Paroxetine: an update of its use in psychiatric disorders in adults

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Authors' objectives
To undertake a review of the major pharmacological features of paroxetine and its use in the management of depression, obsessive-compulsive disorder (OCD), panic disorder, social anxiety disorder, generalised anxiety disorder (GAD) and post-traumatic stress disorder (PTSD).

Searching
MEDLINE, EMBASE and AdisBase were searched. The search terms were 'paroxetine' or 'FG 7051' for MEDLINE, 'paroxetine' or 'BRL 29060' or 'FG 7051' for EMBASE, and 'paroxetine' for AdisBase. The searches were last updated on 21 January 2002. Additional references were identified from the reference lists of published articles. Bibliographical information, including contributory unpublished data, was also requested from the company developing the drug.

Study selection
Study designs of evaluations included in the review
The inclusion criteria for study design stated a preference for large well-controlled trials. The studies presented in the review were randomised controlled trials (RCTs) with at least 100 participants. The duration of the studies ranged from 6 to 24 weeks.

Specific interventions included in the review
Paroxetine (various doses ranging from 10 to 50 mg/day) was compared with placebo or other active comparator such as antidepressants or other selective serotonin re-uptake inhibitors (SSRIs). The antidepressants included amitriptyline (50 to 250 mg/day), imipramine (50 to 275 mg/day), lofepramine (140 to 210 mg/day), clomipramine (150 mg/day), maprotiline (100 to 150 mg/day), mianserin (60 mg/day), mirtazapine (30 to 45 mg/day), nefazodone (200 to 600 mg/day), tianeptine (37.5 mg/day), trazodone (146.1 to 154.3 mg/day) and venlafaxine (75 to 269 mg/day). The SSRIs were fluoxetine (20 to 80 mg/day, sertraline (50 to 200 mg/day) and fluvoxamine (50 to 200 mg/day).

Participants included in the review
The inclusion criteria specified patients with major depressive disorder, dysthymia, OCD, panic disorder, social anxiety disorder, GAD or PTSD.

Outcomes assessed in the review
The inclusion criteria for the outcomes were not stated a priori. The included outcomes were reductions from baseline scores on measurement scales such as the Hamilton Depression Rating Scale, Hopkins Symptom Checklist, Montgomery and Asberg Depression Rating Scale, Bech-Rafaelsen Melancholia Scale, Clinical Global Impressions Scale, Patient's Global Experience, Patient's Global Impression, Raskin Depression Scale and visual analogue scales.

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 review, which was organised first around the comparators, and second around the type of illness being treated by paroxetine.

How were differences between studies investigated?
The authors did not state a method for assessing any differences between the studies.

Results of the review
The number of studies included was not stated. Tables of the included studies showed 7 RCTs of paroxetine versus placebo, 14 RCTs of paroxetine versus tricyclic antidepressants (TCAs), 11 RCTs of paroxetine versus SSRIs, and 8 RCTs of paroxetine versus other antidepressants.

Major depressive illness.
Oral paroxetine (10 to 50 mg/day) was significantly more effective than placebo, at least as effective as TCAs, and as effective as other SSRIs and other antidepressants in the treatment of major depressive disorder. Relapse or recurrence over one year after the initial response was significantly lower with paroxetine (10 to 50 mg/day) than with placebo, and was similar to that with imipramine (50 to 275 mg/day).

The efficacy of paroxetine (10 to 40 mg/day) was similar to that of TCAs and fluoxetine (20 to 60 mg/day) in 6- to 12-week trials in patients aged 60 years and older with major depression. Paroxetine (10 to 40 mg/day) improved depressive symptoms to an extent similar to that of TCAs in patients with co-morbid illness, and was more effective than placebo in the treatment of dysthymia and minor depression.

Other results.
Paroxetine (20 to 60 mg/day) was more effective than placebo after 8 to 12 weeks' treatment of OCD, panic disorder, social anxiety disorder (social phobia), GAD and PTSD. Improvement was maintained, or relapse was prevented, for 24 weeks to one year in patients with OCD, panic disorder, social anxiety disorder or GAD. The efficacy of paroxetine was similar to that of other SSRIs in patients with OCD and panic disorder, and was similar to that of imipramine but greater than that of 2'-chlorodesmethyldiazepam in patients with GAD.

Paroxetine is generally well tolerated in adults, elderly individuals and patients with co-morbid illness, with a tolerability profile similar to that of other SSRIs. The most common adverse events with paroxetine were nausea, sexual dysfunction, somnolence, asthenia, headache, constipation, dizziness, sweating, tremor and decreased appetite.

Authors' conclusions
Paroxetine is generally better tolerated than TCAs and is a first-line treatment option for major depressive disorder, dysthymia or minor depression. Like other SSRIs, paroxetine is also an appropriate first-line therapy for OCD, panic disorder, social anxiety disorder, GAD and PTSD. Given the high degree of psychiatric co-morbidity of depression and anxiety, paroxetine is an important first-line option for the treatment of the psychiatric disorders covered in this review.

CRD commentary
The authors stated the research question, but the review was lacking in detail for all categories of inclusion and exclusion criteria. The literature search was also not reported in detail, although attempts were made to find unpublished or grey literature. It was not stated whether any language restrictions were applied and there were no tests for publication bias.

The quality of the included studies was not formally assessed and the authors have not reported how the articles were selected, or who performed the selection and data extraction. The data extraction was reported briefly in tabular format and briefly discussed in the text of the review, but the participants' characteristics were missing from these details. The studies were not statistically combined and no further tests were conducted to investigate possible differences between
the included studies. The authors' conclusions appear to follow from the results, but are of limited value since the methodological quality of the review process is questionable.

**Implications of the review for practice and research**
The authors did not state any implications for practice or further research.

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