Vilazodone’s comparative merits yet to be demonstrated

The 2010 American Psychiatric Association (APA) guidelines for treating patients with major depression state that the effectiveness of antidepressant medications is generally comparable among and within classes of medications. No antidepressant is considered more effective or faster-acting than others despite each agent’s diverse neuropharmacological profile.

Considering the new antidepressant vilazodone, the question arises, What is its place in therapy relative to the 20+ other antidepressant options? At first pronunciation, one might think “vilazodone” is similar to “trazodone,” but the former’s dual-serotonergic mechanism, recommended dosing, and adverse-effect profile are quite different from the latter’s, as the authors of a review article in this issue of AJHP aptly point out. Vilazodone inhibits the presynaptic reuptake of serotonin through an action similar to that of selective serotonin-reuptake inhibitors (SSRIs), and it produces presynaptic serotonin (5-HT)\textsubscript{1A} agonism similar to that produced by the antianxiety agent buspirone.

Vilazodone should be effective for depression associated with anxiety, and it should be associated with lower rates of adverse sexual effects than SSRIs. The addition of buspirone to SSRI treatment is one strategy recommended by the APA guidelines for managing adverse sexual effects.

Controlled trials involving patients with major depression taking vilazodone hydrochloride 20 or 40 mg over eight weeks showed that the use of the 40-mg dose was associated with a greater decrease in depression rating scale scores relative to the use of a placebo, but it was not better than placebo use for achieving remission (i.e., the virtual absence of depressive symptoms). Remission should be the goal in managing depression, as remission greatly decreases the risk of relapse compared with partial improvement. It is unclear if the use of a higher dose of vilazodone over a longer period of time might lead to remission. None of the premarketing trials demonstrated a faster onset of therapeutic effect than is seen with other antidepressants. Moreover, no studies have evaluated vilazodone for depression associated with anxiety disorders.

Vilazodone lacks trazodone’s potential to produce postsynaptic 5-HT\textsubscript{1A} antagonism and histamine blockade, both of which can contribute to weight gain and sedation, and it lacks significant \(\alpha\)-1-adrenergic antagonist effects, which contribute to orthostatic hypotension and dizziness; these are potential advantages of vilazodone over other antidepressant therapies.

In my view, the ideal trial would entail initiating patients on a vilazodone hydrochloride dose of 10 mg, to be taken with food to minimize nausea and increase bioavailability. The dose could be increased to 20 mg after one week and then to the recommended goal dose of 40 mg after another week. Higher doses have not been systematically evaluated for safety and efficacy.

The authors of the review article in this issue of the journal correctly point out that the theorized advantage of vilazodone’s unique receptor profile is yet to be demonstrated. Controlled trials comparing vilazodone with other antidepressants or an SSRI plus buspirone would greatly facilitate the evaluation of its efficacy, safety, and ultimate place in therapy.

There are not enough data on vilazodone to enable accurate comparisons with other antidepressants reviewed in the APA guidelines. Clinicians are left with potential advantages that remain to be proven and potential concerns that require caution.


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The author has declared no potential conflicts of interest.

DOI 10.2146/ajhp110570