Review: Sedative–hypnotics increase adverse effects more than they improve sleep quality in older persons with insomnia

Glass J, Lanctôt KL, Herrmann N, Sproule BA, Busto UE. **Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits.** BMJ. 2005;331:1169.

Clinical impact ratings: Mental Health ★★★★★☆☆ GIM/FP/GP ★★★★★☆☆ Geriatrics ★★★★★★☆

QUESTION

In older persons with insomnia, what are the benefits and risks of short-term use of sedative–hypnotics?

METHODS

Data sources: MEDLINE, EMBASE/Excerpta Medica, Cochrane Central Register of Controlled Trials, and PsycLIT (1966 to 2003); bibliographies of published reviews; and 3 manufacturers of sedative–hypnotics (unpublished studies).

Study selection and assessment: English-language randomized controlled trials (RCTs) that compared treatment with sedative–hypnotics (prescription or over-the-counter drugs) for ≥ 5 consecutive nights with placebo or another active treatment in persons ≥ 60 years of age who met predetermined criteria for insomnia. Studies excluded patients with psychiatric disorders or severe or acute physical illness that could disrupt sleep, ensured that participants were cognitively able to complete the subjective outcome assessment, and included a washout period between drug treatments. Studies of barbiturates or chloral hydrate or derivatives were excluded. 24 RCTs (n = 2417, age range 56 to 98 y) met the selection criteria and had extractable data. Individual study quality was assessed using the Jadad criteria. 15 RCTs had quality scores ≥ 4 out of 6.

Outcomes: Perceived change in sleep quality, sleep onset latency, total sleep time, number of night awakenings, and adverse events (cognitive, psychomotor, and morning hangover).

MAIN RESULTS

{Mean duration of treatment was 2.2 weeks.}* Meta-analysis showed that participants who received sedatives had slightly better sleep quality, longer total sleep time, and fewer night awakenings than did those who received placebo (Table); results were similar when benzodiazepines only were compared with placebo. Funnel plot analyses suggested possible publication bias favoring positive results for sleep quality and total sleep time ($P \leq 0.05$). Participants who received sedatives had higher risk for cognitive adverse events (Table) and reported more morning or daytime fatigue than did those who received placebo (7 RCTs, n = 829; odds ratio 3.8, 95% CI 1.9 to 7.8) but groups did not differ for psychomotor adverse events (Table). Meta-analysis of 4 trials (n = 1072) showed that 13 patients (CI 7 to 63) would need to be treated with a sedative for 1 additional patient to have an improvement in sleep quality. Meta-analysis of 16 trials (n = 2220) showed that 6 patients (CI 5 to 8) would need to be treated for 1 additional patient to have an adverse effect.

CONCLUSION

In older persons with insomnia, short-term treatment with sedative–hypnotics is twice as likely to produce an adverse effect as improve the quality of sleep.

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*Calculated from data in article.

Sedative–hypnotics vs placebo in older persons with insomnia†

Outcomes	Number of trials (n)	Mean effect size (95% CI)			
Sleep quality	8 (719)	0.14 (0.05 to 0.23)			
Amount of sleep (min)	8 (601)	25 (13 to 38)			
Number of night awakenings	6 (441)	–0.63 (–0.48 to –0.77)			
		Weighted event rates		RRI (CI)	NNH (CI)
		Any sedative	Placebo		
Cognitive adverse effects	10 (712)	3.9%	0.8%	363% (46 to 1281)	34 (10 to 259)
Psychomotor adverse effects	13 (1016)	5.5%	2.5%	118% (–7 to 387)	Not significant

†Abbreviations defined in Glossary; weighted event rates, RRI, NNH, and CI calculated from control event rate and odds ratios reported in article. Analyses based on a random-effects model.

COMMENTARY

The systematic review by Glass and colleagues confirms existing concerns about the dangers of sedative–hypnotic use in older persons, especially benzodiazepines and benzodiazepine-receptor agonists. Older patients were almost twice as likely to have an adverse effect as to have enjoyed improved sleep. This is probably an underestimate of the risk–benefit ratio, as almost all cited trials were industry sponsored, suggesting the possibility of publication bias in the direction of favorable trials.

Why then are benzodiazepines so widely prescribed? First, sleep disorders are common in older persons. Second, drugs and medical conditions (e.g., pain and urinary dysfunction) can interfere with sleep. Without treatment of the underlying problem, hypnotics cannot usually overcome these symptoms and can produce substantial side effects. Given that many patients and physicians look for pharmacologic solutions, there is pressure to prescribe something, even a medication known to have minimal effect. Finally, patients can become dependent on sedatives, often beginning in hospital.

Most trials used self-reported sleep rather than the more accurate measures available in sleep laboratories. Because formal sleep studies suggest that patients sleep better than they actually report (1), more accurate methods may give us better risk–benefit estimates, but will probably still indicate more risk than benefit.

What other tools do we have? Physicians need to discuss reasonable expectations for sleep duration and quality. Encouragement of exercise, proper sleep hygiene, and the treatment of underlying disorders may partially contribute to improved sleep quality. Recent studies have shown that such psychological interventions as stimulus control and sleep restriction provide reliable and durable changes in sleep patterns (2).

Chronically disturbed sleep for older persons is a complex issue and will not be solved by ingestion of a pill, at least not at present. Physicians should be encouraged to think long and hard before initiating such medications and to develop benzodiazepine discontinuation protocols (3).

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