumatic seizures are a common complication of moderate and severe traumatic brain injury. Inheritance of the apolipoprotein E (APOE) epsilon4 allele is associated with increased risk of Alzheimer disease, progression to disability in multiple sclerosis, and poor outcome after traumatic brain injury. Objective: To determine whether inheritance of APOE epsilon4 is associated with increased risk of developing late posttraumatic seizures. Design: Prospective study. Setting: Neurosurgical service at an urban level I trauma center. Patients: Patients admitted with a diagnosis of moderate and severe traumatic brain injury were enrolled. Methods: Six months after injury, patients were contacted to determine functional outcome (according to the Glasgow Outcome Scale-Expanded [GOS-E]) and the presence of late posttraumatic seizures. Genotype at the APOE locus was determined by restriction fragment length polymorphism analysis. Results: DNA and outcome information was obtained from 106 subjects. Six months after injury, 31 (29%) had a poor outcome (GOS-E score, 1-4), 47 (44%) had an intermediate outcome (GOS-E score, 5-6), and 28 (26%) had a favorable outcome (GOS-E score, 7-8). Twenty-one patients (20%) had at least 1 late posttraumatic seizure. The relative risk of late posttraumatic seizures for patients with the epsilon4 allele was 2.41 (95% confidence interval, 1.15-5.07; P = .03). In this cohort, inheritance of APOE epsilon4 was not associated with an unfavorable GOS-E score 6 (P = .47). Conclusions: Inheritance of the APOE epsilon4 allele is associated with increased risk of late posttraumatic seizures. In this cohort, this risk appears to be independent of an effect of epsilon4 on functional outcome. A better understanding of the molecular role of APOE in neurodegenerative diseases may be helpful in developing antiepileptogenic therapies.

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53. Analyzing risk factors for late posttraumatic seizures: A prospective, multicenter investigation

Author(s) Englander J., Bushnik T., Duong T.T., Cifu D.X., Zafonte R., Wright J., Hughes R., Bergman W.

Citation: Archives of Physical Medicine and Rehabilitation, March 2003, vol./is. 84/3 SUPPL. 1(365-373), 0003-9993 (01 Mar 2003)
Publication Date: March 2003
Abstract: Objectives: To ascertain the natural history and to stratify risks for the development of late posttraumatic seizures in individuals with moderate to severe traumatic brain injury (TBI). Design: Prospective, observational study of individuals with TBI admitted to 4 trauma centers within 24 hours of injury. Setting: Four tertiary care trauma centers in urban areas. Participants: A total of 647 individuals (> 16y) with any of the following abnormal computed tomography (CT) scan findings: extent of midline shift and/or cisternal...

Author(s) Chang B.S., Lowenstein D.H.

Citation: Neurology, January 2003, vol./is. 60/1(10-16), 0028-3878 (14 Jan 2003)

Publication Date: January 2003

Abstract: Objective: To review the evidence regarding antiepileptic drug (AED) prophylaxis in patients with severe traumatic brain injury (TBI) in order to make practice recommendations. Methods: The authors identified relevant studies by searching multiple databases and reviewing reference lists of other sources. They included studies that prospectively compared post-traumatic seizure rates in patients given AED prophylaxis vs controls. Each study was graded (class I to IV) according to a standard classification-of-evidence scheme and results were analyzed and pooled. Results: Pooled class I studies demonstrated a significantly lower risk of early post-traumatic seizures (those occurring within 7 days after injury) in patients given phenytoin prophylaxis compared to controls (relative risk 0.37, 95% CI 0.18 to 0.74). Pooled class I and class II studies demonstrated no significant difference in the risk of late post-traumatic seizures (those occurring beyond 7 days after injury) in patients given AED prophylaxis compared to controls (relative risk 1.05, 95% CI 0.82 to 1.35). Serum AED levels were suboptimal in these studies and adverse effects were mild but frequent. Conclusions: For adult patients with severe TBI, prophylaxis with phenytoin is effective in decreasing the risk of early post-traumatic seizures. AED prophylaxis is probably not effective in decreasing the risk of late post-traumatic seizures. Further studies addressing milder forms of TBI, the use of newer AEDs, the utility of EEG, and the applicability of these findings to children are recommended.

