Journal of Psychosomatic Research 88 (2016) 36–41

Contents lists available at ScienceDirect

Journal of Psychosomatic Research

Clinical predictors of depression treatment outcomes in patients with coronary heart disease

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ARTICLE INFO

Article history:
Received 31 May 2016
Received in revised form 15 July 2016
Accepted 17 July 2016

Keywords:
Coronary heart disease
Major depression
Treatment

ABSTRACT

Objectives: Patients with coronary heart disease (CHD) who respond to treatment for depression are at lower risk of mortality than are nonresponders. This study sought to determine whether variables that have been shown to predict both depression treatment outcomes in psychiatric patients and cardiac events in patients with CHD, also predict poor response to depression treatment in patients with CHD.
Methods: One hundred fifty-seven patients with stable CHD who met the DSM-IV criteria for a major depressive episode were treated with cognitive behavior therapy (CBT) for 16 weeks, either alone or in combination with an antidepressant.
Results: The mean Beck Depression Inventory (BDI-II) score was 30.2 ± 8.5 at baseline and 8.5 ± 7.8 at 16 weeks. Over 50% of the participants were in remission (HAM-D-17 score ≤7) at the end of treatment. Of the hypothesized predictors, severe depression at baseline ($p = 0.02$), stressful life events during the first ($p = 0.03$) and last ($p < 0.0001$) 8 weeks of treatment, and the completion of CBT homework assignments ($p = 0.001$) predicted depression outcomes. History of prior episodes, anxiety symptoms, antidepressant therapy at study enrollment, and medical hospitalizations or emergency department visits during treatment did not predict treatment outcome.
Conclusions: Patients who are under considerable stress do not respond as well to evidence-based treatments for depression as do patients with less stress. If future studies support these findings, more work will be needed to better address stressful life events in patients who may otherwise remain at high risk for mortality and medical morbidity following depression treatment.

Depression is a well-established risk factor for mortality in patients with coronary heart disease (CHD). A meta-analysis of 29 studies found depression to be associated with a 2.7 fold increased risk of cardiac-related mortality in the two years following an acute myocardial infarction (MI) [1]. A recent scientific advisory statement from the American Heart Association recommended adding depression to the list of acknowledged risk factors for further cardiac morbidity and mortality in survivors of an acute coronary syndrome (ACS) [2].

There have been only a few controlled trials to determine whether treating depression in patients with CHD improves medical outcomes, and they have been limited by small numbers of cardiac endpoints and small differences in depression outcomes between the intervention and control groups [3–5]. These limitations have made it difficult to detect an effect of depression treatment on cardiac morbidity or mortality, and in fact none of the primary analyses have shown an effect. This has led some to question the value of targeting depression to improve cardiac outcomes [6]. However, secondary analyses have found that patients whose depression symptoms significantly improve with treatment have better survival than those whose symptoms show only minimal or no improvement [7–9]. These findings suggest that survival may improve if depression improves. Similar findings have been reported in a non-randomized trial of exercise training and cardiac rehabilitation in post-MI patients [10] and in a non-randomized [11] and a randomized [12] clinical trial of depression interventions for patients with heart failure.

Given the interest in treating depression in cardiac patients, it is surprising that little is known about the psychiatric and psychosocial variables that predict treatment response in these patients. Some of the factors that have predicted poor responses to depression treatment are also associated with an increased risk of cardiac events in patients with CHD. This may help explain why patients with depression that does not respond to treatment are at higher risk for subsequent morbidity and mortality.

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http://dx.doi.org/10.1016/j.jpsychores.2016.07.011
0022-3999/

We investigated possible biological predictors of depression improvement in this cohort and found that high normal levels of free T4 thyroid hormone predicted poor depression treatment outcome, but elevated markers of inflammation (CRP, TNF, IL-6), poor sleep quality, and low levels of physical activity did not [13]. However, characteristics of the depressive episode and related psychosocial factors also have been shown to predict improvement in depression, and some of these are risk factors for cardiac events. The purpose of this study was to examine whether baseline depression severity [4,14], a history of depressive episodes [4,15–18], comorbid anxiety symptoms [19–22], concurrent medical hospitalizations or emergencies, or stressful life events [23–26], predict a poor response to depression treatment in patients with major depression and stable CHD.

