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Psychology of Chronic Pelvic Pain: Prevalence, Neurobiological Vulnerabilities, and Treatment

Sara R Till, MD, MPH[1], **Sawsan As-Sanie, MD, MPH**[1], and **Andrew Schrepf, PhD**[2]

[1]Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, MI

[2]Department of Anesthesiology, University of Michigan, Ann Arbor, MI

Abstract

Patients with pelvic pain suffer from psychological conditions at a disportionately high rate compared to their peers. We review environmental, genetic, inflammatory, and neurobiological factors that increase vulnerability to developing both of these conditions. We review treatment strategies for chronic pelvic pain in patients who have comorbid psychological conditions, including both non-pharmacologic and pharmacologic options.

Keywords

chronic pelvic pain; endometriosis; depression; anxiety; catastrophizing

Introduction

Chronic pelvic pain (CPP) is a debilitating problem that afflicts 15–20% of women in the United States.[1] CPP is defined as noncyclic pain in the pelvis or abdomen which has been present for at least 6 months and is severe enough to cause functional disability or lead to medical care.[2] However, CPP should not be viewed as a single disease entity, but rather a constellation of symptoms that can be caused separate but frequently overlapping conditions, including endometriosis, pelvic myofascial pain, vulvodynia, interstitial cystitis/bladder pain syndrome (IC/BPS), and irritable bowel syndrome (IBS).

CPP causes significant morbidity and contributes to multiple surgeries and long-term medical therapies at a cost of $2.8 billion annually.[1] Women with CPP suffer tremendously: they use three times more medications, have four times more gynecologic surgery, and are five times more likely to undergo hysterectomy than women without CPP.[1] Pain and suffering often persist despite these treatments, and lead to decreased productivity, diminished emotional well-being, low work productivity, impaired sexual function and reduced quality of life.[3–5]

Psychological factors related to mood are a complicating factor in the morbidity associated with CPP. Women with CPP have much higher rates of psychological disorders compared to

Corresponding author: Sara R Till, MD, MPH, Department of Obstetrics and Gynecology, University of Michigan, 1500 E. Medical Center Dr., Ann Arbor, MI 48109, tillsa@med.umich.edu, T: 734-232-1333, F: 734-647-9727.

their peers without chronic pain. At a tertiary outpatient clinic for CPP, more than 50% of women had moderate to severe anxiety and more than 25% moderate to severe depression.[6] The increased prevalence of depression and anxiety is not unique to pelvic pain, and is well-documented across many other chronic pain conditions.[7–9]

The co-occurrence of pain and psychological distress is an important factor in both evaluation and treatment. Patients with chronic pain and comorbid psychological disorders incur higher health care costs[10], have lower quality of life[11], and report more disability.[12,13] Of particular importance, patients with both depression and chronic pain are more likely to be prescribed opioids than non-depressed patients, and take higher doses of opioids once they are prescribed.[14,15] There are also important consequence for the patient-clinician relationship: many patients with CPP may have felt that their pain complaints have been dismissed or minimized in the past and may be hesitant to divulge details of psychological symptoms for fear that these conditions will detract attention from their pain complaints. However, a comprehensive treatment strategy that addresses both the physical and psychological symptoms appears to result in the best outcomes.[7,8,16] This is because pain and emotion are inextricably linked. Providing a better understanding of the relationship between psychological distress and pain in CPP may help clinicians provide a more comprehensive treatment strategy for their patients.

The objectives of this review are to provide a brief overview of the overlap of CPP and elevated symptoms of psychological distress, to summarize neurobiological vulnerabilities that might predispose patients to both chronic pain and psychological disorders, and to briefly review treatment strategies for patients with comorbid psychological disorders and CPP.

