



Cluster Headache: Clinical Characteristics and Opportunities to Enhance Quality of Life

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Abstract

Purpose of Review Cluster headache is a highly disabling primary headache disorder characterized by severe pain and autonomic features. We present the existing body of literature on psychological factors associated with cluster headache and recommendations to address gaps in current clinical care with regards to psychological treatments for cluster headache.

Recent Findings People with cluster headache often endorse depressive symptoms, are more likely than the general population to report suicidal ideation and behaviors, and experience significantly decreased quality of life. Psychological treatments such as Acceptance and Commitment Therapy may be particularly valuable for patients with cluster headache given that they are transdiagnostic in nature and can therefore simultaneously address the disease burden and common psychiatric comorbidities that present.

Summary Greater understanding of the debilitating nature of cluster headache and behavioral interventions that seek to reduce the burden of the disease and improve the quality of life of people with cluster headache is paramount.

Keywords Cluster headache · Quality of life · Psychological factors · Depression · Suicide · Psychological treatment

Introduction

Cluster headache is a primary headache disorder with a lifetime population prevalence of 0.1% [1] and is more common in men [2]. Cluster headache is characterized by attacks of

severe, unilateral, periorbital pain that last between 15 and 180 min, and occur up to eight times per day [3]. Cluster headache attacks also involve ipsilateral autonomic symptoms including nasal congestion, miosis, and eyelid edema and are accompanied by a sense of restlessness or agitation [3]. Cluster headache remains underdiagnosed and undertreated [4] with many people experiencing a considerable delay to diagnosis, which adds to the disability associated with the disease [2].

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The trigeminovascular systems play an important role in the pain of a cluster attack, as well as parasympathetic nerve fibers in the accompanying autonomic symptoms [5]. The hypothalamus also appears to play a key role in the pattern of cluster attacks [6]. Cluster headache displays chronobiological features, characterized by symptoms that follow circadian and circannual patterns [7], with symptomology that occurs in predictable fashion for individual patients [8, 9]. As attacks occur most often at night, many people with cluster headache endorse anticipatory anxiety related to going to bed due to fear of triggering a cluster attack [10]. People with episodic cluster headache, whose disease manifests in periods occurring at predictable times of year and lasting weeks to months, similarly report anticipatory anxiety between periods worrying about when the next period of attacks will occur, as well as a fear of developing chronic (year-round) cluster headache.

The management of cluster headache typically involves a combination of strategies to abort cluster attacks (e.g., triptans, high-flow oxygen, vagus nerve stimulation) and temporarily reduce the frequency and severity of attacks or shorten a cluster period (e.g., oral steroids, anesthetic occipital nerve blockade \pm steroids, dihydroergotamine), and preventive treatments to chronically suppress attacks (e.g., verapamil, lithium, melatonin, galcanezumab) [6]. However, access to many of these treatments is limited and efficacy is typically modest at best [2]. Even with the best currently available treatment, people with cluster headache experience significant burden.

The pain associated with cluster attacks is so severe that the disorder has been coined “suicide headache” [6]. Many individuals with cluster headache experience such despair, as illustrated by this patient’s description, “During an attack, the pain moves up to a new dimension. You no longer have a headache, you are literally plunged into the pain... There is only one thing that remains of you; your agitated lucidity and the pain that invades everything, takes everything. You would give everything, including your head, your own life, to make it stop” [11•] The recurrent, intense nature of cluster attacks results in significant functional impairments, reduced quality of life [12, 13], psychiatric comorbidities, self-directed violence, and suicidal behaviors. Ultimately, there is a pressing need to effectively manage cluster headache and decrease the substantial burden it has on an individual’s life.

Psychological treatments, including behavioral interventions, hold a promise to improve the quality of life of people with cluster headache through increasing knowledge about the disease, maximizing adherence to effective medical treatment options, and decreasing functional impairments related to cluster headache. We present the existing body of literature on psychological factors and recommendations to address gaps in current clinical care with regards to psychological treatment of cluster headache.

Cluster Headache and Psychological Factors

Quality of Life

Quality of life is a subjective measure of well-being and is operationalized from a multidimensional perspective including the physical, psychological, and social domains [14]. For people living with pain, quality of life is often compromised [15]. Cluster headache is one of the most severe painful conditions a person can experience, rated over 30% more painful than childbirth, pancreatitis, or nephrolithiasis [16•, 17]. It is associated with poorer quality of life during ictal periods [30], especially for those with the chronic subtype [18, 19••].

The US Cluster Headache Survey reported that individuals with cluster headache ($n = 1134$) face many challenges that impede quality of life [20]. Daily living is often adversely impacted by the individual’s difficulty to drive and sleep, engage in cognitive tasks, complete household chores, parent, exercise, participate in family and social activities, and maintain employment [18, 20, 21••, 22]. The survey revealed that almost 20% of people with cluster headache had lost a job due to cluster headache, while 8% were unemployed or on disability due to their headache. A small qualitative study of 20 male patients revealed that patients are adversely impacted by the uncertainty of their condition, intensity and frequency of attacks, skepticism and misunderstanding perceived from social and workplace environments, and physician unawareness resulting in the use of inadequate or ineffective treatments [13].

