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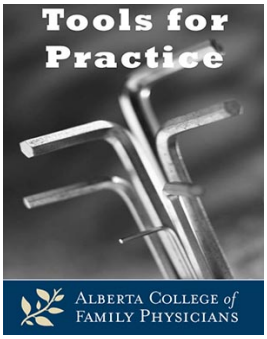

Agitation in Dementia: Are benzos a back-up?

Clinical Question: Are benzodiazepines a reasonable pharmaceutical alternative for management of agitation in demented elders?

Bottom-Line: Many trials are old, most are short and/or small, and the results are inconsistent. Benzodiazepines appear, at best, equivalent to antipsychotics in reducing agitation in the short-term, but superior to placebo. If used, they should be stopped as soon as possible due to potential harms.

Evidence:

- Eight randomized controlled trials (RCTs) comparing benzodiazepines to antipsychotics, placebo, or other drugs:
  - Diazepam vs. thioridazine: Thioridazine statistically better.[1]
    - Nurses rating of improvement: 70% thioridazine vs. 15% diazepam. Number Needed to Treat (NNT)=2.
  - Oxazepam vs. haloperidol vs. diphenhydramine:[2] No statistical difference but oxazepam worse behavioural scores.
  - Alprazolam vs. haloperidol:[3] Both treatments worse than baseline but no statistical difference.
  - Lorazepam vs. olanzapine vs. placebo:[4] Lorazepam 1 mg similar to olanzapine (5 mg and 2.5 mg), and all better than placebo.
    - 40% improved PANSS-EC (measures agitation) at two hours: Lorazepam 72%, olanzapine 62-67%, placebo 37%. Lorazepam NNT=3.
  - Diazepam vs. thioridazine vs placebo:[5] Diazepam worse than thioridazine but better than placebo on some scales.
    - One point improvement on one anxiety scale: 65% Diazepam, 77% thioridazine, 42% placebo.
  - Oxazepam vs. placebo:[6] Oxazepam better.
    - "Moderate improvement" clinical response: Oxazepam NNT=2.
  - Oxazepam vs. placebo:[7] Oxazepam better.
    - "Slight improvement" or better clinical response: Oxazepam NNT=5.
  - Temazepam vs. lorazepam:[8] No statistical difference.

- Limitations:[1-8] Poor description of methods (randomization unclear, etc.), most short (one day to 12 weeks), small (most ≤100 patients), many >25% loss to follow-up, many industry-funded or unclear, etc.
- Harms: Poor reporting of harms. Mild-moderate sedation: Lorazepam (10.3%) vs. olanzapine 5 mg (4.2%) vs. olanzapine 2.5 mg (3%), placebo (3%).[4]

Context:

- Agitation or behavioural issues are very common (up to 75%) in nursing home patients.[9]
- Benzodiazepines are associated with adverse events like falls (57% relative increase) and fractures (34% relative increase). Other medicines, like antidepressants/antipsychotics, are associated with similar risks of these adverse events.[10,11]
- Guidelines for agitation in dementia vary:[9]
  - Some (example British Columbia) discourage benzodiazepines because of adverse events.
  - Others (example American Psychiatric Association and NICE-UK) suggest considering short-acting benzodiazepines as needed for infrequent agitation.

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Disclosure:
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