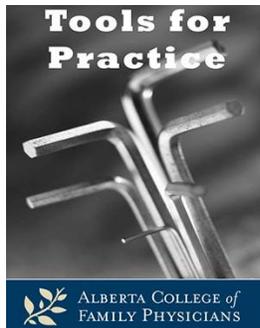


Tools for Practice is proudly sponsored by the Alberta College of Family Physicians (ACFP). ACFP is a provincial, professional voluntary organization, representing more than 4,000 family physicians, family medicine residents and medical students in Alberta. Established over fifty years ago, the ACFP strives for excellence in family practice through advocacy, continuing medical education and primary care research. www.acfp.ca

November 24, 2014



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 benzodiazepines (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

Authors:

Adrienne J Lindblad BSP ACPR PharmD, G Michael Allan MD CCFP

Disclosures:

Authors do not have any conflicts to disclose.

References:

1. Glass J, Lanctôt KL, Herrmann N, *et al.* BMJ. 2005 Nov 19; 331(7526):1169.
2. Holbrook AM, Crowther R, Lotter A, *et al.* CMAJ. 2000 Jan 25; 162(2):225-33.
3. Huedo-Medina TB, Kirsch I, Middlemass J, *et al.* BMJ. 2012 Dec 17; 345:e8343.
4. Buscemi N, Vandermeer B, Friesen C, *et al.* Evid Rep Technol Assess (Summ). 2005 Jun; (125):1-10.
5. Buscemi N, Vandermeer B, Friesen C, *et al.* J Gen Intern Med. 2007 Sep; 22(9):1335-50.
6. Dündar Y, Boland A, Strobl J, *et al.* Health Technol Assess. 2004 Jun; 8(24):iii-x, 1-125.
7. Dündar Y, Dodd S, Strobl J, *et al.* Hum Psychopharmacol. 2004 Jul; 19(5):305-22.
8. Stranks EK, Crowe SF. J Clin Exp Neuropsych. 2014 Sep; 36(7): 691-700.
9. Joya FL, Kripke DF, Loving RT, *et al.* J Clin Sleep Med. 2009; 5(4):377-83.
10. Weich S, Pearce HL, Croft P, *et al.* BMJ. 2014 Mar 19; 348:g1996.
11. Kripke DF, Langer RD, Kline LE. BMJ Open. 2012 Feb 27; 2(1):e000850.
12. Gisev N, Hartikainen S, Chen TF, *et al.* Can J Psychiatry. 2011 Jun; 56(6):377-81.
13. Jaussent I, Ancelin ML, Berr C, *et al.* BMC Med. 2013 Sep 26; 11:212.
14. Towards Optimized Practice. Adult Insomnia: Diagnosis to management. Available for download at: http://www.topalbertadoctors.org/download/439/insomnia_management_guideline.pdf. Accessed July 3, 2014.

Tools for Practice is a biweekly article summarizing medical evidence with a focus on topical issues and practice modifying information. It is coordinated by G. Michael Allan, MD, CCFP and the content is written by practicing family physicians who are joined occasionally by a health professional from another medical specialty or health discipline. Each article is peer-reviewed, ensuring it maintains a high standard of quality, accuracy, and academic integrity.

The ACFP has supported the publishing and distribution of the Tools for Practice library since 2009. If you are not a member of the ACFP and would like to receive the TFP emails, please sign up for the distribution list at <http://bit.ly/signupfortfp>. Archived articles are available at no extra cost on the [ACFP website](#).

You can now earn credits on Tools for Practice! In August 2014, the ACFP launched [GoMainpro, an online accreditation tool](#) to help facilitate MAINPRO® accreditation for the ACFP's Tools for Practice library which has been accredited for Mainpro-M1 credits by the College of Family Physicians of Canada (CFPC). The combination of the CFPC's Direct Entry Program and GoMainpro's tracking and reporting features provide an easy and convenient way to earn Mainpro-M1 credits.

This communication reflects the opinion of the authors and does not necessarily mirror the perspective and policy of the Alberta College of Family Physicians.