Antidepressants Are Effective for the Treatment of Major Depressive Disorder in Individuals Aged 55 Years or Older
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Abstract and Introduction

Abstract


Question

What is the efficacy of antidepressants for the treatment of late life major depressive disorder (MDD)?

Outcomes

Clinical response, defined as a 50% or greater reduction in the Hamilton Depression Rating Scale (HDRS) or the Montgomery-Asberg Depression Rating Scale (MADRS) scores, from baseline to endpoint, or a Clinical Global Impression-Improvement Scale (CGI-I) score <3 at the final visit.

Methods

Design

Systematic review and meta-analysis.

Data Sources

PubMed/Medline was searched from 1 January 1980 to 3 March 2010. The search included antidepressants that had received a letter of approval by the USA, Canadian<EU, Japanese or Australian regulatory agencies for treatment of MDD.

Study selection and analysis: Double-blind, placebo controlled, randomised controlled trials (RCTs) of oral antidepressants used as monotherapy for the treatment of MDD in participants less than 65 years (adult MDD) or 55 years or older (late life MDD). RCTs had to be of a parallel design (crossover studies were excluded) and be at least 4 weeks long. Participants had to have MDD diagnosed according to Diagnostic and Statistical Manual of Mental Disorders III or IV criteria, Research Diagnostic Criteria or Feighner diagnostic criteria. Participants had to be free of treatment resistant depression or other depressive disorders, co-morbid alcohol, substance use or medical disorders. Trials had to use the HDRS, the MADRS or the CGI-I as an outcome measure. The RR of clinical response of adult and late life MDD was calculated by random effects meta-analyses. Meta-regression was performed to compare the RR of response and discontinuation between the adult and late life MDD trials. Antidepressant response rates between age groups were also compared using analysis of variance (ANOVA).
There were 74 trials, with 132 antidepressant versus placebo contrasts and 20,572 participants, included in the analysis. Of these, 59 trials analysed the treatment of adults aged <65 years (adult MDD) and 15 trials analysed the treatment of adults aged ≥55 years (late life depression). The adult and late life MDD trials were similar, except for the age of the participants, the year of publication and the sample-size per treatment arm. The risk of response with antidepressants was significantly higher than with placebo for both adult MDD and late life-MDD (adult MDD RR 1.420, 95% CI 1.354 to 1.488; late life MDD RR 1.304, 95% CI 1.150 to 1.479). There was significant heterogeneity in both sets of trials. Meta-regression found no significant difference in the RR of response or discontinuation in the adult and late life MDD trials. Secondary analysis of trials that included only patients aged 65 years or above (older late life MDD, six trials, 1840 patients), yielded no difference in response rates between antidepressant and placebo therapy (RR 1.128, 95% CI 0.929 to 1.369). The RR of clinical response in the adult MDD trials was significantly higher than the older late life MDD trials, despite there being no difference in the RR of discontinuation. ANOVA (taking into account study characteristics), found that antidepressant response rates were significantly lower in late life MDD and older late life MDD than adult MDD (late life MDD F=8.43, p=0.004; older late life MDD, F=7.34, p=0.008). There was no difference in placebo response rates.

Conclusions

Antidepressants are effective for the treatment of MDD in patients aged 55 years or older (late life MDD). The results of this study suggest that effectiveness may be reduced in patients aged 65 years or older (older late life MDD).

Commentary

The study by Tedeschini et al provides a comprehensive and current review of antidepressant use in the older people with a focus on placebo-controlled randomised trials. Over the past 30 years, epidemiologic studies have consistently demonstrated that the frequency of major depression in community dwelling older people (65+ years of age) is lower than for younger age groups (1–3%), even though suicide rates for older white males are the highest for any age, sex and race demographic. Despite the relatively lower frequency of major depression in community dwelling elders, antidepressant use is as high or higher in this age group than for other age groups across the adult life cycle (around 10% of persons 65+ years of age in the community).

Given this background, what is perhaps most striking is the paucity of studies which focus on the 65+ age group that meet the criteria of the investigators. In these 15 trials, medications were not found to be statistically efficacious; nevertheless, when adults aged 55 or older were included from the trials, the meta-analysis conducted demonstrated the efficacy of antidepressants. These findings raise important questions, alluded to by the authors, regarding antidepressant use in the older people. First, efficacy trials do not immediately translate into effectiveness trials and there is very little data on the actual effectiveness of antidepressants among the older people. Efficacy trials are difficult enough to field in this age group, and much less in the case of effectiveness trials. Yet the major discrepancy between the use of antidepressants in the older people and the evidence base for their use is of great concern. Better designed real world trials are therefore needed to inform practitioners. Second, antidepressants are used for other reasons than to treat depression in late life, including sleep disorders, anxiety and pain syndromes. Translating the data directly into clinical recommendations is therefore not possible.

In summary, I doubt that antidepressant use will drop dramatically given these results. More data is needed if we are to practice evidence-based psychopharmacology in this age group.
References


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