



Practice Guidelines for Treatment of Somatic Pain and Depression

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Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

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ABSTRACT

Background: Somatic pain is often associated with depression. Patients presenting with this combination can be difficult to treat and create a significant financial burden on the medical system. The mechanisms of action linking somatic pain and the myriad of depression are not clearly understood thus highlighting a gap in knowledge between the scientific mechanism, pathogenesis, and psychiatry involved in depression and somatic pain. The objective of this review article is to address etiologic factors and possible mechanisms associating chronic somatic pain and depression. Additionally, this article provides practice guidelines in the management of somatic pain patients with depression.

Methods: Systematic review of literature on human studies published in English language from 2000-2017 using PubMed, EBSCO, and Google Scholar was performed.

Results: Approximately, 76 studies that were recent and relevant were included in the final review. More than 75% of patients with comorbid depression complain of somatic pain such as headache, neck pain, stomach or back pain including generalized body pain. Socio-demographic factors (advanced age, female gender, marital/relationship status, low educational level), clinical correlates (pain location, duration, score, use of medications), psychosocial correlates (pain self-efficacy, coping skills, quality of life), medical conditions (type 2 diabetes mellitus, fibromyalgia, connective tissue diseases, musculoskeletal or autoimmune disorders), and patient determinants (doctor

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shopping, aberrant medication-related behaviors like prescription drug misuse or abuse, early refills) are associated with somatic pain in patients with psychiatric comorbidities. Practice guidelines include improving provider-patient relationship, detailed history taking, performing physical exam, obtaining laboratory and radiologic exams, administering validated screening method for pain and depression scales, pharmacotherapy with multi-target agents, psychotherapy, functional restoration program, physiotherapy for chronic pain, self-management strategies (yoga, mindfulness) and including a multi-disciplinary treatment team.

Conclusion: This article has important implications for clinical practice as it not only highlights the epidemiology and correlates of somatic pain and depression but also provides practice guidelines for managing somatic pain patients with comorbid depression.

Keywords: Somatic; pain; depression; treatment; practice guideline.

1. INTRODUCTION

Somatic pain is a common clinical presentation in patients suffering from underlying depression that is often underreported and goes undiagnosed [1]. Patients presenting with somatic pain symptoms in the form of non-specific headache, vague body aches and musculoskeletal pain often have multiple doctor's office visits and go through various primary care clinics, including behavioral, and pain specialty clinics. For resolution of pain symptoms, such patients' engagement in doctor shopping activities and subsequent interaction with diverse specialty providers' may lead to multiple clinical assessments, laboratory and radiologic exams that may not be necessary or effective in the management of patient care.

Frequent healthcare visit with presentation of somatic pain symptoms is also associated with twice the annual health care costs [2]. A study involving a cohort of neurology patients reported that somatic pain and depression often coexist, persist for an extended time period, and have long-term negative effects on health status; such patients have greatest utilization of healthcare services and significant health impairment [3]. Hence, somatic pain in depressed patients not only proves to be costly for the patient, community, and healthcare system but also serves as a source of iatrogenic problems from unnecessary invasive procedures and ongoing discomfort to the patient. Somatic pain patients are thus often caught up in a merry go round circle between pain somatization compounding pain that again manifests as somatic pain symptoms necessitating frequent doctor office visits without an in-depth evaluation of pain causing depression and vice-versa. Such patients can be difficult to treat, and often pose a significant challenge for providers. Therefore,

somatic pain in patients suffering from depression poses a major public health problem.

Validated screening instruments with excellent psychometric properties like the Patient Health Questionnaire (PHQ-9) are routinely administered in clinics to screen and assess the severity of underlying depression that could help explain the somatic pain symptoms [4]. Although, screening instruments are available in clinics to assess underlying depression associated with somatic pain symptoms, but, they are subjective, as they assess responses based on patient self-report and do not have an objective criteria or reflect personal experiences of individual patients. Nevertheless, the exact mechanism of action linking the association between depression and pain is not clear and often not measurable through subjective questionnaires. Additionally, the myriad of somatic pain symptoms in underlying depression that is poorly understood, highlights a knowledge gap between scientific mechanism, pathogenesis and the psychiatry associated with somatic pain. Here we review the etiological factors and possible mechanisms of action associating somatic pain and depression. This article has important implications in clinical practice as it also provides practice guidelines for managing somatic pain patients with depression.

