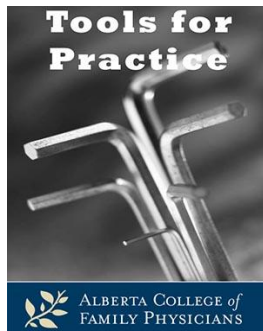


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Z-drugs for sleep: Should we “Catch Some Z’s”?

Clinical Question: Are Z-drugs (zopiclone, zolpidem, and eszopiclone) safe and effective in insomnia?

Bottom-line: Z-drugs help people fall asleep faster (~13-22 minutes) and perhaps get ~5% more time sleeping while in bed. Z-drugs may increase the risk of mild infections (one in 43 patients) and have some inconsistent cognitive effects like reduced verbal memory or attention.

Evidence:

- Seven systematic reviews¹⁻⁷ (with duplicate publications⁴⁻⁷), including 3-48 randomized controlled trials (RCTs) (96-10,926 patients). Some focused primarily on benzodiazepine (with Z-drugs secondarily considered).^{1,2} Compared to placebo, Z-drugs significantly affected:
 - Falling asleep faster: ~13-22 minutes.³⁻⁵
 - Total sleep time: Not statistically different³⁻⁵ except by patient diary, 32 minutes more.^{4,5}
 - Perceived sleep quality: No difference in two meta-analyses.^{1,3} Another showed “moderate” improvement (standard mean difference 0.48).⁴
 - Time asleep while in bed: no difference³ or improved ~5%.^{4,5}
 - Limitations: Not all outcomes evaluated in all reviews, short duration (example mean 34 days³), used multiple comparisons, funded by manufacturers or funding source not reported,^{5,7} and possible publication bias.¹
- Adverse effects:
 - Meta-analysis of 20 RCTs (367 patients, mean age 37) found no significant effects on speed of processing, working/verbal memory or attention nine hours after drug administration compared to “control” except for:
 - “Moderate” negative effects (effect sizes 0.42-0.56) on verbal memory (zopiclone and zolpidem) and attention (zolpidem).⁸
 - Meta-analysis of 36 placebo-controlled RCTs (13,211 patients) found significantly increased infections (6.9% vs. 4.6%, number needed to harm 43 over 36 days). Most infections likely mild (example pharyngitis).⁹
 - Z-drugs (and other sedative-hypnotics) have been associated with increased mortality in some,^{10,11} but not all,^{12,13} cohort studies.

- Numerous potential confounders (like Z-drug patients sicker) and causation unproven.

Context:

- Compared to benzodiazepines, there is no difference in time to fall asleep,^{2,6} sleep quality^{1,6} or adverse events.¹ Total sleep time may be better with benzodiazepines (23 minutes).²
- Guidelines recommend zopiclone for short-term (<7 consecutive nights) or long-term (<3 nights/week) as an adjunct to cognitive and behavioural therapies.¹⁴

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Disclosures:

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