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# **EEG for children with complex febrile seizures (Review)**

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#### [Intervention Review]

# **EEG** for children with complex febrile seizures

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#### ABSTRACT

#### Background

Febrile seizures can be classified as simple or complex. Complex febrile seizures are associated with fever that lasts longer than 15 minutes, occur more than once within 24 hours, and are confined to one side of the child's body. It is common in some countries for doctors to recommend an electroencephalograph (EEG) for children with complex febrile seizures. A limited evidence base is available to support the use of EEG and its timing after complex febrile seizures among children.

# Objectives

To assess the use of EEG and its timing after complex febrile seizures in children younger than five years of age.

#### Search methods

For the latest update of this review, we searched the Cochrane Epilepsy Group Specialized Register (23 January 2017), the Cochrane Central Register of Controlled Trials (CENTRAL) via the Cochrane Register of Studies Online (CRSO, 23 January 2017), MEDLINE (Ovid, 23 January 2017), and ClinicalTrials.gov (23 January 2017). We applied no language restrictions.

#### Selection criteria

All randomised controlled trials (RCTs) that examined the utility of an EEG and its timing after complex febrile seizures in children.

# Data collection and analysis

The review authors selected and retrieved the articles and independently assessed which articles should be included. Any disagreements were resolved by discussion and by consultation with the Cochrane Epilepsy Group. We applied standard methodological procedures expected by Cochrane.

#### Main results

Of 41 potentially eligible studies, no RCTs met the inclusion criteria.

#### Authors' conclusions

We found no RCTs as evidence to support or refute the use of EEG and its timing after complex febrile seizures among children. An RCT can be planned in such a way that participants are randomly assigned to the EEG group and to the non-EEG group with sufficient sample size. Since the last version of this review, we have found no new studies.

#### PLAIN LANGUAGE SUMMARY

#### EEG for children with complex febrile seizures

#### Background

Febrile seizures (fits) can be classified as simple or complex. Complex febrile seizures are associated with a high temperature (fever), last longer than 15 minutes, occur more than once within 24 hours, and are confined to one side of the child's body. It is common in some countries for doctors to recommend an electroencephalograph (EEG), which records electrical activity in the brain, on children with complex febrile seizures. The EEG may help identify why the seizures occur and predict the risk of future seizures.

#### Study characteristics

We searched scientific databases for randomised controlled trials (clinical studies where people are randomly put into one of two or more treatment groups; these are regarded as a gold standard for trial design) that compared EEG with no EEG or a delayed EEG (occurring at second seizure) in children under five years of age with a first complex febrile seizure. We planned to look at the number of seizures that occurred at 1, 6, 12, and 24 months after EEG.

#### Key results and quality of the evidence

We attempted to search all possible sources but were unable to find any randomised controlled trials to address the issue up to 23 January 2017. We concluded that there is no high-quality evidence to support or refute the use of an EEG and its timing after complex febrile seizures in children. Well-designed randomised controlled trials are therefore required. We intend to update this review regularly with the hope that new randomised studies will be reported in the future.

# BACKGROUND

# **Description of the condition**

According to the US National Institutes of Health and the International League Against Epilepsy, febrile seizures can occur between the ages of one month and five years (Freeman 1980; ILAE 1993), and are associated with fever with no intracranial infection or defined cause (Freeman 1980). Febrile seizures can be classified as simple or complex. Simple febrile seizures are generalised tonic or tonic-clonic convulsions lasting less than 15 minutes that occur only once in a 24-hour period in a neurologically and developmentally normal child. If focal features are present, the seizures last longer than 15 minutes, the child has a pre-existing neurological condition, and the seizures occur multiple times (recurrent within 24 hours) or within the same febrile event, the febrile seizures are referred to as complex (Francis 2006; Gordon 2001; Kliegman

1996; Waruiru 2004). The incidence of febrile seizures varies from 2% to 5% in Western Europe and the USA (Joshi 2005; Waruiru 2004), from 5% to 10% in India, and is reported to be 8.8% in Japan and 14% in Guam (Waruiru 2004). Data from low- to middle-income countries are limited (Waruiru 2004).

