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Review

A systematic review of epileptic seizures in adults with subdural haematomas

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ABSTRACT

Background: Posttraumatic epileptic seizures (PTS) are a serious complication in patients with subdural haematoma (SDH). However, to date, several studies have shown discordances about SDH-associated seizures in terms of incidence, risk factors and prophylactic antiepileptic treatment.
Objective: The aim of this study was to analyse the incidence, risk factors of PTS and the role of prophylactic antiepileptic treatment in patients with SDH.
Data sources: A systematic literature review examining PTS in patients with SDH was performed using PubMed gateway, Cochrane Central Register of Controlled Trials, and Excerpta Medica dataBASE between September 1961 and February 2016. Search terms included subdural haematoma, seizure, epilepsy, prophylactic antiepileptic drugs, anticonvulsive medication, and risk factors.
Data selection: Human-based clinical studies focusing on epileptic seizures in patients with SDH.
Data extraction and synthesis: PRISMA statements were used for assessing data quality. Two independent reviewers extracted data from included studies and disagreement was solved by consensus. Twenty-four studies were identified for inclusion into the study.
Results: Overall incidence of early PTS (ePTS) and late PTS (lPTS)/2 years was 28% and 43% in acute SDH (aSDH) whereas the incidence of e- and lPTS was lower in chronic SDH (cSDH; 5.3% vs. 10%). Overall risk factors for PTS in patients with aSDH were: 24 h postoperative Glasgow Coma Score (GCS) score below 9 (OR 10.5), craniotomy (OR 3.9), preoperative GCS below 8 (OR 3.1). In patients with cSDH the risk factors were alcohol abuse (OR 14.3), change of mental status (OR 7.2), previous stroke (OR 5.3) and density of haematoma in computer tomography (OR 3.8). Age, sex, haematoma size/side and midline shifts were not significant risk factors for PTS in both types of SDH. In prevention of PTS phenytoin and levetiracetam showed similar efficacy (OR 1.3), whereas levetiracetam was associated with significantly lower adverse effects (OR 0.1).
Limitations: Most of the studies were of retrospective nature with a small sample size. Due to the inclusion criteria, some studies had to be excluded and that might lead to selection bias.
Conclusions: PTS are a serious complication in patients with SDH, particularly in aSDH. The "prophylactic use" of antiepileptic drugs might be beneficial in patients with cumulative risk factors.

1. Introduction

Post-traumatic epileptic seizures (PTSs) are a serious complication after traumatic brain injury (TBI), particularly in patients with subdural haematomas (SDHs). The prevalence of PTSs in SDHs is reported to be 24% in acute SDHs (aSDHs) and 11% in chronic SDHs (cSDHs) [1–3]. Despite the high prevalence of PTSs in SDHs, which patients are at risk of developing PTSs and could eventually profit from a prophylactic antiepileptic medication remains a matter of speculation. In fact, some retrospective studies showed that older age, chronic alcoholism and the severity of trauma were associated with PTSs [4,8–11]; however, classifying PTSs is more complex than it seems at first sight. In the literature, PTSs are classified by arbitrary time limits into three groups: immediate seizures occur within 24 h after insult; early acute symptomatic seizures within 7 days after insult; and late unprovoked seizures

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7 days after insult. It seems important to differentiate between those groups due to the different underlying pathophysiology, which might be associated with different seizure recurrence rates. Unfortunately, the time limits are not used consistently: some authors delineate between early and late seizures at 14 days. Compared to early PTSs (ePTSs), late PTSs (lPTSs) have a much higher risk of recurrence of seizures (<20% compared to >60%). Although the risk of PTS is highest within 24 h after TBI as an acute symptom, lPTSs can occur up to 20 years after TBI, thereby suggesting clinical alertness. In particular, injuries involving SDHs are likely to increase both ePTSs and lPTSs in children and adults compared to other TBIs [3]. The prognosis after an SDH depends on multiple factors such as age, Glasgow coma scale (GCS), size of haemorrhage and time from the SDH until treatment, but the occurrence of a PTS is an independent marker of poor functional and social outcome [5–8,10,19].

Antiepileptic drugs (AEDs) are standard treatment for lPTSs, but their use in ePTSs remains controversial. There have been some prospective studies verifying the positive effect of prophylactic AEDs like phenytoin, which was largely used in the past as the gold standard in reducing ePTSs [13]. Recently, more tolerable AEDs like levetiracetam, which have a similar efficacy, were introduced into the market to replace the standard AEDs [55]. However, to date, there have been no prospective controlled studies describing the value of prophylactic AEDs exclusively focusing on SDHs. One retrospective study showed a significant reduction of epileptic seizures by administering prophylactic AEDs [2,15], but other retrospective studies were not able to show any advantage of prophylactic AEDs [16,17,25]. Therefore, further studies are needed to clarify the ongoing debate about the benefit of using prophylactic AEDs in patients with SDHs.