Prevalence of psychological disorders in patients with CPP

Prevalence of many psychological disorders are higher among patients with CPP compared to the general population. This review will focus primarily on conditions of depression and anxiety, as well as the cognitive construct of pain catastrophizing given that these factors have been studied most thoroughly in this population. However, clinicians should be aware that personality disorders and substance abuse disorders are also more prevalent among patients with chronic pain, but are not covered in this brief review. Referral to psychiatry for more thorough assessment should be offered when appropriate. It is important to note that patients do not need to meet formal diagnostic criteria for a mood disorder to be affected by symptoms of depression, anxiety, and catastrophizing, and brief, high-quality measures exist to measure these symptoms on a continuum.[17,18]

Depression

Major depressive disorder is characterized by persistent feelings of sadness, loss of interest in previously enjoyed activities (anhedonia), and issues with decreased appetite, energy, and sleep. Women are at higher risk for depression compared to men. Pain symptoms are a frequent complaint among patients with depression, with approximately 65% of patients with depression reporting some type of chronic pain symptoms.[8] Patients who have both depression and chronic pain not only report greater functional limitations and worse overall

quality of life, but also do not have as robust a response to treatment compared to patients with depression alone or chronic pain alone.[8]

Among patients with CPP, prevalence of depression ranges from 26–52%, compared to 5–10% prevalence in the general population.[6,19–22] CPP patients who have concurrent depression experience more severe pain and report significantly lower quality of life compared to CPP patients without depression.[20,23]

Anxiety

Generalized anxiety disorder is highly prevalent among patients with chronic pain conditions. This condition is characterized by pervasive or excessive worry that interferes with daily activities, sleep, and concentration. It is frequently associated with muscle tension or fatigue. Women are at higher risk for anxiety disorders compared to men.

Among patients with CPP, prevalence of anxiety ranges from 39–73%, compared to 12% prevalence in the general population.[6,19,20,22] Similar to findings with concurrent depression, CPP patients who have concurrent anxiety disorders experience more severe pain and report significantly lower quality of life compared to CPP patients without anxiety.[20,23] Anxiety and depression are frequent seen together in patients with CPP.[20]

Catastrophizing

Catastrophizing is a cognitive construct, rather than a mood or psychological condition. It is a maladaptive cognitive and emotional coping response, in which patients tend to ruminate on and amplify pain symptoms and display feelings of helplessness and pessimism.[24,25] Some researchers argue that catastrophizing is more accurately defined as a distress response as opposed to a coping mechanism.[26] Catastrophizing appears to predict which patients will transition from an acute pain condition to a chronic one.[27] Chronic pain patients with higher degree of catastrophizing reported more physical disability, depression, and pain severity despite treatment.[28]

Many researchers have focused on the impact of catastrophizing in patients with CPP, but few have published data regarding the prevalence of the construct in this population. In one study of patients with CPP, 42% of patients displayed moderate to severe catastrophizing.[24] In patients with CPP, catastrophizing is strongly associated with pain severity[23] and worse health-related quality of life.[25] CPP patients with higher catastrophizing do not improve in response to a variety of treatment strategies to as great an extent as those with low catastrophizing.[24,29,30]

Catastrophizing, anxiety, and depression are highly collinear, although they are considered different constructs.[24,26] This overlap makes it difficult to tease out their individual contributions when studying chronic pain. Williams proposed a biopsychosocial approach to pain assessment, in which anxiety and depression are considered affective vulnerability factors that may predispose to pain, whereas catastrophizing is considered a belief or attitude in response to pain.[22]

Mechanism

The preponderance of evidence suggests common etiology for comorbid chronic pain and psychological disorders, rather than a unidirectional relationship. The underlying etiology is likely multifactorial with contributions from environmental, genetic, and neurobiological factors.

