



Interactions between analgesic drug therapy and mindfulness-based interventions for chronic pain in adults: protocol for a systematic scoping review

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Abstract

Introduction: Most current chronic pain treatment strategies have limitations in effectiveness and tolerability, and accumulating evidence points to the added benefits of rational combinations of different therapies. However, most published clinical trials of treatment combinations have involved combinations of 2 drugs, whereas very little research has been performed to characterize interactions between drug and nondrug interventions. Mindfulness-based interventions (MBIs) have been emerging as a safe and potentially effective treatment option in the management of chronic pain, but it is unclear how MBIs can and should be integrated with various other pain treatment interventions. Thus, we seek to review available clinical trials of MBIs for chronic pain to evaluate available evidence on the interactions between MBIs and various pharmacological treatments.

Methods: A detailed search of trials of MBIs for the treatment of chronic pain in adults will be conducted on the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, and PsycINFO from their inception until the date the searches are run to identify relevant randomized controlled trials. Primary outcomes will include the following: (1) what concomitant analgesic drug therapies (CADTs) were allowed; (2) if and how trials controlled for CADTs and analyzed their interaction; and (3) results of available analyses of interactions between the MBI and CADT.

Perspective: This review is expected to synthesize available evidence describing the interactions between MBIs and various studied drug therapies for chronic pain. Available evidence may help inform the rational integration of MBIs with drug therapy for chronic pain.

Keywords: Chronic pain, Mindfulness, Analgesic therapy, Clinical trials, Systematic review, Meditation

1. Introduction

Chronic pain is a significant health problem given its prevalence, impact on quality of life, economic burden, and difficult management. Chronic pain is generally described as pain that persists over

3 months or past the normal time for tissue healing.¹⁵ However, in most people, the duration of pain is much longer.^{9,37} For example, one Canadian study found that over 45% of people with chronic pain have experienced pain for over 10 years.³⁷ Chronic pain has major negative impacts on daily living activities and work-related outcomes, such as employment status and days missed from work.⁴ Individuals living with chronic pain have double the risk of suicide compared with those who do not.^{27,38} Chronic pain is one of the most common reasons for medical visits and is estimated to affect 1.5 billion people worldwide.^{8,10,12} Approximately 30% of adults in the United States and up to 19% of adults in Canada experience chronic pain.^{20,36} Chronic pain costs \$635 billion per year in the United States and \$43 billion per year in Canada when direct health care and productivity costs are considered, which exceed the annual costs from cancer, heart disease, and diabetes.^{20,28} Despite the limited evidence supporting the efficacy and safety of opioids for chronic noncancer pain, they have been the mainstay of treatment in the United States for the past 2 decades. The high opioid prescriptions have been associated with increases in opioid-related mortality due to accidental overdose and in the number of individuals with opioid-misuse disorders.^{3,21} This emphasizes the importance of advancing knowledge on nonopioid treatment regimens, including alternatives, which might replace or enhance the effectiveness of drug therapies.

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The use of mindfulness-based interventions (MBIs) for the management of chronic pain has received considerable attention in the last 3 decades due to its potentially beneficial effects on pain intensity, depressive symptoms, quality of life, as well as emerging evidence regarding its safety.^{23,30,31,35,41} Recent studies have consistently shown a positive relationship between mindfulness and positive psychological health, with clinical uses including the treatment of depression, stress reduction, and tobacco cessation—as well as for chronic pain.^{17,25,39} Although there are variations between mindfulness techniques, their basic procedures and goals are similar.⁷ Mindfulness involves nonjudgmentally observing one's own thoughts, feelings, and sensations in the present moment without attempting to change them.²⁴ A well-studied MBI is mindfulness-based stress reduction.²² Mindfulness-based stress reduction is an evidence-based, structured 8-week group program consisting of 8 weekly 2-hour workshops and a full day session half-way through the course.^{32,34} Mindfulness-based stress reduction includes instruction on mindfulness meditation, body scans, and hatha yoga to facilitate awareness of physical and mental experiences. In addition, participants commit to perform daily 45-minute homework tasks that include meditation and yoga.^{22,32}

A large body of evidence supports the possible benefits of MBIs for patients with chronic pain.^{11,23,26,31,35} Although mindfulness may directly reduce pain intensity, the primary goal of mindfulness is to improve functioning and distress.³⁵ The practice of mindfulness is believed to result in the spontaneous uncoupling of the sensory component from the cognitive emotional component of pain.²⁴ This emotional component can amplify pain and contribute to the development of depression and anxiety, as well as contribute to avoidance of activity, thereby exacerbating disability.⁷ Thus, understanding and controlling the cognitive and emotional components of pain aims to reduce the amount of suffering and disability.

