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[Intervention Review]

Antidepressants for insomnia in adults

Hazel Everitt¹, David S Baldwin², Beth Stuart¹, Gosia Lipinska³, Andrew Mayers⁴, Andrea L Malizia⁵, Christopher CF Manson⁶, Sue Wilson⁷

¹Primary Care and Population Sciences, Faculty of Medicine, University of Southampton, Southampton, UK. ²University Department of Psychiatry, Faculty of Medicine, University of Southampton, Southampton, UK. ³UCT Sleep Sciences, Department of Psychology, University of Cape Town, Cape Town, South Africa. ⁴Department of Psychology, Faculty of Science and Technology, Bournemouth University, Poole, UK. ⁵Department of Neurosurgery, The Burden Centre, Frenchay hospital, Bristol, UK. ⁶University Department of Psychiatry, Faculty of Medicine, University of Southampton, Southampton, UK. ⁷Centre for Neuropsychopharmacology, Division of Brain Sciences, Imperial College London, London, UK

Contact: Hazel Everitt, Primary Care and Population Sciences, Faculty of Medicine, University of Southampton, Aldermoor Health Centre, Aldermoor Close, Southampton, SO16 5ST, UK. h.a.everitt@soton.ac.uk.

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ABSTRACT

Background

Insomnia disorder is a subjective condition of unsatisfactory sleep (e.g. sleep onset, maintenance, early waking, impairment of daytime functioning). Insomnia disorder impairs quality of life and is associated with an increased risk of physical and mental health problems including anxiety, depression, drug and alcohol abuse, and increased health service use. hypnotic medications (e.g. benzodiazepines and 'Z' drugs) are licensed for sleep promotion, but can induce tolerance and dependence, although many people remain on long-term treatment. Antidepressant use for insomnia is widespread, but none is licensed for insomnia and the evidence for their efficacy is unclear. This use of unlicensed medications may be driven by concern over longer-term use of hypnotics and the limited availability of psychological treatments.

Objectives

To assess the effectiveness, safety and tolerability of antidepressants for insomnia in adults.

Search methods

This review incorporated the results of searches to July 2015 conducted on electronic bibliographic databases: the Cochrane Central Register of Controlled Trials (CENTRAL, 2015, Issue 6), MEDLINE (1950 to 2015), Embase (1980 to 2015) and PsycINFO (1806 to 2015). We updated the searches to December 2017, but these results have not yet been incorporated into the review.

Selection criteria

Randomised controlled trials (RCTs) of adults (aged 18 years or older) with a primary diagnosis of insomnia and all participant types including people with comorbidities. Any antidepressant as monotherapy at any dose whether compared with placebo, other medications for insomnia (e.g. benzodiazepines and 'Z' drugs), a different antidepressant, waiting list control or treatment as usual.

Data collection and analysis

Two review authors independently assessed trials for eligibility and extracted data using a data extraction form. A third review author resolved disagreements on inclusion or data extraction.



Main results

The search identified 23 RCTs (2806 participants).

Selective serotonin reuptake inhibitors (SSRIs) compared with placebo: three studies (135 participants) compared SSRIs with placebo. Combining results was not possible. Two paroxetine studies showed significant improvements in subjective sleep measures at six (60 participants, P = 0.03) and 12 weeks (27 participants, P < 0.001). There was no difference in the fluoxetine study (low quality evidence).

There were either no adverse events or they were not reported (very low quality evidence).

Tricyclic antidepressants (TCA) compared with placebo: six studies (812 participants) compared TCA with placebo; five used doxepin and one used trimipramine. We found no studies of amitriptyline. Four studies (518 participants) could be pooled, showing a moderate improvement in subjective sleep quality over placebo (standardised mean difference (SMD) -0.39, 95% confidence interval (CI) -0.56 to -0.21) (moderate quality evidence). Moderate quality evidence suggested that TCAs possibly improved sleep efficiency (mean difference (MD) 6.29 percentage points, 95% CI 3.17 to 9.41; 4 studies; 510 participants) and increased sleep time (MD 22.88 minutes, 95% CI 13.17 to 32.59; 4 studies; 510 participants). There may have been little or no impact on sleep latency (MD -4.27 minutes, 95% CI -9.01 to 0.48; 4 studies; 510 participants).

