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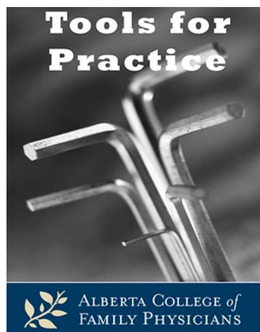

Atypical antipsychotics for anxiety: Worth worrying about?

Clinical Question: Are atypical antipsychotics (alone or added to antidepressants) effective in managing anxiety disorders?

Bottom Line: Atypical antipsychotics have similar efficacy to antidepressants in generalized anxiety disorder (GAD), but are more poorly tolerated and do not improve response rates when added to antidepressants. In obsessive-compulsive disorder (OCD), approximately one in 4-8 people will have a response when antipsychotics are added to antidepressants, while one in nine will stop due to adverse effects.

Evidence:

- All included results statistically significant unless mentioned.
  - GAD: Highest quality systematic review of nine randomized controlled trials (RCTs) (4,387 patients).[1]
    - Quetiapine versus placebo (four RCTs, 2,262 patients):
      - Response: Number Needed to Treat (NNT)=6. Inconsistent results.
      - Remission: NNT=10. Inconsistent results.
      - Withdrawal due to adverse events: Number Needed to Harm (NNH)=9.
    - Quetiapine versus antidepressants (two RCTs, 858 patients):
      - Similar efficacy but quetiapine more withdrawal due to adverse effects NNH=11.
    - Quetiapine (one RCT, 22 patients), risperidone (two RCTs, 457 patients), or olanzapine (one RCT, 24 patients) versus placebo added to antidepressants:
      - No differences except olanzapine one improved anxiety rating.
  - OCD: Highest quality systematic review of 11 RCTs (396 patients):[2]
    - Antipsychotic versus placebo added to antidepressants:
      - Olanzapine: Not different.
      - Quetiapine: Response NNT=8 (borderline significance p=0.07).
        - Stopping early due to adverse effects NNH=9 over 12 weeks.
      - Risperidone: Response NNT=4.
        - No difference in stopping early for adverse effects.
    - No RCTs versus placebo or antidepressants.

- Other reviews found similar results.[3-10] Aripiprazole may be beneficial in OCD, based on two RCTs (79 patients).[7]
- Limitations: Short-term (≤16 weeks); all manufacturer-sponsored, often small sample sizes, unclear randomization and blinding procedures in most studies.[1,2]

Context:

- No evidence for panic and too little evidence (two RCTs, 27 patients) for social phobia.[1]
- NNT~5-6 over 10-13 weeks for response from antidepressants in GAD and OCD.[11,12]
- For depression, atypical antipsychotics have stronger evidence for augmentation of antidepressants than therapy alone.[13]
- Canadian guidelines recommend atypical antipsychotics typically 3rd line (alone or adjunct) for most anxiety disorders, with risperidone and aripiprazole 1st line adjuncts in OCD.[14]

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