Response and discontinuation rates of newer antidepressants: a meta-analysis of randomized controlled trials in treating depression

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Authors' objectives
To examine the differences between newer and older antidepressants in response and discontinuation rates.

Searching
MEDLINE (was searched from 1989 to 1996 for RCTs of nefazodone, mirtazapine or venlafaxine. The reference lists of retrieved articles were also examined.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were included. The length of treatment ranged from 6 to 8 weeks.

Specific interventions included in the review
The newer antidepressants were nefazodone, mirtazapine, and venlafaxine. The older antidepressants included tricyclic antidepressants (TCAs), notricyclic antidepressants (NTCAs) and selective serotonin re-uptake inhibitors (SSRIs). A wide range of doses were given.

Participants included in the review
The participants suffered from major depression, as defined by the American Psychatric Association's criteria (DSM-III, DSM-IIIR) or the Research Diagnostic Criteria.

Outcomes assessed in the review
The response and discontinuation rates were measured. The response rate was computed by dividing the number of responders whose Hamilton Depression Rating Scale score was reduced by at least 50% (or less than 3 on the Clinical Global Impression scale) on their last visits, by the total number of participants. Since several factors affect patients dropping out of psychiatric treatments, only those discontinuation rates due to lack of efficacy or adverse effects were concerned. The discontinuation rates were calculated by dividing the number of drop-outs by the total number of participants.

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

Assessment of study quality
The author does not state that they assessed validity.

Data extraction
Data were extracted on an intention-to-treat basis.

Methods of synthesis
How were the studies combined?
Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for each rate comparison. Separate meta-analyses were carried out for each of the overall comparisons between newer and older antidepressant response rates, newer antidepressant and TCA discontinuation rates, and newer antidepressant and NTCA-SSRI discontinuation rates.
This approach was taken because no efficacy difference has been found among the older antidepressants, and NTCA-SSRIs are more tolerable than TCAs. For each overall comparison, the ORs were calculated using Peto's method (see Other Publications of Related Interest).

How were differences between studies investigated?
Heterogeneity was analysed for each overall comparison using a chi-squared test.

Results of the review
There were 18 studies included in the review: 12 double-blind placebo-controlled studies and 6 double-blind studies. There were 1,889 participants included in the overall comparison of the response rates for newer and older antidepressants. There were 851 and 783 patients included, respectively, in the overall comparisons of the discontinuation rates for newer antidepressants and TCAs, and newer antidepressants and NTCA-SSRIs.

Significant heterogeneity was found in the discontinuation rates compared for the newer antidepressants and TCAs (chi-squared 18.11, d.f.=7, p= 0.01). Two studies were excluded because they used low doses and caused significant heterogeneity. When these studies were excluded, the discontinuation rates were homogeneous.

The pooled OR of the newer and older antidepressants was 1.29 (95% CI: 1.07, 1.55), indicating a higher response of the newer antidepressant group.

In the overall comparison of the newer antidepressant and TCA discontinuation rates, the OR was 0.54 (95% CI: 0.38, 0.77); this showed a significantly lower discontinuation rate of the newer antidepressant group.

In the overall comparison of the newer antidepressant and NTCA-SSRI discontinuation rates, the pooled OR was 0.94 (95% CI: 0.66, 1.35), showing no significant difference between them.

Authors' conclusions
Newer antidepressants offered a slight but significantly superior efficacy to older antidepressants, which probably include SSRIs. The overall discontinuation rate of the newer antidepressant group was also lower than that of the TCA group, but not that of NTCA-SSRIs. However, the efficacy difference between newer antidepressants and SSRIs should be viewed as a preliminary result, since very few studies have compared their efficacy.

CRD commentary
The author presented a well-defined research question. The primary studies were combined appropriately. Some details of the individual studies were presented; however, more information on the patients' characteristics would have been appropriate, such as age, gender and socioeconomic status. The search was fairly narrow and could have been extended to include PsycLIT and EMBASE databases, and an attempt to find unpublished studies. It was unclear whether the author chose to search MEDLINE between 1989 and 1996, or whether the articles retrieved in the search were published during this period. The inclusion and exclusion criteria were not reported, and the validity of the included studies was not assessed.

The author's conclusions follow logically from the results.

Implications of the review for practice and research
The author states that because SSRIs are first-line treatments for major depressive disorder at present, the lower discontinuation rate of newer antidepressants, compared with TCAs, seems to have little impact in practice. The finding that newer antidepressants have a superior efficacy to older ones seems to be important. Viewed in conjunction with the finding that SSRIs are not more efficient than TCAs and NTCA-SSRIs, the superior efficacy of newer antidepressants found in the present analysis may indicate their superior effect over SSRIs. This result should be viewed as preliminary since very few studies have compared their efficacy. More studies with head-to-head comparisons of newer antidepressants and SSRIs are needed.
Bibliographic details

PubMedID
9676069

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
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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.