There may have been little or no difference in adverse events between TCAs and placebo (risk ratio (RR) 1.02, 95% CI 0.86 to 1.21; 6 studies; 812 participants) (low quality evidence).

'Other' antidepressants with placebo: eight studies compared other antidepressants with placebo (one used mianserin and seven used trazodone). Three studies (370 participants) of trazodone could be pooled, indicating a moderate improvement in subjective sleep outcomes over placebo (SMD -0.34, 95% CI -0.66 to -0.02). Two studies of trazodone measured polysomnography and found little or no difference in sleep efficiency (MD 1.38 percentage points, 95% CI -2.87 to 5.63; 169 participants) (low quality evidence).

There was low quality evidence from two studies of more adverse effects with trazodone than placebo (i.e. morning grogginess, increased dry mouth and thirst).

Authors' conclusions

We identified relatively few, mostly small studies with short-term follow-up and design limitations. The effects of SSRIs compared with placebo are uncertain with too few studies to draw clear conclusions. There may be a small improvement in sleep quality with short-term use of low-dose doxepin and trazodone compared with placebo. The tolerability and safety of antidepressants for insomnia is uncertain due to limited reporting of adverse events. There was no evidence for amitriptyline (despite common use in clinical practice) or for long-term antidepressant use for insomnia. High-quality trials of antidepressants for insomnia are needed.

PLAIN LANGUAGE SUMMARY

Antidepressants for insomnia

Why is this review important?

Insomnia (having difficulty falling or staying asleep) is common, approximately one in five people report sleep problems in the preceeding year. Insomnia can cause daytime fatigue, distress, impairment of daytime functioning and reduced quality of life. It is associated with increased mental health problems, drug and alcohol abuse, and increased healthcare use. Management depends on the duration and nature of the sleep problem. It may involve: treating coexisting medical problems; providing advice on sleep habits and lifestyle (known as sleep hygiene); medicines and psychological therapies such as cognitive behavioural therapy (CBT, which is a talking therapy).

Medicines called hypnotics (for example, temazepam and 'Z' drugs) are most commonly used to treat insomnia and are known to help sleep, but can have problems such as tolerance (needing to take more of the medicine to get the same effect) and dependence (physical or mental problems if the medicine is stopped). Guidelines recommend only short-term use of hypnotics (two to four weeks). However, millions of people worldwide take long-term hypnotic medicines.

Antidepressants are widely prescribed for insomnia despite not being licensed for this use, and uncertain evidence for their effectiveness. This may be because of the concerns regarding hypnotic medicines. Psychological treatments such as CBT are known to help insomnia, but availability is limited. Thus, alternative medicines, such as antidepressants (used to treat depression) and antihistamines (used to treat allergies), are sometimes tried. Assessing the evidence for the unlicensed use of these medicines is important.

Who will be interested in this review?

People with sleep problems and their doctors will be interested in this review to better understand the research evidence and enable informed decision-making regarding using antidepressants for insomnia.

What questions did this review aim to answer?



The aim was to find out how well antidepressants work in treating insomnia in adults, how safe they are and if they have any side effects.

Which studies did we include in the review?

We included randomised controlled trials (clinical studies where people were randomly put into one of two or more treatment groups; these trials provide the most reliable and highest quality evidence) of adults with an insomnia diagnosis. People could have had other conditions (comorbidities) in addition to insomnia. We included any dose of antidepressant (but not combinations with another antidepressant) compared with placebo (pretend treatment), other medicines for insomnia (e.g. benzodiazepines or 'Z' drugs), a different antidepressant, waiting list control or 'treatment as usual.'

What did the evidence from the review tell us?

We reviewed 23 studies with 2806 people with insomnia. Overall, the quality of the evidence was low due to a small number of people in the studies, and problems with how the studies were undertaken and reported. We often could not combine the individual study results. There was low quality evidence to support short-term (i.e. weeks rather than months) use for some antidepressants. There was no evidence for the antidepressant amitriptyline, which is commonly used in clinical practice, or to support long-term antidepressant use for insomnia. The evidence did not support the clinical current practice of prescribing antidepressants for insomnia.

What should happen next?

High quality trials of antidepressants for insomnia are needed to provide better evidence to inform clinical practice. Additionally, health professionals and patients should be made aware of the current paucity of evidence for antidepressants commonly used for insomnia management.