Cochrane Library

Cochrane Database of Systematic Reviews

Stiripentol add-on therapy for focal refractory epilepsy (Review)

Brigo F, Igwe SC, Bragazzi NL

Brigo F, Igwe SC, Bragazzi NL.
Stiripentol add-on therapy for focal refractory epilepsy.
Cochrane Database of Systematic Reviews 2018, Issue 5. Art. No.: CD009887.
DOI: 10.1002/14651858.CD009887.pub4.

www.cochranelibrary.com

WILEY

[Intervention Review]

Stiripentol add-on therapy for focal refractory epilepsy

Francesco Brigo[1], Stanley C Igwe[2], Nicola Luigi Bragazzi[3]

[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy. [2]Department of Neuropsychiatry, Federal Teaching Hospital, Abakaliki, Nigeria. [3]Department of Health Sciences, Postgraduate School of Public Health, Genoa, Italy

Contact address: Francesco Brigo, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, P.le L.A. Scuro, 10, Verona, Verona, 37134, Italy. dr.francescobrigo@gmail.com.

Editorial group: Cochrane Epilepsy Group.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 5, 2018.

Citation: Brigo F, Igwe SC, Bragazzi NL. Stiripentol add-on therapy for focal refractory epilepsy. *Cochrane Database of Systematic Reviews* 2018, Issue 5. Art. No.: CD009887. DOI: 10.1002/14651858.CD009887.pub4.

ABSTRACT

Background

This is an updated version of the Cochrane review last published in 2015 (Issue 10). For nearly 30% of people with epilepsy, seizures are not controlled by current treatments. Stiripentol is a new antiepileptic drug (AED) that was developed in France and was approved by the European Medicines Agency (EMA) in 2007 for the treatment of Dravet syndrome as an adjunctive therapy with valproate and clobazam, with promising effects.

Objectives

To evaluate the efficacy and tolerability of stiripentol as add-on treatment for people with focal refractory epilepsy who are taking AEDs.

Search methods

For the latest update, we searched the following databases on 21 August 2017: Cochrane Epilepsy Specialized Register, CENTRAL , MEDLINE, ClinicalTrials.gov, and the WHO International Clinical Trials Registry Platform (ICTRP). We contacted Biocodex (the manufacturer of stiripentol) and epilepsy experts to identify published, unpublished and ongoing trials.

Selection criteria

Randomised, controlled, add-on trials of stiripentol in people with focal refractory epilepsy.

Data collection and analysis

Review authors independently selected trials for inclusion and extracted data. Outcomes investigated included 50% or greater reduction in seizure frequency, seizure freedom, adverse effects, treatment withdrawal and changes in quality of life.

Main results

On the basis of our selection criteria, we included no new studies in the present review. Only one study was included from the earlier review (32 children with focal epilepsy). This study adopted a 'responder enriched' design and found no clear evidence of a reduction in seizure frequency (≥ 50% seizure reduction) (risk ratio (RR) 1.51, 95% confidence interval (CI) 0.81 to 2.82, low-quality evidence) nor evidence of seizure freedom (RR 1.18, 95% CI 0.31 to 4.43, low-quality evidence) when add-on stiripentol was compared with placebo. Stiripentol led to a greater risk of adverse effects considered as a whole (RR 2.65, 95% CI 1.08 to 6.47, low-quality evidence). When specific adverse events were considered, confidence intervals were very wide and showed the possibility of substantial increases and small reductions in risks of neurological (RR 2.65, 95% CI 0.88 to 8.01, low-quality evidence) or gastrointestinal adverse effects (RR 11.56, 95% CI 0.71 to 189.36, low-quality evidence). Researchers noted no clear reduction in the risk of study withdrawal (RR 0.66, 95% CI 0.30 to 1.47, low-quality evidence), which was high in both groups (35.0% in add-on placebo and 53.3% in stiripentol group, low-quality evidence). The external validity of

this study was limited because only responders to stiripentol (i.e. patients experiencing a ≥ 50% decrease in seizure frequency compared with baseline) were included in the randomised, add-on, placebo-controlled, double-blind phase. Furthermore, carry-over and withdrawal effects probably influenced outcomes related to seizure frequency. Very limited information derived from the only included study shows that adverse effects considered as a whole seemed to occur significantly more often with add-on stiripentol than with add-on placebo.

Authors' conclusions

Since the last version of this review was published, we have found no new studies. Hence, we have made no changes to the conclusions of this update as presented in the initial review. We can draw no conclusions to support the use of stiripentol as add-on treatment for focal refractory epilepsy. Additional large, randomised, well-conducted trials are needed.

PLAIN LANGUAGE SUMMARY

Stiripentol as an add-on treatment for focal refractory epilepsy

Background

Epilepsy is one of the more common chronic neurological disorders; it affects 1% of the population worldwide. A large proportion of these people (up to 30%) continue to have seizures despite adequate therapy with antiepileptic drugs (AEDs), used singularly (as monotherapy) or in combination (polytherapy). These individuals are regarded as having refractory epilepsy. Stiripentol is a new AED that was developed in France and was approved in 2007 by the European Medicines Agency (EMA) for the treatment of Dravet syndrome as adjunctive therapy with valproate and clobazam, with promising effects. This review appraised evidence for the use of stiripentol as add-on treatment for focal refractory epilepsy in individuals taking AEDs.

Results

On the basis of our review criteria, we included only one study in the review (32 children with focal epilepsy). This study adopted a 'responder enriched' design and found no clear evidence of seizure reduction (≥ 50%) nor of seizure freedom with add-on stiripentol compared with placebo. Add-on stiripentol led to greater risk of adverse effects considered as a whole (risk ratio (RR) 2.65, 95% confidence interval (CI) 1.08 to 6.47) compared with placebo. Generalisation of study results to a more widespread population is limited by the fact that only responders to stiripentol (i.e. patients experiencing a decrease in seizure frequency of at least 50% compared with baseline) were included in the randomised, add-on, placebo-controlled, double-blind portion of the study. Also, the very small sample size with the correspondingly high dropout rate prevents generalisation of study results. Finally, because of the adopted design, carry-over and withdrawal effects probably influenced outcomes related to seizure frequency.

Quality of evidence

We judged the included study to be at low to unclear risk of bias. Using GRADE methodology, we rated the quality of evidence as low.

Currently, no available evidence supports the use of stiripentol as add-on treatment for focal refractory epilepsy. Additional large, randomised, well-conducted trials on this topic are needed.

The evidence is current to August 2017.