1. Methods

1.1. Eligibility screening and recruitment

Patients were recruited between May 2009 and August 2013 at cardiology offices and diagnostic laboratories affiliated with Washington University School of Medicine and Barnes-Jewish Hospital of St. Louis. Consenting patients with CHD documented by coronary angiography, a history of coronary revascularization, or hospitalization for ACS, completed the Patient Health Questionnaire (PHQ-9) [27]. Patients were excluded from the study if they refused to participate or if their physician did not approve enrollment in the study, or if they had significant cognitive impairment, psychotic features, a comorbid psychiatric disorder other than an anxiety disorder, a high risk of suicide, current substance abuse, hospitalization for ACS or coronary artery bypass graft (CABG) surgery within the previous two months, advanced malignancy, or a disability that would affect compliance with the study protocol. Patients who had been taking a therapeutic dose of an FDA-approved selective serotonin reuptake inhibitor (SSRI) antidepressant for at least 30 days were eligible to participate as long as all of the other eligibility criteria were met. Patients who were not excluded and who screened positive for depression on the PHQ-9 (total score ≥10) were scheduled for a structured diagnostic interview. Those who met the DSM-IV criteria for a major depressive episode, scored ≥16 on the Beck Depression Inventory (BDI-II), and gave written informed consent were enrolled. The study was approved by the Human Research Protection Office at Washington University School of Medicine in St. Louis.

1.2. Assessments

1.2.1. Depression interview and structured Hamilton (DISH)

The DISH [28] was administered to diagnose major depression using the DSM-IV criteria and to measure the severity of depression from an embedded version of the Hamilton Rating Scale for Depression (HAM-D-17). The DISH includes a screen for exclusionary psychiatric conditions, and assesses psychiatric history including previous major depressive episodes and psychiatric treatment. A HAM-D-17 score of ≤7 was used to define depression remission in this study.

1.2.2. Beck Depression Inventory-II (BDI-II)

The 21-item BDI-II was administered to measure the self-reported severity of depression symptoms. The BDI-II was the primary measure of treatment outcome [29].

1.2.3. Beck Depression Anxiety Inventory (BAI)

The 21-item BAI was administered to assess self-reported severity of anxiety symptoms [30].

1.2.4. Stressful life events questionnaire (SLEQ)

Based on the work of Caspi and colleagues [31], the SLEQ assesses the occurrence of 14 types of stressful life events including medical illness of the participant or significant other, death of a family member or close friend, financial problems, problems with close interpersonal relationships, loss of a job, changing residence, and other life threatening or otherwise traumatic situations. The participants were asked to report events that had occurred in the 12 months prior to baseline, and during the previous 8 weeks at the 8th and 16th week of the intervention. They were also asked to rate the severity of perceived stress associated with each event on a four point scale (0 = not or only minimally stressful, 3 = very stressful). The total stress score at each assessment occasion is the sum of the stress ratings for that period.

1.3. Treatment

The study treatment protocol is described in more detail elsewhere [13]. Briefly, participants received up to 12 sessions of CBT over four months. Those who had already been taking a therapeutic dose of an SSRI antidepressant for at least four weeks prior to enrollment were given CBT and asked to remain on this antidepressant for the 16 weeks of the study. Patients who were not taking an antidepressant at enrollment initially received only CBT. However, if their BDI-II score did not improve by 30% or more by the 5th week of treatment, or by 50% or more by the 8th week, they were prescribed 50 mg of sertraline until the end of the 16-week treatment period. Thus, participants received up to two recognized depression treatments during the four-month treatment period. Nonresponse to adequate trials of at least two evidence-based treatments is a common definition of treatment-resistant depression [32,33].

Individual CBT was provided in weekly 50- to 60-minute sessions by one of two therapists, a psychiatric social worker and a master's level counseling psychologist, both with extensive training and experience with CBT for depression in patients with CHD [34,35]. Brief telephone contacts between CBT sessions were also allowed as needed. Each case was reviewed in group supervision meetings held weekly with one of the investigators (KEF) to provide clinical guidance and to assure fidelity to the CBT protocol. The general principles and therapeutic techniques of the intervention were guided by treatment manuals [36,37], while adapting behavioral activation plans to address medical safety concerns as needed [38].

1.4. Treatment adherence

1.4.1. Cognitive behavior therapy

Patients' attendance (in-person and telephone sessions) and homework completion were recorded for the duration of treatment. CBT homework assignments are described in the treatment manuals. These include rating the mood associated with specific thoughts or activities, identifying and correcting cognitive distortions, applying problem solving techniques learned during sessions, and planning and engaging in pleasant activities.

1.4.2. Medications

Patients were asked to bring their pill bottles to each psychotherapy session and psychiatrist visit and these were counted and recorded by the research nurse. Patients who forgot to bring their bottle or who missed a treatment session were contacted by telephone and asked to count the remaining pills. The percentage of prescribed pills that were taken and the percentage of CBT homework that was completed during the course of treatment were the primary measures of adherence.

1.5. Medical events

Hospitalizations and emergency department visits were monitored and recorded throughout the 16 weeks of the intervention. Participants' medical records were reviewed at the end of the study to confirm the reported events and assure that all events were recorded.