2. METHODS

Online databases (PubMed, Medline, EBSCO, Psychinfo) along with articles from Google Scholar were searched from 2000-2017. Only articles published in the English language were included. Key reviews and original research articles for the adult population were included using the following terms: "pain", "somatic", "symptoms", "psychiatry", "neuro-psychiatric", "depression", "anxiety", "primary care", "clinic",

“etiology”, “prevalence”, “epidemiology”, “pathology”, “pathogenesis”, “practice”, “guidelines”. These search terms were used in combination with each other using the conjunction “AND” and “OR”. The search was supplemented by a manual review of the reference list from relevant articles. The search yielded more than 400 articles. A total of 250 articles were included for the initial review. The articles were each reviewed individually. Articles were excluded for duplication, animal studies, studies emphasizing on pain or depression associated with cancer, HIV, surgery, autoimmune or specific diseases. Approximately, 76 articles that were recent and clinically relevant to the topic or subheadings were included in the final review.

3. RESULTS

3.1 Epidemiology

A review of literature resulted in numerous publications reporting the presentation of somatic pain associated with depression. More than 75% of patients with comorbid depression reported somatic pain such as headache, neck pain, stomach, or back pain including generalized body pain [5,6]. Majority of the epidemiological studies conducted in Europe report a positive correlation among patients with depression and physical pain symptoms. For example, in Norway, 75% of patients with major depression report at least one non-affective complaint [7]. One study indicated that patients with depression and physical pain symptoms have more depressive symptoms, score higher on somatic symptoms, suffer more everyday disabilities, and frequently visit a general practitioner [7]. Among depressed patients unexplained painful physical symptoms or medically unexplained pain complaints are prevalent [7].

Population survey studies indicate that the prevalence of co-occurrence of somatic pain and one depressive symptom is 28%; while those with chronic pain (lasting more than 3 months) and an established diagnosis of major depressive disorder (MDD) is 43% [8]. In other studies, approximately 45-50% of patients with a diagnosed psychiatric condition, self-report their somatic pain symptoms [9,10]. One large study reported that depressive symptoms are present in 80.4% of subjects with higher prevalence in women; among them 56.2% had major depression and 17.8% had dysthymia/mild depression [11]. Majority of pain complaints

associated with underlying mood disorders are localized in the neck and back (71.6%), including headache (64.7%) and joints or limbs (61.3% vs. 58.5%) [11].

Patients with depression commonly present to the clinic with low back pain [12]. Prevalence of chronic low back pain (39.5-40%) and headache (43%) is high among patients with depression [13,14]. Prevalence of chronic pain involving multiple sites is reported to be 50.4% and is higher among patients with a mood disorder (major depression or bipolar disorder) than those without a mood disorder [15]. A similar study indicated that patients with major depression reported significantly higher proportion of chronic pain than those without depression [16]. In this cohort of chronic pain patients, when depression symptoms are unrecognized and untreated, they become worse with poor health outcome and pose considerable economic burden [17,18]. Thus, prior studies indicate that these conditions often coexist and therefore, clinicians should be aware that both depression and somatic pain will need to be treated together in order to observe any significant improvement among this cohort of patient population.

3.2 Etiology and Pathogenesis

Although there is an observed association between somatic pain and depression, it is difficult to assess causality or temporality of association. Prior studies failed to identify a specific cause-effect relationship since either the somatic pain or depression can precede the other. One possible research question arises is that whether it is the depression that is presenting as somatic pain, or is it the somatic pain presenting with symptoms of depression?

