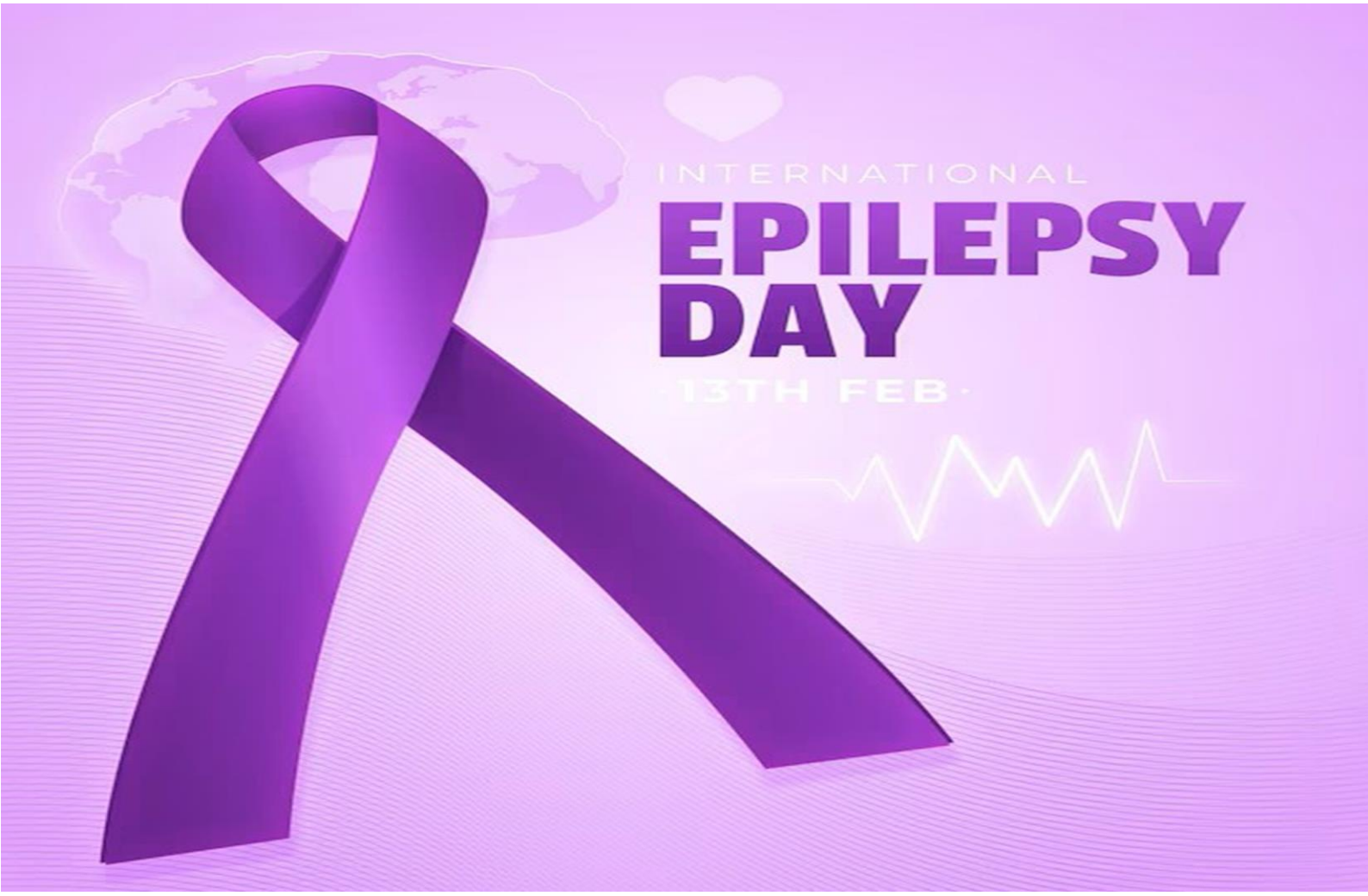
Cochrane Cameroon



INTERNATIONAL EPILEPSY DAY 2025

This document provides up-to-date evidence on the causes and treatment of Epilepsy to health professionals.

Enjoy your read!

