Second-generation antidepressants

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Clinical question

In adults suffering from depression, are some second-generation antidepressants more effective than others?

Evidence

- A 2008 systematic review[1] compared benefits and harms of second-generation antidepressants.
  -No important difference in effectiveness. The few statistical differences found were not clinically important (eg, escitalopram 1.13 points better than citalopram on the 60-point MADRS scale [minimal clinically important difference ≥2]); sponsorship might have played a role in these subtle differences.
  -Adverse events: similar amount (61% of patients had ≥1), but types vary.
- A 2009 systematic review[2] examined response to treatment and withdrawal, and identified some small differences in efficacy and acceptability.
  -Efficacy top 4: mirtazapine, escitalopram, venlafaxine, and sertraline.
  -Acceptability top 4: escitalopram, sertraline, bupropion, and citalopram.
- Both reviews had validity concerns, like the use of indirect comparisons, but the 2009 review had additional issues with treating all depression scales as the same (and they are not), and using odds ratios that could exaggerate differences.

Context

- Considerable bias exists in antidepressant evidence: Few studies are high quality[1,3] and positive trials are selectively published[4,5] (and republished[5]) while more than 60% of negative trials are never published.[4]
- Industry-sponsored trials favour their products (about 5%) over any other antidepressants.[3]
- Escitalopram,[6] venlafaxine,[7] and sertraline[8] have each been shown to be superior to all others; this puts conclusions of each into question.
- A trial comparing bupropion, venlafaxine, and sertraline as second-line therapy found no difference.[9]
- On average, 54% of patients taking antidepressants and 37% of those given placebos get a 50% reduction in symptoms in 8 to 12 weeks.[10]

Bottom line

Among second-generation antidepressants, there is little or no reliable difference in effectiveness. The frequency of adverse events is also similar, but the types of adverse events do vary.

Implementation

Regular assessment of depression and response to therapy is an important part of management. Standardized scales, such as the PHQ-9, can help providers monitor progress and determine treatment.[11] Results should be discussed with patients and used to supplement clinical decision making.[12,13] For information about the PHQ-9 and for a copy of the scale itself, visit the MacArthur Initiative on Depression and Primary Care website (**www.depression-primarycare.org**).

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