Review: Selective serotonin reuptake inhibitors differ from tricyclic antidepressants in adverse events

Trindade E, Menon D. Selective serotonin reuptake inhibitors (SSRIs) for major depression. Part I: Evaluation of the clinical literature. Ottawa: Canadian Coordinating Office for Health Technology Assessment, 1997 Aug. Report 3E.

Objective
To compare the efficacy, completion rates, and adverse event rates of selective serotonin reuptake inhibitors (SSRIs) with tricyclic antidepressants (TCAs) in treating depression.

Data sources
Studies were identified by searching MEDLINE, EMBASE, PsyCINFO, International Pharmaceutical Abstracts, Pascal, Health Planning & Administration, Mental Health Abstracts, PharmacoEconomics & Outcomes News, and Current Contents databases (1980 to May 1996); scanning bibliographies of retrieved articles; hand searching journals; and consulting researchers.

Study selection
Studies were selected if they were double-blind, randomised controlled trials; used antidepressant therapy for 4 to 12 weeks; and reported numerical or graphical data. Studies were excluded if they reanalysed data from previous studies.

Data extraction
Data were extracted on efficacy, study completion, and adverse events.

Main results
162 randomised controlled trials were reviewed. SSRIs and TCAs were equally effective, and the study completion rates did not differ. SSRIs increased the occurrence of 7 adverse events and decreased the occurrence of 3 adverse events compared with TCAs (Table). Incidence of palpitations, urinary disturbance, fatigue, tremor, hypotension, blurred vision, anorexia, and sweating did not differ.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>SSRI weighted EER (CI)</th>
<th>TCA weighted CER (CI)</th>
<th>RRR (95% CI)</th>
<th>Weighted NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry mouth</td>
<td>21% 55% 61% (54 to 66)</td>
<td>34% 3 (3 to 4)</td>
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<tr>
<td>Constipation</td>
<td>10% 22% 46% (33 to 56)</td>
<td>12% 9 (7 to 13)</td>
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<tr>
<td>Dizziness</td>
<td>13% 23% 45% (30 to 56)</td>
<td>10% 10 (8 to 11)</td>
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</table>

Outcomes | SSRI weighted EER (CI) | TCA weighted CER (CI) | RRI (CI) | Weighted NNH (CI) |
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<tbody>
<tr>
<td>Nausea</td>
<td>22% 12% 83% (53 to 119)</td>
<td>10% 11 (8 to 15)</td>
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<tr>
<td>Diarrhoea</td>
<td>13% 5% 130% (17 to 355)</td>
<td>8% 13 (8 to 55)</td>
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<tr>
<td>Anxiety</td>
<td>13% 7% 77% (18 to 161)</td>
<td>6% 16 (10 to 22)</td>
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<tr>
<td>Agitation</td>
<td>14% 8% 66% (6 to 195)</td>
<td>6% 19 (10 to 37)</td>
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<tr>
<td>Insomnia</td>
<td>12% 7% 60% (25 to 105)</td>
<td>5% 22 (15 to 24)</td>
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<tr>
<td>Nervousness</td>
<td>15% 11% 44% (9 to 91)</td>
<td>4% 29 (17 to 91)</td>
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<tr>
<td>Headache</td>
<td>17% 14% 31% (12 to 53)</td>
<td>3% 33 (19 to 12)</td>
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</tbody>
</table>

†SSRI = selective serotonin reuptake inhibitor. Other abbreviations defined in Glossa RRR, RRI, ARR, ARI, NNT, NNH, and CI calculated from data in article.

Conclusion
Selective serotonin reuptake inhibitors do not differ from tricyclic antidepressants in efficacy or completion rate. The question is usually answered by using the proxy measure dropout rates from trials, and this review shows that even when standard SSRI doses are compared with low-dose TCAs, efficacy does not differ. This finding is less surprising than it may seem: the evidence that high doses of TCAs are required is flimsy and based on a handful of small trials. SSRIs are pharmacologically "cleaner" and, therefore, we are often told, have fewer side effects. This systematic review shows that even when standard SSRIs report nausea and anxiety, whereas those on TCAs complain of constipation and dry mouth. SSRIs were associated with greater total number of side effects than TCAs, a finding that may have many interpretations but runs counter to the promotional literature. Which drug is better tolerated? This question is usually swayed by the large difference in adverse events except in adult outpatients who were more likely to drop out on TCA.

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