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Editorial

Epilepsy is a chronic non-communicable disease of the brain that affects 50 million people around the world. It is manifested through repeated seizures, with brief episodes of involuntary shaking affecting either a part of the body (partial seizures), or the entire body (generalised seizures). These seizures may sometimes lead to a syncope and lack of control over bladder and bowel movements. These seizures are caused by excessive electrical discharges within a cluster of neuronal cells.
Their frequency can also fluctuate, from occurring less than once a year to several times a day (WHO, 2024).

Key facts

- Epilepsy is a neurological disorder that can affect people of any age;
- Around 50 million people worldwide are affected, making it one of the most common neurological disorders;
- Around 80% of people with epilepsy live in low- or middle-income countries.
- It is estimated that 70% of people with epilepsy could be seizure-free if their condition were properly identified and treated;
- The premature mortality rate among people with epilepsy is almost three times higher than in the general population.

Causes of epilepsy

- Epilepsy cannot be transmitted. Although there are many pathological processes that can cause epilepsy, the origin of the disease remains undetermined in around 50% of cases worldwide. The causes of epilepsy are classified as structural, genetic, infectious, metabolic, immune or of unknown origin. To give a few examples:
- Brain damage caused by trauma before or during birth (oxygen deficiency, trauma during childbirth or low birth weight);
- Cerebral malformations associated with congenital anomalies or genetic disorders; A serious brain injury, such as a stroke, which reduces the amount of oxygen in the brain; An infection affecting the brain, such as meningitis, encephalitis or neurocysticercosis; Certain genetic disorders and brain neoplasia.

Treatement

- In low- and middle-income countries, around 75% of people with epilepsy do not have access to the treatment they need;
- Epilepsy can be treated and even cured in around 70% of cases, thanks to a wide range of effective anti-epileptic drugs (AEDs). Despite the existence of numerous AEDs and the relatively low cost of some of them, almost three quarters of people with epilepsy in low- and middle-income countries do not receive treatment;
- Non-adherence to treatment, which is widespread for chronic illnesses, is reported in the literature to be high for anti-epileptic drugs, and studies have shown a higher prevalence of seizures in those who have not adhered to their AEDs. In addition, poor adherence to AEDs has been reported to increase morbidity and mortality, and thus impair quality of life and productivity (Doumbe, 2020).

Audience for this synthesis of systematic reviews:

Decision-makers and professionals and all other stakeholders involved in the fight against neurological disorders.

Why was this synthesis produced?

To provide up-to-date evidence on the causes and treatemnts of Epilepsy.

What is a systematic review?

A summary of studies that answers a clearly formulated question and uses systematic and explicit methods to identify, select and critically appraise relevant studies. Data from different studies are extracted and can be analyzed together using meta-analysis techniques.

The situation in Cameroon

In Cameroon, studies have shown that people are well aware of epilepsy, but the disease is still surrounded by many taboos and rejection, leading to the exclusion of these patients. People living with epilepsy suffer from stigmatisation, overprotection and exclusion. In the absence of a medical response, parents of epileptic children often turn to traditional healers, exorcist priests and pastors of revivalist churches.

In Cameroon, precise statistics on the disease are not yet available, yet the disease is rampant in anonymity, especially in rural areas. Epilepsy is a common, chronic neurological pathology that can develop at any stage of life, from infancy to adulthood. It encompasses a range of epileptic diseases of varying severity, depending on a number of parameters: the age of onset of the first seizures, the cause of the seizures, their nature, their frequency, and the response to anti-epileptic treatments (MINSANTE, 2023).

Epilepsy in the elderly is defined as the onset of seizures after the age of 60. The prevalence of epilepsy increases with age, as does that of associated neurological pathologies (stroke, dementia). As life expectancy increases, we can expect to see a rise in the number of people affected by epilepsy.

Treatment

In Cameroon, adherence to anti-epileptic drugs is often neglected, affecting up to 82.35% of patients. Predictors of non-adherence include forgetting one or more doses of antiretroviral treatment, lack of financial resources, drug shortages and lack of information about the disease. It is essential to put in place communication and patient education strategies to reinforce compliance and minimise the effects of non-compliance, such as recurrent attacks and reduced quality of life. It is also necessary to put pressure on the authorities, in particular the Ministry of Public Health, to make AEDs more geographically and financially accessible. This could be achieved through the use of high-quality generic medicines (Doumbe, 2020).

