DOI: 10.53469/jcmp.2024.06(11).20

A Brief Discussion on Chronic Subdural Hematoma Based on the "Kidney Generates Marrow" Theory and the "Meridian" Doctrine.

Kai Li[1], Xiaoxuan Fan[2,*]

[1]Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China
[2]Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang 712000, Shaanxi, China
**Correspondence Author*

Abstract: ***Chronic subdural hematoma is a typical neurological disease that occurs in middle-aged and elderly people and seriously affects the quality of life of middle-aged and elderly people. In recent years, with the further deepening of the understanding of CSDH in traditional Chinese medicine theory, it has been found that "kidney deficiency and medullary deficiency and loss of choroids" play a key role in the pathogenesis of CSDH. Combined with the theory of "kidney medulla" and "vein" in traditional Chinese medicine and its comprehensive explanation of its mechanism in modern medicine, the pathogenesis of CSDH was analyzed, and the clinical efficacy of the "kidney and marrow" method and the "pulse and essence" method of CSDH treatment were discussed, so as to pursue a more reasonable TCM diagnosis and treatment plan and further give full play to the unique TCM medical advantages of CSDH. It provides reference significance for the treatment of CSDH of "tonifying the kidney and generating marrow, clearing the pulse and consolidating the roots".***

Keywords: Renal myeloid, Choroid, Renal deficiency, Chronic subdural hematoma, Theory, Clinical research.

1. Introduction

Chronic subdural hematoma (CSDH) is one of the common diseases in neurosurgery, but its etiology is not yet fully understood. Some factors pointing to the pathogenesis of CSDH, including the formation of subdural space, local inflammatory response, neomembrane neovascularization and rebleeding, and local hyperfibrinolysis, have begun to be proposed in recent literature. The prevalence of chronic subdural hematoma (CSDH) is increasing year by year with the acceleration of China's aging population, indicating that the prevention and treatment of CSDH are still essential [1]. The literature points out that the incidence rate in people under 65 is nearly 3.4/100,000, while the incidence rate in people over 65 is as high as 8/100,000 to 58/100,000 [2]. The high incidence rate in the elderly may be because there is a gap between the brain and the dura mater in the elderly group, which sows the risk of disease, however, the probability of brain atrophy in young people is much lower compared to the elderly, thus the probability of CSDH is also much lower [3]. With the continuous in-depth study of CSDH by traditional Chinese medicine in recent years, it has been found that "kidney deficiency and marrow reduction, and the loss of control of blood vessels" are closely related to the pathogenesis of CSDH. Exploring the pathogenesis and clinical efficacy of CSDH, and leveraging the unique advantages of traditional Chinese medicine in the prevention and treatment of CSDH, based on the "kidney generates marrow" theory and "collateral" theory, provides a reference for the future understanding of the pathogenesis of CSDH and clinical syndrome differentiation and treatment by traditional Chinese medicine.

It is generally believed that CSDH is caused by head trauma leading to the aggregation of brain microvessels compressing the subdural space blood, causing the rupture of bridging veins, inducing an inflammatory response, and promoting the further proliferation of fibroblasts, leading to subdural bleeding in the brain. A outer envelope is formed. The root cause of the CSDH hematoma is the rupture of bridging veins [4]. However, most studies nowadays show that many CSDH patients do not have a clear history of trauma [5]. In response to this, Professor Fan Xiaoxuan believes that CSDH patients without a clear history of trauma may be due to brain atrophy causing a gap between the brain and the meninges, leading to long-term leakage of liquid in the veins to form a hematoma, which also more reasonably explains why aging can be one of the recognized influencing factors of CSDH. Some literature also points out that brain atrophy in elderly patients may cause the elongation of bridging veins, making the cerebral vessels more fragile, and minor head trauma can lead to the rupture of bridging veins, leading to the occurrence of CSDH [6,7]. At present, the academic community generally believes that aging is one of the key prerequisites for the occurrence of CSDH, and the rupture of bridging veins is the main cause of CSDH hematoma, with the main mechanism being neovascularization and rebleeding. The "kidney generates marrow" theory is the main theoretical basis for delaying aging in modern traditional Chinese medicine, and Professor Wu Yiling [8] proposed that the collateral system is highly related to the vascular system, which makes the "collateral" theory closely linked with bridging veins and neocapillaries. Therefore, the "kidney generates marrow" theory and the "collateral" theory can be used as one of the theoretical bases for the treatment of CSDH by traditional Chinese medicine.

