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Exploration on the Correlation between Cluster Headache and Anxiety State Based on the "Liver Governing Dispersal" Function

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Abstract: Cluster headache, known for its severe pain intensity, remains a significant medical challenge both domestically and internationally. The incidence of cluster headache is notably higher in individuals with anxiety, yet Traditional Chinese Medicine (TCM) lacks a systematic consensus on its pathogenesis. Conventional Western medical treatments often yield poor results, making it difficult to cure, which severely impacts patients' quality of life, disrupts their work, and leads to economic losses. Guided by the theory of the "Liver Governing Dispersal" function, this paper explores the pathogenesis of cluster headache from the perspective of emotional disorders. Based on its clinical characteristics and modern research, it is concluded that cluster headache is often accompanied by an anxiety state. The discussion centers on liver qi stagnation, which obstructs the flow of qi, leading to pain ("obstruction causes pain"), and the impairment of the circulation of qi, blood, and body fluids, resulting in inadequate nourishment of the head and face, which also causes pain ("malnourishment causes pain"). This in-depth analysis holds significant importance for the prevention and treatment of this disease.

1. Introduction

Cluster Headache (CH) is a primary trigeminal autonomic cephalalgia and one of the most severe types of primary headaches. It typically manifests as unilateral attacks accompanied by intense craniofacial pain [1], primarily localized to the orbital, supraorbital, or temporal regions, or any combination of these areas. It is often associated with ipsilateral autonomic symptoms such as conjunctival injection, lacrimation, nasal congestion, rhinorrhea, forehead and facial sweating, miosis, ptosis, and/or eyelid edema, as well as irritability and restlessness. Each attack lasts between 15 to 180 minutes, with a frequency ranging from once every two days to eight times per day [2]. Some patients exhibit an annual rhythmic pattern, with attacks more likely occurring in spring and autumn. In recent years, the prevalence of CH has been reported as 1 in 1, 000 individuals [3]. The intense pain during cluster episodes, coupled with its chronic and refractory nature, significantly impacts patients' quality of life and work productivity. Moreover, prolonged anxiety and other mental states

can lead to hypothalamic dysfunction, contributing to headache onset [4]. Studies have shown that approximately 55% of CH patients experience suicidal tendencies during attacks, earning it the nickname "suicide headache" [5]. In Traditional Chinese Medicine (TCM), CH falls under the categories of "headache" or "head wind" within the broader classification of "pain disorders" [6]. It is often attributed to emotional distress, liver qi stagnation, imbalance of qi and blood, and blockage of meridians. Based on Professor Zhang Qiming's theory of the "Liver Governing Dispersal" function from Morphology of Traditional Chinese Medicine and modern research advancements, this paper explores the correlation between cluster headache and anxiety states. The aim is to leverage the significant advantages of TCM in alleviating patients' life stressors and provide new insights and methods for clinical treatment.

2. The Connotation and Modern Extension of the Theory of “Liver Governing Dispersal”

In Traditional Chinese Medicine (TCM), the concept of "Liver Governing Dispersal" is one of the most central physiological functions, primarily reflected in regulating the flow of qi, modulating emotions, and maintaining the circulation of qi and blood. Some scholars suggest [7] that the liver's dispersing function is closely related to the neuro-endocrine-immune network, serving as the core of modern psychological stress theory and having significant correlations with the TCM theory of the "seven emotions" (joy, anger, worry, pensiveness, sadness, fear, and fright). In TCM, the seven emotions are considered an essential aspect of disease etiology. Furthermore, modern Western medical research indicates [8] that brain regions such as the hippocampus, hypothalamus, and amygdala play a critical role in regulating the liver's dispersing function, particularly in emotional regulation.Professor Qiming Zhang [9], in his work Morphology of Traditional Chinese Medicine, explains that the liver's dispersing function (governing visceral movement) involves the visceral nervous system generating and transmitting visceral sensory and motor signals to control visceral movements. The subconscious nervous system generates subconscious mental activities, while the emotional nervous system produces internal emotional experiences. Specifically, the subconscious nervous system consists of the central nervous system responsible for subconscious mental activities, and the emotional nervous system comprises the central nervous system that enables individuals to generate internal experiences in response to external stimuli. Thus, the liver's dispersing function is closely linked to emotional regulation.Additionally, classical TCM texts, such as Wai Jing Wei Yan, state: "The liver prefers dispersal and dislikes stagnation, " highlighting the liver's physiological characteristic of favoring free flow and aversion to depression. Pathologically, the liver and emotional disorders share common mechanisms, such as dysregulation of immune and nervous system functions, leading to alterations in the levels and actions of various neurotransmitters, cytokines, gut microbiota, and hormones [10]. When the liver's dispersing function operates normally, qi and blood are harmonized, emotions are balanced, and mental well-being is maintained. This enhances efficiency in work, life, and learning, ultimately improving overall happiness and quality of life.