Some national non-governmental initiatives taken to fight epilepsy

- The NGO Community Development and Epilepsy Foundation (CODEF) works to provide care for epilepsy and HIV/AIDS in rural communities in Cameroon. It raises public awareness, facilitates access to medical care, offers psychosocial support and defends the rights of people suffering from these diseases.
- With the support of the Ministry of Public Health, the Cameroonian League against Epilepsy is taking action in Cameroon to combat this disease. These efforts include information campaigns, consultations for patients, and training sessions for general practitioners, nurses, and school and college teachers on the medical and social management of epilepsy (MINSANTE, 2024).

1. Transcranial magnetic stimulation for treatment of epilepsy

Background

Epilepsy is a common neurological disorder that appears in various forms. Many individuals with epilepsy have satisfactory seizure control with the use of antiepileptic medications. Yet, nearly a third of people with epilepsy suffer from frequent and uncontrolled seizures despite the use of medication, or are unable to tolerate the side effects of those medications. Surgery is an option for some people with uncontrolled seizures, but it is invasive and not suitable for all individuals. As a result, there remains a substantial unmet need for safe, effective therapies for these harder-to-treat epilepsies.

Transcranial magnetic stimulation (TMS) is one of several newer treatments that can potentially offer people with epilepsy a safe and non-invasive alternative to surgery. Long used as a research tool to study brain function, TMS has also been studied as a possible treatment for a number of nervous system conditions, including epilepsy. This non-surgical and painless treatment uses induced magnetic currents to regulate brain function in order to reduce the tendency to have seizures.

Objective

We aimed in this review to evaluate the evidence for the use of repetitive transcranial magnetic stimulation (rTMS) in individuals with epilepsy compared with other available treatments in reducing seizure frequency, improving quality of life, reducing epileptiform discharges (abnormalities on brain electrographic testing that suggest underlying brain disturbance or seizure tendency), antiepileptic medication use, and side effects.

Methods

The latest search for trials was 2 June 2020. We assessed the evidence from eight randomised controlled trials (studies in which participants are assigned to one of two or more treatment groups using a random method) involving a total of 241 participants comparing rTMS to control treatments (sham treatment, antiepileptic medication, or low-frequency rTMS).

Results

Some of the included trials showed that rTMS reduces the number of seizures individuals had compared to before the therapy, but other trials did not show any significant differences in seizure frequency. Four trials showed a reduction in epileptiform discharges

following rTMS treatment. One study measured changes in quality of life in seven participants; although not statistically analysed they found that a greater proportion of study participants reported increased quality of life scores with active treatments compared to the sham treatment. One trial reported an increase in antiepileptic medication in a single individual but they had received the control treatment. Side effects were uncommon; the most frequently reported side effect was headache (and the majority of individuals completed the treatment with rTMS). However, one study showed an increase in seizure frequency in two individuals: one during the rTMS treatment (who discontinued the treatment early), and one weeks after the treatment.

Certainty of the evidence

Overall, we judged the certainty of the evidence for the main outcome of reduction in seizure frequency to be low due to unclear information in the published papers about study design and the unclear presentation of results. One included study commented on quality of life, but involved only seven participants.

The evidence is current to June 2020.

Authors' conclusions

Implications for practice

There is some evidence to suggest that repetitive transcranial magnetic stimulation (rTMS) is safe and in some cases effective at reducing epileptiform discharges on electroencephalography (EEG). A narrative review of the currently available studies included two studies that showed a significant effect on seizure frequency, and six studies that did not show a significant effect. Given the variability in technique and outcome reporting, which prevented meta-analysis, definitive evidence for the efficacy of rTMS for seizure reduction in focal drug-resistant epilepsies is still lacking.

Citation: Walton D, Spencer DC, Nevitt SJ, Michael BD. Transcranial magnetic stimulation for the treatment of epilepsy. Cochrane Database of Systematic Reviews 2021, Issue 4. Art. No.: CD011025. DOI: 10.1002/14651858.CD011025.pub3.

2. Antiepileptic drug monotherapy (single drug treatment) for epilepsy

Background

Epilepsy is a common neurological disorder in which abnormal electrical discharges from the brain cause recurrent seizures. We studied two types of epileptic seizures in this review: focal seizures that start in one area of the brain, and generalised onset tonic-clonic seizures that start in both cerebral hemispheres simultaneously.

For around 70% of people with epilepsy, seizures can be controlled and, for the majority, seizures are controlled with a single antiepileptic drug. Currently in the UK, National Institute for Health and Care Excellence (NICE) guidelines for adults and children recommend carbamazepine or lamotrigine as the first treatment options to try for individuals with newly diagnosed focal seizures and sodium valproate for individuals with newly diagnosed generalised tonic-clonic seizures; however, a range of other antiepileptic drug treatments are available.