2. Traditional Medical Theories of "Kidney Generating Marrow" and "Collaterals" in Understanding Chronic Subdural Hematoma (CSDH)

The "Kidney Generates Marrow" theory, first recorded in "Suwen Xuanming Wuqi" states: "The kidney governs the bones and generates marrow." "Suwen Yinyang Yingxiang Dalun" says: "The kidney generates bone marrow." "Suwen Liujie Zangxiang Lun" further states: "The kidney stores essence, which can generate marrow." "This all indicates that

the generation of marrow relies on the nourishment of the kidney's essence and energy." "Ling Shu Jingmai," "Ling Shu Hai Lun," and "Suwen Gu Kong Lun" all record the pathway of the foot taiyang bladder meridian, describing the collaterals that "belong to the kidney," "belong to the brain," and "connect to the kidney," providing detailed descriptions. "Ling Shu Hai Lun" says: "The Du meridian penetrates the spine, reaches the wind palace, and enters the brain." Below the wind palace is the spinal canal, filled with spinal cord, which, after this connection, communicates with the brain, proving that through the Du meridian, the spinal cord and brain marrow are interconnected, and through the Du meridian, it can be seen that the spinal canal communicates with the brain. "Ling Shu Jingmai": "The branch of the Du meridian, called Changqiang, goes up along the spine, disperses on the head... separates to go to the taiyang meridian, and enters the spine," indicating that the Changqiang collateral has the most direct connection with the taiyang meridian and the head, and "goes up along the spine" and "enters the spine" further strengthen the connection between the Du meridian and the taiyang meridian. Therefore, some people directly advocate that the Du meridian is the collateral of the brain. Traditional Chinese medicine theory holds that CSDH belongs to the categories of "headache" and "dizziness" [9]. "Ling Shu Xie Qi Zang Bing Xing" mentions: "The twelve meridians and three hundred and sixty-five collaterals, their blood and qi all go to the face and walk through the empty orifices." This further explains that the collaterals are interwoven and converge in the head orifices, which is the place where the body's blood and qi are most vigorous. Therefore, the role of collaterals in enriching brain marrow and nourishing brain nerves is very important. The "Kidney Generates Marrow" theory and the "collateral" doctrine indicate that the kidney is the production base of marrow, and when kidney energy is sufficient, the marrow has a source of transformation. Marrow acts on the brain through collaterals. If kidney energy is insufficient or collaterals are not nourished and become obstructed, it will lead to a vacuum in the brain marrow, leading to the onset of headaches or dizziness. "Medical Record · Participation in Western Record" mentions: The brain is the sea of marrow, which is actually formed by the true yin and yang of the kidney, brewed and combined, and rises along the Du meridian to be injected into the brain, pointing out that the collaterals of the Du meridian originate in the kidney, and the essence produced by the kidney is transported along the collaterals to the brain, so the brain marrow is abundant, the mind is clear, and the whole body is relaxed. The "kidney-marrow-collateral-brain" central axis that runs through the whole body plays a key role in transmitting brain and facial activities, and body movement information. "Classification and Treatment" says: "The kidney is the root of qi." Academician Wu Yiling points out that the innate essence of the human body converges into marrow, and the accumulation of essence forms the brain, so there is the concept of "the brain is the sea of marrow." At the same time, "transforming essence into qi," the qi formed is the true qi, which is transformed from the innate essence and hidden in the kidneys. Academician Wu also believes that the "pulse" in the concept of traditional Chinese medicine basically coincides with the "blood vessel" in the concept of Western medicine. The "Sun pulse" mentioned in traditional Chinese medicine is very closely related to microvessels from a microscopic perspective [10]. Therefore, we can roughly consider that the functions of generating blood, promoting blood, and capturing blood in the kidney's true qi in traditional Chinese medicine theory are highly unified with the roles of promoting angiogenesis, blood flow dynamics, and improving vascular stability in Western medicine concepts. This is also in harmony with the three reasons for the formation of pathological collaterals in collateral disease theory, including uncontrolled collateral proliferation, obstruction of collaterals, and aging of collateral vessels. Therefore, it can be said that marrow is the material basis of true qi, and the true qi generated by the kidney is the key guarantee for marrow to enter the brain through collaterals. It also emphasizes the reference value of the "kidney-marrow-collateral-brain" central axis that runs through the whole body. It further confirms the close connection between the "Kidney Generates Marrow" theory and the "collateral" doctrine in traditional medicine and CSDH, and it is also very important to study the "kidney-marrow-collateral-brain" central axis from the perspective of modern medicine.