Temporal Influence

The temporal relationship between chronic pain conditions and psychological disorders is still unclear, but is certainly both reciprocal and synergistic. In a prospective cohort study of over 4000 older adults, depression or anxiety at baseline doubled the risk for development of chronic pain within 3-year follow-up period. However, the inverse was also true: pain at baseline was equally associated with development of anxiety or depression at follow-up.[31]

Several prospective studies have attempted to further determine how the risk of developing mood disorders relates to pain, and vice versa. There is increasing evidence that pain may be a stronger risk factor for developing depression or anxiety than the inverse. A recent prospective cohort study examining over 5000 adults free of depression or anxiety disorders at baseline indicated that any degree of pain severity or pain interference doubled the risk of developing depression or anxiety over the 3-year follow-up period, compared to no pain at baseline.[32] Another prospective cohort study of over 2000 older adults demonstrated that chronic pain at baseline was associated with new-onset depression at 12-year follow up, but that depression at baseline was not significantly associated with new-onset chronic pain.[33] These studies do not support the view that pain is an expression of psychological distress, but rather, that pain and mood imbalances mutually influence each other and may co-occur in part due to common neurobiological vulnerabilities.

Genetic Vulnerabilities

Twin studies suggest that genetic factors explain 40% or more of the variance in the prevalence of CPP.[34,35] This is similar to the estimated heritability of chronic pain with a widespread manifestation (48–54%).[36] There are also significant phenotypic correlations between CPP and other chronic pain disorders including irritable bowel syndrome (phenotypic correlation =.25) and chronic widespread pain (phenotypic correlation =.22) indicating common heritable risk.[35] What is less widely appreciated in the field of chronic pain is that common genetic factors are believed to mutually influence chronic pain and mood disorders. In a recent twin study of chronic low back pain and symptoms of anxiety/depression, the relationship between negative mood and pain disappeared entirely once genetic factors are fully accounted for by examining monozygotic case-control twin sets, suggesting that common genetic factors play a major role in their co-occurrence.[37] A prospective twin study of over 1200 adults without depression or anxiety at baseline showed that chronic low back pain doubled risk for depression or anxiety at 4-year follow-up.[38] However, the association was no longer significant once the psychologically discordant twin pairs were analyzed in a case-control manner, indicating that the genetic factors which predispose to psychological disorders may have a stronger effect than the experience of chronic pain. These findings are supported by another recent twin study showing a

significant phenotypic correlation (.32) between chronic widespread pain and depression.[39] Genome wide associated studies (GWAS) of pain – those that attempt to identify specific single nucleotide polymorphisms (SNPs) that confer risk – are still in the early stages of development in the pain field.[40] Nonetheless, some of the most widely studied SNPs have been associated with multiple painful conditions include variants of catechol-O-methyltransferase (*COMT*) and opioid receptor mu 1 (*OPRM1*),[41,42] both of which have also been linked independently to mood regulation and response to anti-depressant treatment.[43,44] *COMT* variants modulate the breakdown of catecholamines like dopamine, epinephrine, and norepinephrine, while variants in *OPRM1* modulate aspects of the endogenous mu-opioid receptor system. Recent preliminary work focusing on CPP suggests that variants in *COMT* are associated with primary vulvodynia and dyspareunia and variants in *OPRM1* are associated with impairments of the endogenous 'pain control' system in primary dysmenorrhea.[45,46] There are also several SNPs related to inflammation and inflammatory control that have been independently linked to pain and mood. Variants in the *IL-10, IL-1, and TNF* gene families have been linked to multiple pain conditions.[39] IL-10 is an inflammation regulating cytokine, while IL-1 and TNF family cytokines primarily reflect pro-inflammatory pathways, though the balance of these factors is affected by complex interactions and feedback mechanisms. A review of clinical studies examining genes controlling cytokine activity found that functional variants of TNF and IL-1 are linked to the response to anti-depressant treatment and the presence of MDD, though results were not consistent across all studies.[47] It has long been speculated that variation in innate immune activity plays a role in the ontogeny of mood disorders for a subset of patients and the same may be true in chronic pain conditions. IL-1 polymorphisms have been associated with endometriosis and vulvodynia.[48,49]

