

Newer generation antidepressants for depressive disorders in children and adolescents

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[†]This review is an abridged version of a Cochrane review previously published in the Cochrane Database of Systematic Reviews, 2012, Nov 14, Issue 11: CD004851 (doi: 10.1002/14651858.CD004851.pub3) (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.

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See commentary on pp. 75–80, this issue.

Background

Depressive disorders are common in young people and are associated with significant negative impacts. Newer generation antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs), are often used; however, evidence of their effectiveness in children and adolescents is not clear. Furthermore, there have been warnings against their use in this population due to concerns about increased risk of suicidal ideation and behaviour.

Objectives

To determine the efficacy and adverse outcomes, including definitive suicidal behaviour and suicidal ideation, of newer generation antidepressants compared with placebo in the treatment of depressive disorders in children and adolescents.

Search methods

For this update of the review, we searched the Cochrane Depression, Anxiety and Neurosis Review Group's Specialised Register (CCDANCTR) to October 2011. The CCDANCTR includes relevant randomised controlled trials from the following bibliographic databases: CENTRAL (the Cochrane Central Register of Controlled Trials) (all years), EMBASE (1974–), MEDLINE (1950–) and PsycINFO (1967–). We searched clinical trial registries and pharmaceutical company websites. We checked reference lists of included trials and other reviews, and sent letters to key researchers and the pharmaceutical companies of included trials from January to August 2011.

Selection criteria

Published and unpublished randomised controlled trials (RCTs), cross-over trials and cluster trials comparing a newer generation antidepressant with a placebo in children and adolescents 6 to 18 years of age and diagnosed with a depressive disorder were eligible for inclusion. In this update, we amended the selection criteria to include newer generation antidepressants rather than SSRIs only.

Data collection and analysis

Two or three review authors selected the trials, assessed their quality, and extracted trial and outcome data. We used a random-effects meta-analysis. We used risk ratio (RR) to summarise

dichotomous outcomes and mean difference (MD) to summarise continuous measures.

Main results

Nineteen trials of a range of newer antidepressants compared with placebo, containing 3335 participants, were included. The trials excluded young people at high risk of suicide and many comorbid conditions and the participants are likely to be less unwell than those seen in clinical practice. We judged none of these trials to be at low risk of bias, with limited information about many aspects of risk of bias, high drop out rates and issues regarding measurement instruments and the clinical usefulness of outcomes, which were often variously defined across trials. Overall, there was evidence that those treated with an antidepressant had lower depression severity scores and higher rates of response/remission than those on placebo. However, the size of these effects was small with a reduction in depression symptoms of 3.51 on a scale from 17 to 113 (14 trials; $N = 2490$; MD -3.51 ; 95% confidence interval (CI) -4.55 to -2.47). Remission rates increased from 380 per 1000 to 448 per 1000 for those treated with an antidepressant. There was evidence of an increased risk (58%) of suicide-related outcome for those on antidepressants compared with a placebo (17 trials; $N = 3229$; RR 1.58; 95% CI 1.02 to 2.45). This equates to an increased risk in a group with a median baseline risk from 25 in 1000 to 40 in 1000. Where rates of adverse events were reported, this was higher for those prescribed an antidepressant. There was no evidence that the magnitude of intervention effects (compared with placebo) were modified by individual drug class.

Authors' conclusions

Caution is required in interpreting the results given the methodological limitations of the included trials in terms of internal and external validity. Further, the size and clinical meaningfulness of statistically significant results are uncertain. However, given the risks of untreated depression in terms of completed suicide and impacts on functioning, if a decision to use medication is agreed, then fluoxetine might be the medication of first choice given guideline recommendations. Clinicians need to keep in mind that there is evidence of an increased risk of suicide-related outcomes in those treated with antidepressant medications.

Assessed as up to date: 28 October 2011