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55. Repinotan (BAY x 3702): a 5HT1A agonist in traumatically brain injured patients.

Author(s) Ohman, J, Braakman, R, Legout, V, Traumatic Brain Injury Study Group

Citation: Journal of neurotrauma, Dec 2001, vol. 18, no. 12, p. 1313-1321, 0897-7151 (December 2001)

Publication Date: December 2001

Abstract: Repinotan is a high-affinity, selective, full agonist of the 5HT1A-receptor subtype with neuroprotective properties. This paper presents the results of a randomized, double-blind, placebo-controlled study examining the safety and tolerability of three different doses of repinotan in patients with severe traumatic brain injury. Sixty patients were enrolled to receive repinotan (0.5, 1.25, or 2.50 mg/day) or placebo, by continuous i.v. infusion for 7 days postinjury or best Glasgow Coma Scale (GCS) score of <10 during the first 24 hours post-TBI. Subjects were enrolled from August 1993 through September 1997 and followed for up to 24 months, until death or their first late posttraumatic seizures.

Interventions: Not applicable. Main Outcome Measures: Cumulative probability, relative risk, and survival analyses were used to stratify risks for development of late posttraumatic seizures on the basis of demographic factors, etiology of injury, initial GCS, early posttraumatic seizures, time post-TBI, types of intracerebral lesion by CT scan, and number and types of intracranial procedures. Results: Sixty-six individuals had a late posttraumatic seizures; 337 had no late posttraumatic seizures during full 24-month follow-up; 167 had no late posttraumatic seizures during time followed (<24mo); and 54 were placed on anticonvulsants without a late posttraumatic seizures, whereas 23 died before their first late posttraumatic seizures. The highest cumulative probability for late posttraumatic seizures included biparietal contusions (66%), dural penetration with bone and metal fragments (62.5%), multiple intracranial operations (36.5%), multiple subcortical contusions (33.4%), subdural hematoma with evacuation (27.8%), midline shift greater than 5mm (25.8%), or multiple or bilateral cortical contusions (25%). Initial GCS score was associated with the following cumulative probabilities for development of late posttraumatic seizures at 24 months: GCS score of 3 to 8, 16.8%; GCS score of 9 to 12, 24.3%; and GCS score of 13 to 15, 8.0%. Conclusions: Stratification by CT scan findings and neurosurgical procedures performed were the most useful findings in defining individuals at highest risk for late posttraumatic seizures. &lt;#xa9; 2003 by the American Congress of Rehabilitation Medicine and the American Academy of Physical Medicine and Rehabilitation.

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days. Repinotan treatment had no apparent adverse effects on intracranial pressure, hemodynamic parameters or laboratory parameters. No seizures occurred during treatment, and the incidence and severity of adverse events was as expected for this indication. No serious adverse events were considered related to drug treatment, with the possible exception of one case of inappropriate ADH secretion. No further safety concerns were raised during the 3 months following treatment. On a descriptive basis, the proportion of patients having good outcome or moderate disability (Glasgow Outcome Scale) was somewhat greater in repinotan-treated patients (60%) than in placebo (50%).

Source: Medline
Available in fulltext from JAMA: Journal of the American Medical Association at ProQuest

56. Stimulating consciousness and cognition following severe brain injury: a new potential clinical use for lamotrigine.

Author(s) Showalter, P E, Kimmel, D N
Citation: Brain injury, Nov 2000, vol. 14, no. 11, p. 997-1001, 0269-9052 (November 2000)
Publication Date: November 2000

Abstract: No medications clearly enhance consciousness or cognition following severe brain injury. This series (n = 13) suggests that lamotrigine may stimulate improvement of patients with impairment equivalent to level I-III on the Rancho Los Amigos Cognitive Scale. After a serendipitous clinical result, severely brain injured patients who were taking an anticonvulsant had an opportunity to start lamotrigine. This cohort had been transferred to this rehabilitation unit 14-304 (mean 73.9) days and started lamotrigine 20-310 (mean 87.5) days after acute brain injury. Compared to this unit's experience with patients with similar severe brain injuries, more patients (n = 10) were discharged to the community and fewer to skilled nursing facilities (n = 3) than were expected. This preliminary and provocative case series corresponds to basic science results, and further investigation of lamotrigine is warranted.

