Antiepileptics for aggression and associated impulsivity (Review)

Huband N, Ferriter M, Nathan R, Jones H

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2010, Issue 2

http://www.thecochranelibrary.com

[Intervention Review]

Antiepileptics for aggression and associated impulsivity

Nick Huband[1], Michael Ferriter[2], Rajan Nathan[3], Hannah Jones[2]

[1]Section of Forensic Mental Health, Institute of Mental Health, Nottingham, UK. [2]Literature and Evidence Research Unit (LERU), Institute of Mental Health, Nottinghamshire Healthcare NHS Trust, Woodbeck, UK. [3]Division of Psychiatry, University of Liverpool, Liverpool, UK

Contact address: Nick Huband, Section of Forensic Mental Health, Institute of Mental Health, Nottinghamshire Healthcare Trust, Room B06, The Gateway Building, University of Nottingham, Innovation Park, Triumph Road, Nottingham, NG7 2TU, UK. nick.huband@nottingham.ac.uk.

Editorial group: Cochrane Developmental, Psychosocial and Learning Problems Group.
Publication status and date: New, published in Issue 2, 2010.
Review content assessed as up-to-date: 4 October 2009.

Citation: Huband N, Ferriter M, Nathan R, Jones H. Antiepileptics for aggression and associated impulsivity. *Cochrane Database of Systematic Reviews* 2010, Issue 2. Art. No.: CD003499. DOI: 10.1002/14651858.CD003499.pub3.

ABSTRACT

Background

Aggression is a major public health issue and is integral to several mental health disorders. Antiepileptic drugs may reduce aggression by acting on the central nervous system to reduce neuronal hyper-excitability associated with aggression.

Objectives

To evaluate the efficacy of antiepileptic drugs in reducing aggression and associated impulsivity.

Search strategy

We searched CENTRAL, MEDLINE, EMBASE, CINAHL, PsycINFO, *meta*Register of Controlled Trials (*m*RCT) and ClinicalTrials.gov to April 2009. We also searched Cochrane Schizophrenia Group's register of trials on aggression, National Research Record and handsearched for studies.

Selection criteria

Prospective, placebo-controlled trials of antiepileptic drugs taken regularly by individuals with recurrent aggression to reduce the frequency or intensity of aggressive outbursts.

Data collection and analysis

Three authors independently selected studies and two authors independently extracted data. We calculated standardised mean differences (SMDs), with odds ratios (ORs) for dichotomous data.

Main results

Fourteen studies with data from 672 participants met the inclusion criteria. Five different antiepileptic drugs were examined. Sodium valproate/divalproex was superior to placebo for outpatient men with recurrent impulsive aggression, for impulsively aggressive adults with cluster B personality disorders, and for youths with conduct disorder, but not for children and adolescents with pervasive developmental disorder. Carbamazepine was superior to placebo in reducing acts of self-directed aggression in women with borderline personality disorder, but not in children with conduct disorder. Oxcarbazepine was superior to placebo for verbal aggression and aggression against objects in adult outpatients. Phenytoin was superior to placebo on the frequency of aggressive acts in male prisoners and in outpatient men including those with personality disorder, but not on the frequency of 'behavioral incidents' in delinquent boys.

Authors' conclusions

The authors consider that the body of evidence summarised in this review is insufficient to allow any firm conclusion to be drawn about the use of antiepileptic medication in the treatment of aggression and associated impulsivity. Four antiepileptics (valproate/divalproex, carbamazepine, oxcarbazepine and phenytoin) were effective, compared to placebo, in reducing aggression in at least one study, although for three drugs (valproate, carbamazepine and phenytoin) at least one other study showed no statistically significant difference between treatment and control conditions. Side effects were more commonly noted for the intervention group although adverse effects were not well reported. Absence of information does not necessarily mean that the treatment is safe, nor that the potential gains from the medication necessarily balance the risk of an adverse event occurring. Further research is needed.

PLAIN LANGUAGE SUMMARY

Antiepileptic drugs for treating recurrent aggression

Various medicines, which are collectively termed 'antiepileptic drugs', have been used to treat persistent aggression. This review systematically examines the evidence supporting this practice. From the evidence available, we were unable to draw any firm conclusion about using these medicines to treat aggression. Four antiepileptic drugs (valproate/divalproex, carbamazepine, oxcarbazepine and phenytoin) helped to reduce aggression in at least one study. However, for three of these drugs (valproate, carbamazepine and phenytoin) we found at least one other study where there was no significant improvement. Further research is needed to clarify which antiepileptic drugs are effective for whom. Such research is best carried out using carefully designed clinical trials. Such trials need to take account of the type of aggression displayed, the severity of the aggression, and any other disorders experienced by the participants.