Sertraline: a review of its use in the management of major depressive disorder in elderly patients

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Authors' objectives
The authors' objective appeared to be to assess the efficacy of sertraline in elderly people with major depressive disorder. The review also includes evidence on the pharmacodynamics and pharmacokinetic profile of sertraline. This abstract refers only to that part of the review dealing with the therapeutic use of sertraline.

Searching
MEDLINE, EMBASE and AdisBase were searched from 1980 to May 2002; the search terms were reported. In addition, the bibliographies of published articles were reviewed for further studies. Bibliographic information, including contributory unpublished data, were also requested from the company developing the drug. Abstracts were apparently included in the review.

Study selection
Study designs of evaluations included in the review
The study designs eligible for inclusion in the therapeutic use section were not explicitly stated, although for the article as a whole, large randomised controlled trials (RCTs) were included where possible. The studies included in the assessment of therapeutic use were double-blinded RCTs.

Specific interventions included in the review
Studies of sertraline were eligible for inclusion. The studies included in the assessment of therapeutic use compared sertraline (50 to 200 mg/day) with placebo, fluoxetine (20 to 40 mg), nortriptyline (25 to 100 mg), amitriptyline (50 to 150 mg) and imipramine (150 mg). The studies lasted 8 or 12 weeks.

Participants included in the review
Studies of patients aged 60 years or more with major depressive disorder were eligible for inclusion. The studies included in the assessment of therapeutic use were of elderly out-patients who had mean baseline depression scores per treatment group ranging from 21.4 to 25.2 on the Hamilton Depression Rating Scale (HDRS) or 27.8 to 30.3 on the Montgomery-Asberg Depression Rating Scale (MADRS). One included study was of depressed patients with Alzheimer's disease.

Outcomes assessed in the review
The outcomes that had to be assessed before the studies were included were not explicitly stated. In the review, therapeutic use was assessed using the HDRS, MADRS, Clinical Global Impression (CGI) and subscales, Profile of Moods States (POMS) and the Quality of Life Enjoyment and Satisfaction Scale. Response rates were also assessed, but were defined differently in different studies. Adverse reactions were also assessed.

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

Assessment of study quality
The authors do not report the method used to assess quality, or how the quality assessment was performed.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data
extraction. The following information were tabulated: author, details of sertraline dose and comparator drug, sample size, study duration, method used to assess the outcomes, baseline depression score and results.

**Methods of synthesis**
How were the studies combined?
The studies were grouped by comparator drug and a narrative synthesis was undertaken.

How were differences between studies investigated?
Differences between the studies were not discussed in the review.

**Results of the review**
Five RCTs (1,434 patients) appear to have been included.

Sertraline (50 to 100 mg) versus placebo (1 RCT, 748 patients): sertraline significantly improved depression at 8 weeks compared with placebo. The mean decrease from the baseline HDRS was 7.7 with sertraline versus 6.5 with placebo (P<0.01). The response rates (CGI improved by 1 or 2 from baseline) were 46 and 35% with sertraline and placebo, respectively (P<0.01). The values quoted in the review were taken from a graph.

Sertraline (50 to 100 mg) versus fluoxetine (1 RCT, 236 patients): there was no significant difference between sertraline and fluoxetine in depression at 12 weeks in terms of the HDRS score, response rates, quality of life, CGI Severity, CGI Improvement, CGI Efficacy Index rating, MADRS or POMS. The mean decrease from the baseline HDRS was 11.3 with both sertraline and fluoxetine. The response rates (at least 50% decrease in HDRS from baseline) were 73 and 71% with sertraline and fluoxetine, respectively.

Sertraline (50 to 150 mg) versus nortriptyline (1 RCT, 210 patients): there was no significant difference between sertraline and nortriptyline at 12 weeks in terms of the HDRS score, response rates, CGI Severity, CGI Efficacy Index rating or Global Satisfaction. However, sertraline significantly improved some aspects of quality of life compared with nortriptyline: physical health (P=0.01), psychosocial health (P=0.01), leisure time satisfaction (P=0.02) and social health satisfaction (P=0.004). The mean decrease from the baseline HDRS was 14.4 with sertraline versus 13.0 with nortriptyline. The response rates (not defined) were 72 and 61% with sertraline and nortriptyline, respectively.

Sertraline (50 to 200 mg) versus amitriptyline (1 RCT, 185 patients): there was no significant difference between sertraline and amitriptyline at 8 weeks in terms of the HDRS score or response rates when using data from evaluable patients. An intention-to-treat analysis found that amitriptyline was significantly better when using the HDRS score (P value not reported). The mean decrease from the baseline HDRS was 13.3 with sertraline versus 14.2 with amitriptyline. The response rates (not defined) were 69 and 63% with sertraline and amitriptyline, respectively.

Sertraline (50 mg) versus imipramine (1 RCT, 55 patients): there was no significant difference between sertraline and imipramine in depression at 8 weeks, response rates or MADRS. The mean decrease from the baseline MADRS was 14.4 with sertraline versus 12.8 with imipramine. The response rates (at least 50% decrease in HDRS from baseline) were 56 and 61% with sertraline and imipramine, respectively.

Adverse reactions (percentages taken from graph, hence approximate).

Nortriptyline (1 RCT) and amitriptyline (1 RCT) significantly increased constipation and dry mouth compared with sertraline: constipation was approximately 40% with nortriptyline versus 10% with sertraline, while dry mouth was 78% with nortriptyline versus 40% with sertraline (P<0.001). Sertraline significantly increased nausea compared with both nortriptyline and amitriptyline: approximately 24% with sertraline versus 12% with nortriptyline (P<0.5).

**Authors’ conclusions**
Sertraline was an effective treatment for major depressive disorders in elderly people and was well tolerated. The authors also state that sertraline was more effective than placebo and as effective as fluoxetine, nortriptyline and imipramine.
CRD commentary
The review question was clear in terms of the intervention and participants of interest. The authors failed to define inclusion criteria for the diagnosis of depression or in terms of eligible outcomes. The eligibility criteria for study design were not explicitly defined, but only double-blind RCTs appear to have been included in the assessment of therapeutic effectiveness. Several relevant sources were searched and the terms used in the search strategy were given. However, it was unclear whether any language restrictions had been applied. Abstracts appear to have been included, although again this was not explicitly stated. The methods used for the study selection, data extraction and quality assessment were not described, thus it is not possible to assess the potential for bias in any of these processes. Relevant information on the included studies was tabulated, including the basis used to estimate results (evaluable patients or intention-to-treat analysis). The studies were appropriately grouped by comparator drug and a narrative synthesis was undertaken. There seemed to be considerable variability in the response rates in the sertraline arms across studies (from 46 to 73%), but potential reasons for this were not discussed.

The authors’ conclusions appear to follow from the evidence presented, although it must be highlighted that all comparisons of treatments were based on single RCTs and the generalisability of these results is uncertain. The review was conducted by Adis International Limited.

Implications of the review for practice and research
Practice: The authors state that sertraline may have advantages over other antidepressants (tricyclics and the serotonin re-uptake inhibitors paroxetine, fluoxetine and fluvoxamine) in treating elderly people with depression since it has a relatively low potential for drug interactions.

Research: The authors did not state any implications for further research.

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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.