3. Correlation Factors and Exploration

3.1. Theoretical Exploration of the Dispersing Function and Cluster Headache

Traditional Chinese Medicine (TCM) has a history of over two thousand years in the treatment of headaches, accumulating extensive clinical experience. The most critical etiology is attributed to the liver's failure in dispersing and draining, which disrupts the flow of qi and blood throughout the body, disturbs the mind, and prevents the proper nourishment of the brain and head. This leads to symptoms such as qi and blood failing to ascend, resulting in inadequate nourishment of the head and face, as well as the stagnation of phlegm and blood stasis, which obstruct the clear orifices and cause pain

due to malnourishment.With the increasing intensity of social competition, the incidence of emotion-related diseases has been rising steadily. The medical model has also evolved into a comprehensive "biological-psychological-social" framework. Prolonged emotional imbalance and chronic anxiety can trigger and exacerbate cluster headache (CH) [11]. TCM, based on its holistic perspective, recognizes that the occurrence and progression of diseases are influenced by multiple factors. Among these, the interaction of "wind, fire, phlegm, stasis, and deficiency" can lead to meridian blockages, resulting in pain symptoms.The nature of CH pain is often described as distending pain, which, in TCM pain differentiation, is associated with liver qi stagnation due to impaired dispersing function. The autonomic symptoms of CH, such as tearing, and non-autonomic symptoms, such as restlessness and agitation, are clinical manifestations caused by dysfunction of the liver's dispersing function, which disrupts the visceral nervous system.

3.2. Theoretical Exploration of the Dispersing Function and Anxiety State

In Traditional Chinese Medicine (TCM), "liver failing to disperse and regulate" includes both excessive and insufficient dispersing functions, which directly affect the movement of qi and lead to corresponding emotional disorders. Among these, liver qi stagnation caused by insufficient dispersing function is the most critical pathological mechanism underlying anxiety states. The Suwen: Treatise on Regulating the Channels states, "When qi and blood are disharmonious, all kinds of diseases arise, " indicating that imbalances in the body can lead to various health issues. Under normal physiological conditions, the liver qi thrives, ascends, flows freely, and remains unobstructed, representing an ideal state of the human body. Therefore, regulating emotions is a central aspect and key component of the liver's dispersing function [14].

When the liver's dispersing function is insufficient, it leads to qi stagnation, causing individuals to experience an anxious state. Common emotional disorders such as anxiety disorders, depression, and bipolar disorder fundamentally stem from an imbalance in the body's qi movement, where qi and blood fail to circulate properly throughout the body. Treatment often focuses on soothing the liver and relieving stagnation to restore the smooth flow of qi. Anxiety is an unpleasant emotional response to perceived threats or adverse situations. When anxiety persists, it can lead to significant psychological distress, uncontrollable fear, and even intense autonomic nervous system symptoms, progressing into pathological anxiety [15].In daily life, an anxious state manifests as noticeable emotional distress, such as irritability, anger, tension, restlessness, and sleep disturbances, accompanied by symptoms of autonomic nervous system dysfunction. Currently, the prevailing understanding in TCM is that the root of anxiety lies in the liver, with liver dysfunction and failure to disperse and regulate being the primary etiology and pathogenesis [16]. Anxiety state is a syndrome triggered by specific factors, encompassing psychological, somatic, and motor symptoms of anxiety. It exists on a spectrum between normal anxiety and anxiety disorders, not only as a distinct condition but also as a contributing factor that interacts with and influences other clinical diseases.