A child with febrile seizures usually does not need to be hospitalised. However, when the seizure is prolonged or is accompanied by a serious infection, or when the source of the infection cannot be determined, hospitalisation for observation may be recommended. Prolonged daily use of oral antiepileptic drugs to prevent febrile seizures is usually not recommended because of their potential for adverse effects and their questionable effectiveness in preventing such seizures (Kliegman 1996; Offringa 2012).

#### **Description of the intervention**

An electroencephalograph (EEG) records brain waves detected by electrodes placed on the scalp. Reporting of paroxysmal EEG abnormalities in children with febrile seizures may vary widely (Panayiotopoulos 2005). The reasons may be related to differences in participant selection by different authors, the criteria used in different studies to define paroxysmal discharges, or the timing of the EEG.

The American Academy of Pediatrics practice parameter on febrile seizures recommends that an EEG should not be part of a routine investigation after a simple febrile seizure in neurologically normal children because of its lack of usefulness in predicting recurrence risk or future epilepsy (American Academy of Pediatrics 1996; Joshi 2005; Kuturec 1997). The quality standards subcommittees of the American Academy of Neurology, the Child Neurology Society, and the American Epilepsy Society recommend an EEG in the initial evaluation of the first afebrile seizure, as an abnormal EEG predicts recurrence (Hirtz 2000; Joshi 2005). The precise role of EEG in the evaluation of children with complex febrile seizure has not been established; however, it is common for both paediatricians and specialists to recommend EEGs on these children in some countries (Joshi 2005; Millichap 1991). An EEG taken within the first week after a febrile seizure is termed an 'early EEG', whereas an EEG taken anytime between the first week and one month after the seizure activity is termed a 'late EEG'. Few retrospective studies have attempted to assess the use of EEGs in complex febrile seizure (Maytal 2000; Yucel 2004).

# How the intervention might work

An EEG performed in the evaluation of complex febrile seizures may help identify the nature of the underlying acute or remote cerebral pathology and predict the risk of future seizures.

# Why it is important to do this review

Much uncertainty remains about the use of an EEG and its timing in children with complex febrile seizures, hence the need to carry out this review. This is an update of a previously published review in the Cochrane Database of Systematic Reviews published in 2014 and first update published in 2015, which found no evidence to support or refute the use of EEG for children with complex febrile seizures.

# **OBJECTIVES**

To assess the use of EEG and its timing after complex febrile seizures in children younger than five years of age.

# METHODS

# Criteria for considering studies for this review

#### Types of studies

We planned to include parallel-group randomised controlled trials (RCTs).

# Types of participants

Participants in the studies eligible for inclusion were children of either sex younger than five years of age with a first episode of complex febrile seizure.

We would include children in the review only:

- if the EEG was performed after the first complex febrile seizure episode; or
- if recruitment of children into the study was delayed and the EEG was performed before the child's second seizure.

We excluded studies in which children had other neurological disorders (e.g. behavioural disorders, cerebral palsy, mental retardation).

#### Types of interventions

The intervention was EEG investigation. We selected two comparisons.

- Children without administration of an EEG versus children with administration of an EEG (early or late or at any time).
- Children with administration of an early EEG versus children with administration of a late EEG.

#### Types of outcome measures

# **Primary outcomes**

- 1. Proportions of children developing seizures of any type after follow-up periods of one month, six months, 12 months, and two years in two comparison groups of EEG versus no EEG and early EEG versus late EEG. We decided to include any type of seizure in this outcome. We recorded the available outcome measures with respect to a particular time period. In addition, we planned to contact the original trial authors to enquire whether outcome measurements had been recorded for other time periods of interest. We believe that the most important clinically relevant time period was two years.
- 2. Risk of recurrence between no EEG and EEG (early EEG, late EEG, or any other time), which will act as a surrogate outcome.

- 3. Total number of seizure episodes in each group during twoyear follow-up.
  - 4. Time to development of seizures as time-to-event outcome.
- 5. Adverse events (although the EEG may not cause any adverse event per se, adverse events may be related to sedation given to children and may be transient).

#### Search methods for identification of studies

#### **Electronic searches**

We ran searches for the original review on 18 October 2012, and ran subsequent searches on 17 October 2013, 6 July 2015, and 23 January 2017. For the latest update, we searched the following databases using the search strategies shown in Appendix 1.