The choice of the first antiepileptic drug for an individual with newly diagnosed seizures is of great importance and should be made taking into account high-quality evidence of how effective the drugs are at controlling seizures and whether they are associated with side effects. It is also important that drugs appropriate for different seizure types are compared to each other.

Review methods

The antiepileptic drugs of interest to this review were carbamazepine, phenytoin, sodium valproate, phenobarbitone, oxcarbazepine, lamotrigine, gabapentin, topiramate, levetiracetam, zonisamide, eslicarbazepine acetate, and lacosamide. In this review, we evaluated the evidence from 89 randomised controlled clinical trials comparing two or more of the drugs of interest based on how effective the drugs were at controlling seizures (i.e. whether people had recurrence of seizures or had long periods of freedom from seizures (remission)) and how tolerable any related side effects of the drugs were. We were able to combine data for 14,789 people from 39 of the 89 trials; for the remaining 7251 people from 50 trials, data were not available to use in this review. No data were available from people receiving eslicarbazepine acetate.

We performed two types of analysis in this review; firstly, we combined data available where pairs of drugs had been compared directly in clinical trials and, secondly, we performed an analysis to combine all information from the clinical trials across the 'network' of 11 drugs. This analysis allowed us to compare drugs in the network that had not previously been compared to each other in clinical trials.

Key results

Our 'network' analysis showed that, for people with focal seizures and for people with generalised seizures, the oldest drugs (phenobarbitone and phenytoin) were better options in terms of seizure control than the other drugs but that these older drugs were the worst in

terms of long-term retention (stopping the treatment) compared to the newer drugs such as lamotrigine and levetiracetam. Sodium valproate was the best option of all the drugs for achieving control and remission of generalised tonic-clonic seizures.

The most commonly reported side effects across all drugs were drowsiness or fatigue, headache or migraine, gastrointestinal disturbances (stomach upsets), dizziness or faintness, and rash or skin disorders.

Quality of the evidence

This review provides high-quality evidence for individuals with focal seizures and moderate- to high-quality evidence for individuals with generalised tonic-clonic seizures, as less information was available for some of the drugs of interest for people with this seizure type.

Conclusions

The results of this review support the NICE guidelines that carbamazepine and lamotrigine are suitable first treatment options for individuals with focal onset seizures, and also show that levetiracetam would be a suitable first treatment. Results of this review also support the use of sodium valproate as the first treatment for individuals with generalised tonic-clonic seizures and show that lamotrigine and levetiracetam would be suitable alternative first treatments, particularly for those who are pregnant or considering becoming pregnant, for whom sodium valproate may not be an appropriate treatment option.

How up-to-date is this review?

The evidence is current to April 2021.

Authors' conclusions

Implications for practice

Current guidelines from the National Institute for Health and Care Excellence (NICE) in the UK for adults and children recommend carbamazepine or lamotrigine as first-line treatment for focal onset seizures, and sodium valproate for generalised onset seizures (NICE 2012); however, given the range of treatment options available to individuals with new onset seizures, including many recently licensed 'second generation' and 'third generation' antiepileptic drugs (AEDs), the choice of first-line treatment for an individual must be made based on the highest-quality evidence of the relative effectiveness and tolerability of AEDs compared to one another.

Results of this review demonstrate that generally the earliest licensed AEDs, such as phenytoin and phenobarbitone, provide increased seizure control, in terms of delaying recurrence of first seizure and earlier remission, compared to newer AEDs. However, this comes at the expense of earlier treatment failure, and it is newer AEDs such as lamotrigine and levetiracetam that perform the best in terms of treatment retention. Considering the optimum balance of efficacy (seizure control) and tolerability (treatment retention), for individuals with focal seizures, carbamazepine, lamotrigine and levetiracetam seem to be the best treatment options, whereas for individuals with generalised tonic-clonic seizures (with or without other seizure types), sodium valproate, lamotrigine and levetiracetam seem to be the best treatment options. Zonisamide and lacosamide, the most recently licensed AEDs for monotherapy treatment, may be an effective treatment option for individuals with focal onset seizures; however, further evidence from randomised controlled trials is needed. Only a small number of participants with generalised seizures have been randomised to lacosamide in clinical trials so effectiveness evidence is very limited, and no published clinical trial has evaluated zonisamide for individuals with generalised seizures.

