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Review article

Efficacy and tolerability of antidepressants in people aged 65 years or older with major depressive disorder – A systematic review and a meta-analysis

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ABSTRACT

Background: There has been a steady increase in the prescription of antidepressants for the elderly. This study comprises a systematic review of randomized, placebo-controlled trials of antidepressants for treatment of depressive disorder in people aged 65 years or more.
Methods: PubMed, EMBASE, Cochrane Library, CINAL, and PsycINFO were searched until May 2016. Where appropriate, the results were synthesized in meta-analyses.
Results: Twelve trials met the inclusion criteria. For patients with major depressive disorder, selective serotonin re-uptake inhibitors (SSRI) were not superior to placebo in achieving remission (OR: 0.79, 95% CI: 0.61–1.03) or response (OR=0.86, 95% CI: 0.51–1.10) after 8 weeks of treatment (three trials). However, maintenance treatment with SSRIs was superior to placebo in preventing relapse (OR: 0.22, 95% CI: 0.13–0.36; NNT=5, 95% CI: 3–6; two trials). Duloxetine was superior to placebo in achieving remission (OR: 1.78, 95% CI: 1.20–2.65; NNT=9, 95% CI: 6–20; three trials) and response (OR: 1.83, 95% CI: 1.96–4.08; two trials) in recurrent major depression after 8 weeks, but increased the risk of adverse events that can be problematic in the elderly.
Limitations: The quality of evidence was generally low or moderate, emphasizing the uncertainty of the results. Study populations only partly covered the heterogeneous population of elderly with depressed mood, limiting the generalizability.
Conclusion: The results underscore the importance of close monitoring of the effects of antidepressants in treatment of elderly patients with a depressive disorder. Methods for early detection of non-responders and effective treatment options for this group are needed.

Contents

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1. Introduction

The rate of depression among the elderly in Europe is estimated to be about 10–15% (Castro-Costa et al., 2007; Copeland et al., 1999). For nursing home residents the prevalence might be as high as 20–25% (Rovner et al., 1991). Depression in the elderly is associated with decreased quality of life (Gurland, 1992) and increased mortality (Gallo et al., 2005). Moreover, depression is expected to take second place, following only heart disease, in its contribution to the global burden of disease, measured as disability-adjusted life years (Chapman and Perry, 2008). Major depressive disorder (MDD) is the most prevalent mental disorder among elderly patients (Hybels and Blazer, 2003), but despite the high prevalence and the serious sequelae, the condition often remains undetected, untreated or inadequately treated (Richardson et al., 2012; Wilson et al., 1999).

The use of antidepressants in elderly people has increased steadily, especially among the older-old (Sonnenberg et al., 2008). Systematic reviews to date suggest that antidepressants can be efficacious in treatment of depression in the elderly (Kok et al., 2012; Mottram et al., 2006; Nelson et al., 2008; Tedeschini et al., 2011). The latter review included a subset of studies on patients aged 65 years or more, in whom antidepressants were not efficacious (Tedeschini et al., 2011). Thus the outcome might depend on the age threshold for inclusion in the studies. The literature search for the review in question was undertaken in 2010, limited to PubMed/MEDLINE publications and did not assess the risk of bias. There is therefore a need for an updated review, with special reference to treatment of depressive disorder in elderly subjects. There is also a need to address tolerability or adverse events (AE) in this age group.

Although antidepressants are commonly used as treatment for both depression and anxiety disorders in the elderly, there are few studies investigating AE, not only in short-term clinical trials but also during maintenance treatment. A population-based cohort study of elderly people diagnosed with depression failed to show reduced risk of adverse outcomes using SSRI and other antidepressants compared with tricyclic antidepressants (Coupland et al., 2011). A recent study suggested an association between SSRI treatment and reduced bone marrow density, but the independent effect of depression or antidepressant medication on bone loss is unclear (Stubbs et al., 2016a).

The present study comprises an updated systematic review of efficacy and tolerability of antidepressant treatment in patients with depression, aged 65 or more, with special reference to remission, response and AEs. Head-to-head comparisons of two active substances frequently result in a better outcome for the sponsored drug, possibly due to a high risk of sponsor bias (Heres et al., 2006; Rochon et al., 1994). The present review was therefore limited to placebo-controlled trials.

2. Method

2.1. Protocol and registration

This systematic review was part of a larger project investigating the efficacy and tolerability of treatments for depression in the elderly, conducted within the framework of the Swedish Agency for Health Technology Assessment and Assessment of Social Services, SBU (www.sbu.se/en/), a public agency conducting health technology assessments. The inclusion criteria and method of analysis were specified in advance at SBU (Ref. No. UTV2013/142), and are available upon request.

2.2. Eligibility criteria

Only studies published in English were considered (although this limit was not applied to the literature search).

Population: Individuals aged 65 years or more diagnosed with depressive disorder in accordance with the definitions by American Psychiatric Association (A.P.A., 1994) or the World Health Organization (W.H.O., 1992). Studies which included individuals with bipolar disorders were excluded. Only studies that pertained study participants diagnosed with major depressive disorder (MDD) were identified.

Interventions: Commercially available antidepressants, including: Fluoxetine, Citalopram, Paroxetine, Sertraline, Fluvoxamine and Escitalopram (SSRIs); Moclobemide (reversible monoamine oxidase inhibitor); Amitriptyline (tricyclic antidepressant); Duloxetine and Venlafaxine (serotonin–norepinephrine reuptake inhibitors); Mianserin (tetracyclic antidepressant); Mirtazapine (noradrenergic and specific serotonergic antidepressant); Reboxetine (norepinephrine reuptake inhibitor); Agomelatine (melatonergic antidepressant); Vortioxetine (serotonin modulator and stimulator) and Bupropion.

Comparator: Placebo.

Outcomes: Rates of remission, response, and treatment