Antidepressants and their effect on sleep
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CRD summary
This review examined the effect of antidepressants on sleep in depressed patients and others. The authors concluded that the effect of antidepressants on sleep varies between compounds within antidepressant classes, as well as between classes. As a full validity assessment was not carried out, and there were issues with the review methodology, the reliability of this conclusion is not clear.

Authors' objectives
To assess the effects of antidepressants on sleep.

Searching
CINAHL, EMBASE, MEDLINE and PsycINFO were searched from inception to May 2005.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) with a minimum of 5 patients per group, and which were double-blind, were eligible for inclusion in the review. The duration of the included studies ranged from 3 days to 1 year.

Specific interventions included in the review
Studies of antidepressant drugs were eligible for inclusion. Eligible studies used placebo or alternative antidepressants as the comparator interventions. The included studies considered the following classes of antidepressants: tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), selective serotonin re-uptake inhibitors (SSRIs) and others. The individual antidepressants used in the included studies were: amitriptyline, paroxetine, milnacipran, fluoxetine, moclobemide, sertraline, belflostatone, lorazepam, mirtazapine, imipramine, alprazolam, trazodone, femoxetine, maprotiline, fluvoxamine, brofaromine, trimipramine, citalopram, nortriptyline, doxepin, bupropion, tolazolatone, mianserin, nefazodone, dothiepin, zolpedim, buspironote, nomifensine, clobazam, melitracen, flupentixol, maprotiline and venlafaxine.

Participants included in the review
Studies of patients taking antidepressant medications were eligible for inclusion. Both individuals with depression and those being treated for other conditions were eligible for inclusion. The included studies involved healthy volunteers and patients with the following conditions: fibromyalgia, cancer, bruxism, depression, opiate withdrawal, marijuana withdrawal, alcohol dependence, gastric conditions, rheumatism, hip or knee arthroplasty, chronic or severe pain, panic or agoraphobia, insomnia with or without depression, conditions related to geriatric status, and manic depression with psychosis. Both in- and out-patients were included. A number of studies had elderly populations. Both male and female participants were included.

Outcomes assessed in the review
Studies reporting sleep-related outcomes were eligible for inclusion. The included studies reported outcomes such as disturbed sleep, drowsiness, sedation and difficulty waking, alertness, arousal, rapid eye movement (REM) sleep, insomnia, early morning waking, sleep quality, slow-wave sleep, total sleep time, sleep efficiency, sleep latency, waking after sleep onset, and length of such awakenings. Other outcomes, including depression and anxiety, were also reported.

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
Only double-blind RCTs were eligible for inclusion in the review; the authors did not state that they performed a subsequent assessment of validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. For each study, the level of statistical significance of differences between treatments was presented.

Methods of synthesis
How were the studies combined?
The studies were discussed in a lengthy narrative.

How were differences between studies investigated?
The studies were grouped according to the antidepressant drug(s) used and patient group, and differences between the studies were discussed in the narrative synthesis.

Results of the review
A total of 120 studies with over 21,312 participants were included in the review. The sample sizes ranged from 10 to 1,168.

TCAs, MAOIs and SSRIs.
Sedation was reported with all TCAs except desipramine. Insomnia was reported with all TCAs except amitriptyline. With the exception of trimipramine, REM sleep suppression was reported with all TCAs, especially clomipramine.

Insomnia, sedation and REM sleep suppression were all reported with all MAOIs.

Insomnia and REM sleep suppression were reported with all SSRIs.

Other agents.
Insomnia was seen with venlafaxine and moclobemide. REM sleep suppression was found with venlafaxine, trazodone and bupropion. Sedation was reported with mirtazapine, nefazodone, maprotiline, trazodone and mianserin.

Authors’ conclusions
The effect of antidepressants on sleep varies between compounds within antidepressant classes. Differences were found in sedative or alerting effects, measures of sleep, REM sleep and the extent of sleep-related side-effects.

CRD commentary
The review question was reasonably clear although the inclusion criteria for the intervention and participants were broad; this resulted in the inclusion of at least 30 different drugs and a wide variety of participants. The search was adequate, but the authors did not report making attempts to identify unpublished studies, which may increase the possibility that some relevant studies were not included in the review. Only double-blind RCTs were included in the review, but the authors did not report whether they performed an additional validity assessment. The methods used to select studies, assess validity and extract the data were not described, so it is not known whether any efforts were made to reduce reviewer errors and bias.

The decision to combine the studies in a narrative appeared appropriate given the differences among the studies, but the narrative was limited to reporting results for only some studies listed in the tables and there was little attempt at a synthesis of the evidence. Differences among the studies, especially with respect to patient groups, outcome measures and comparator drugs, made interpretation of the evidence difficult. The authors’ conclusions are extremely general in nature and reflect the wide scope of the review. However, given the lack of a full validity assessment, differences
between the studies and the methodological issues discussed above, it is not possible to determine how reliable these conclusions are.

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

The authors did not state any implications for practice or further research.

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