Neurobiological links to pain and comorbid psychiatric conditions are complex and suggest that each set of symptoms exacerbates the other, mutually amplify each other, or worsen in response to stress [19]. One study indicated a higher level of pro-inflammatory cytokine, P-selectin associated early micro-vascular changes as detected by Enzyme linked immuno-sorbent assays (ELISA) in a depressed population with somatic pain [20]. Another study highlights a dysregulation of the serotonergic and noradrenergic neurons or neural pathways of the raphe nucleus and locus-coeruleus (directly link pain and symptoms of depression) might provoke or enhance either or both conditions [21]. These studies point at the neurobiological evidence associating somatic pain and depression.

Functional MRI (fMRI) studies indicate structural and functional changes in the brain among patients with psychiatric comorbidities (depression) along with neuroendocrine, autonomic, and immune dysregulation; including exaggerated cortisol response to ACTH hormone [22]. Another possible mechanism suggested is an increased central (spinal and supraspinal) pain sensitization and altered cerebral processing of painful stimuli in patients with depression and therefore an established altered pain perception is reported in patients with depression [23,24].

3.3 Socio-demographic Factors

Advanced age, female gender, and lower educational level are associated with somatic pain in patients with psychiatric comorbidities [25]. Bodily aches and somatic pain symptoms in the absence of definitive diagnosis and comorbid depression are prevalent in women during midlife, especially during menopause [26]. Women are more prone to present with somatic symptoms of chronic pain in primary care clinics that is often mediated by depression [27]. One study reported that among women with chronic pelvic pain, a history of physical or sexual abuse is associated with higher levels of depression compared to women who reported no abuse [28].

Marital status is associated with coping of pain and depression [29]. For women in chronic pain, being happily partnered is associated with less pain-related disability, more adaptive affective and cognitive responses to daily pain changes than unhappily partnered and un-partnered patients [30]. In this context, one longitudinal study reported that loneliness is a significant risk factor for the development of pain and depression [31]. Therefore, relationship status plays a pivotal role in coping with affective responses among patients with chronic pain.

3.4 Clinical Correlates

Somatic pain correlates are primarily psychiatric conditions such as depression and anxiety [32]. One study reported that a higher number of pain locations including joint pain, pain duration greater than 90 days, daily use of pain medication, and a higher chronic pain grade score are associated with worsening of depression and anxiety disorders [33]. Another study reported similar findings except that the depression severity was not associated with pain duration ($p=0.15$) or the age of the patient

($p=0.24$) [34]. Clinical correlates of somatic symptoms in depression are severity of depression, higher scores for generalized anxiety disorder, somato-sensory amplification, and difficulty identifying and communicating emotional distress (alexithymia) [35]. Conversely, determinants of chronic nonspecific shoulder pain are depression, burnout, and alexithymia [36]. The commonly co-occurring comorbid psychiatric conditions associated with chronic pain often negatively reinforce each other and are associated with higher somatization scores [37,38]. Therefore, it is important to recognize and treat clinical correlates of pain if one is to improve outcomes.

Patients with somatoform disorder often present with medically-unexplained physical symptoms with comorbid psychiatric conditions (anxiety, depression) [39]. The somatic pain symptoms are often recurrent, multiple, and associated with various gastrointestinal, sexual, or neurologic features [40]. Other clinical correlates for somatic pain and psychiatric comorbidities include personality disorder, hypochondriasis, malingering, and substance use disorders [41-43].

Personality disorders occur in approximately 40-50% of patients with chronic pain according to some studies, with the most prevalent subtypes being borderline, paranoid, and obsessive-compulsive personality [44]. With respect to borderline personality disorder, the presence of chronic pain and somatization may be reflective of self-regulation difficulties inherent to the personality [44]. Severe headaches and migraine are common in patients with borderline personality disorder [45]. Therefore, somatic preoccupation along with mood disorders appears to be prevalent in this population with underlying personality disorders.

3.5 Psychosocial Correlates

Psychosocial correlates including health perception, sense of coherence, pain self-efficacy, and health-related-quality-of-life (HRQOL) are associated with somatic musculoskeletal pain and depression [46]. Nearly half of primary care patients with chronic pain screen positive for one or more anxiety disorders and are adversely associated with impairment across multiple domains of HRQOL [47]. Other psychosocial factors such as perceived poor social support and passive coping responses are also associated with depression and perceived pain intensity [48].

