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Short Communication

Mindfulness Based Therapies for Autoimmune Diseases and Related Symptoms

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Abstract

Over the past few decades, there have been minimal advances in effective new behavioral or psychotherapeutic interventions for people living with autoimmune diseases such as systematic lupus erythematosus. This is problematic due to the severe, debilitating and potentially life-threatening nature of these diseases. Mindfulness based interventions, such as Mindfulness Based Stress Reduction, have demonstrated effectiveness in a wide range of patient populations and we hypothesize such treatment would also benefit patients with autoimmune disorders and related symptoms. We further hypothesize that these therapies will work by impacting physiological mechanisms, such as inflammatory markers, associated with such disease symptoms. We present our findings below.

Keywords

Mindfulness; autoimmune disorders; mind-body; MBSR; MBCT

1. Introduction

Autoimmune disorders are a group of conditions in which structural or functional damage to cells/tissues/organs/organ systems is produced by the correlation of immunologically competent cells or antibodies against the normal component of the body. There are multiple autoimmune diseases known to modern medicine, including inflammatory diseases such as rheumatoid arthritis, psoriatic arthritis, and multiple sclerosis, among others. Specific symptoms associated with these diseases include chronic fatigue, joint and other pain, swelling, skin rashes, and anemia [1]. Symptoms range from subtle to life-threatening, often wax and wane, and impact multiple organ systems [1]. Autoimmune disease appears to be on the rise [2]. According to Nakawaza [2], type 1 diabetes increased by 23% between 2001 and 2009. The incidence of celiac disease, a condition where the body's immune system attacks the small intestine, is also on the rise according to the U.S. National Institutes of Health and the University of Chicago Celiac Disease Center [3]. Patients with autoimmune disorders often suffer from additional neuropsychiatric and psychological comorbidities [4-6]. For example, throughout their lives, 65% of patients with SLE will be diagnosed with a mood or anxiety disorder, including major depression (47%), specific phobia (24%), panic disorder (16%), obsessive-compulsive disorder (9%), and bipolar disorder (6%) [7]. There is evidence for biological etiologies of neuropsychiatric SLE implicating neuroactive autoantibodies such as anti-ribosomal-P antibodies, antiphospholipid antibodies, anti-glutamate receptor antibodies (a subset of anti-double stranded DNA antibodies that cross react with N-methyl-D-aspartate (NMDA) receptor subunit 2), anti 16-6 idiotype (anti double stranded DNA idiotype), anti-gamma-aminobutyric acid type B receptor (GABAR(B)) antibodies and anti-endothelial cell antibodies [4, 8-10]. However, definitive pathophysiologic mechanisms that explain the breadth of psychiatric and psychological symptoms remains elusive. Overall, the negative psychological impact associated with symptoms may be significant and can exert a considerable negative impact on patients' quality of life [7].

2. Current Treatments

Treatment of symptoms related to autoimmune disorders is multifaceted and primarily involves education and pharmacologic management of physical symptoms, as well as addressing related cardiovascular risk factors, associated infections, psychological issues, and treatment complications [10-14]. Treatment of psychological issues may be an additional component of care [15, 16]. Contemplative approaches to psychosocial treatment in the form of mindfulness-based interventions (MBIs) are increasing and have been found to be effective in treating both psychological and medical conditions, as well as associated symptoms characterized by intrusive pain, such as arthritis and fibromyalgia [17, 18]. MBI techniques aimed generally at the reduction of psychological symptoms of distress and enhancement of quality of life are used to cultivate the mental quality of mindfulness, an

open minded, flexible, and nonjudgmental awareness of whatever is happening at each successive moment of perception. The objects of both direct and pre-reflexive perception range from somatic interoceptive, kinesthetic, and proprioceptive experiences (bodily sensations, movements, awareness of breath, etc.) to internal psychological states (feelings, thoughts, images, etc.) as well as external stimuli experienced through the senses. Sustained development of mindful attention to these objects leads to improved self-regulation and orientation to a patients' objective experience [19].

One of the most well-studied mindfulness-based interventions (MBI) is Mindfulness Based Stress Reduction developed by Jon Kabat-Zinn at the University of Massachusetts [19-21]. Rooted in core Buddhist principles that all physiological suffering arises from a judgmental mind, MBSR in a 8-week structured course consisting of weekly two and a half hour group sessions, aims at cultivating the nonjudgmental mental quality of attention, mindfulness, through a variety of experiential contemplative practices including sustained formal meditation (focused attention and open monitoring sitting sessions, hatha yoga, body scan, walking and eating meditation) as well as informal practices that can be incorporated into daily life (momentary pauses in activity, mindful communication, movement). With regular training these practices result in the reduction of the habitual tendency to automatically and compulsively engage in and react to one's own physical and mental states as well as environmental conditions [21].

