Antipsychotics for agitation in dementia

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Clinical question

What are the benefits and harms of antipsychotics for agitation in dementia?

Bottom line

Antipsychotics provide little improvement over placebo on agitation scales. However, a 50% improvement in behaviour occurs in about 46% of those taking antipsychotics versus about 33% taking placebo. Harms are serious (eg, 1 increased death in 80 over 3 months) and common. Antipsychotics should be reserved for severe aggression, and withdrawal should be attempted as soon as possible.

Evidence

Evidence includes 6 systematic reviews (5 to 16 RCTs of 856 to 5110 patients that lasted 10 to 12 weeks).[1-6] Results are statistically significant unless indicated otherwise.

- Placebo had large effects (eg, 11-point increase on a 144-point scale—a clinically meaningful difference).[7]
- Studies of atypical antipsychotics revealed the following:
  -Mean improvement on multiple scales was trivial (eg, 3 on a 144-point scale [not likely clinically meaningful]).[1-3]
  -Individual antipsychotics had generally similar results.[2,5]
  -Some patients attained 50% improvement on scales (eg, 46% with risperidone vs 33% with placebo, number needed to treat [NNT] = 8).[4]
  -Harms included stopping owing to adverse events (number needed to harm [NNH] = 13 to 39).[2] Serious harms included death (NNH = 77 to 84)[1,4] and cerebrovascular events (NNH = 48 to 104).[1,2,4]
  -Mini-Mental State Examination score was 0.73 points worse (statistically, not clinically, significant).[4]
  -Other harms were somnolence (NNH = 7 to 11), gait abnormalities (NNH = 11 to 20), extrapyramidal symptoms (NNH = 16 to 44), and peripheral edema (NNH = 20 to 25).[1,2,4]
- First-generation antipsychotics (eg, haloperidol) appear to have similar rates of harms but inconsistent benefits.[6]

Context

- Cholinesterase inhibitors, selective serotonin reuptake inhibitors, trazodone, and valproate provide no meaningful improvement in agitation.[8-11]
  -Benzodiazepines might approach antipsychotics in efficacy for agitation but also have harms.[12]
- Stopping antipsychotics might reduce death (NNT = 4 at 2 years) with little effect on neuropsychiatric symptoms.[13]

Implementation

Medical, psychological, and environmental triggers should be assessed and targeted in patients with agitation.[14] Pain is a common cause of agitation in dementia, occurring in 57% of patients, and pain resolution can improve agitation.[15] A 3 *R*s approach (repeat, reassure, redirect) is recommended.[14] In severe aggression that threatens the safety of the patient or others, use atypical antipsychotics to target symptoms without sedating the patient.[16] The lowest effective dose should be used for the shortest time. A deprescribing algorithm is available.[16]

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Competing interests
None declared

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