Baseline self-rated health is associated with post-pain depression and chronic depression trajectories [49]. The post-pain depression trajectory describes a pattern of low depression at baseline and increasing symptoms following pain onset while chronic depression trajectory has persistent high depression symptoms irrespective of pain onset among middle aged adults [49].

In a surgical population, a prospective cohort study of over 600 patients demonstrated that among psychological variables, the preoperative fear and anxiety of long-term consequences of surgery was associated with worse chronic pain-related dysfunction, and conversely optimism favored a good surgical outcome and was associated with an overall better outcome [50]. These studies highlight the importance of identifying the underlying psychosocial processes that are often associated with somatic pain and psychiatric comorbid conditions.

3.6 Medical Conditions

Somatic pain and depression often coexist in patients with medical conditions like type 2 diabetes mellitus [51], skeletal and autoimmune disorders such as osteoarthritis [52] and rheumatoid arthritis [53]. Additionally, self-reported symptoms of pain and depression are observed in fibromyalgia and other musculoskeletal disorders [53]. They are also prevalent in neurodegenerative disorders such as Parkinson's disease (PD), restless leg syndrome [54] and Alzheimer's disease (AD) [55].

Chronic fatigue syndrome (CFS) is often associated with pain and depression [56]. CFS patients exhibit oxidative stress induced damage that increases autoimmunity, which subsequently increase specific inflammatory biomarkers that can explain part of the biological mechanism of somatic pain symptoms and depression in these patients [56]. Thus, comorbid medical conditions are often associated with somatic pain and depression.

3.7 Patient Determinants

Doctor-shopping behavior (seeking multiple providers for the same complaint) is often observed in anxious, worried and depressed patients with chronic pain who also exhibit a high level of demand and cost for healthcare-related services [57]. Aberrant medication-related

behavior including prescription medication misuse or abuse, requests for early refills of controlled substances, borrowing or stealing prescriptions from friends or family, and prescription diversion is observed to a greater extent among chronic pain patients with depression or anxiety [58]. Apart from the psychiatric comorbidities of depression, anxiety, and somatization disorder these chronic pain patients who abuse opioids also have substance abuse issues [59]. Malingering behavior for personal incentives such as litigation, financial reward, or seeking disability status is not unsurprisingly associated with exaggerated somatic complaints and intentionally poor effort on performance testing [60,61]. Primary care patients with somatic pain and comorbid psychiatric problems including hypochondriacal health anxiety have frequent doctor visits and higher medical care utilization [62]. Thus, patient determinants and individual patient characteristics play a significant role in associating somatic pain symptoms to comorbid psychiatric conditions.

3.8 Practice Guidelines

Prior studies have detailed practice guidelines in the management of somatic pain symptoms in patients with psychiatric comorbidities including depression [63-76]. These include:

1. Establish a good therapeutic alliance with somatic pain patients with comorbid depression. Such patients can be difficult to treat and a caring, compassionate patient-provider relationship that is trustworthy is the key to successful management.
2. Obtain a detailed history, perform thorough physical exam, and formulate a differential diagnosis that is necessary to rule out an organic pathology of pain before associating somatic pain with psychiatric comorbidities.
3. Establish diagnosis and discuss the treatment plan/regimen with the patient.
4. Administer validated screening instruments and pain scales with excellent psychometric properties [patient health questionnaire (PHQ-9), Generalized Anxiety Disorder (GAD-7), pain catastrophizing and interference scale etc.] to assess clinical condition, severity of symptoms and to monitor progress.
5. Obtain laboratory exams (CBC with diff, BMP etc.) as underlying hemodynamic