During the last few years, several studies have reported a correlation between SDHs and epileptic seizures, but many studies disagree about SDH-associated seizures. In the present study, we performed the first systematic review on epileptic seizures in SDHs. The objective of this study was to identify and summarize the incidence and risk factors of SDH-associated seizures and the current state of prophylactic use of AEDs.

2. Methods

A systematic review was performed following the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and was approved by the Clinical Ethics Committee of the University of Frankfurt (Nr.509/15) [32,51].

2.1. Data sources and data searches

A broad search for all studies describing epileptic seizures in patients with SDHs using the PubMed gateway of the MEDLINE database, the Cochrane Central Register of Controlled Trials (CENTRAL) and the Excerpta Medica dataBASE (EMBASE) was performed from 1961 to February 2016. Additionally, we researched the reference lists of those studies. The following keywords were used individually or in combination with “AND”: subdural haematoma; SDH (acute/chronic); seizure; epilepsy; prophylactic antiepileptic drugs; anticonvulsive medication; risk factors of seizure.

2.2. Study selection

Inclusion required human-based clinical studies that focused on epileptic seizures in patients with SDHs. Exclusion criteria included studies reporting only paediatric patients (<18 years old), language other than English, redundant data and deficient insufficient disaggregation to identify incidence or risk factors of PTSs. Case reports, presentations and conference abstracts were excluded as well. The study selection process is illustrated in Fig. 1.

2.3. Data extraction and synthesis

Two reviewers performed eligibility assessment independently in an unblinded standardized manner. Two independent review authors acquired the literature, selected the studies and extracted data from the included studies. Disagreement between reviewers was resolved by consensus [51]. In the case of no agreement, third third author was authorized to decide.

In total, 982 studies were identified. After screening the titles and abstracts, 42 studies were identified as addressing subdural haematomas and epileptic seizures. Among those studies, 18 were excluded (not in English, redundant, not disaggregated, no manuscript available) and 24 were included. Among these studies, 17 investigated seizure incidence, 11 explored risk factors for seizures and 10 studies examined prophylactic antiepileptic treatment. For all parameters, we distinguished between aSDHs and cSDHs. The incidence that we describe in this review is a crude incidence estimate and not from population-based studies. Furthermore, we tried to analyse immediate, early and late PTSs separately; however, the majority of the studies considered immediate PTSs and ePTSs as one category. Due to the lack of granularity provided in the reviewed literature we were only able to distinguish between ePTSs and lPTSs.

2.4. Statistical analysis

GraphPad Prism (6.0, GraphPad Software Inc., USA) was used for statistical analysis. Parametric data were analysed between group differences using an unpaired t-test. For categorical variables, we used Fisher’s exact or the Chi-square test. For dichotomy risk factors, we counted odds ratios (ORs) with 95% confidence intervals (CI_{95}). A p-value ≤ 0.05 was regarded as statistically significant.

3. Results

In total, 17 studies reporting incidence of seizures in patients with acute and chronic SDHs were analysed [3,5,10–12,15,17,21,25,27–30,33–37]. Two of the 17 studies (11.7%) reported PTSs in SDHs, without differentiating the type of SDH. Nine of the 17 studies (52.9%) distinguished between ePTSs and lPTSs, but none of them differentiated between immediate PTSs and ePTSs. Therefore immediate PTSs and ePTS were considered as one category. Other studies did not differentiate between these entities and referred to PTS as one entity, which we classified as unspecified PTS. Eleven of the 17 studies (64.7%) analysed additionally risk factors for PTSs in SDHs. Apart from two prospective studies [11,39], all other studies were retrospectively analysed with an evidence level of 3.

3.1. Incidence of PTS in patients with acute subdural haematoma

The results are illustrated in Table 1. In total, three studies were identified as describing the incidence of PTS in patients with aSDHs. About 40 years ago, Jennett [36] reported that 58 out of 159 patients with aSDHs (36%) developed ePTSs, which was the highest incidence among all intracranial haematomas. Recently, similar results (24%, 25%) were reported by Temkin and Rabinstein et al. [3,10]. The mean time to occurrence of ePTS was one day, indicating the highest incidence within 24 h after onset [5]. Furthermore, two of those studies analysed cumulative lPTS incidence in aSDHs within a two-year period. In both studies, the incidence of lPTS was more than 40% [3,36]. One prospective study