Summary
GAD Psychopharmacology Algorithm

Presented by:
David Osser, MD
Associate Professor of Psychiatry
Harvard Medical School

Contents

Introduction: GAD Psychopharmacology Algorithm ................................................................. 3
Diagnosing GAD (Node 1) ........................................................................................................... 3
Comorbidities and Special Populations ....................................................................................... 3
First-Line Recommendation: An SSRI (Node 3) ......................................................................... 3
Alternatives to an SSRI as the First-Line Choice (Node 3A) ......................................................... 3
Buspirone for GAD (Node 3A) .................................................................................................... 4
Hydroxyzine for GAD (Node 3A) ............................................................................................... 4
Pregabalin and Gabapentin for GAD (Node 3A) ......................................................................... 4
Bupropion for GAD (Node 3A) .................................................................................................. 4
Benzodiazepines for GAD .......................................................................................................... 4
Partial Response to an SSRI (Node 3B) ...................................................................................... 4
Try a Second SSRI or an Alternative (Node 4) .......................................................................... 4
What to Do After Two Failed Trials: Tried an SNRI? (Node 5) ................................................... 5
GAD Psychopharmacology Algorithm: Conclusions .................................................................. 5
Introduction: GAD Psychopharmacology Algorithm

- There are FDA-approved drugs and other options that have sufficient evidence base for GAD treatment
- FDA-approved
  - SSRIs: escitalopram, paroxetine
  - SNRIs: venlafaxine, duloxetine
  - Benzodiazepine: alprazolam
  - Azapirone (buspirone)
- Off-label
  - Other SSRIs and benzodiazepines
  - Hydroxyzine, pregabalin, bupropion, kava, lavender oil, gabapentin

Diagnosing GAD (Node 1)

- Awareness of the changes from DSM-III to DSM-IV and DSM-5 is important
  - Pharmacotherapy trial results with DSM-III criteria may not be that applicable to GAD patients meeting the current DSM-5 criteria
  - Probably no disorder in the DSM has changed as much over the years as GAD

Comorbidities and Special Populations

- Usually, insomnia is a symptom, not a disease
  - Consider differential diagnosis in GAD patients and treat accordingly
- Avoid benzodiazepines in patients with anxiety who are substance abusers
- Avoid antidepressants in bipolar patients with anxiety
- In patients with comorbid PTSD and GAD, use prazosin added to antidepressants for PTSD-related sleep disturbances, daytime hyperarousal and irritability symptoms

First-Line Recommendation: An SSRI (Node 3)

- Escitalopram and sertraline seem the best SSRI options for first-line use in GAD
  - Escitalopram is FDA-approved and sertraline is not
- SSRIs have many side effects and informed consent should be obtained, as with all prescribing

Alternatives to an SSRI as the First-Line Choice (Node 3A)

- If the risks of adverse effects from an SSRI are unacceptable, there are other options to consider (not necessarily in order of preference):
  - Duloxetine (preferred over venlafaxine)
  - Buspirone
  - Hydroxyzine
  - Pregabalin
  - Bupropion
Buspirone for GAD (Node 3A)

- Advantages of buspirone over benzodiazepines include no abuse potential and mild side effect profile

Hydroxyzine for GAD (Node 3A)

- Hydroxyzine has low abuse potential, sedating properties and lacks sexual side effects
  - Comparable to benzodiazepines in efficacy and tolerability
  - The European Pharmacy Commission limited its maximum dose to 100 mg/day because of QTc prolongation risk

Pregabalin and Gabapentin for GAD (Node 3A)

- Pregabalin is approved in Europe and South America for GAD
  - Not approved in the U.S. for GAD (rejected twice)
- Pregabalin causes sedation, is expensive and can be helpful in patients with insomnia and GAD
- Gabapentin costs less than pregabalin, but there are concerns about its potential for misuse

Bupropion for GAD (Node 3A)

- There is evidence suggesting bupropion has an antianxiety effect

Benzodiazepines for GAD

- Avoid benzodiazepines as a first-line option
  - Contraindicated in patients with sleep apnea
  - Avoid in patients with substance use disorders

Partial Response to an SSRI (Node 3B)

- If the patient seemed to have a partial response and side effects were acceptable, think about whether this improvement was more likely due to placebo effect rather than a real medication effect
  - Get patient input
  - If you conclude it was placebo, do not augment but instead switch (go to Node 4)
- The three augmenters that seem the most likely to help and be reasonably safe are hydroxyzine, pregabalin, and benzodiazepines

Try a Second SSRI or an Alternative (Node 4)

- After failure on an initial SSRI, a second SSRI is the standard recommendation
  - SSRIs are not identical in spectra of receptor activity
  - A different SSRI might have a better constellation of effects
- Other alternatives at this point include: buspirone, hydroxyzine, pregabalin, bupropion, benzodiazepines, venlafaxine and herbs (Kava, Rhodiola rosea, and lavender oil)
What to Do After Two Failed Trials: Tried an SNRI? (Node 5)

- The patient is very treatment-resistant to pharmacotherapy by this point, having had two good, adequate trials of medication
- We add two alternatives:
  - Second-generation antipsychotics: they have a substantial side effect burden and we would still avoid olanzapine
  - Valproate is also an option with a small evidence base for GAD

GAD Psychopharmacology Algorithm: Conclusions

- Algorithms should not be followed rigidly
- Add clinical experience and special considerations for individual patients