Overall, the high-certainty evidence provided by this review is in line with NICE guidelines that carbamazepine and lamotrigine are suitable first-line treatments for individuals with focal onset seizures and also demonstrates that levetiracetam may be a suitable alternative. High-certainty evidence from this review is also in line with the use of sodium valproate as the first-line treatment for individuals with generalised tonic-clonic seizures (with or without other seizure types) and also demonstrates that lamotrigine and levetiracetam would be suitable alternative first-line treatments, particularly for those of childbearing potential, for whom sodium valproate may not be an appropriate treatment option. Evidence for the relative effectiveness of other AEDs for individuals with generalised seizures is limited and of moderate certainty; further evidence from randomised controlled trials recruiting individuals with generalised tonic-clonic seizures (with or without other seizure types) is needed.

Citation: Nevitt SJ, Sudell M, Cividini S, Marson AG, Tudur Smith C. Antiepileptic drug monotherapy for epilepsy: a network meta-analysis of individual participant data. Cochrane Database of Systematic Reviews 2022, Issue 4. Art. No.: CD011412. DOI: 10.1002/14651858.CD011412.pub4.

3. Rapid versus slow withdrawal of antiepileptic medicines

Background

Epilepsy is a disorder where recurrent seizures (fits) are caused by abnormal electrical discharges of the brain. Antiepileptic medicines are used to prevent these seizures. Regular intake of antiepileptic medicines may have long-term side effects. When in remission (free of seizures for some time), it is logical to attempt to stop the medicines. Two important issues are how and when to stop them.

Aim of the review

This review analyzed studies for evidence regarding rapidity of withdrawal of antiepileptic medicines. We included randomized controlled trials (clinical studies where people are randomly put into one of two or more treatment groups) evaluating the rapid or slow withdrawal (tapering down) of these medicines after varying periods of seizure control in people with epilepsy.

Results

We included only two small studies conducted in 206 children with epilepsy. The included studies found no difference in the proportion of participants remaining seizure-free between the rapid- and the slow-tapering groups at different time points. There were no data for other measures such as status epilepticus (a long seizure), death, illness relating to seizures, and quality of life. We found no completed trials investigating antiepileptic medicine withdrawal in adults.

Currently, one Italian trial is ongoing that is investigating if a slow or a rapid withdrawal schedule of antiepileptic medicine influences return of seizures (relapse) in adults with epilepsy who have been seizure free for at least two years (no preliminary results available).

Reliability of the evidence

Evidence from the two included studies was of very low reliability. Both studies were conducted in a small number of participants and there were not enough data to detect a difference between the groups. Furthermore, they included only children, hence the results cannot be generalized to adults. Therefore, no reliable evidence is currently available on the optimal rate of tapering of antiepileptic medicines.

The evidence is current to November 2021.

Authors' conclusions

Implications for practice

The conclusions remain the same as the previous update (Ayuga Loro 2020). In view of methodological deficiencies and small sample size of the two included studies, we are unable to derive any firm conclusions regarding the optimal rate of tapering of antiepileptic drugs (AEDs). Further trials are needed to assess the optimal rate of tapering of AEDs in adults and children whose seizures are well controlled with medication.

Citation: Ayuga Loro F, Gisbert Tijeras E, Brigo F. Rapid versus slow withdrawal of antiepileptic drugs. Cochrane Database of Systematic Reviews 2022, Issue 1. Art. No.: CD005003. DOI: 10.1002/14651858.CD005003.pub4

4. Antidepressants for people with epilepsy and depression

Background

Depressive disorders occur in approximately one-third of people with epilepsy, often requiring antidepressant treatment. However, depression often goes untreated in people with epilepsy, partly due to fear that antidepressants might cause seizures. There are different classes of antidepressants, however they all aim to increase key nerve chemicals in the brain, thereby alleviating depressive symptoms.

Characteristics of studies

We found ten studies that included 626 patients with epilepsy and depression treated with an antidepressant. Four were randomised controlled trials, and six were non-randomised prospective cohort studies. The studies observed the effect of different antidepressants, mainly a class of antidepressant called a selective serotonin reuptake inhibitor (SSRI). One randomised controlled trial and one prospective study also observed the effect of cognitive behavioural therapy on depression.