4. Modern Medical Perspectives on Cluster Headache

Cluster headache (CH) is classified as a primary headache disorder, which mainly includes migraines, tension-type headaches, trigeminal autonomic cephalalgias, and other primary headaches. Among the trigeminal autonomic cephalalgias, CH is the most common [17]. Early Western medical studies have shown that the pathogenesis of CH [18] involves the trigeminovascular system pathway, the trigeminal-autonomic reflex, and abnormal synchronous activity in the hypothalamus. Activation of the trigeminovascular system triggers the trigeminal-autonomic reflex, and the complex interaction between these two systems promotes the release of specific neuropeptides such as calcitonin gene-related peptide (CGRP) and pituitary adenylate cyclase-activating polypeptide 38 (PACAP38) [19].

Additionally, the hypothalamus plays a role in central pain processing. CH patients often exhibit reduced plasma testosterone levels and a diminished response to thyroid-stimulating hormone [20].The hypothalamus, located below the dorsal thalamus, is involved in regulating hormone secretion, emotional behavior, wakefulness, and sleep cycles, among other physiological functions [22]. CH attacks can disrupt patients' sleep patterns and reduce sleep quality [23], significantly impacting their daily lives and predisposing them to psychological disorders. Common triggers for CH attacks include alcohol consumption, weather changes, sleep disturbances, cold wind, and emotional changes [24]. Among these, decreased sleep quality and stress-related responses such as anxiety have been shown to increase the incidence of CH [21].

5. Correlation Between the Dispersing Function and the Mechanism of Cluster Headache with Comorbid Anxiety

In Traditional Chinese Medicine (TCM), cluster headache (CH) is categorized under "headache" or "head wind" within the broader classification of "pain disorders." Its fundamental pathogenesis is attributed to the disharmony of qi and blood and the obstruction of meridians [25]. It is often associated with external pathogenic factors and emotional disturbances [26]. Ancient TCM texts state, "The head is the meeting point of all yang energies and the residence of clear yang." The brain, located at the highest point of the body, gathers the yang qi of all meridians, and the qi and blood of the internal organs converge here. The liver, belonging to the wood element and associated with wind, is characterized by its dynamic and rapid nature. When liver fire flares up and scorches the brain's orifices, it can lead to headaches, as described by the principle, "Rebellious liver qi induces headaches." Prolonged consumption of yin and blood can lead to malnourishment of the liver meridian, or insufficient yin failing to control yang, causing yang hyperactivity in the upper body, which can also trigger headaches. From the perspective of TCM pain mechanisms, this is described as "yang qi stagnation, obstruction of brain collaterals, pain due to obstruction, and impaired circulation of qi, blood, and body fluids, leading to malnourishment of the brain and pain due to deficiency."When the liver's dispersing function is normal, it regulates the flow of qi throughout the body, maintaining the harmonious balance of the internal organs and ensuring the smooth circulation of qi and blood, thereby reducing the likelihood of developing such diseases. Conversely, "liver failing to disperse and regulate" results in impaired qi movement, stagnation of clear yang, and obstruction of brain collaterals, leading to headache symptoms. As stated in Lin Zheng Zhi Nan Yi An: Headache, "Headache is caused by the failure of clear yang to ascend and wind-fire taking advantage of deficiency to rise." Dan Xi Xin Fa: Six Stagnations proposes, "When qi and blood flow harmoniously, no disease arises; once stagnation occurs, various diseases emerge." Additionally, Xu Chunfu, in Gu Jin Yi Tong Da Quan: Eyebrow Ridge Pain, suggests that the etiology of this condition is related to liver fire flaring upward, and individuals prone to anger are more susceptible to the disease.Anxiety states in TCM fall under the category of "depression disorders." The liver's role in dispersing and regulating emotions is a vital physiological function. Adverse emotional factors can negatively impact the liver and other organs, triggering or exacerbating headache symptoms, making it a significant etiological factor. Research on comorbidities in CH patients often focuses on emotional disorders such as anxiety and depression. During attacks, patients frequently experience irritability, anger, and hostility toward others, and in severe cases, may exhibit bizarre behavior or mental abnormalities. The long-term burden of the disease and anxiety states can lead to suicidal tendencies [12]. Approximately one-quarter of Chinese CH patients experience pre-cluster symptoms such as facial discomfort, anxiety, and insomnia [13]. This reveals that headache patients often suffer from qi stagnation and prolonged illness, making them more prone to comorbid anxiety states.

