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Pharmacologic and hormonal treatments for menopausal sleep disturbances: A network meta-analysis of 43 randomized controlled trials and 32,271 menopausal women

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Background
Sleep problems are common among menopausal women. This network meta-analysis aimed at investigating efficacy and tolerability of pharmacologic/hormonal interventions for menopausal sleep disturbances.

Aims & Objectives
The current network meta-analysis had been published on Sleep Med Rev. 2021 Jun;57:101469. In brief, this network meta-analysis aimed at investigating efficacy/tolerability of pharmacologic/hormonal interventions for menopausal sleep disturbances. Major databases were searched for randomized controlled trials (RCTs) examining pharmacologic or hormonal interventions with either placebo or active controlled designs.

Methods
Primary outcomes were improvements in sleep disturbance severity/tolerability reflected by overall dropout rates, whereas secondary outcome was discontinuation rates from adverse events.

Results
Analysis of 43 RCTs with 25 treatment arms involving 32,271 women during or after menopausal transition (age: 61.24±4.23, duration: 90.83±66.29 weeks) showed therapeutic benefit of melatonin-fluoxetine [SMD=-2.47 (95% CI:-4.19–-0.74)] for sleep disturbances in this population compared to that of placebo. Subgroup analysis of 15 RCTs on vasomotor symptoms demonstrated superior benefits of gabapentin [SMD=-1.04 (95% CI:-1.90–-0.18)], oral combined hormone therapy [SMD=-0.62 (95% CI:-1.06–-0.18)], and bazedoxifene-conjugated estrogens [SMD=-0.50 (95% CI:-0.96–-0.04)] to placebo/control. Although our study also showed therapeutic benefits of raloxifene-only [SMD=-1.86 (95% CI:-3.09–-0.63)] and raloxifene-oral estrogen [SMD=-2.64 (95% CI:-4.64–-0.63)], the results were only from two studies in which the former focused on patients with fibromyalgia; therefore, these findings should be judiciously interpreted. Dropout rates were comparable between interventions and placebo/control. Raloxifene-only was associated with the lowest dropout rate [RR=0.32 (95% CI:0.03–3.52)], whereas eszopiclone [RR=3.84 (95% CI:1.14–12.87)] and oral combined hormone therapy [RR=2.51 (95% CI:1.04–6.07)] were associated with higher rates of adverse event-related discontinuation.

Discussion & Conclusion
The results support combined estrogen-progesterone therapy for menopausal sleep disturbances associated with vasomotor symptoms but showed no significant effects of hypnotics in this clinical setting.