- changes and metabolic derangements (hypo/hyperkalemia) can present as vague aches and somatic pain.
6. Consider obtaining advanced radiological imaging to visualize underlying anatomic abnormalities or pathological conditions that might be responsible for their pain.
 7. Obtain consultation with psychiatrists, psychologists, neurologists, pain management specialists, and surgeons when necessary.
 8. Pharmacotherapy with multi-target agents that act on several neurochemical pathways (serotonin, norepinephrine) like duloxetine (SNRI) have minimal side-effects and demonstrate dual action since they target both depression and pain [66-67]. Antidepressant medications targeting postsynaptic 5HT_{1A} (serotonergic receptors) have demonstrated efficacy in affective/mood, anxiety disorders and pain [68]. The anti-hyperalgesic and antinociceptive effects of antidepressants like tricyclics (amitriptyline), SNRI-duloxetine, and atypical antidepressant-mirtazapine are proven effective in chronic pain, pain-induced anxiety and comorbid depression [69-71]. There is a weaker body of evidence to support SSRI medications, though some studies have indicated they may be efficacious to a degree for neuropathic pain [72,73].
 9. After initiating pharmacotherapy, monitor for effectiveness, focusing on functional improvements such as sleep, activity, concentration, mood, opioid-reduction, and even employment status. If the side-effects are intolerable or improvement is not observed, consider increasing the dose or switching to a new class of medication.
 10. Advise contraception and provide family planning counseling for women of childbearing age as these pharmacologic agents could have teratogenic potential.
 11. Cognitive behavioral psychotherapy (CBT) for depression and pain should be used in combination with pharmacotherapy as part of comprehensive treatment plan for somatic pain patients with psychiatric comorbidities.
 12. Functional restoration programs (FRP) and physiotherapy for chronic pain have been demonstrated to significantly improve health-related quality of life compared to standard treatment [74].
 13. Self-management strategies (mindfulness, yoga, self-physical therapy, meditation), complimentary and alternative medicine (CAM) modalities (acupuncture, chiropractic care, medical massage) are often pooled with mainstream medical therapies, a practice referred to as integrative medicine. These are proven in sum to be beneficial for the treatment of chronic pain, anxiety, and depression [75].
 14. Procedural-based treatments should be used with great caution in patients with exaggerated somatic complaints, as this population has been shown to be at a higher risk of false-positive results from diagnostic procedures.
 15. Patients prescribed controlled substances should sign treatment agreements with clear treatment goals and undergo regular comprehensive urine drug tests that not only screen for illicit substances but also monitor for compliance to non-opioid pain medication regimens.
 16. Treatment-resistant patients ideally would benefit most from evaluation and treatment by a multidisciplinary pain management team that includes primary care physicians, psychiatrists, psychologists, pain specialists, physiotherapists, pharmacists, nurse practitioners, counselors, and social workers, all of whom work together closely on a daily basis in a shared workspace. This is typically the model at the authors' medical center and in other centers of excellence around the country. Treated within this paradigm, these challenging patients receive an adequate biopsychosocial evaluation, and treatment plans that emphasize education, optimization of psychological comorbid conditions, functional restoration, and prudent medication management, while simultaneously de-emphasizing passive modalities that possess the potential for iatrogenesis such as poorly monitored medication use, procedures and surgery.

4. CONCLUSION

Somatic pain is associated with depression. No study has been convincing in providing a definitive etiology or pathogenesis of causality of somatic pain manifestation in patients with comorbid psychiatric disorders and vice-a-versa. It is uncertain as to whether the pain itself is leading to a progressed disease state that manifests itself as a psychiatric illness, or if it is the psychiatric illness that is creating the

physiological somatic pain response. Although, prior studies have observed this association and have characterized traits and patient populations at increased risk; nevertheless, the exact mechanism linking the two conditions is not clearly understood.

Associated factors highlighting somatic pain symptoms in patients with depression include socio-demographic factors, clinical correlates, psychosocial correlates, medical conditions and patient determinants. This article addresses the epidemiology and factors associating comorbid psychiatric conditions in somatic pain patients. Additionally, this article details practice guidelines in the management of this patient cohort. This article will enable practitioners to identify a patient's individual risk, and prophylactically treat somatic pain symptoms at the initial stages to avoid progression to chronic pain syndrome or treatment refractory psychiatric disease states, all of which pose a significant public health problem. Adherence to these guidelines will not only improve patient outcome but also decrease public health cost and economic burden to healthcare.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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