Inflammation

Under conditions of acute illness or infection a collection of symptoms sometimes described as *sickness behaviors* develop that include increased sensitivity to pain and heightened negative emotionality.[50] These changes are mediated by pro-inflammatory cytokine production that reach the central nervous system through volume diffusion, afferent nerves, and brain structures that are not immunologically privileged.[50] This general phenomenon is familiar to anyone who has experienced food poisoning or a transient infection. What is not widely-appreciated is that chronic inflammation occurring at lower levels affects many of the same signaling pathways and can produce a similar battery of symptoms.[51,52] Elevated levels of the pro-inflammatory cytokine interleukin IL-6 have been noted in women with endometriosis,[53–55] dysmenorrhea,[56] and IC/BPS,[57] though the results across studies have not been consistent. A systematic review of risk factors for non-cyclic pelvic pain suggests that pelvic inflammatory disease predisposes women to develop CPP[58] and a recent prospective study has shown that elevated plasma IL-1β, another pro-inflammatory cytokine, predicts the development of endometriosis.[59] Higher levels of plasma/serum cytokines have been linked meta-analytically to the presence of mood disorders cross-sectionally,[60] and more persistent elevations in inflammatory markers are prospectively linked to worsening depressive symptoms in older women.[61]

Furthermore, index markers of inflammation, those that reflect systemic or circulating levels of inflammatory activity like IL-6, do not tell the whole story. It has now been repeatedly demonstrated that the provoked immune response, that which occurs when immune cells are met with a challenge, distinguishes pain patients from controls. Toll-like receptors (TLRs) are highly conserved elements of the innate immune system found on sentinel immune cells. One of the primary functions of TLRs is to respond to tell-tale signs of infection or damage by releasing pro-inflammatory cytokines.[62] Animal models of chronic pain demonstrate convincingly that TLRs located on spinal glial cells (non-neuronal cells that act protectively while supporting metabolism and structure) play a critical role in the process of pain sensitization.[62] Work in women with IC/BPS shows parallels to this phenomenon, as women with IC/BPS show heightened inflammatory responses when their monocytes/lymphocytes are isolated and stimulated with a TLR-2 agonist.[63] Furthermore, when these same cells are stimulated with a TLR-4 agonist, the subsequent response predicts the degree of widespread pain, genitourinary pain severity, and dyspareunia.[63,64] A recent review considers the evidence for TLRs and inflammatory sensitization pathways in visceral pain with a special emphasis on the high female preponderance of these conditions.[65] Beyond their role in pain, TLRs appear to play potentially important roles in mood disorders. Individuals with major depression have an elevated expression of TLR4s in circulating immune cells, expression which decreases following treatment with cognitive behavioral therapy and antidepressant treatment.[66,67] A recent review of the literature shows how TLRs, and particularly TLR4, can potentiate negative emotionality through inflammatory signaling as well as interactions with the central stress response.[68]

Both TLRs and their inflammatory products also interact peripherally and centrally with the hypothalamic-pituitary-adrenal (HPA) axis and its immune-modulating glucocorticoids. In CPP, altered diurnal cortisol patterns have been noted in IC/BPS,[57] endometriosis with pelvic pain,[69] and dysmenorrhea.[70] Both diurnal cortisol patterns, and the cortisol response to experimental stress have been linked to mood disorders, particularly major depression.[71,72]

Brain function

Pain is both a sensory experience and an emotional response. Some regions of the brain figure prominently in the relay of painful physical sensory information and these include the thalamus, insula, and secondary somatosensory cortex,[73] while other regions are more closely associated with affective processes such as the hippocampus, amygdala, and cingulate cortex.[74] Functional neuroimaging however has revealed large overlap between neural activity brought on by physical pain, social pain, and induced negative emotions. A recent review found that the insula, thalamus, and two regions of the cingulate cortex to be consistently activated by both psychological and physical pain paradigms.[75] Similarly, there is considerable overlap between the regions activated during experimental social exclusion and physical pain, especially the anterior insula and dorsal anterior cingulate cortex.[76] In addition to shared regions of activation by physical and “social pain”/social exclusion, there is evidence that there may be shared mechanisms for physical and social *pain relief: a*cetaminophen reduces the activation in the dACC and anterior insula brought about by social exclusion. Machine learning algorithms designed to detect the neural signature of

remitted depression find regions long thought to regulate emotion, such as the hippocampus, but also regions well-described in the pain literature, such as the anterior insula, anterior cingulate cortex, and thalamus.[77] These studies are not described to suggest that pain and negative emotion have no distinguishing features at the neural level, but to reinforce that the neural representation of physical pain and negative emotion are built from many common pieces.

