Sustained response versus relapse: the pharmacotherapeutic goal for obsessive-compulsive disorder
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CRD summary
This review assessed evidence for long-term pharmacological management of obsessive compulsive disorder (OCD) using serotonin reuptake inhibitors and concluded that data showed some serotonin reuptake inhibitors remained effective over long-term treatment. Relapse prevention was an achievable goal for OCD pharmacotherapy. A number of flaws in the reporting raised serious concerns about the reliability of the authors’ conclusions.

Authors’ objectives
To review the evidence for the long-term pharmacological management of obsessive compulsive disorder (OCD) with serotonin reuptake inhibitors (SRIs).

Searching
The authors searched MEDLINE (1966-2006), EMBASE (1966-2006), PsycINFO (1970-2006) and Cochrane Central Register of Controlled Trials. Search terms were not reported.

Study selection
Randomised controlled trials (RCTs) of pharmacotherapy for OCD that incorporated a maintenance, discontinuation or relapse-prevention component were eligible for inclusion in the review. Studies included in the review evaluated fluvoxamine, sertraline, fluoxetine, paroxetine, clomipramine, citalopram and escitalopram across a range of doses.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

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

Data extraction
In studies evaluating relapse prevention, the relative risk ratio and corresponding 95% confidence intervals (CI) for the number of responders who relapsed in the treatment and placebo groups was calculated. For trials using multiple doses of medication, summary statistics were calculated for the highest dose.

The authors did not state how data were extracted for the review.

Methods of synthesis
Relative risk ratios from relapse-prevention RCTs were combined in a meta-analysis. Statistical heterogeneity was assessed and quantified using $\chi^2$ and $I^2$ tests.

The results of other RCTs were presented in a narrative synthesis.

Results of the review
The authors appeared to include 25 placebo controlled RCTs (n=unclear) in the review, of which five (n=757) were included in the relapse prevention meta-analysis.

Definitions of response and remission varied between studies. RCTs reported a range of thresholds on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS).

Five placebo-controlled RCTs evaluated the long-term efficacy of serotonin reuptake inhibitors. One RCT reported
fluoxetine at doses of 20, 40 and 60 mg over 24 weeks; the 60 mg group improved significantly more than others. One RCT reported significant improvement in OCD symptoms for sertraline over 40 weeks follow up. The final RCT found significant benefits of escitalopram 10 mg, escitalopram 20 mg and paroxetine 40 mg compared to placebo over 24 weeks follow up, with highly significant differences for escitalopram 20 mg and paroxetine.

Five placebo-controlled RCTs (n=757) reported relapse prevention outcomes. These trials evaluated paroxetine, fluoxetine, sertraline and escitalopram. When combined in a meta-analysis, the pooled relative risk ratio of relapse was significantly lower in the serotonin reuptake inhibitor than placebo groups (relative risk ratio was 0.52, 95% CI: 0.41 to 0.66, p<0.00001).

**Authors’ conclusions**
Persuasive data showed some serotonin reuptake inhibitors remained effective over long-term treatment and that relapse prevention was an achievable goal for OCD pharmacotherapy.

**CRD commentary**
The review question was reasonably clearly defined in terms of the participants, interventions, and study designs of interest. The authors searched three electronic databases, but did not report search terms or attempts to identify studies through other sources. Therefore relevant studies may potentially have been missed. Though some issues around sample size are briefly mentioned, no attempt was made to formally assess the validity of the included studies. Though inclusion was limited to placebo-controlled RCTs, a number of additional studies were incorporated into the text of the review and appear to inform its conclusions. A subgroup of included RCTs were pooled in a meta-analysis, though important details of this analysis (e.g. use of fixed or random effects models) were not reported. The authors do not report any attempts to minimise the potential for errors and bias in the selection or extraction of studies for the review. The number of flaws in the reporting of this review raise serious concerns about the reliability of the authors’ conclusions.

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

**Research**: The authors stated that further research on the basic mechanisms mediating medication withdrawal was needed. They recommended that future studies defined relapse as a worsening of five Y-BOCS points from randomisation.

**Practice**: The authors stated that long-term treatment with serotonin reuptake inhibitors was indicated to prevent relapse in OCD, and that clinicians and patients needed to consider the risks of relapse when making decisions about maintenance treatment.

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