Improving quality of life is an important treatment target for psychological interventions. In chronically painful conditions, psychological treatments designed to improve quality of life can also improve treatment trajectories, and reduce symptoms of psychiatric comorbidities [15, 23].

Depression

Living with excruciating periods of intense pain from cluster headache attacks can negatively impact mental health. Given the importance of mood in the cluster headache population, there is surprisingly little evidence evaluating depression in cluster headache.

Rates of depression are highly variable across studies (6 to 57%) and depend on population and definition of depression [20, 24]. For example, data from the Observatory of Migraine and Headaches project in France found that among 2074 patients with cluster headache, 43% met formal criteria for depression [25], which is similar to an online cross-sectional European study which found that 41% of people with cluster headache met cutoff criteria for depression on a self-report measure [26]. On the other hand, a retrospective analysis of 7589 patients with cluster headache from the USA

found that 20% had received a formal diagnosis of major depressive disorder; this was still double the rate of major depressive disorder in the control population (10%) population [27]. Further, a large population-based, prospective study in Taiwan reported that people with cluster headache ($n=673$) are 5.6 times greater risk of developing depression per ICD-9 criteria, compared to people with migraine ($n=2692$) and people without migraine or cluster headache ($n=2692$) [28]. In all, evidence consistently indicates that people with cluster headache are at greater risk of having depression compared to control populations.

Among people with cluster headache, risk factors for the development of depression in people with cluster headache include a higher number of cluster periods per year [28], chronic cluster headache, and currently being in an active cluster period [29–31]. It is unclear whether the relationships between depression and cluster headache are unidirectional or bidirectional. However, people with cluster headache describe their depression as stemming in part from both the pain from cluster headache attacks and the interictal burden of pain-related fear from future attacks [26]. Existing evidence suggests depression is commonly comorbid with cluster headache, that higher cluster headache disease activity is associated with depressed mood. Depressive symptoms, burden of current pain, and fear of future painful attacks are all potential treatment targets for psychological interventions for cluster headache.

Suicide

The link between suicide and cluster headache was first described in 1939; “our patients were disabled by pain so severe that several had to be constantly watched for fear of suicide” [32]. Endorsement of suicidal ideation remains common in people with cluster headache. An observational study examined claims data from the Truven Health Analytics market scan, over a 5-year period, and found that people with cluster headache were 2.5 times more likely to have suicidal ideation than controls (those without a cluster or other headache diagnosis) [27]. In the US Cluster Headache Survey with people diagnosed with cluster headache living in the USA ($n=1134$), 55% of participants reported suicidal ideation, with 2% reporting a suicide attempt [20]. Similarly, data from the Korean Cluster Headache Registry found that 64% of people with cluster headache reported passive suicidal ideation, 36% reported active suicidal ideation, 6% reported have a suicidal plan, and 2% reported having attempted suicide [12]. Data from this study indicated that suicidal behavior were less common interictally as opposed to during attacks and active cluster periods. This suggests that active cluster headache symptoms substantially impair quality of life. Suicidal attempts are alarmingly high, especially within clinical settings. For example, 51% of people

with cluster headache presenting to one of four outpatient neurology clinics in Flanders, Belgium ($n=85$), reported a previous suicide attempt [33].

The rates of suicidal behavior in people with cluster headache are unacceptably high. It is possible that comorbid depression exacerbates suicidal behaviors, but suicide may also serve as a way for a person to alleviate the excruciating pain associated with cluster headache. For example, Schindler and colleagues recently described that during attacks, patients may carry out self-injurious behaviors (e.g., striking head, punching the wall), but this behavior is not necessarily suicidal in nature; rather, it is likely an extreme aspect of the restlessness associated with cluster attacks and, further, a method to distract from head pain (i.e., conditioned pain modulation) [34••]. A recent cross-sectional survey study by Koo and colleagues found that in a sample of 100 people with cluster headache, 47% endorsed a lifetime history of suicidal ideation compared to just 26.7% in 135 controls matched for age, sex, and other socioeconomic and educational factors. Interesting in this study, suicidal ideation was associated with the psychological phenomenon of demoralization and was not associated with a lifetime history of depression [35••]. This study highlights the importance of screening for both depression and demoralization in patients with cluster headache.

It is concerning that the rates of suicidal ideation and behaviors continue to be high in people with cluster headache; there is a necessity for adequate management of cluster headache symptoms both in the ictal and interictal periods. Providers should ensure they consistently assess suicidal ideation at every clinical encounter. It may be particularly beneficial to ensure strong connections with mental health staff in order to assist with management of suicidal ideation and behaviors. The high rates of suicidal ideation and behaviors reveal an urgent need to develop strategies to mitigate the burden of cluster headache on patients’ lives. If the burden of cluster headache is not adequately addressed, consequences in this population may be fatal.