Given the well-recognized limitations of any one modality of treatment for chronic pain, the evolving concept of multimodal therapy has led to the concurrent use of 2 or more different treatment modalities for chronic pain. However, the evidence base to support the rational use of specific treatment combinations is quite limited.²¹ Because MBIs and drug therapies likely reduce pain by different mechanisms, their combined use could provide added benefit. However, there have been no reports of interaction effects of the combination of MBIs with any specific analgesic drugs. Thus, we aim to perform a systematic scoping review to systematically review MBI trials with respect to concurrent drug therapy used during each trial, evaluate the current state of the literature, and look at the evidence for the efficacy and safety of MBI and drug combination therapy compared with monotherapy.

2. Objectives

The objective of this overview is to review the available clinical trials of MBIs for chronic pain to describe the landscape of mindfulness-based trials with respect to drug therapy and evaluate the available evidence on the interactions between MBIs and various drug treatments.

3. Methods

This protocol is developed in accordance with PRISMA-P guidelines³³ and will be registered in the PROSPERO register (protocol number pending).

3.1. Sources of evidence

We will conduct a detailed search on CENTRAL, MEDLINE, EMBASE, and PsycINFO from their inception until the date the

searches are run. The search will include terms relating to MBIs, chronic pain, and relevant clinical pain outcomes. The search strategy for MEDLINE was developed in consultation with a librarian specializing in literature searches.

We will also review the bibliographies of any randomized controlled trials identified for relevance, as well as search clinical trial databases (ClinicalTrials.gov) and the World Health Organization International Clinical Trials Registry Platform to identify additional published or unpublished data.

3.2. Report selection

3.2.1. Types of studies

The review will include randomized controlled trials that evaluate the efficacy of MBIs in the treatment of chronic pain. Studies with less than 10 participants will be excluded to minimize small study bias.

3.2.2. Types of participants

We will include studies with adults aged 18 years and over-reporting any type of chronic pain for at least 3 months. Chronic pain can include persistent (eg, chronic low back pain and fibromyalgia) and intermittent (eg, migraine) pain.

3.2.3. Types of interventions

We will focus on any MBI administered for the treatment of chronic pain. To provide a discrete set of results, we will focus on “mindfulness,” “mindfulness-based stress reduction,” “mindfulness-oriented recovery enhancement,” “mindfulness-based cognitive therapy,” “mindfulness meditation,” “mindfulness awareness in body-oriented therapy,” or any intervention that is a modification of these mindfulness-based therapies. This will allow the current state of mindfulness trials with respect to concomitant drug therapy to be summarized. We will exclude studies where mindfulness is only a component of the intervention.

3.2.4. Comparators

Studies comparing the MBI can be compared with usual care, wait-list control, or an active comparator.

3.3. Data collection, extraction, and management

Two reviewers will independently evaluate studies for eligibility. Screening will be performed on titles and abstracts, and full-text screening will be performed on citations felt to be potentially eligible. Disagreements between the reviewers will be resolved by discussion and consensus. If necessary, a third reviewer will be consulted.

Data from selected studies will be extracted independently by two reviewers using standardized extraction forms. The forms will capture information about the chronic pain conditions of participants, type of mindfulness-based treatment investigated, primary and secondary outcome measures, and other study characteristics.

3.4. Outcomes

3.4.1. Primary outcomes

Our primary outcomes will include the following: (1) What concomitant analgesic drug therapies the trial participants were receiving, (2) if and how trials controlled for what concomitant

analgesic drug therapies the participants were receiving, and (3) if trials analyzed the interaction between the MBI and the concomitant drug therapies the trial participants were receiving. As an example, we will report on any subgroup analyses on the effect of the MBI with or without a specific concomitant analgesic drug. For the trials that analyzed the interaction between mindfulness and drug therapy, we will also look at what the results were in terms of pain intensity and pain relief (eg, MBI and drug combination therapy compared with monotherapy in reducing pain intensity).