- Cochrane Epilepsy Group Specialized Register (23 January 2017).
- Cochrane Central Register of Controlled Trials (CENTRAL) via the Cochrane Register of Studies Online (CRSO, 23 January 2017).
  - MEDLINE (Ovid, 1946 to 23 January 2017).
- US National Institutes of Health Ongoing Trials Register Clinical Trials.gov (clinical trials.gov/) (23 January 2017).

#### Searching other resources

We searched the references of all studies retrieved in full to identify additional research papers. We contacted authors of relevant articles and experts in the field to ask about additional research papers and unpublished trials. We looked for conference proceedings for trials relevant to our review. We decided not to impose language restrictions.

# Data collection and analysis

#### Selection of studies

Two review authors (PBS (methodology expert), SJ (content expert)) conducted the searches and independently carried out an initial screening of the titles of research papers (Lefebvre 2011). The review authors independently screened the abstracts of papers deemed potentially relevant. We retrieved the full text for all articles whose abstracts were relevant. When full-text articles were not available, we contacted the study authors and asked them to provide the full text of the article. We decided to use this search methodology during screening of the cross-references of the full-text retrieved articles and articles suggested by authors and experts in the field. Two review authors (PBS, SJ) independently reviewed the full-text articles and classified each into one of the following

groups: included studies; excluded studies; or studies pending decision (if required, we contacted study authors to request additional details of the study).

We recorded the information on the eligibility assessment form included in Appendix 2.

We attempted to identify duplicate publications by assessing similar study types, same place, or same authors (maybe with different sequence). We used reference management software (Mozilla with Zotero) to identify and exclude duplicate publications. In cases of doubt, we contacted the study authors to avoid inclusion of duplicate publications in this review.

We agreed to resolve any disagreements by discussion and to reach a final decision by consensus or by consultation with the Cochrane Epilepsy Group. We used standard methodological procedures expected by Cochrane.

#### Data extraction and management

We could not extract the data in the present review, as no study met the inclusion criteria. We planned to conduct the data extraction process as follows.

Two review authors (PBS, SJ) planned to independently extract required data from the full-text articles of the included studies. (We have included the data extraction form in Appendix 3.) The data extraction form has the following five components.

- Identification of study.
- Characteristics of included studies with a brief description in tabular form of methods, participants, interventions and outcomes, and notes on specific issues (if any).
- 'Risk of bias' table, as per guidelines of the *Cochrane Handbook for Systematic Reviews of Interventions* (Altman 2011).
  - Measurements of treatment effects extracted.
- Information pertaining to any discrepancy noted in records of the clinical trial registry.

We agreed to resolve any disagreements by discussion and to reach a final decision by consensus or by consultation with the Cochrane Epilepsy Group. We agreed to follow the guidelines of the Quality of Reporting of Meta-Analyses (QUOROM) statement, and PRISMA (formerly QUOROM) (Moher 2009).

We have provided a list of excluded studies with reasons for exclusion in tabular form (see Characteristics of excluded studies table). We planned to report in tabular form the details of any ongoing studies in terms of methods, interventions and outcomes, or trial registration numbers; however, we found no ongoing studies.

# Assessment of risk of bias in included studies

We could not assess the risk of bias in the present review, as no study met the inclusion criteria.

We planned to report risk of bias as recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* for 'Risk of bias'

tables (Appendix 4) (Altman 2011). We planned to fill the description for each domain with a quote from the article or correspondence and then comment with judgement regarding particular bias (yes, no, or unclear). We would undertake a summary assessment of risk of bias for each outcome (across domains) within and across studies and to make judgements about the risk of bias as low, unclear, or high. We planned to report a 'Risk of bias' graph and a 'Risk of bias' summary figure. Two review authors (PBS, SJ) intended to independently assess the risk of bias. Any disagreements would have been resolved by discussion and through consensus or by consultation with the Cochrane Epilepsy Group.

#### Measures of treatment effect

We could not measure the treatment effect in the present review, as no study met the inclusion criteria. We planned to measure treatment effect as follows.