Psychological Treatment for Cluster Headache

Given the substantial impact cluster can have on quality of life, depression, and even suicidal behavior, it is surprising so little research has examined psychological and behavioral treatments to improve the lives of people with cluster headache. Substantial research in migraine and tension-type headache has demonstrated that stress is an important precipitating factor for headache attacks, and that stress management techniques can reduce headache activity and improve quality of life [36, 37]. Relaxation techniques, such as deep breathing, progressive muscle relaxation, and imagery, have been integrated into almost every behavioral treatment protocol for headache. Biofeedback, which

integrates relaxation techniques with psychophysiological assessment to provide targeted feedback about the efficacy of relaxation, has commonly been used to extend the benefits of relaxation approaches. Therefore, it is not surprising that some of the earliest research in cluster headache reported case series describing the potential utility of relaxation and biofeedback techniques in cluster headache. These case series ($n = 2-11$) in the 1970s and 1980s suggest that relaxation and biofeedback strategies might have some benefit for patients with cluster headache for symptom reduction [38–41]. However, there are several reasons to doubt that relaxation strategies alone would produce a large impact on cluster headache. Stress is unlikely to be as important of a factor for the initiation and maintenance of cluster headache compared to migraine and tension-type headache, given the differing mechanisms of action [42]. Although relaxation strategies can be important components of any psychological treatment for health conditions, it is unlikely to be, alone, as important of an intervention for cluster as it is for other primary headache disorders.

Integrative care models combine multiple disciplines in the treatment of chronic medical conditions like pain and headache disorders [43]. A recent health services report of a multidisciplinary headache center found some evidence that people with cluster headache could benefit from an integrated care model, which for this particular health system included neurology, physical therapy, nursing, and health psychology. Psychological therapy included cognitive behavioral therapy strategies for stress management, biofeedback, and relaxation strategies [44]. Of the 1346 patients seen in this headache center, 49 were diagnosed with cluster headache. Patients with cluster headache treated in this integrative model experienced significant reductions in attack intensity and duration [44].

To our knowledge, no studies to date have evaluated psychological interventions of any kind for cluster headache in a controlled setting. Integrating psychological treatment into routine care of patients with cluster headache is a good idea in theory, but psychologists lack strong evidence for which treatments to provide specifically to patients with cluster headache, and have no real knowledge of what outcomes can be expected to be achieved with psychological intervention.

Gaps in Care and Areas for Future Research

Cluster headache remains undertreated. Given the observed associations between cluster headache, psychiatric comorbidities, suicidality, and quality of life impairments, there is a substantial need to develop treatments that have long-lasting effects to reduce the burden of this disease. Many behavioral and pharmacotherapies aim to decrease symptoms of a disease. However, interventions that target minimizing disability, while still living with the symptoms of the disease, may prove more beneficial for cluster headache. Acceptance and

Commitment Therapy (ACT) is a “third-wave” behavioral therapy [45], which may show promise for helping people with cluster headache. At its core, ACT emphasizes the culmination of mindfulness skills, while guiding people to work toward living a value-based life while accepting that pain is a normal and inevitable human experience [46, 47]. ACT is transdiagnostic in nature and therefore may be particularly valuable for patients with cluster headache, simultaneously addressing the disease burden and common psychiatric comorbidities that present [48]. ACT can be brief and easily integrated into medical settings [48]. To date, there have been a plethora of trials reporting on the efficacy of ACT for a range of medical and psychological disorders [49–51]. The literature demonstrates that ACT-based treatments for chronic pain result in enhanced quality of life [52–55]. A recent multicenter, phase II, randomized trial reported that ACT was feasible for people with high-frequency episodic migraine and resulted in a decrease in the number of headache days [56•]. Interestingly, although the focus of ACT is not on targeting specific disease symptomatology but rather on guiding individuals to live a value-based life, many people report the added benefit of a decrease in their symptoms. Dindo and colleagues demonstrated that participation in a 1-day ACT intervention resulted in significant improvements in depression in people with migraine and comorbid depression, highlighting the potential impact of this transdiagnostic treatment [57]. While evidence exists regarding the benefits of ACT for various medical and psychological diseases, future research examining the potential benefits of ACT for people with cluster headache is warranted and may provide hope for people living with this debilitating disease.

Conclusions

Cluster headache is a highly disabling primary headache disorder. Currently available medical management strategies are suboptimal and often inaccessible. While suppressing the symptoms and treating underlying diseases have proven to be challenging, there is ample room to explore other methods of disease management in cluster headache. Given high comorbidity of affective disease, poor quality of life, and high suicidality in these patients, there are many behavioral and psychological factors to consider, but there are no current recommendations for psychological interventions in treating people with cluster headache. Third-wave behavioral interventions such as Acceptance and Commitment Therapy may show promise for improving the quality of life of people living with cluster headache. Greater understanding of the debilitating nature of cluster headache [11•] and behavioral treatments that provide opportunities and seek to reduce the burden of the disease and improve the quality of life of people with cluster headache is paramount.

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Compliance with Ethical Standards

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- Of major importance

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