3.4.2. Secondary outcomes

Secondary outcomes include how MBI and drug combination treatment differs from monotherapy in managing secondary features of chronic pain such as depression, physical and mental health-related quality of life, and functional disability. Secondary outcomes will also include participants experiencing any adverse event and participants experiencing any serious adverse event.

3.5. Analysis plan

3.5.1. Analysis of outcomes

A descriptive approach will be used to report the primary outcomes because the outcomes will likely be varied across studies. We will also use a descriptive approach to evaluate how the combination treatment differs from the individual treatments in managing secondary features of chronic pain such as depression, physical and mental health-related quality of life, and functional disability. Analysis of trial outcomes will be categorized according to the type of control intervention used in the trial. The interaction between MBIs and drug therapy will be evaluated to the degree that each trial accounted for drug effects.

3.5.2. Analysis of risk of bias

Risk of bias for each study will be independently assessed by 2 reviewers using criteria outlined in the Cochrane Handbook for Systematic Review of Interventions (25). For any studies that include both an MBI and an analgesic drug as the trial interventions, risk of bias will be assessed separately for each intervention. Disagreements between reviewers will be resolved with discussion and consensus. If necessary, a third reviewer will be consulted. We will assess the following for each study: (1) random sequence generation for possible selection bias; (2) allocation concealment for possible selection bias; (3) blinding of participants and personnel for possible performance bias; (4) blinding of outcome assessment for possible detection bias; (5) incomplete outcome data for possible attrition bias; (6) selective reporting for possible reporting bias; and (7) size of study for possible biases confounded by small sample size. Each category will be assigned a low, unclear, or high risk of bias and presented with a "Risk of bias" graph and "Risk of bias" summary.

3.5.3. Dealing with missing data

No pooled analysis is planned in this review. Missing data regarding concomitant drug therapy will be used to aid in the describing the landscape of trials investigating MBIs for chronic pain patients with respect to drug therapy.

4. Discussion

Chronic pain is a common and complicated health issue that has a marked negative impact on patients' quality of life, physical and mental health, relationships, and productivity.^{2,6} In North America,

physicians have increasingly prescribed opioids for chronic pain in efforts to reduce pain intensity, despite the lack of rigorous research demonstrating its long-term effectiveness.^{13,18,19} Deaths from prescription opioid overdoses quadrupled in the last 15 years in the United States, with >210,000 prescription opioid-related deaths since 1999, emphasizing the need for an alternative approach to chronic pain management.¹ Efforts by the government and regulatory bodies to curb the opioid crisis is unlikely to be an effective solution to the chronic pain crisis.⁴⁰ The nature of attention given to the opioid crisis may worsen the stigma associated with the proper use of prescription opioids, and result in patients being aggressively tapered off prescription opioids without other treatment options to help control their pain.¹⁶ Therefore, the issue of chronic pain should be managed in a larger context than simply the opioid crisis.⁴⁰ Other primary pharmacological modalities for chronic pain management include antidepressants, anticonvulsants, nonsteroidal anti-inflammatory drugs, and muscle relaxants.²¹ However, because of the dose-limiting adverse effects and limited efficacy of many these therapies, there is still a significant unmet need for sufferers as many patients with chronic patients are still in pain despite treatment.^{21,29} Furthermore, despite advancements in chronic pain research, finding a safe alternative for chronic pain remains a large challenge.²⁹ Emerging evidence supports the safe use of MBIs in reducing pain intensity as well as improving secondary features of chronic pain.^{5,14,23,35} However, little is known about the current state of MBI trials with respect to concomitant drug therapy. In addition, there is no consensus regarding the clinical effects of MBIs in combination with current drug therapies for chronic pain. This review seeks to elucidate the current state of the literature and clinical effects of this combination, provide information to health care professionals on how MBIs can be integrated into patients' multidisciplinary chronic pain management strategy, and improve the quality of life of chronic pain patients. Understanding the unique effects of MBIs and its combination with drug therapy on chronic pain can also help patients formulate realistic expectations of mindfulness therapy and potentially facilitate adherence, which may help patients live productive lives despite discomfort.

Disclosures

The authors have no conflict of interest to declare.

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