Psychopharmacology Algorithm for Management of Generalized Anxiety Disorder

ABSTRACT

Background: This is a 2014 revision of previous algorithms for the psychopharmacology of generalized anxiety disorder (GAD) under the auspices of the Psychopharmacology Algorithm Project at the Harvard South Shore Program. It differs from previous versions of GAD algorithms in proposing alternatives to SSRIs and SNRIs for GAD in the event of inadequate response or unacceptable side effects.

Methods: Previous algorithms and associated references were evaluated. Studies and reviews published from 2008-2013 were obtained from PubMed and reviewed with a focus on their potential to justify changes in the recommendations of prior algorithms. Exceptions to the main algorithm for special patient populations, such as women of childbearing potential and pregnant women, adolescents, the elderly, and those with common medical and psychiatric comorbidities were considered. Efficacy and tolerability in both acute and maintenance management were the basis for prioritizing treatments. If efficacy, tolerability, and safety were comparable, then costs were considered.

Results: SSRIs titrated to their therapeutic doses is still the first-line medication for GAD with maintenance for 12 months if response is satisfactory. If response is inadequate, then the recommendation is to try a different SSRI. An alternative is benzodiazepine for selected patients or bupropion. Gabapentin may be considered despite minimal evidence and the absence of efficacy evaluations as it is very similar to pregabalin, which has undergone many clinical trials and has been approved in Europe for GAD, though it is not FDA-approved in the United States for this indication. However, despite their similarities, gabapentin is not a scheduled drug, has a more favorable safety profile, and is more affordable than pregabalin. If there is an unsatisfactory response to the second SSRI, then the recommendation is an SNRI. For patients with a partial response after an SSRI trial, then the recommendation is to consider augmenting with hydroxyzine or buspirone, although consideration may also be given to gabapentin. Other alternatives to SSRIs and SNRIs include hydroxyzine or a TCA, mirtazapine or quetiapine if weight gain is not a concern, and a benzodiazepine if no history of substance use. Treatment-resistant patients may be tried on newer alternative approaches like kava or agomelatine, the latter not available in the United States.

Conclusions: This 2014 revision of the GAD algorithm responds to issues raised by new treatments under development such as pregabalin and organizes the evidence systematically for practical clinical application.

Psychopharmacology Algorithm for Generalized Anxiety Disorder

1. Met criteria for DSM 5 diagnosis of GAD
2. Evaluate
3. Had adequate trial of SSRI?
   - Yes, partial response
   - Augment with:
     - Hydroxyzine
     - Buspirone
     - Gabapentin
     (No second-generation antipsychotic until third trial.)
3A. Yes, partial response
   - Try an SSRI
3B. No
   - Try an SNRI or Try Alternative from 4A or Try a Second Generation Antipsychotic
   - Quetiapine
   - Ziprasidone
   (Other second-generation antipsychotics have not been studied as monotherapy. Avoid olanzapine.)
4. Tried second SSRI?
   - Yes, but no response
   - Try another SSRI or Try Alternative:
     - Benzodiazepine
     - Bupropion
     - Gabapentin
     - Hydroxyzine
     - TCA
     - Mirtazapine
     - Kava
     - Agomelatine (not available in the United States)
     (No second-generation antipsychotic until third trial.)
4A. No
   - Yes, but no response
5. Tried SNRI?
   - Yes, partial response
5A. No
   - Consider at each stage:
     - Insomnia
     - Substance Use
     - Women of Childbearing Potential
     - Pregnant Women
     - Elderly
     - Comorbidities
       - Medical
       - Psychiatric
         - GAD with bipolar disorder: valproic acid, lithium, or second generation antipsychotic
         - GAD with OCD: SSRI dosing difference
         - GAD with PTSD: prazosin

REFERENCES