6. Prevention and Treatment Strategies for Cluster Headache with Comorbid Anxiety

Ancient medical practitioners' understanding of the etiology and pathogenesis of headache primarily evolved through four stages: an initial focus on external pathogens, the development of the "head wind" theory, the recognition of internal injury headaches, and finally the differentiation between external and internal causes of headache. With the advancement of time and technology, modern physicians have deepened their understanding of headache pathogenesis, recognizing that it involves multiple factors such as "wind, fire, phlegm, stasis, depression, deficiency of yin essence, dual deficiency of yin and yang, and deficiency of qi and blood." In terms of treatment, methods such as calming the liver, clearing fire, resolving phlegm, removing stasis, promoting circulation, and nourishing yin and blood are commonly employed, all of which have shown good efficacy. Therefore, by soothing liver qi and regulating qi movement, the condition can be alleviated. Clinical studies have also found that blood deficiency with liver hyperactivity is a fundamental pathogenesis and syndrome of internal injury headaches, and treatments focusing on nourishing blood and soothing the liver have shown significant effects [27].In Western medicine, the acute treatment of CH primarily involves high-flow pure oxygen inhalation, combined with intranasal administration of zolmitriptan or subcutaneous injection of sumatriptan, as pure oxygen promotes cerebral vasoconstriction [28] and affects the activity of catecholamines and serotonin. However, pure oxygen is not easily accessible and requires specialized equipment. Pharmacological treatments often include triptans, ergotamines, and steroids, but these come with significant side effects and are not suitable for long-term use. Triptans, for example, are believed to exert their therapeutic effects on CH by acting on the hypothalamus, the trigeminovascular system, and the release of inflammatory neuropeptides [29]. CH is a sudden and severe condition, classified as a refractory neurological disorder. Currently, clinical outcomes are inconsistent [30-32].Based on the theory of "Liver Governing Dispersal, " it is believed that CH with comorbid anxiety is often associated with factors such as wind-heat, phlegm-dampness, blood stasis, and liver fire obstructing qi movement [33]. In contemporary society, where pressures from various aspects of life are increasing, many patients experience recurrent episodes due to anxiety states, leading to poor prognosis.

7. Summary

With the increasing pressures of survival, work, and mental stress, the incidence of cluster headache (CH) has shown a rising trend in recent years. Currently, CH remains a major challenge in the field of headache disorders due to its complex symptoms and unclear pathological mechanisms. Research on comorbidities has primarily focused on emotional disorders such as anxiety and depression, though many aspects still require further investigation. Western medicine has yet to develop a specific and effective treatment plan for this condition. This paper explores the correlation between cluster headache and anxiety states based on the theory of the "Liver Governing Dispersal" function, integrating modern research. By applying the theoretical perspective of "pain due to obstruction and malnourishment, " it reveals that "liver qi stagnation and impaired circulation of qi, blood, and body fluids lead to insufficient nourishment of the brain, resulting in headaches." Thus, soothing liver qi and regulating qi movement can alleviate anxiety states, thereby reducing the clinical symptoms caused by CH. This approach holds significant clinical value for the prevention and treatment of cluster headache.Furthermore, as society progresses, there is growing emphasis on psychological therapy in clinical practice. By alleviating patients' suffering and improving their quality of life, this provides new insights for disease management. However, the perspectives discussed above are primarily based on TCM theories and some research findings, and further modern scientific studies are needed for validation. Additionally, there are differences between TCM theories and modern medical perspectives, so a comprehensive approach considering individual differences is

essential when applying these principles in practice.

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