Effect of ropinirole on sleep outcomes in patients with restless legs syndrome: meta-analysis of pooled individual patient data from randomized controlled trials

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CRD summary
This review concluded that ropinirole improved sleep quantity and adequacy and lessened sleep disturbance and daytime somnolence in patients with moderate to severe primary restless leg syndrome. The authors acknowledged a number of limitations of their review and the conclusions should be treated with some caution.

Authors' objectives
To evaluate the effect of ropinirole compared with placebo on sleep in patients with restless legs syndrome.

Searching
MEDLINE, ClinicalTrials.gov and the global clinical trials register of GlaxoSmithKline Inc. were searched between 1980 and January 2007; search terms were not reported.

Study selection
Randomised controlled trials (RCTs) that evaluated the impact of ropinirole on sleep in patients with restless legs syndrome compared to placebo were eligible for inclusion. Included studies had to use the Medical Outcomes Study (MOS) sleep scale over at least 12 weeks or the Clinical Global Impression-Improvement (CGI-I) scale to assess sleep outcomes. Studies designed to assess maintenance treatment or long-term safety were excluded. Studies where ropinirole was an adjunct treatment were excluded.

Included studies were restricted to those of moderate to very severe primary restless leg syndrome requiring treatment only at night. Mean age of participants was approximately 54 years. The proportion of males was 37%. Most participants reported risk factors for sleep disturbance (alcohol use, caffeine use, comorbid conditions and concomitant drugs). Most participants were recruited in USA and UK.

The authors did not state how many reviewers performed the study selection.

Assessment of study quality
Only double-blinded RCTs were included in the review; the authors did not report that they used a systematic quality assessment or checked the integrity of individual patient data (IPD).

Data extraction
Individual patient data were obtained for eligible RCTs. The review concentrated on four of the six domains of the MOS sleep scale (quantity, adequacy, disturbance of sleep and daytime somnolence); three of these were converted to a scale from zero to 100. CGI-I was considered a secondary outcome. Mean changes from baseline in sleep scores were calculated. Last observation carried forward was used if patients did not complete 12 week assessments.

The authors did not report how many reviewers performed data extraction.

Methods of synthesis
For primary analysis of MOS sleep domains, a mixed-effects analysis of covariance was used. For secondary analysis of the proportion of patients classified as responders (CGI-I), logistic regression was used. Changes in sleep duration from baseline at 12 weeks between ropinirole and placebo were calculated along with 98.75% confidence intervals (CI) for intention to treat (ITT) and per protocol populations. Age, gender and concomitant conditions were controlled for in the analyses. Changes in sleep scale scores and the proportion of patients rated as responders on the CGI-I scale, along with adjusted odds ratio and 95% CI, were reported.
Results of the review
Six trials met the inclusion criteria (n=1,679 participants, range 73 to 381).

Improvement in sleep at 12 weeks was 41 minutes per night for ropinirole and 22 minutes per night for placebo (p<0.001). Compared to baseline, ropinirole resulted in a 21% greater increase in sleep adequacy scores, 14% less sleep disturbance and 8% less daytime somnolence than placebo. On the CGI-I scale, 62.8% of patients who received ropinirole were rated responders compared to 47.4% of patients who received placebo (adjusted odds ratio 1.88, 95% CI 1.52 to 2.31).

Authors’ conclusions
Ropinirole improved sleep quantity and adequacy and lessened sleep disturbance and daytime somnolence in patients with moderate to severe primary restless leg syndrome.

CRD commentary
The review addressed a clear review question supported by appropriate inclusion criteria. The search was limited and studies may have been missed. Attempts were made to identify unpublished/ongoing trials in order to reduce publication bias. It was unclear whether language restrictions were applied and language bias could not be ruled out. Methods used to select studies were not reported and bias could not be ruled out. Individual patient data were obtained, but no checking and validation of the integrity of the data was reported. The manufacturer of ropinirole provided funding to the centre that undertook the review.

The authors acknowledged a number of limitations of their review and their conclusions should be treated with some caution.

Implications of the review for practice and research
The authors did not state implications for practice and research.

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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.