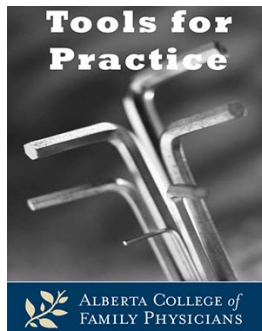


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Benzodiazepines in Generalized Anxiety Disorder: Calm Your Nerves?

Clinical Question: Are benzodiazepines effective in generalized anxiety disorder (GAD)?

Bottom-Line: In GAD, benzodiazepines are more effective than placebo and similar to antidepressants. They cause more withdrawals for adverse effects than placebo but less than antidepressants. They are recommended second-line generally due to concerns of dependence. The evidence quality is generally poor, trials are short-term, and none used benzodiazepines as adjunctive therapy.

Evidence:

- Compared to placebo:
 - Systematic review (23 Randomized Controlled Trials (RCTs), 2,326 patients) of diazepam, lorazepam, and alprazolam:¹
 - Fewer withdrawals for no efficacy with benzodiazepines: RR 0.29 (0.18-0.45).
 - Number Needed to Treat=7 over 4-6 weeks.^{2,3}
 - More withdrawals for adverse effects: RR 1.54 (1.17-2.03).
 - Other systematic reviews found benzodiazepines more effective than placebo.^{4,5}
- Compared to tricyclic antidepressants:
 - One systematic review (three RCTs, 617 participants):⁶
 - Two RCTs found tricyclics better for psychiatric symptoms, while one found benzodiazepines better for somatic symptoms (another found no difference in somatic symptoms).
 - Another RCT found no difference in efficacy.
 - Two RCTs found benzodiazepines had fewer adverse effects (one no difference).
- Compared to paroxetine or venlafaxine:
 - One systematic review (two RCTs, 709 participants):⁶ No difference in efficacy.
 - Adverse Effects: Venlafaxine had more drop-outs for adverse effects than diazepam (9-13% versus 2%, Number Needed to Harm=9-14 over eight weeks).⁷ Adverse effects not reported in paroxetine study.⁸
- As adjunct to antidepressants: No RCTs found.

Context:

- Many studies conducted by manufacturers; small sample sizes, short-term (often ≤8weeks); data on randomization, blinding procedures and randomization concealment often not described; most studies involved middle-aged adults, limiting application to others.
- Rather than titrating to effect or as needed use, many studies used fixed doses of benzodiazepines with wide dosing ranges (example: alprazolam 2-6 mg/day in divided doses).^{1-3,6}
- Benzodiazepines may have effects on cognition, performance and dependence,⁴ although the magnitude of these effects are not well understood.
- Adjunctive benzodiazepines use is supported by evidence in early panic disorders.^{9,10}
- Onset of effect is more rapid with benzodiazepines than antidepressants.⁸
- Guidelines suggest benzodiazepines are second-line in GAD.¹¹

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Disclosure:

Authors do not have any conflicts to disclose.

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