We planned to calculate the proportions of children developing seizures after follow-up periods of one month, six months, 12 months, and two years. We also planned to calculate risk of recurrence between no EEG and EEG (early EEG, late EEG, or any other time), total number of seizure episodes in each group during the two-year follow-up, time to development of seizures as time-to-event outcome, and adverse events (if any). We planned to use odds ratio for dichotomous outcomes and mean difference for continuous data. For data provided in other forms, we decided to convert extracted data to the above measures. We planned to extract or calculate 95% confidence intervals for all data. In the case of insufficient information, we would contact study authors to ask for additional details.

# Unit of analysis issues

We did not anticipate any unit of analysis issues.

# Dealing with missing data

We contacted study authors to ask for missing data such as method of randomisation if not stated in the paper or whether an outcome of interest that was not reported had been analysed. The reasons for missing data would have been useful in the imputation of missing data.

#### Assessment of heterogeneity

We could not assess the heterogeneity in the present review, as no study met the inclusion criteria. We planned to assess heterogeneity as follows.

We planned to assess clinical heterogeneity by comparing participant factors, interventional factors, outcome factors, and methodological heterogeneity by study methods. We also planned to assess statistical heterogeneity by measuring variability in interventional effects by visually comparing the overlap of confidence intervals on forest plots. If confidence intervals for the results of individual studies have poor overlap, this might indicate the presence of statistical heterogeneity. We also planned to measure statistical heterogeneity using the  $I^2$  statistic, interpreting it as follows (Deeks 2011).

- 0% to 40%: might not be important.
- 30% to 60%: may represent moderate heterogeneity.
- 50% to 90%: may represent substantial heterogeneity.
- 75% to 100%: considerable heterogeneity.

#### Assessment of reporting biases

We planned during this stage to determine primary and secondary outcomes of the included studies from clinical trial registries (if possible) to assess any discrepancies in reporting, which we would have reported had we found any. We planned to assess funnel plot asymmetry if we identified more than 10 studies. Reasons for asymmetry include publication bias, outcome reporting bias, and heterogeneity.

# **Data synthesis**

We did not attempt data synthesis in the present review, as no study met the inclusion criteria. We planned to perform data synthesis as follows.

We planned to analyse each trial and record data on the data extraction form. The review authors would independently enter the results of each study using Review Manager 5 (RevMan 2014). We planned to carry out a meta-analysis according to Cochrane guidelines (Higgins 2011); the most common method available using Review Manager 5 is the Mantel-Haenszel method. If RCTs were clustered, we would have used the inverse method. In case of heterogeneity, we planned to carry out a thorough assessment (see Assessment of heterogeneity).

# Subgroup analysis and investigation of heterogeneity

We did not attempt subgroup analysis and investigation of heterogeneity in the present review, as no study met the inclusion criteria. We agreed upon the following process.

We planned to carry out subgroup analyses based on sex, duration of disease, duration of hospitalisation, and length of follow-up. In cases of significant heterogeneity, we might have followed the steps outlined below.

- Recheck extraction and recording of data.
- Change from random-effects to fixed-effect model.
- Perform sensitivity analysis (see Sensitivity analysis).
- Explore heterogeneity by subgroup analysis.
- Present systematic review without meta-analysis.

#### Sensitivity analysis

Sensitivity analysis is a repeat primary analysis in which alternative decisions and ranges of values are substituted for decision making related to assessment of the robustness of conclusions.

We did not attempt sensitivity analysis in the present review, as no study met the inclusion criteria.

We planned to carry out the following steps in a sensitivity analysis.

- Some studies have larger effects than others because random error means that multiple replications of the same study will produce different effect estimates due to sampling variation, even if replications would yield the right answer on average. The results of smaller studies are subject to greater sampling variation and hence are less precise. Imprecision is reflected in the confidence interval around the intervention effect estimate from each study and in the weight given to the results of each study in a meta-analysis. More precise results are given more weight.
- In cases of missing values, use of the following imputation methods, of which many methods for imputation techniques have been proposed, is suggested. In cases of dichotomous data, best case-worst case analysis is performed to find out how the risk factor or the result value may vary in different situations. For continuous data, the last value takes the role of the missing value. These imputations are important because RCTs have to be analysed as intention-to-treat analyses.
  - Use random-effects rather than fixed-effect model.

