COCHRANE CORNER

Cholinergic medication for antipsychotic-induced tardive dyskinesia[†]

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[†] This review is an abridged version of a Cochrane review previously published in the *Cochrane Database of Systematic Reviews*, 2018, March 19, Issue 3: CD000207 (doi: 10.1002/14651858.CD000207.pub2) (see www.Cochranelibrary.com for information). Cochrane reviews are regularly updated as new evidence emerges and in response to feedback, and the Cochrane Database of Systematic Reviews should be consulted for the most recent version of the review.

We thank the Cochrane Review Group for their support in publishing these reviews.

See commentary on pp. 289–294, this issue.

Background

Tardive dyskinesia (TD) remains a troublesome adverse effect of conventional antipsychotic (neuroleptic) medication. It has been proposed that TD could have a component of central cholinergic deficiency. Cholinergic drugs have been used to treat TD.

Objectives

To determine the effects of cholinergic drugs (arecoline, choline, deanol, lecithin, meclofenoxate, physostigmine, RS 86, tacrine, metoxytacrine, galantamine, ipidacrine, donepezil, rivastigmine, eptastigmine, metrifonate, xanomeline, cevimeline) for treating antipsychotic-induced TD in people with schizophrenia or other chronic mental illness.

Search methods

An electronic search of the Cochrane Schizophrenia Group's Study-Based Register of Trials (16 July 2015 and April 2017) was undertaken. This register is assembled by extensive searches for randomised controlled trials in many electronic databases, registers of trials, conference proceedings and dissertations. References of all identified studies were searched for further trial citations.

Selection criteria

We included reports identified by the search if they were of controlled trials involving people with antipsychotic-induced TD and chronic mental illness, who had been randomly allocated to either a cholinergic agent or to a placebo or no intervention. Two review authors independently assessed the methodological quality of the trials.

Data collection and analysis

Two review authors extracted data and, where possible, estimated risk ratios (RR) or mean differences (MD), with 95% CI. We analysed data on an intention-to-treat basis, with the assumption that people who left early had no improvement. We assessed risk of bias and created a 'Summary of findings' table using GRADE.

Main results

We included 14 studies investigating the use of cholinergic drugs compared with placebo published between 1976 and 2014. All studies involved small numbers of participants (5 to 60 people). Three studies that investigated the new cholinergic Alzheimer drugs for the treatment of TD are new to this update. Overall, the risk of bias in the included studies was unclear, mainly owing to poor reporting; allocation concealment was not described, generation of the sequence was not explicit, studies were not clearly blinded, we are unsure whether data are incomplete, and data were often poorly or selectively reported.

We are uncertain about the effect of new or old cholinergic drugs on no clinically important improvement in TD symptoms when compared with placebo; the quality of evidence was very low (RR = 0.89, 95% CI 0.65–1.23; 27 people, 4 RCTs). Eight trials found that cholinergic drugs may make little or no difference to deterioration of TD symptoms (low-quality evidence, RR = 1.11, 95% CI 0.55–2.24; 147 people). Again, owing to very low-quality evidence, we are uncertain about the effects on mental state (RR = 0.50, 95% CI 0.10–2.61; 77 people, 5 RCTs), adverse events (RR = 0.56, 95% CI 0.15–2.14; 106 people, 4 RCTs) and leaving the study early (RR = 1.09, 95% CI 0.56–2.10; 288 people, 12 RCTs). No study reported on social confidence, social inclusion, social networks or personalised quality of life.

Authors' conclusions

TD remains a major public health problem. The clinical effects of both older cholinergic drugs and new cholinergic agents, now used for treating Alzheimer's disease, are unclear, as too few, too small studies leave many questions unanswered. Cholinergic drugs should remain of interest to researchers and currently have little place in routine clinical work. However, with the advent of new cholinergic agents now used for treating Alzheimer's disease, scope exists for more informative trials. If these new cholinergic agents are to be investigated for treating people with TD, their effects should be demonstrated in large well-designed, well-conducted and well-reported randomised trials.