Additional MBIs based on MBSR have been developed to work more specifically with different populations and conditions. Mindfulness Based Cognitive Therapy (MBCT) [22] was developed as a method for the prevention of relapses of major depression. Like MBSR, MBCT was developed as a secular, clinical intervention that further combines the practice and clinical application of the 8-week mindfulness training with the tools of cognitive therapy that draws a direct correlation between the way events are perceived and feeling about them and, in turn, how one behaves. MBCT therapists teach clients, through practices such as mindfulness meditation and breathing exercises, to be aware and transform negative thought patterns that can cause a downward spiral into a depressed state. Another MBI, Mindfulness Awareness Practices (MAPs [23] is group programming based in MBSR/MBCT models that includes sitting mindfulness meditation exercises, movement, and body scan to promote awareness of self, other, and environment. Duration of MAPs programing varies between 6-8-week long periods with practice sessions gradually lengthening over the course of the program.

Biological markers associated with mindfulness practice include reduced urine cortisol levels and increased number of white blood cells [24]. Mindfulness has been found to reduce anxiety, stress and depression in individuals with chronic physical and mental health conditions [25]. It reduces fatigue and pain, increases quality of life and self-efficacy, and positively impacts various biological and immunological markers in autoimmune disorders such as arthritis, heart disease, diabetes, cancer and asthma [26-29].

Reviews of randomized controlled trials (RCTs) demonstrate that MBIs can exert beneficial effects on stress-related ailments, psychiatric disorders, and disease symptomatology [21]. The research base documenting the effectiveness of MBIs relies heavily on participants' self-reports of their own health status, which can be prone to bias. Additionally, while a more recent, yet relatively small body of literature also exists examining how MBIs affect objective biological markers of human health, there is

no comprehensive literature reviews conducted to evaluate how mindfulness meditation influences biological processes that are most centrally involved in disease pathogenesis. Markers of immune system activity are particularly relevant in this context, given that immune system dynamics have been implicated in several major mental and physical health problems, including asthma, rheumatoid arthritis, metabolic disorders, neurodegenerative disorders, certain types of cancer, and SLE. Therefore, in the present review, we examined the question of whether MBIs can influence peripheral biomarkers of immune system activity associated with symptoms that are typically gathered via self-report from patients suffering from autoimmune disorders.

3. Methodology

3.1 Study Design

To test our hypothesis that MBIs can be used for autoimmune disorders and will impact physiology in a positive manner, we conducted a review of the use and impact of mindfulness based or mind-body interventions in patients with symptoms associated with the autoimmune disorders with a focus on SLE. Utilizing the PubMed and OVID databases in the summer of 2016, we searched the following specific terms: Systemic Lupus Erythematosus; SLE; mindfulness; mind-body interventions; yoga; fatigue; pain; poor immunological status, and cross referenced with physiological terms: Cytokines; Chemokines; inflammatory response; immunological response; genetic. Our criteria for inclusion included that the article had to clearly focus on a clinical application of mindfulness or mind-body interventions administered to human patients with symptoms of SLE, include minimal information regarding the impact on immunological functioning, inflammation or other relevant biological aspect of SLE disease process, be written in or translated into English, and not be a single case design. After reading each manuscript, we followed up by obtaining all relevant articles referenced, and eventually obtained 21 studies which met our criteria.

3.2 Results

Of the 21 studies reviewed, 10 used a standard Mindfulness Based Stress Reduction (MBSR) intervention [30-39], 5 used adapted versions of MBSR or Mindfulness Based Cognitive Therapy (MBCT) [40-44], 2 used Mindful Awareness Practices (MAPS) [45, 46], 3 used customized Mindfulness Based Interventions (MBI) [47-49] and one used a residential mindfulness retreat [50]. The largest number of studies used MBSR as the contemplative intervention. All studies included autoimmune disorders and symptoms common to such. There were 943 total subjects in these 10 studies, with predominantly female participants. They included participants suffering from respiratory infections, HIV+, and rheumatoid arthritis, and explored the effects of MBSR on various biological, immunological, and psychological parameters. Changes in biological/immunological markers were observed in 8 out of the 10 MBSR studies [31-33, 35-39] with 2 MBSR studies reporting no significant changes [30, 34]. In terms of psychological functioning, 8 studies reported improvements in psychological functioning [30-32, 34, 36-38], 1 study did not measure these changes [35], and 1 found no changes [33]. These results support that non-pharmacological treatment can positively impact psychological functioning

as well as biological markers and may thus be used to complement standard medical treatment. Five studies used an adapted version of MBSR/MBCT and included 530 participants [40-44], of which more than 80% were females. These studies included patients suffering from rheumatoid arthritis and breast cancer patients. Out of these studies, 3 reported positive changes in immune markers associated with reductions in disease symptomatology and disease progression [44, 48, 49]. Two studies reported improvements in pain, self-efficacy, and other psychological outcomes [40, 42] while an additional two studies reported no change in psychological outcomes [43, 47] and one study that did not assess psychological functioning [41].