While the above sensitivity analyses were prespecified, it was not possible to specify all sensitivity analyses, as issues may develop only in the course of completing the review. Where sensitivity analysis influenced the robustness of our conclusion, we planned to attempt to resolve the uncertainty by contacting trial authors and consulting the Cochrane Epilepsy Group. As it might not have been possible to report all sensitivity analyses in detail, we planned to provide a summary table. Sensitivity analysis would have helped us to explore the influence of various factors.

#### 'Summary of findings' tables

We planned to provide 'Summary of findings' tables, prepared using GRADEpro software (GRADEpro 2014). We planned to report a rating of overall quality of evidence for each outcome, as well as conclusions, and implications for practice and research (Appendix 5). Two review authors (PBS, SJ) would independently prepare the 'Summary of findings' tables. Any disagreements would have been resolved by discussion and through consensus or by consultation with the Cochrane Epilepsy Group.

# **Description of studies**

#### Results of the search

With the help of the Information Specialist of the Cochrane Epilepsy Group, our searches identified 41 potentially eligible studies. A summary of the search results is shown in Appendix 6. Literature searches identified four studies in this update. After assessing the titles and abstracts, we excluded all 41 studies; therefore, no studies were eligible for inclusion in the review (see Characteristics of excluded studies table).

#### Included studies

None of the studies met the inclusion criteria, thus no studies were included in the present review.

#### **Excluded studies**

We excluded all 41 studies because the study design and the intervention were not of interest to this review (see Excluded studies; Characteristics of excluded studies table).

#### Risk of bias in included studies

We included no studies in this review, hence risk of bias is not applicable.

### **Effects of interventions**

In the absence of any suitable studies for this review, analyses were not possible. Although we could not attempt data collection and analysis as specified in the protocol, we decided to describe the process of different aspects of data collection and analysis, as the review will be updated regularly and the full protocol may not be easily accessible to all users of this evidence.

We could not provide 'Summary of findings' table in the present review, as no study met the inclusion criteria.

# DISCUSSION

#### Summary of main results

We did not find any RCTs of EEG for children with complex febrile seizures. Hence, there is currently no randomised highquality evidence to report for an EEG and its timing after complex febrile seizures in children younger than five years of age.

# RESULTS

# Overall completeness and applicability of evidence

We performed a comprehensive search of the literature as described in Appendix 6, and assessed 41 studies that may have been relevant to the review. We excluded all 41 studies, so we identified no RCTs.

# Quality of the evidence

We found no studies.

# Potential biases in the review process

None.

# Agreements and disagreements with other studies or reviews

We found no other similar review. However, a few published nonrandomised studies to date have looked specifically at complex febrile seizures and the role of EEG in their evaluation (Joshi 2005; Maytal 2000; Yucel 2004). In one retrospective review of 33 neurologically normal children with EEGs within one week of complex febrile seizures, Maytal and colleagues found no children with abnormalities, but Yucel and colleagues reported abnormalities in 71 of 159 children with complex febrile seizures analysed retrospectively over seven years. In Yucel 2004, 16 children had abnormal EEG records in the first week. Of the 71 children with abnormal EEG records, 51 were diagnosed with epilepsy on followup. One other study by Joshi and colleagues showed that children with complex febrile seizures are approximately 3.5 times more likely to display an abnormal EEG within seven days post ictus in comparison with children with complex febrile seizures in whom the EEG was performed beyond the seven-day period post ictus. Hence, conflicting reports describe the utility of EEG and its timing after complex febrile seizures among children.

# AUTHORS' CONCLUSIONS

#### Implications for practice

Although it is common for both paediatricians and specialists in some countries to recommend electroencephalographs (EEG) for children with complex febrile seizures (Joshi 2005; Millichap

1991), evidence to support or refute the use of EEG and its timing after complex febrile seizures among children is lacking. We have found no new studies since the last version of this review.

### Implications for research

This review highlighted the absence of randomised controlled trials (RCTs) investigating the utility of EEG and its timing after complex febrile seizures in children. We found no RCT evidence to support or refute the utility of EEG and its timing after complex febrile seizures in children. A randomised controlled trial can be planned in such a way that participants are randomly assigned to an EEG group and a non-EEG group with sufficient sample size. Hence, well-designed RCTs are required to confirm or refute the utility of EEG. These clinical trials should follow good clinical practice guidelines with an emphasis on methodological issues such as randomisation, blinding of outcome assessment, intention-to-treat analysis, and scientific means to reduce bias.

