The pharmacological management of childhood anxiety disorders: a review

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CRD summary
This review examined the effectiveness of pharmacological treatments, including selective serotonin re-uptake inhibitors (SSRIs) and tricyclic antidepressants for obsessive compulsive disorder and other anxiety disorders in children aged under 18 years. The authors concluded that evidence supports the use of such agents, including SSRIs. Poor reporting of review methodology means that the reliability of this conclusion cannot be determined.

Authors' objectives
To examine the pharmacological treatment of paediatric anxiety disorders including obsessive compulsive disorder (OCD).

Searching
MEDLINE, PsycINFO and the Cochrane Library were searched; the search terms were reported. In addition, a manual search of references was carried out. Studies published between 1985 and 2006 were eligible for inclusion in the review.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) with a minimum of 10 participants were eligible for inclusion. Both parallel and crossover trials were included in the review.

Specific interventions included in the review
Studies that compared pharmacological treatments with placebo and had a focus on short-term treatment of less than 6 months were eligible for inclusion. The duration of treatment in the included studies ranged from 8 to 32 weeks. The included studies examined selective serotonin re-uptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs); some also examined cognitive-behavioural therapy (CBT).

Participants included in the review
Studies of children and adolescents aged under 18 years with anxiety disorders were eligible for inclusion. Where reported, the included studies had participants with ages ranges from 5 to 17 years. Studies of children with OCD and with other anxiety disorders, including generalised anxiety disorder (GAD), social phobia (SP), elective mutism and separation anxiety disorder (SAD), were included in the review.

Outcomes assessed in the review
Inclusion criteria required that 'reasonable outcomes' be assessed. These were defined as the Clinical Global Impressions-Improvement scale, or anxiety measurement scales validated in the paediatric population. Adverse effects were also included 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, but it appears that the studies were assessed for blinding.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data
extraction. Data were extracted on intervention and dose, population characteristics, the primary outcome of anxiety or OCD symptoms, and adverse events. Effect sizes or numbers-needed-to-treat (NNT) were extracted where possible.

**Methods of synthesis**

How were the studies combined?
The studies were combined in an extensive narrative.

How were differences between studies investigated?
The studies were grouped according to the anxiety disorder and the intervention under investigation, and differences were discussed in the narrative synthesis.

**Results of the review**

Twenty-one RCTs with 1,805 participants were included in the review.

**SSRIs in OCD (8 RCTs).**

Three RCTs compared fluoxetine with placebo and found effect sizes ranging from 0.2 to 0.6 in favour of fluoxetine. One large RCT found that fluvoxamine was more effective than placebo, with an effect size of 0.3. Two large RCTs found that paroxetine was more effective than placebo (effect sizes or NNTs not reported). Two RCTs compared sertraline with placebo: one reported an NNT of 6, the other found that CBT combined with sertraline was superior to either treatment alone, all treatment options being superior to placebo (effect sizes: sertraline 0.67, CBT 0.97, combination 1.4).

**TCAs in OCD (3 RCTs).**

Three small RCTs compared clomipramine with placebo and found, respectively, effect sizes of 0.8 and 0.97 and an NNT of 4.

**SSRIs in other anxiety disorders (5 RCTs).**

Two RCTs assessed SSRIs for anxiety disorders in general. One found that fluvoxamine was more effective than placebo in treating children with SAD, GAD or SP (effect size 1.1, NNT 2). The other RCT found a similar result in the same population when comparing fluoxetine with placebo (effect size 0.4, NNT 4). One small RCT assessed sertraline for GAD and found an effect size of 1.9 and an NNT of 1. A large RCT assessed paroxetine for SP and found an NNT of 3. A final small RCT assessed fluoxetine for elective mutism and found an effect size of 0.67.

**TCAs in other anxiety disorders (5 RCTs).**

Three small RCTs compared imipramine with placebo; two showed effectiveness for, respectively, school phobia (NNT 3) and school refusal in conjunction with at least one anxiety disorder (effect size 0.3, NNT 3; treatment combined with CBT). The third found little evidence of effectiveness (NNT 100). One RCT found no evidence of effectiveness for imipramine combined with alprazolam for school phobia and related anxiety, and another no significant difference from placebo or clomipramine in the treatment of school phobia.

Side-effects were also reported.

**Authors' conclusions**

There is good evidence to support the efficacy of several pharmacological treatments, including SSRIs, to treat paediatric anxiety and OCD, although unanswered questions remain.

**CRD commentary**

The review question and inclusion criteria were clear but often broad given the small evidence base. The authors
searched several relevant databases, although they did not report searching for unpublished studies. This might have increased the possibility that some relevant studies were not included in the review. The authors did not state that they carried out a formal validity assessment, although at least one key criterion of validity appears to have been assessed. The authors did not report using methods designed to reduce bias and error in this assessment, in the selection of studies for the review, or in the extraction of data.

The decision to employ a narrative synthesis is likely to have been appropriate given the clinical heterogeneity documented in the evidence tables. The conclusions are supported by the results of the systematic review; although it is not clear to what extent they were also informed by a second non-systematic review which was included in the report. However, given the lack of a validity assessment and the poor reporting of the review methodology, it is difficult to determine the reliability of the conclusions.

**Implications of the review for practice and research**

Practice: The authors did not state any implications for practice.

Research: The authors stated there were no comparative trials for SAD, GAD and SP, and that there were also no large definitive studies of medication in paediatric post-traumatic stress disorder or specific phobias.

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