Source: Medline
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Citation: JAMA, Jun 2000, vol. 283, no. 23, p. 3075-3081, 0098-7484 (June 21, 2000)
Publication Date: June 2000

Abstract: Traumatic brain injury (TBI) is a principal cause of death and disability in young adults. Rehabilitation for TBI has not received the same level of scientific scrutiny for efficacy and cost-efficiency that is expected in other medical fields. To evaluate the efficacy of inpatient cognitive rehabilitation for patients with TBI. Single-center, parallel-group, randomized trial conducted from January 1992 through February 1997 at a US military medical referral center. One hundred twenty active-duty military personnel who had sustained a moderate-to-severe closed head injury, manifested by a Glasgow Coma Scale score of 13 or less, or posttraumatic amnesia lasting at least 24 hours, or focal cerebral contusion or hemorrhage on computed tomography or magnetic resonance imaging. Patients were randomly assigned to an intensive, standardized, 8-week, in-hospital cognitive rehabilitation program (n=67) or a limited home rehabilitation program with weekly telephone support from a psychiatric nurse (n=53). Return to gainful employment and fitness for military duty at 1-year follow-up, compared by intervention group. At 1-year follow-up, there was no significant difference between patients who had received the intensive in-hospital cognitive rehabilitation program vs the limited home rehabilitation program in return to employment (90% vs 94%, respectively; P=.51; difference, 4% [95% confidence interval -5% to 14%]) or fitness for duty (73% vs 66%, respectively; P=.43; difference, 7% [95% CI, -10% to 24%]). There also were no significant differences in cognitive, behavioral, or quality-of-life measures. In a post-hoc subset analysis of patients who were unconscious for more than 1 hour (n = 75) following TBI, the in-hospital group had a greater return-to-duty rate (80% vs 58%; P=.05). In this study, the overall benefit of in-hospital cognitive rehabilitation for patients with moderate-to-severe TBI was similar to that of home rehabilitation. These findings emphasize the importance of conducting randomized trials to evaluate TBI rehabilitation interventions. JAMA. 2000;283:3075-3081

Source: Medline
Available in fulltext from JAMA: Journal of the American Medical Association at
58. Increased incidence and impact of nonconvulsive and convulsive seizures after traumatic brain injury as detected by continuous electroencephalographic monitoring.

**Author(s)** Vespa, P M, Nuwer, M R, Nenov, V, Ronne-Engstrom, E, Hovda, D A, Bergsneider, M, Kelly, D F, Martin, N A, Becker, D P