Updating the review: in accordance with Cochrane policy, we plan to update this review every two years (or sooner, should we find any important study that fulfils the inclusion criteria).

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  - Family members for continuous inspiration and support.

#### REFERENCES

#### References to studies excluded from this review

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#### Berg 2008 {published data only}

Berg AT. Risk of recurrence after a first unprovoked seizure. *Epilepsia* 2008;**49(Suppl 1)**:13–8.

# Bernasconi 1998 {published data only}

Bernasconi A, Andermann F, Cendes F, Dubeau F, Andermann E, Olivier A. Nocturnal temporal lobe epilepsy. *Neurology* 1998;**50**(6):1772–7.

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Burneo JG, Knowlton RC, Martin R, Faught RE, Kuzniecky RI. Race/ethnicity: a predictor of temporal lobe epilepsy surgery outcome?. *Epilepsy & Behavior* 2005;7(3):486–90.

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Conry J, Ng YT, Peng G, Lee D, Isojarvi J. Efficacy and safety of clobazam for lgs patients who completed all 15 weeks of the phase iii contain trial. *Epilepsy Currents* 2014; 14:390.

#### Drayer 1982 {published data only}

Drayer B, Suslavich F, Luther J, Rommel A, Allen S, Dubois P, et al. Clinical trial of iopamidol for lumbosacral myelography. *Electroencephalography* 1982;3(1):59–64.

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Fallah R, Gofrani M. Comparison of intravenous lidocaine and midazolam infusion for refractory convulsive status epilepticus in children. *Journal of Pediatric Neurology* 2007; **5**(4):287–90.

# Ghazavi 2016 {published data only}

Ghazavi A, Abbasi E, Nikibakhsh A, Sadeghi E, Sadeghimanesh J. Comparison of prophylactic effect of clobazam and diazepam in children with simple febrile convulsion (SFC). *International Journal of Tropical Medicine* 2016;**11**(2):21–3.

# Gradisnik 2015 {published data only}

Gradisnik P, Zagradisnik B, Palfy M, Kokalj-Vokac N, Marcun-Varda N. Predictive value of paroxysmal EEG abnormalities for future epilepsy in focal febrile seizures. *Brain and Development* 2015;37(9):868–73. [DOI: 10.1016/j.braindev.2015.02.005

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Grahn A, Hagberg L, Nilsson S, Blennow K, Zetterberg H, Studahl M. Cerebrospinal fluid biomarkers in patients with varicella-zoster virus CNS infections. *Journal of Neurology* 2013;**260**(7):1813–21.

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Grigsby J, Kramer RE, Schneiders JL, Gates JR, Brewster SW. Predicting outcome of anterior temporal lobectomy

using simulated neural networks. *Epilepsia* 1998;**39**(1): 61–6.

#### Gumus 2015 {published data only}

Gumus H, Bayram AK, Poyrazoglu HG, Canpolat DG, Per H, Canpolat M, et al. Comparison of effects of different dexmedetomidine and chloral hydrate doses used in sedation on electroencephalography in pediatric patients. *Journal of Child Neurology* 2015;**30**(8):983–8. [DOI: 10.1177/0883073814549582

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Heijbel J, Blom S, Bergfors PG. Simple febrile convulsions. A prospective incidence study and an evaluation of investigations initially needed. *Neuropadiatrie* 1980;**11**(1): 45–56.

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Huang Y, Yang L, Wang S, Wang G. Alterative application of five anticonvulsants according to the half life for the treatment of status epilepticus in children with severe viral encephalitis. *Neural Regeneration Research* 2007;**2**(9):561–4.

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Knudsen FU. Effective short term diazepam prophylaxis in febrile convulsions. *Journal of Pediatrics* 1985;**106**(3): 487–90.

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Mahmoudian T, Zadeh MM. Comparison of intranasal midazolam with intravenous diazepam for treating acute seizures in children. *Epilepsy & Behavior* 2004;**5**(2):253–5.

