How Long Before Antidepressants Work: Happy News?

Clinical Question: How quickly do the effects of antidepressants become clinically evident?

Bottom-line: Antidepressants begin to work as early as one week and continue to provide incremental benefits on depressive symptoms weekly for at least six weeks.

Evidence:
A large meta-analysis addresses this question:

- A meta-analysis\(^1\) of 28 trials (5872 depressed patients) looked at response to SSRI medications, compared to placebo at a series of time intervals up to six weeks:
  - At week one, the average patient gets about 1/3 of the six-week absolute benefit.
  - The incremental benefit is greatest at week one and the magnitude of the additional benefits gradually declines week by week.
  - To get a ≥50% reduction in the Hamilton Rating Scale for Depression (HRSD orHAM-D)
    - At one week, Numbers Needed to Treat (NNT)=25.
    - At six weeks, NNT=9.

Context:
- The results of the study above confirm those of another meta-analysis,\(^2\) which also found that antidepressants result in statistically significant improvement in clinically important outcomes within the first week.
- Since previous trials involved fewer patients, they were underpowered to adequately assess early response; this led to the misconception that SSRIs always take four to six weeks to work.
- Note: NNT describes the benefit of SSRI over placebo, but the placebo response in depression is high. In practice, we will see more than one in every 25 or nine patients improve at weeks one and six, respectively.

Original Authors:
G Michael Allan MD CCFP & Ron Shute MD CCFP
Updated: Ricky D Turgeon BSc(Pharm) ACPR PharmD
Reviewed: G. Michael Allan MD CCFP

References:

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