In a recent resting-state functional neuroimaging study comparing female UCPPS patients to matched healthy controls, UCPPS patients showed increases in connectivity between the posterior cingulate cortex and several regions that have been implicated in both physical pain and emotional processing, including the insula, thalamus, striatum, hippocampus, and amygdala.[78] In a study of women with endometriosis and CPP, higher levels of excitatory neurotransmitter were found in the anterior insula and increased connectivity between the anterior insula and medial prefrontal cortex. This connectivity was furthermore associated with greater pain intensity, anxiety, and depression.[79] An earlier study of women with vulvar vestibulitis found increased activation of the insula and frontal cortical areas upon experimental pressure in the painful area compared to healthy women,[80] findings echoed and expanded in a more recent study indicating increased activation of the insula, thalamus, cingulate cortex in women with vulvodynia experiencing pain at the thumbnail.[81,82]

Overview of treatment strategies

General approach

Addressing peripheral pain generators in CPP, such as endometriosis, is an important but incomplete strategy. This is because amplification and even generation of pain can occur in the central nervous system (CNS), a process sometimes called central pain amplification. Central pain amplification is characterized by widespread or multifocal pain, fatigue, sleep disturbances, and memory difficulties.[83–86] This mechanism is thought to play a key role in many chronic pain conditions, including fibromyalgia, interstitial cystitis, irritable bowel syndrome, chronic low back pain, and chronic headaches. Clinical, psychophysical, and neuroimaging characteristics of central pain amplification have been demonstrated in patients with CPP.[79,82,87–89] Psychological distress and central pain amplification are not interchangeable concepts, but both may respond to some of the same treatment strategies.

Therefore, a multimodal, personalized approach that addresses peripheral pain generators, central pain amplification, and overlapping psychological disorders is crucial for effective management of these challenging patients. An integrative model involving active communication with primary care providers, psychiatrists, and mental health counselors provides the framework for comprehensive and thoughtful care. Particularly in patients with more complex psychological conditions, such as bipolar disorder or schizophrenia, deliberate coordination of medication initiation or change with psychiatry can prevent symptom exacerbations. Discussing comorbid psychological disorders with your CPP patient requires careful presentation. Clearly acknowledging that you believe that their pain symptoms and psychological conditions are distinct issues is important to maintain rapport and credibility. However, helping them to understand how these two conditions can exacerbate one another may be essential to their willingness to initiate treatment for their

psychological condition. As detailed above, there is much overlap between epidemiology and underlying mechanisms of pain and mood disorders. While those with both fare less well than having pain alone, mood disorder is often a consequence rather than cause of pain. Treating pain without addressing a concurrent mood disorder is less likely to be effective, and many treatments actually help both symptoms, possibly due to improvements in brain metabolites and connectivity changes that are common in both pain and mood.

This review focuses on treatments that are likely to be effective in patients with comorbid CPP and psychological disorders, and does not represent a comprehensive discussion of treatments for CPP. Several prior reviews have discussed surgical options for CPP,[90,91] pharmacologic treatments,[92] and non-pharmacologic strategies[93] in more detail. Additionally, this review focuses primarily on CPP treatments rather than psychological therapies, although there may be overlapping efficacy in some areas. Some of the treatments reviewed here have not been extensively studied in CPP and much of the data is extrapolated from other chronic pain conditions. Furthermore, many of the pharmacologic treatment options are used off-label, meaning that the US Food and Drug Administration (FDA) has not approved the medication specifically for use in chronic pain. This should be discussed during your counseling.