# Mamelle 1982 {published data only}

Mamelle JC, Mamelle N, Plasse JC, Revol M, Gilly R. The efficacy of sodium valproate compared with that of phenobarbitone and placebo in the prophylaxis of febrile convulsions. *Pediatrics* 1982;**37(6)**:433–45.

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# Natriashvili 2005 {published data only}

Natriashvili G, Natriashvili S, Kapanadze N. Mexidol in treatment of children with generalized epilepsy and febrile seizures. *Georgian Medical News* 2005;**122**:40–4.

#### NCT01370044 {published data only}

NCT01370044. Carbon dioxide (Carbogen) for the treatment of febrile seizures (CARDIF). clinicaltrials.gov/show/NCT01370044 (first received 17 October 2013).

# NCT01694524 {published data only}

NCT01694524. Nervous system infections among patients with febrile seizure. clinicaltrials.gov/show/NCT01694524 (first received17 October 2013).

#### NCT01738841 {published data only}

NCT01738841. Safety study of measles-mumpsrubella-varicella (MMRV) vaccine, Priorix-Tetra<sup>TM</sup> in children living in the Philippines. clinicaltrials.gov/show/ NCT01738841 (first received17 October 2013).

#### NCT01884766 {published data only}

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<sup>\*</sup> Indicates the major publication for the study

# CHARACTERISTICS OF STUDIES

# Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion		
Aksu 2011	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Berg 2008	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Bernasconi 1998	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Burneo 2005	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Conry 2014	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Drayer 1982	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Fallah 2007	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Ghazavi 2016	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Gradisnik 2015	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Grahn 2013	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Grigsby 1998	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Gumus 2015	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Heijbel 1980	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Huang 2007	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Kaminska 1999	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Knudsen 1985	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Mackintosh 1970	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Mahmoudian 2004	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Mamelle 1982	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Mamelle 1984	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		
Natriashvili 2005	Study did not make a comparison between EEG and no EEG or early EEG and late EEG		

# (Continued)

NCT01370044	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
NCT01694524	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
NCT01738841	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
NCT01884766	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
NCT01906619	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
NCT01931813	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
NCT01946594	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
NCT02374450	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
Novotny 2010	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
O'Brien 2008	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
Pavlidou 2006	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
Pina-Garza 2005	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
Reijs 2007	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
Rosati 2003	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
Rose 2005	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
Rosenfeld 2014	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
Rosman 1987	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
Strengell 2009	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
Tsuboi 1988	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			
Vecchi 2016	Study did not make a comparison between EEG and no EEG or early EEG and late EEG			

EEG: electroencephalograph.

# DATA AND ANALYSES

This review has no analyses.

# WHAT'S NEW

Date	Event	Description
23 January 2017	New citation required but conclusions have not changed	Conclusions are unchanged.
23 January 2017	New search has been performed	Searches were updated on 23 January 2017; no new studies were identified

# HISTORY

Date	Event	Description
3 February 2016	Amended	Copyedits made to the Plain language summary.
6 July 2015	New search has been performed	Searches updated 6 July 2015.
6 July 2015	New citation required but conclusions have not changed	No new relevant studies identified; conclusions are unchanged

# **CONTRIBUTIONS OF AUTHORS**

Develop search strategy: PBS, SJ with Information Specialist.

Search for trials: PBS, SJ with Information Specialist.

Obtain copies of trials: PBS, SJ, and SE with Information Specialist.

Select trials to include: PBS, SJ, and SE.
Draft the final review: PBS, SJ, and SE.

# **DECLARATIONS OF INTEREST**

Pankaj B Shah: None known. Saji James: None known. S Elayaraja: None known.

# SOURCES OF SUPPORT

#### Internal sources

• No sources of support supplied

#### **External sources**

• National Institute for Health Research (NIHR), UK.

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# DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We did not attempt the data collection analysis and 'Summary of findings' table, as no study met the inclusion criteria. We decided to describe the process of different aspects of data collection and analysis in the present review, as it will be updated regularly and the full protocol may not be easily accessible to all users of this evidence.

# INDEX TERMS

# **Medical Subject Headings (MeSH)**

\*Electroencephalography; \*Seizures, Febrile; Time Factors

# MeSH check words

Child, Preschool; Humans