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Review article

Systematic review and meta-analysis of interventions for depression and anxiety in persons with multiple sclerosis

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ABSTRACT

Background: Depression and anxiety are common in persons with multiple sclerosis (MS), and adversely affect fatigue, medication adherence, and quality of life. Though effective treatments for depression and anxiety exist in the general population, their applicability in the MS population has not been definitively established.
Objective: To determine the overall effect of psychological and pharmacological treatments for depression or anxiety in persons with MS.
Methods: We searched the Medline, EMBASE, PsycINFO, PsycARTICLES Full Text, Cochrane Central Register of Controlled Trials, CINAHL, Web of Science, and Scopus databases using systematic review methodology from database inception until March 25, 2015. Two independent reviewers screened abstracts, extracted data, and assessed risk of bias and strength of evidence. We included controlled clinical trials reporting on the effect of pharmacological or psychological interventions for depression or anxiety in a sample of persons with MS. We calculated standardized mean differences (SMD) and pooled using random effects meta-analysis.
Results: Of 1753 abstracts screened, 21 articles reporting on 13 unique clinical trials met the inclusion criteria. Depression severity improved in nine psychological trials of depression treatment ($N=307$; SMD: −0.45 (95% CI: −0.74, −0.16)). The severity of depression also improved in three pharmacological trials of depression treatment (SMD: −0.63 ($N=165$; 95%CI: −1.07, −0.20)). For anxiety, only a single trial examined psychological therapy for injection phobia and reported no statistically significant improvement.
Conclusion: Pharmacological and psychological treatments for depression were effective in reducing depressive symptoms in MS. The data are insufficient to determine the effectiveness of treatments for anxiety.

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1. Introduction

Psychiatric comorbidity is common in persons with multiple sclerosis (MS), with a lifetime prevalence of depression as high as 24% (Marrie et al., 2015); and of anxiety disorders as high as 21.9% (Marrie et al., 2015). Depression and anxiety are associated with more fatigue (Brown et al., 2009), lower quality of life (Fruehwald et al., 2001; Janssens et al., 2003), and reduced adherence to disease-modifying therapy (DiMatteo et al., 2000; Turner et al., 2009). Although the adverse effects of depression and anxiety in MS are well-recognized, they remain undertreated. Well-developed evidence to guide the treatment of depression and anxiety in MS is lacking (Minden et al., 2014), therefore health care providers must rely on the general psychiatry and psychology literature for treatment recommendations. Effective treatments for depression and anxiety exist in general and medical populations (van Straten et al., 2010; Gartlehner et al., 2011; Roshanaei-Moghaddam et al., 2011; Cuijpers et al., 2013, 2014; Hunsley et al., 2014; Bandelow et al., 2015), but MS-specific considerations, such as cognitive impairment, fatigue, and urinary retention, may affect the safety, tolerability and effectiveness of treatments tested in the general population. Therefore disease-specific investigations of interventions to reduce depression and anxiety in MS are essential (Koch et al., 2011; Minden et al., 2014).

The aim of this systematic review and meta-analysis was to summarize, critically appraise, and quantify the findings of controlled trials of pharmacological and psychological interventions for depression and anxiety in persons with MS.

2. Methods

Using an *a priori* published protocol (Fiest et al., 2015), we conducted this systematic review following the Cochrane Handbook for Systematic Reviews, and reported the findings according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria (Moher et al., 2009; Chandler et al., 2013).

2.1. Populations, interventions, comparators, settings and study designs

We included studies meeting these criteria: (1) randomized controlled trial conducted in any setting; (2) published in any language; and (3) conducted in a depressed or anxious population of adults with MS. Definite diagnoses of MS were required based on the prevailing criteria used when the trial was conducted. Depression and anxiety could have been defined by a clinical interview, or by self-report using a screening tool. Otherwise, we did not pre-specify criteria regarding the definition of depression or anxiety, but rather evaluated which approaches were used by individual trials to identify the specific instruments used. We excluded trials if the study population was < 18 years old.

2.2. Outcome measures

To ensure relevant, patient-oriented outcomes were examined, we held meetings with primary care providers and individuals living with MS. Based on recommendations from these stakeholders, the primary research question was: “What is the efficacy of pharmacological and psychological treatments for depression or anxiety in persons with MS?”. We compared the severity of depression and/or anxiety on any tool at post-assessment between the treatment and control groups using the standardized mean difference (SMD) of depression and/or anxiety scores. Secondary outcomes were: differences in participant's quality of life and fatigue, proportion of participants achieving remission of depression or anxiety, and participants achieving at least a 50% reduction in depressive or anxious symptoms. The final research question was “What is the tolerability of pharmacological or psychological treatment for depression or anxiety in MS?” for which we examined the drop-out rate and any side effects.

2.3. Search strategy

An Information Specialist (M.F.) developed the search strategies in consultation with experts in neurologic disease (J.M., R.A.M.) and psychiatric disorders (S.P., J.W., L.G., K.F., J.S., J.B.). We searched