Efficacy and safety of naltrexone use in pediatric patients with autistic disorder
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CRD summary
The authors concluded that naltrexone may benefit children with autistic disorder, particularly those with self-injurious behaviour, if other attempted therapies have failed. Given the small sample sizes and unknown quality of the included studies, the reliability of the results is unknown.

Authors’ objectives
To assess the efficacy and safety of naltrexone in paediatric patients with autistic disorder (AD).

Searching
MEDLINE (1966 to May 2006) and International Pharmaceutical Abstracts (1971 to May 2006) were searched using the keywords provided. The reference lists of retrieved articles were checked for additional studies.

Study selection
Study designs of evaluations included in the review
The inclusion criteria did not specify what types of study designs were eligible for inclusion. The review included case reports, case series, randomised controlled trials (RCTs) including crossover trials, and non-controlled trials.

Specific interventions included in the review
Studies that described or evaluated the efficacy and/or safety of naltrexone were eligible for inclusion. Dosages varied from 0.4 mg/kg every third day to 2 mg/kg per day. Duration varied from one dose to treatment for 6 months.

Participants included in the review
Paediatric patients with AD were eligible for inclusion. The participants were aged from 2 to 21 years. Some studies included participants with self-injurious behaviour and/or mental retardation.

Outcomes assessed in the review
The inclusion criteria did not specify measures of efficacy and/or safety. Methods used to express patient response included 18 different rating scales,checklists or assessments, as well as physiological measurements (details were reported in the review).

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were combined in a narrative.

How were differences between studies investigated?
The authors grouped the studies by study design.

Results of the review
The authors reported on 25 studies (number of participants unclear): 3 case reports, 8 case series and 14 clinical studies. It is noted, however, that some of the studies included some of the same participants.

The available research was characterised by small sample sizes, short duration and use of a variety of methods to evaluate outcomes.

Naltrexone was generally effective in decreasing self-injurious behaviour. It may also attenuate hyperactivity, agitation, irritability, temper tantrums, social withdrawal and stereotyped behaviours. Participants may also have experienced improved attention and eye contact after treatment. The most commonly reported adverse event was transient sedation.

**Authors’ conclusions**
Children affected with AD, particularly those with self-injurious behaviour, may benefit from naltrexone if other attempted therapies have failed. Short-term studies did not report any serious adverse effects.

**CRD commentary**
The inclusion criteria were clearly reported in terms of the participants and intervention, but remained broad for the outcomes. The authors searched two databases and screened the references of included studies. However, it is not clear if non-English papers and unpublished studies were sought, thus potentially introducing language and publication bias. The authors did not state how many reviewers were involved in selecting the studies and extracting the data, thereby introducing the potential for reviewer bias. In addition, the validity of the studies was not formally assessed. While the authors stated that some of the studies were well-designed, it is not possible to determine the overall quality of the included studies. There may also be some overlap in participants between some included studies, thus introducing the potential for bias.

The authors’ decision to describe the results in a narrative synthesis was appropriate given the heterogeneity between the studies. Details of the studies were presented in the tables and text of the review. Given the small sample sizes and unknown quality of the included studies, the reliability of the results is unknown.

**Implications of the review for practice and research**
Practice: The authors stated that use of naltrexone may be attempted in a child with AD and self-injurious behaviour, starting with a low dose (such as 0.5 mg/kg daily) and titrating upwards according to response and/or adverse effects.

Research: The authors stated that further large, long-term RCTs are needed to elucidate the efficacy and safety of naltrexone.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.