Non-pharmacologic options

Pelvic physical therapy is widely used in CPP. This specialized area of physical therapy focuses on muscles and fascia of the pelvic floor, abdominal wall, back, and hips. Therapists utilize a number of therapeutic techniques, including manual therapy, mobilization, muscle motor control, acupressure, and biofeedback. Additionally, they often integrate pain education, mindfulness strategies, cognitive-behavioral techniques, and motivational interviewing, which are useful tools for any patient but exceedingly valuable for patients with significant anxiety or high catastrophizing.[94]

Despite excellent anecdotal success, there is relatively little high-quality research on pelvic physical therapy for CPP. Several small, single-cohort studies of patients with pelvic floor myofascial pain demonstrated significant improvement in pain severity and decreased use of pain medications with a pelvic physical therapy intervention.[95–97] Patients with coccydynia and vulvodynia also had significant improvements in pain following a course of pelvic physical therapy.[98,99]

Cognitive behavioral therapy (CBT) has been extensively studied in many chronic pain conditions.[100] CBT was initially developed as a treatment for depression, but has since been adapted to treat many other psychological conditions and chronic pain disorders. CBT is a goal-directed psychological therapy in which patients learn to recognize how their thoughts and behaviors impact their pain and functioning, and learn how to alter those thoughts and behaviors. CBT techniques for chronic pain include education about contribution of thoughts, emotions, and behaviors to the physical symptoms or emotional experience of chronic pain, cognitive restructuring and reframing, relaxation techniques to minimize autonomic arousal, graded activity and pacing, sleep hygiene, problem solving strategies, coping skills, and interpersonal skills.[101,102]

While most patients with chronic pain would likely benefit from education regarding pacing, sleep, and coping mechanisms, this intervention is likely to be highly impactful for patients with comorbid chronic pain and psychological disorders. In particular, CBT has been associated with significant improvements in catastrophizing in patients with chronic pain conditions.[103,104] Increasing adaptive coping skills and pain-related self-efficacy helps to mitigate the additive insult of these comorbid disorders.

The data supporting CBT for treatment of other chronic pain conditions is much more robust than that for treatment of CPP, but there is increasing evidence of its efficacy in this population. Among patients with vulvodynia, CBT interventions resulted in improved pain, dyspareunia, sexual function, and anxiety.[99,105] Similarly, patients with endometriosis reported improved pain, dyschezia, and quality of life.[106] These patients also demonstrated parallel changes on functional MRI.[107]

Exercise has been widely studied and has proven to be an effective treatment for many chronic pain conditions. Exercise interventions are associated with improvements in pain, quality of life, mood, sleep, physical function, and social and emotional function in patients with chronic pain.[108–113] Exercise interventions may include strength training, flexibility, aerobic activity, or a combination. Each of the activity types seems to have specific benefits. Although it does not appear than a single modality is more significantly effective than the others, aerobic activity and strength training have the most robust evidence for improved pain symptoms.[111]

However, this is an intervention that requires education, planning, and flexibility in order to avoid exacerbation of pain symptoms. Patients with chronic pain conditions who are planning to begin an exercise intervention should plan to “start low, go slow,” meaning that they should start at a low intensity and short duration and slowly build up over a period of weeks to months. Pacing is a critical skill to incorporate into exercise interventions. Many patients have a tendency to avoid activity during a pain flare and then try to “catch up” once they are feeling better, which often precipitates another pain flare. Instead, experts recommend that patients continue to do their planned duration of exercise on their regular schedule regardless of how good or bad they feel that day. If patients do experience a pain flare as they are increasing activity levels, they should decrease the intensity and duration back to a level that they feel is tolerable but should not avoid activity all together. Once the pain flare subsides, they can slowly increase intensity and duration again.[102]

While all patients with chronic pain conditions would likely benefit from a thoughtful exercise intervention, patients with comorbid psychological conditions may see dual symptom improvements. Exercise interventions resulted in improved mood, depression, and anxiety in patients with various chronic pain conditions.[111,112,114]

