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Prophylactic antidepressant treatment following acute coronary syndrome: A systematic review of randomized controlled trials

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ABSTRACT

Major depressive disorder is significantly increased in patients following acute coronary syndrome resulting in twofold increased mortality compared with patients without depression. The depression diagnosis is often missed leading to considerable undertreatment. This systematic review assesses the current evidence of primary prophylactic treatment of depression in patients after acute coronary syndrome. The study protocol was prospectively registered at PROSPERO (registration number CRD42015025587). A systematic review were conducted and reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. PubMed, Embase, PsychINFO, CINAHL, and Cochran Library was searched. Two independent reviewers screened the records. The inclusion criteria were randomized controlled trials on adult patients with acute coronary syndrome treated prophylactically with an antidepressant intervention of any kind. A validated assessment tool should measure depression and depressive symptoms. Languages were limited to articles written in English. Six articles were included. Four studies utilized different components of case and disease management, health coaching, or relaxational audiotapes as intervention compared with usual care or with no formal program of rehabilitation. None of the studies showed any significant prophylactic effect against depression. One study with a program of health education and counselling and another study with a pharmacological antidepressant showed significant prophylactic effect on depression and depressive symptoms. All six included studies were associated with high risk of bias. There is not strong evidence of the effects of any type of routine antidepressant prophylaxis in patients following acute coronary syndrome. Further high quality studies are warranted.

Contents

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1. Introduction

Major depressive disorder was significantly increased in patients following acute coronary syndrome (ACS) (Thombs et al., 2006; Jiang et al., 2002) with a rate ratio of 1.28 compared with a comparable reference population (Osler et al., 2016). The prevalence of depression (13,7%) was constant at least 18 months following myocardial infarction (Hanssen et al., 2009). The risk of depression was comparable to the risk in patients after stroke after controlling for sex, age, and level of handicap (hazard ratio (HR) 1.08; p = 0.72) (Aben et al., 2003). Other register-based literature has shown prevalence of depression to be higher in patients following stroke compared to myocardial infarction (Jorgensen et al., 2016a).

The prevalence of antidepressant prescription has increased considerably during the last decades, reaching 10–15% by 2005 in patients after ACS (Czarny et al., 2011). A nationwide Danish retrospective cohort study found that 12% of patients were treated with antidepressants within two years after their ACS – almost two times more than those without ACS (Jorgensen et al., 2016b).

Recurrent or new onset depression in patients with ACS had higher mortality rates than patients with no depression (Osler et al., 2016; Meijer et al., 2011; van Melle et al., 2004). A recent patient level meta-analysis showed that hazard ratios for the association between post-myocardial infarction depression and all-cause mortality was 1.32 (95% CI 1.26–1.38, P < 0.001) but was attenuated after adjustment for disease severity (HR = 1.23) (Meijer et al., 2013). However, depression was still an independent risk factor for all-cause mortality and cardiovascular events, which was acknowledged by the American Heart Association (Lichtman et al., 2014), who has made recommendations for screening of depression following ACS (Lichtman et al., 2008).

The pathophysiology of post-ACS depression remains unclear and several mechanisms have been put forth (Jiang et al., 2002; Carney et al., 2002) including dysfunction of the autonomic nervous system, heart rate variability and an increase of the inflammation response (Jiang et al., 2002; Huffman et al., 2013; Carney and Freedland, 2009; Carney et al., 2005; Poole et al., 2011; Ross, 1999; Kaptoge et al., 2014; Pizzi et al., 2010; Howren et al., 2009). Cytokines have been associated with atherosclerotic plaque formation, progression, and rupture; and as such they were major contributors to the pathogenesis of coronary artery disease and myocardial infarction (Huffman et al., 2013). Depression have also been linked to increased levels of interleukins (especially CRP, IL-1, and IL-6), both in patients with and without a history of cardiac disease (Pizzi et al., 2010; Howren et al., 2009). Platelet activity and aggregation is yet another possible link between depression and ischemic heart disease as serotonin plays an important role in platelet function (Pizzi et al., 2009). Of potential direct mechanisms, Huffman J.C. et al (Huffman et al., 2013). mention neural-immune interaction via the serotonin receptors effect on cardiac outcomes, and increased cytokines which may elevate the degradation of tryptophan (precursor to serotonin) resulting in overall lover serotonin levels (Huffman et al., 2013).