Two studies used Mindful Awareness Practices (MAPs) and included 88 total participants with more than 80% female participants [45, 46]. These studies included people with sleep disturbances and breast cancer survivors. Both of these studies found improvements in immunological markers which indicates that biological markers can be altered by using mindful awareness practices. Both studies also reported improvements in sleep quality and sleep disturbances and other psychological outcomes. Three studies incorporated different components of mindfulness with varied duration to target immune markers in normal samples, obese women, and in patients with ulcerative colitis [31, 33, 48]. These studies included 137 participants and 72% were females; one study included 100% obese women. All studies found changes in immunological markers, of which two studies reported an increase in telomerase activity and one study reported decrease in TNF-α which suggests that even integrating different components of mindfulness and varying duration from a standard MBSR program can result in improvements of biological markers. In fact, all three studies increased the duration of their intervention which also indicates that spending more hours and weeks in mindfulness may show greater improvements in the outcomes. Similarly, all three studies have reported improvements in mental health, perceived control, and quality of life. This may lend support for the idea that increasing the duration of the intervention may result in more beneficial outcomes.

Although varied immunological markers were measured in these selected studies, there is evidence that MAPs, MBSR, and mind-body therapy all have a significant effect on decreasing TNF-alpha levels. In the HIV population both Creswell et al. [35] and Seyed Alinaghi et al. [32] noted significant increases in CD4+ T lymphocyte activity after MBSR treatment. Furthermore, changes in T cell activity was noted outside the HIV population by Lengacher et al. [41] following similar MBSR treatment. NF-kB concentrations appears to be responsive to MAPs as well as MBSR according to three studies. Telomerase activity is noted to increase after mindfulness-based interventions [48]. One study noted an increase in IL-10 activity following MBSR, but there exists contradicting evidence involving IL-8. IL-6 is measured in five studies but only in Bower et al. [46] is there a measurable decrease after MAPs. In the four other studies looking at MBSR and MBCT there appears to be no effect on IL-6 concentrations.

4. Discussion

In our review of the current literature on treatment with MBSR, adapted versions of MBSR/MBCT, and MAPs as contemplative interventions for patients suffering from autoimmune disease processes or symptoms similar to such, we found a correlation with respective biomarker changes and

improvements in psychological functioning for subjects in a majority of studies that assessed these parameters. There are additional notable limitations to the generalizability of the above conclusions. The gender of patients is significantly skewed with some studies consisting of 80% female patients. There appears to be general consensus regarding the psychological benefits of mindfulness-based interventions correlated with improvements in the occurrence of negative emotions including anxiety, stress, and increased experiences of positive emotions including optimism, feelings of support, and better coping in a variety of treatment lengths and variations. The relationship between mindfulness-based interventions and various physiological markers of disease activity is not as clear. This is exemplified in the Zautra et al. [42] study which show inconsistent evidence regarding expected IL-6 response for different modalities of mindfulness interventions. These findings suggest that there is no consensus that increasing emotional regulation positively impacts cytokine activation. Principle questions still remain regarding the underlying mechanisms that dictate the complex immunologic cascade and its responses to mindfulness intervention that lead to the detected biomarker changes. Additionally, factors such as previous psychiatric history, age, baseline health, baseline behavior (i.e. sleep and diet), and adherence to therapy have all been proposed as potential confounders to observed biomarker changes resulting after mindfulness therapies.

Another limitation is the variable quality of the studies reviewed in this manuscript. Notable within most of the studies are the small study sizes that are not necessarily powered to answered to key questions. For example, in Zautra et al. [42], we find too few subjects to provide reliable analysis regarding biomarker changes once subgroups accounting for previous depression history were made. In Seyed Alinaghi et al. [32], key questions regarding CD4 responses were inconclusive due to inconsistent blood sampling, poor randomization procedures, and the lack of a control group for the MBSR group. In the Moynihan et al. [38] study, biomarker changes could not be completely interpreted due to the lack of baseline antibody measurements and appropriate controls for biomarker changes.

Despite the above limitations, the results of these studies do appear to support that MBIs are not harmful and may have a positive impact on patient outcomes. Studies that show MBSR affecting immune pathways involving TNF-alpha, IL-10, modulations in T-Cell activity demonstrate potential pertinence to immune pathways implicated in autoimmune mechanisms of SLE and other diseases [39, 42, 46, 50]. Together these studies offer initial evidence that MBSR and its variants may be a positive addition to pharmacotherapy, may promote psychological well-being, and potentially enhance physiologic and immunologic responses.

We propose that information collected in this review can be incorporated to augment existing interventions for patients with autoimmune disorders or related symptoms, with a design to target the specific symptoms and underlying immune pathways and markers, while also honoring the limitations of the patient population. For example, interventions associated with longer sessions and longer duration of intervention may be more impactful, but may be less well tolerated by individuals who are in pain or have limited mobility. Thus, finding a length of intervention that can positively impact physiological markers yet be tolerated by patients is important and may involve reducing the 8-week length of traditional MBSR. Additionally, adapting the yoga or other physical components of traditional MBSR may be needed in order to accommodate patients with limited mobility. Designing

an effective yet accessible MBI for this patient population is a challenge, and our hope is that this manuscript may begin to help inform such research, despite its not insignificant limitations.

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Author Contributions

JKP designed the study and all authors (JKP, DC, NA, JMP, NL, YRX, SM, NS, PK, JL, LH) helped conduct the literature review, write up the results, and edit multiple versions of the manuscript and the final manuscript.

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Competing Interests

The authors have declared that no competing interests exist.

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