While there is more extensive data for exercise in other chronic pain conditions, a number of recent high-quality studies have been performed in patients with CPP. Two randomized controlled trials examining a yoga intervention demonstrated improvements pain and quality of life in patients with CPP.[115,116] In patients with dysmenorrhea, pain symptoms improved as a result of an exercise intervention in four randomized controlled trials.[117–120]

Pharmacologic options

Serotonin norepinephrine reuptake inhibitors (SNRI), such as duloxetine and venlafaxine, increase available amount of norepinephrine and serotonin by inhibiting reuptake in the descending pain modulatory pathways, which appears to decrease pain sensitivity.[121,122] Duloxetine is FDA-approved for treatment of several chronic pain conditions, including fibromyalgia and chronic low back pain. Milnacipram is approved for fibromyalgia and venlafaxine for neuropathic pain. In patients with fibromyalgia, duloxetine resulted in significant improvements in pain and quality of life.[123,124] SNRIs are generally well tolerated with few bothersome side effects. Additionally, SNRIs are also quite effective for treatment of depression and anxiety, so may be a good choice in patients with these comorbid conditions. There is no data regarding SNRIs for treatment of CPP.

Tricyclic antidepressants (TCA), such as amitriptyline and nortriptyline, also increases available amount of norepinephrine and serotonin by inhibiting reuptake in the descending pain modulatory pathways, decreasing pain sensitivity.[125] TCAs were initially developed for treatment of mood disorders, but have largely been replaced by more effective and well tolerated medications such as SSRIs. TCAs have been widely used off-label for many chronic pain conditions, despite only modest symptom improvement in most studies.[126] Additionally, their use is often limited by bothersome anticholinergic side effects, specifically sedation, drowsiness, dry mouth, and constipation. Slow titration does seem to minimize risk of side effects, and many side effects diminish with continued use. Data is limited in CPP, but amitriptyline did show modest efficacy in one study.[127]

Cyclobenzaprine is a centrally active muscle relaxer which has a tricyclic structure and is suspected to function in a manner similar to TCAs, likely by increasing available amount of norepinephrine and serotonin. However, it does not appear to have any antidepressant effect. Cyclobenzaprine is frequently used off-label in fibromyalgia and is associated with improved pain, sleep, and fatigue in several studies.[128,129] Drowsiness is a frequently reported side effect, so nighttime administration may improve tolerability and maximize sleep benefits. Cyclobenzaprine has not been studied in CPP.

Gabapentinoids, such as gabapentin and pregabalin, are centrally acting calcium channel blockers. Mechanism of action is not entirely clear, but it does appear to decrease availability of glutamate and substance P, thereby decreasing activity of the ascending pain pathways. Additionally, it acts as a membrane stabilizer and has some anti-inflammatory effects.[130] Gabapentinoids have been widely used off-label for a variety of chronic pain conditions, including fibromyalgia and peripheral neuropathy. Gabapentinoids are typically well tolerated with drowsiness and dizziness the most commonly listed side effects, which often improve over time. Side effects can be minimized by slow titration and by giving most or all of the daily dose at night with smaller doses during the day.[86] In patients with fibromyalgia, gabapentinoids were associated with improved pain, sleep, quality of life, fatigue, and anxiety.[131] Data is CPP is limited, but several small studies indicated improved pain and mood.[127,132] In an RCT comparing gabapentin and amitriptyline in patients with CPP, gabapentin resulted in greater pain improved and better tolerability.[127]

Conclusion

Comorbid psychological conditions are highly prevalent among patients with chronic pelvic pain and are associated with increased pain severity and decreased quality of life. The overlapping relationship between chronic pain conditions and psychological disorders is complex, but it appears that there are environmental, genetic, inflammatory, and neurobiological factors that increase vulnerability to developing both of these conditions. Patients with both CPP and psychological disorders are best served with a comprehensive, multimodal treatment approach which incorporates both non-pharmacologic and pharmacologic options, as well as coordination with primary care or psychiatric colleagues.

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