Besides the association between post-ACS depression and mortality, patients suffering from depression related to ACS were less likely to engage in health promoting behaviours, including maintenance of a healthy diet, regular exercise, adherence to medications (Rieckmann et al., 2006; Carney et al., 1995; May et al., 2010), stress reduction, and completion of cardiac rehabilitation programs following myocardial infarction (Blumenthal et al., 1982; Ziegelstein et al., 2000). This was associated with an increased risk of cardiac events (Gehi et al., 2007; Wessel et al., 2004). Patients with cardiac disease and clinical depression, who were hospitalized and treated for their depression on the other hand showed enhanced effect on adherence to diet, exercise, and medication (Bauer et al., 2012). Thus, suggesting these negative behavioural factors would be modifiable with the correct treatment.

Moderate to severe depression were found to be significantly under-recognized and undertreated among patients with ACS (Amin et al., 2006; Huffman et al., 2006), which leads to patients receiving inadequate treatment. In the general population studies suggests that, despite the severity and possible complications of depression, only half of those with depression will seek professional help (World Health Organization, 2000). Given the high risk of patients developing depression and the problems inherent with diagnosing depression, there is increasing interest in prophylactic therapies that may prevent abnormal mood and improve outcome after ACS. The aim of this current systematic review was to review the prophylactic treatment of depression in patients after ACS.

2. Method

The systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Liberati et al., 2009). The systematic review was registered on PROSPERO (Booth et al., 2011a, 2011b) with registration number: CRD42015025587.

We used the following PICOS (P: population, I: intervention, C: comparator/control, O: outcomes, S: study design) (Liberati et al., 2009) when constructing the eligibility criteria and the search strategy; P: humans, adults, ≥18 years, diagnosed with ACS, I: antidepressant treatment of any kind, C: placebo or active treatment, O: depression and depressive symptoms, and S: randomized controlled trails (RCT). Studies in English comparing pharmaceutical agents with placebo, psychotherapy against standard care, or any other antidepressant treatment against standard care to prevent depression in patients with ACS were included. No restriction on dose, administration, timing of the intervention, or to other outcomes being assessed in the studies was chosen.

The search was carried out using PubMed, Embase, PsycINFO, CINAHL, and the Cochrane Library (PubMed: 1966 - now, Embase: 1974 - now, PsycINFO: 1806 - now, CINAHL: 1981 - now, Cochrane Library: date of inception - now). Contact with the study authors was made if the data were not extractable from text or figures in the article. The search was conducted on 19th of December 2015. The same search terms were use in the databases, however, the mesh terms were modified to fit to the search criteria of the respective databases. No limits were set for language; thus all records were manually screened with regard to being English. No limits were set with regard to the years of publication. No attempt was made to include potential ongoing trials. The reference list of all included studies was manually reviewed to identify additional relevant studies. The exact search terms for PubMed were: (coronary artery disease OR ischemic heart disease OR myocardial infarction OR acute myocardial infarction OR unstable angina OR acute coronary syndrome OR coronary bypass surgery OR atherosclerosis) AND (antidepressant OR tricyclic antidepressant OR selective serotonin reuptake inhibitor OR serotonin-noradrenaline reuptake inhibitor OR noradrenergic and specific serotonergic antidepressants OR mono amino oxidase inhibitors OR melatonin OR agomelatine OR Psychotherapy OR Psychological intervention OR Cognitive behavioural therapy OR psychodynamic psychotherapy OR interpersonal psychotherapy OR intervention OR counselling OR mindfulness OR family therapy OR psychosocial intervention OR stress management OR behavioural OR social support OR exercise) AND (prevention OR primary prevention OR secondary prevention OR tertiary prevention OR prophylactic OR prophylaxis) AND (depression OR depressive symptoms OR depressive disorder OR mood OR mood disorder).