**Citation:** Journal of neurosurgery, Nov 1999, vol. 91, no. 5, p. 750-760, 0022-3085

**Publication Date:** November 1999

**Abstract:** The early pathophysiological features of traumatic brain injury observed in the intensive care unit (ICU) have been described in terms of altered cerebral blood flow, altered brain metabolism, and neurochemical excitotoxicity. Seizures occur in animal models of brain injury and in human brain injury. Previous studies of posttraumatic seizures in humans have been based principally on clinical observations without a systematic approach to electroencephalographic (EEG) recording of seizures. The purpose of this study was to determine prospectively the incidence of convulsive and nonconvulsive seizures by using continuous EEG monitoring in patients in the ICU during the initial 14 days post-injury. Ninety-four patients with moderate-to-severe brain injuries underwent continuous EEG monitoring beginning at admission to the ICU (mean delay 9.6±/-5.4 hours) and extending up to 14 days postinjury. Convulsive and nonconvulsive seizures occurred in 21 (22%) of the 94 patients, with six of them displaying status epilepticus. In more than half of the patients (52%) the seizures were nonconvulsive and were diagnosed on the basis of EEG studies alone. All six patients with status epilepticus died, compared with a mortality rate of 24% (18 of 73) in the nonseizure group (p < 0.001). The rates of early seizures were higher and similar when using either valproate or phenytoin (15% in the phenytoin treatment group and 4.5% in the valproate arms of the study; p = 0.14, relative risk [RR] = 2.9, 95% confidence interval [CI] 0.7-13.3). The rates of late seizures did not differ among treatment groups (15% in patients receiving the 1-week course of phenytoin, 16% in patients receiving the 1-month course of valproate, and 24% in those receiving the 6-month course of valproate; p = 0.19, RR = 1.4, 95% CI 0.8-2.4). The rates of mortality were not significantly different between treatment groups, but there was a trend toward a higher mortality rate in patients treated with valproate (7.2% in patients receiving phenytoin and 13.4% in those receiving valproate; p = 0.07, RR = 2.0, 95% CI 0.9-4.1). The incidence of serious adverse events, including coagulation problems and liver abnormalities, was similar in phenytoin- and valproate-treated patients. Valproate therapy shows no benefit over short-term phenytoin therapy for prevention of early seizures and neither treatment prevents late seizures. There was a trend toward a higher mortality rate among valproate-treated patients. The lack of additional benefit and the potentially higher mortality rate suggest that valproate should not be routinely used for the prevention of posttraumatic seizures.

**Source:** Medline

59. Valproate therapy for prevention of posttraumatic seizures: a randomized trial.


**Citation:** Journal of neurosurgery, Oct 1999, vol. 91, no. 4, p. 593-600, 0022-3085

**Publication Date:** October 1999

**Abstract:** Seizures frequently accompany moderate to severe traumatic brain injury. Phenytoin and carbamazepine are effective in preventing early, but not late, posttraumatic seizures. In this study the authors compare the safety and effectiveness of valproate with those of short-term phenytoin for prevention of seizures following traumatic brain injury. The study was a randomized, double-blind, single-center, parallel-group clinical trial. Treatment began within 24 hours of injury. One hundred thirty-two patients at high risk for seizures were assigned to receive a 1-week course of phenytoin, 120 were assigned to receive a 1-month course of valproate, and 127 were assigned to receive a 6-month course of valproate. The cases were followed for up to 2 years. The rates of early seizures were low and similar when using either valproate or phenytoin (1.5% in the phenytoin treatment group and 4.5% in the valproate arms of the study; p = 0.14, relative risk [RR] = 2.9, 95% confidence interval [CI] 0.7-13.3). The rates of late seizures did not differ among treatment groups (15% in patients receiving the 1-week course of phenytoin, 16% in patients receiving the 1-month course of valproate, and 24% in those receiving the 6-month course of valproate; p = 0.19, RR = 1.4, 95% CI 0.8-2.4). The rates of mortality were not significantly different between treatment groups, but there was a trend toward a higher mortality rate in patients treated with valproate (7.2% in patients receiving phenytoin and 13.4% in those receiving valproate; p = 0.07, RR = 2.0, 95% CI 0.9-4.1). The incidence of serious adverse events, including coagulation problems and liver abnormalities, was similar in phenytoin- and valproate-treated patients. Valproate therapy shows no benefit over short-term phenytoin therapy for prevention of early seizures and neither treatment prevents late seizures. There was a trend toward a higher mortality rate among valproate-treated patients. The lack of additional benefit and the potentially higher mortality rate suggest that valproate should not be routinely used for the prevention of posttraumatic seizures.

