A Systematic Approach to Pharmacotherapy for Geriatric Major Depression

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KEYWORDS

• Major depressive disorder • Geriatrics • Old age • Antidepressant agents • Drug therapy • Guidelines • Algorithm • Stepped care

KEY POINTS

- The effectiveness of antidepressants depends in large part on the way they are used. Under usual care conditions, the outcomes of antidepressant pharmacotherapy for geriatric depression have been shown to be mediocre at best.
- Trying to individualize treatment by matching each patient with a specific antidepressant based on the patient's symptoms and an antidepressant putative side-effect profile is ineffective. Instead, the outcomes of antidepressant pharmacotherapy for geriatric depression can be improved markedly when antidepressants are prescribed following an algorithmic ("stepped-care").
- Published guidelines and algorithms for the antidepressant pharmacotherapy for geriatric depression are informed by published evidence but they do not necessarily conform to this evidence. This article presents an updated algorithm for the antidepressant pharmacotherapy for geriatric depression that is based on the authors' interpretation of the available evidence.

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INTRODUCTION

Approximately 14% of older Americans are now taking an antidepressant.[1–3] However, this broad use has not been associated with a notable decrease in the burden of geriatric depression.[4,5] This article, based on a selective review of the literature, explores several explanations for this paradox. First, the possible explanations that antidepressants are not effective in the treatment of depression or that the results of randomized, controlled clinical trials (RCTs) are not applicable to the treatment of depression in real-world clinical settings, are discussed and rejected. Instead, the authors propose that the efficacy of antidepressants depends in large part on the way they are used. Evidence is presented to support the proposition that the use of antidepressant pharmacotherapy is associated with better outcomes when guided by a treatment algorithm (a stepped-care approach) as opposed to an attempt to individualize treatment. Published guidelines and pharmacotherapy algorithms developed for the treatment of geriatric depression are reviewed. Finally an updated algorithm is proposed, based on the authors' interpretation of the available evidence.

ARE ANTIDEPRESSANTS EFFECTIVE FOR THE TREATMENT OF MAJOR DEPRESSIVE DISORDER?

Some investigators have proposed that antidepressants are either not effective or only minimally effective except in patients with the most severe depression, pointing out the small effect sizes in meta-analyses including both published and unpublished placebo-controlled RCTs of antidepressants (eg, Refs.[6–8]). Several analyses have been published specifically to refute these results (eg, Refs.[9–12]) or show that psychotropic medications (including antidepressants) are as efficacious as drugs used to treat general medical conditions.[13] The debate about the true efficacy of antidepressants (ie, whether there is a meaningful difference in the remission or response rates experienced by patients randomized to an antidepressant or a placebo) continues.[14–16] Regardless of the degree to which antidepressants are more efficacious than placebo, patients treated with active antidepressants should experience at least the improvement associated with the use of a placebo. However, some published data suggest that patients whose depression is treated under usual care (nonstudy) conditions are actually less likely to respond to antidepressant treatment or to experience remission of their depressive symptoms than depressed patients who receive a placebo in an RCT. Poor outcomes for depressed patients treated under usual care conditions have been reported in both those treated by primary care providers (PCPs) and those treated by psychiatrists. For instance, Meyers and colleagues[17] reported that only 30% of adult patients with a major depressive disorder (MDD) who were treated by a psychiatrist experienced remission of their major depressive episode after 3 months, a rate lower than the 30% to 40% rate of remission typically associated with placebo in RCTs of adults with MDD.[12,13]

ARE THE RESULTS OF RANDOMIZED CONTROLLED TRIALS OF ANTIDEPRESSANTS APPLICABLE TO REAL-WORLD GERIATRIC PRACTICE?

Some investigators have proposed that antidepressants are not as effective in clinical practice as in RCTs because patients who participate in RCTs are not representative of patients treated in real-world clinical practice. This argument is supported by some published data showing that, because of the required eligibility criteria they have to meet to participate, depressed subjects included in RCTs differ from the population from which they are drawn.[18,19] However, the gap between the efficacy of antidepressants when used in an RCT and their lower effectiveness when used under usual care