Results

Taking all the evidence into account, the review found that there is very limited evidence that antidepressants decrease depressive symptoms more than other treatments, placebo, or no treatment in epilepsy. There was limited information on the effect of antidepressants on seizure control, however in the studies reporting this outcome there did not appear to be any significant worsening of seizures. The evidence is current to February 2021.

Quality of the studies

We assessed the studies with regard to bias and quality. Overall, the quality of the evidence was rated as moderate to low for the clinical trials and low to very low for the

non-randomised prospective cohort studies. Large, high quality trials of antidepressants are needed to examine how different classes of antidepressant compare, and what impact they are likely to have on seizure control.

Authors' conclusions

Implications for practice

Existing evidence on the effectiveness of antidepressants in treating depressive symptoms associated with epilepsy is still very limited. There is low to moderate certainty evidence from two RCTs that venlafaxine, sertraline, and CBT may reduce depressive symptoms. Sertraline and CBT may improve quality of life, but moderate certainty evidence did not find one superior to the other. We have no high certainty evidence to inform the choice of antidepressant drug or class of drug for treating depression in people with epilepsy. None of the treatments appeared to increase seizure activity, but there are no available comparative data on antidepressant classes and safety in relation to seizures.

Citation: Maguire MJ, Marson AG, Nevitt SJ. Antidepressants for people with epilepsy and depression. Cochrane Database of Systematic Reviews 2021, Issue 4. Art. No.: CD010682. DOI: 10.1002/14651858.CD010682.pub3.

5. Immunomodulatory interventions (treatments that target the immune system) for focal epilepsy

Key messages

Immunomodulatory interventions are treatments that target the immune system.

Focal epilepsy is characterised by seizures arising from a specific area of the brain.

Immunomodulatory interventions were significantly more effective than placebo in reducing seizure frequency in children and adults with focal epilepsy.

What is epilepsy?

Epilepsy is a common neurological condition affecting approximately 50 million people worldwide. Focal epilepsy is characterised by seizures arising from a specific area of the brain. Approximately one-third of patients with epilepsy continue to have seizures despite treatment with antiepileptic drugs. Therefore, the development of effective new therapies for the treatment of epilepsy is of considerable importance. Recently, it has been suggested that the immune system and how it responds to injury may play an important role in this process. As such, immunomodulatory interventions - treatments that target the immune system - may represent a therapeutic approach for focal epilepsy.

What did we want to find out?

We wanted to find out if treatments that target the immune system are better than placebo, in children and adults with focal epilepsy. We also wanted to find out if these treatments are safe.

What did we do?

We searched for studies that looked at treatments that target the immune system in children and adults with focal epilepsy. We compared and summarised the results of the studies and rated our confidence in the evidence, based on factors such as study methods and sizes.

What did we find?

Treatments that target the immune system may be effective in reducing seizure frequency in adults with focal epilepsy. These treatments are more often associated with an increase in adverse effects such as dizziness, headache, fatigue, and gastrointestinal disorders, but it is not possible to draw any conclusions about the safety of these agents in children and adults with focal epilepsy.

What are the limitations of the evidence?

We are moderately confident in the evidence due to missing outcome data and imprecise results from the studies. Further high-quality research is needed to fully evaluate the efficacy and tolerability of immunomodulatory interventions.

How up to date is this evidence?

The evidence is up-to-date to November 2021.

Authors' conclusions

Implications for practice

The results of this review prove that the addition of immunomodulatory treatment to people with focal epilepsy could substantially improve the course of the disease in some people. It is not possible to draw any conclusions about the safety of these agents in children and adults with epilepsy.

Citation: Panebianco M, Walker L, Marson AG. Immunomodulatory interventions for focal epilepsy. Cochrane Database of Systematic Reviews 2023, Issue 10. Art. No.: CD009945. DOI: 10.1002/14651858.CD009945.pub3.

Conclusion

On 13 February 2025, International Epilepsy Day is a crucial moment to educate the public about the difficulties faced by people with epilepsy and to dismantle the prejudice and stigma associated with this neurological condition. This Day highlights the daily lives of people with epilepsy, promoting solidarity, education and access to appropriate treatment.

It not only raises awareness, but also encourages research to optimise epilepsy treatment, while emphasising the need for social and medical support to improve patients' well-being. This Day is therefore a reminder that epilepsy can affect anyone, but that with awareness and understanding, progress can be made in helping people with the condition.

Others sources:

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