Aripiprazole for autism spectrum disorders (ASD), a Cochrane Review

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Autism spectrum disorders (ASD) include autistic disorder, Asperger's disorder and pervasive developmental disorder - not otherwise specified (PDD-NOS). Antipsychotics have been used as a medication intervention for irritability related to ASD. Aripiprazole, a third-generation, atypical antipsychotic, is a relatively new drug that has a unique mechanism of action different from that of other antipsychotics. This review updates a previous Cochrane review on the safety and efficacy of aripiprazole for individuals with ASD, published in 2011 (Ching 2011).

Objectives

To assess the safety and efficacy of aripiprazole as medication treatment for individuals with ASD.

Search methods

In October 2015, we searched the Cochrane Central Register of Controlled Trials (CENTRAL), Ovid MEDLINE, Embase, the Cumulative Index to Nursing and Allied Health Literature (CINAHL) and seven other databases as well as two trial registers. We searched for records published in 1990 or later, as this was the year aripiprazole became available.

Selection criteria

Randomised controlled trials (RCTs) of aripiprazole (administered orally and at any dosage) versus placebo for treatment of individuals with a diagnosis of ASD.

Data collection and analysis

Two review authors independently collected, evaluated and analysed data. We performed meta-analysis for primary and secondary outcomes, when possible. We used the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach to rate the overall quality of the evidence.

Main results

We included three trials in this review. Two were included in the previous published review, and the results of one, placebo-controlled discontinuation study were added to this review. Although we searched for studies across age groups, we found only studies conducted in children and youth. Included trials had low risk of bias across most domains. High risk of bias was seen in only one trial with incomplete outcome data. We judged the overall quality of the evidence for most outcomes to be moderate.

Two RCTs with similar methods evaluated use of aripiprazole for a duration of eight weeks in 316 children/adolescents with ASD. Meta-analysis of study results revealed a mean improvement of -6.17 points on the Aberrant Behavior Checklist (ABC) - Irritability subscale (95% confidence intervals (CIs) -9.07 to -3.26, two studies, 308 children/adolescents, moderate-quality evidence), -7.93 points on the ABC - Hyperactivity subscale (95% CI -10.98 to -4.88, two studies, 308 children/adolescents, moderate-quality evidence) and -2.66 points on the ABC - Stereotypy subscale (95% CI -3.55 to -1.77, two studies, 308 children/adolescents, moderate-quality evidence) in children/adolescents taking aripiprazole relative to children/adolescents taking placebo. In terms of side effects, children/adolescents taking aripiprazole had a greater increase in weight, with a mean increase of 1.13 kg relative to placebo (95% CI 0.71 to 1.54, two studies, 308 children/adolescents, moderate-quality evidence), and had a higher risk ratio (RR) for sedation (RR 4.28, 95% CI 1.58 to 11.60, two studies, 313 children/adolescents, moderate-quality evidence) and tremor (RR 10.26, 95% CI 1.37 to 76.63, two studies, 313 children/adolescents, moderate-quality evidence). A randomised, placebo-controlled discontinuation study found that 35% of children/adolescents randomised to continue intervention with aripiprazole relapsed with respect to their symptoms of irritability, compared with 52% of children/adolescents randomised to placebo, for a hazard ratio of 0.57 (95% CI 0.28 to 1.12, 85 children/adolescents, low-quality evidence).

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Authors' conclusions

Evidence from two RCTs suggests that aripiprazole can be effective as a short-term medication intervention for some behavioural aspects of ASD in children/adolescents. After a short-term medication intervention with aripiprazole, children/adolescents showed less irritability and hyperactivity and fewer stereotypies (repetitive, purposeless actions). However, notable side effects, such as weight gain, sedation, drooling and tremor, must be considered. One long-term, placebo discontinuation study found that relapse rates did not differ between children/adolescents randomised to continue aripiprazole versus children/adolescents randomised to receive placebo, suggesting that re-evaluation of aripiprazole use after a period of stabilisation in irritability symptoms is warranted. Studies included in this review used criteria from the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (APA 2000) for ASD diagnosis; however, the diagnostic criteria for ASD changed significantly with release of the fifth edition of the DSM (DSM-5) in 2013 (APA 2013).

COCHRANE CORNER

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