**Source:** Medline
A phase II study of moderate hypothermia in severe brain injury.

Author(s) Clifton, G L, Allen, S, Barrodale, P, Plenger, P, Berry, J, Koch, S, Fletcher, J, Hayes, R L, Choi, S C

Citation: Journal of neurotrauma, Jan 1993, vol. 10, no. 3, p. 263, 0897-7151 (1993)

Publication Date: January 1993

Abstract: Forty-six patients with severe nonpenetrating brain injury [Glasgow Coma Scale (GCS) 4-7] were randomized to standard management at 37 degrees C (n = 22) and to standard management with systemic hypothermia to 32 to 33 degrees C (n = 24). The two groups were balanced in terms of age (Wilcoxon's rank sum test, p > 0.95), randomizing GCS (chi-square test, p = 0.54), and primary diagnosis. Cooling was begun within 6 h of injury by use of cooling blankets. Metocurine and morphine were given hourly during induction and maintenance of hypothermia. Rewarming was at a rate of 1 degree C per 4 h beginning 48 h after intravascular temperature had reached 33 degrees C. Muscle relaxants and sedation were continued until core temperature reached 35 degrees C. There were no cardiac or coagulopathy-related complications. Seizure incidence was lower in the hypothermia group (Fisher's exact test, p = 0.019). Sepsis was seen more commonly in the hypothermia group, but difference was not statistically significant (chi-square test). Mean Glasgow Outcome Scale (GOS) score at 3 months after injury showed an absolute increase of 16% (i.e., 36.4-52.2%) in the number of patients in the Good Recovery/Moderate Disability (GR/MD) category as compared with Severe Disability/Vegetative/Dead (SD/V/D) (chi-square test, p > 0.287). Based on evidence of improved neurologic outcome with minimal toxicity, we believe that phase III testing of moderate systemic hypothermia in patients with severe head injury is warranted.

Source: Medline

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Evaluation of Seizure-like Episodes in Survivors of Moderate and Severe Traumatic Brain Injury
AM Hudak, K Trivedi, CR Harper… - The Journal of head …, 2004 - journals.lww.com Background: Transient paroxysmal alterations of consciousness or behavior are common sequelae of moderate and severe traumatic brain injury (TBI). Clinicians caring for patients with such episodes often diagnose them as epileptic seizures, a frequent and well-studied ...
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The impact of prophylactic treatment on post-traumatic epilepsy after severe traumatic brain injury

R Formisano, C Barba, MG Buzzi… - Brain …, 2007 - informahealthcare.com

Aim: To assess the incidence of late post-traumatic epilepsy (PTE) in patients with very severe traumatic brain injury (TBI) who either received or did not receive anti-epileptic prophylactic treatment. Methods: Two populations were studied: 55 patients who

Preventing and treating posttraumatic seizures: the human experience

NR Temkin - Epilepsia, 2009 - Wiley Online Library

... severe TBI is associated with about a 17-fold increase in risk, which translates into more than 15% of people with severe TBI developing epilepsy ... About one-third of those who ultimately develop posttraumatic epilepsy (PTE) have their first unprovoked seizure within 3–4 ...

A population-based study of risk of epilepsy after hospitalization for traumatic brain injury

PL Ferguson, GM Smith, BB Wannamaker… - …, 2010 - Wiley Online Library

... this study with those which have different follow-up times (up to 20 years), are restricted to moderate and severe TBI, or consist of ... n = 11, 10%) was PTE assigned solely on a positive response to whether they took medicines to control their seizure disorder or epilepsy ...

Role of intravenous levetiracetam in seizure prophylaxis of severe traumatic brain injury patients


Abstract Traumatic brain injury (TBI) can cause seizures and the development of epilepsy. The incidence of seizures varies from 21% in patients with severe brain injuries to 50% in patients with war-related penetrating TBI. In the acute and sub-acute periods following ...

Epilepsy after head injury


... of Neurology Practice parameter: antiepileptic drug prophylaxis in severe traumatic brain injury: report of ... Evaluation of topiramate neuroprotective effect in severe TBI using microdialysis. ... Antiepileptogenesis and seizure prevention trials with antiepileptic drugs: meta-analysis of ...

Nonconvulsive seizures after traumatic brain injury are associated with hippocampal atrophy

PM Vespa, DL McArthur, Y Xu, M Eliseo, M Etchepare… - Neurology, 2010 - AAN Enterprises

... Posttraumatic seizures occur in nearly one-quarter of patients with severe TBI and may be a specific therapeutic target with cEEG ... Hippocampus, amygdala, and basal ganglia morphometrics in children after moderate-to-severe traumatic brain injury. ...

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