3. The modern medical interpretation of the "Kidney Generates Marrow" theory and the "Collateral" Doctrine in Relation to Chronic Subdural Hematoma (CSDH)

Modern medical research has found that the quality of life of patients with Chronic Subdural Hematoma (CSDH) is closely related to traditional Chinese medicine (TCM) syndrome types. Academician Fan Yongping and his team [11] conducted a study on 106 CSDH patients who were diagnosed and treated at the Traditional Chinese Medicine Clinic of Beijing Tiantan Hospital, affiliated with Capital Medical University, from September 2016 to March 2019. The diagnosis revealed that 22.6% of the patients had kidney deficiency type CSDH, and blood stasis type patients even reached 100%, thereby confirming the important role of kidney deficiency and blood stasis in the pathogenesis of CSDH. With the continuous progress of modern medicine, some scholars have used morphological experiments to discover that fear can damage the kidney essence of female mice, leading to changes in the ultramicrostructure of the brain of the next generation of mice, thereby confirming the close relationship between the kidney and the brain. Moreover, studies have shown that people with neurological diseases are more likely to have kidney diseases [12]. In addition, some experts have pointed out that insufficient kidney yang may cause disorders in the hypothalamic-pituitary-adrenal cortex axis on the kidney. This close relationship between the brain and the kidney reflects the holistic view guided by the theory of traditional Chinese medicine, suggesting that the abundance or decline of kidney essence not only affects the function of the kidneys but also influences the filling of marrow and the function of the brain [13]. This indicates that the "Kidney Generates Marrow" theory is not only limited to human reproduction and growth development but also involves issues with the human nervous system.

In recent years, studies have also found that the method of unblocking collaterals, guided by the theory of "collaterals," can significantly improve the brain's ability to process information [14]. Tongxinluo Capsule is a new medicine that tonifies qi and nourishes blood, and it is developed based on

the research of TCM collateral theory. According to literature reports, the content of TXB2 in the plasma significantly decreased after taking Tongxinluo Capsule ($P<0.05$). The content of 6-keto-PGF1α in the plasma increased, and the ratio of TXB2/6-keto-PGF1α significantly decreased ($P<0.05$), so it can be speculated that Tongxinluo Capsule has the effect of inhibiting the hypercoagulable state of blood, improving vascular tension, and protecting brain nerves [15]. Some articles have also pointed out that the four collateral-unblocking traditional Chinese medicines, whole scorpion, earthworm, centipede, and ground beetle, play a key role in inhibiting the formation of cerebral thrombosis [16]. Some scholars collected specimens of the dura mater and hematoma capsule walls from 102 patients with chronic subdural hematoma during surgery at the Second Affiliated Hospital of Nanhua University. Using immunohistochemical analysis to study the expression levels of CD34, SMA, TGF-β, Smad2/3, and the presence of VMI, and observing samples at different time points. The expression of CD34, SMA, TGF-β, and Smad2/3 on the hematoma capsule was higher than that on the dura mater, and the expression of VMI on the hematoma capsule was lower than that on the dura mater, showing a gradually decreasing trend. This confirms that there are continuously forming capillaries on the CSDH capsule, suggesting that the progression of CSDH may be related to the continuous growth of immature capillaries [17]. At the same time, some literature has pointed out that increased vascular permeability, local inflammatory reactions, or the formation of immature blood vessels can all lead to blood vessel damage, thereby causing vascular leakage and gradually increasing the subdural hematoma [18]. Some scholars have also pointed out that the mechanism of CSDH formation is closely related to vascular aging, local inflammatory reactions, the formation of immature blood vessels, and increased vascular permeability [19]. With in-depth research, some articles have pointed out that the neovascularization of the capsule and abnormal local inflammatory reactions may lead to the occurrence of CSDH [20]. Professor Fan Xiaoxuan also believes that angiogenesis and inflammatory reactions are the basis for the continued development of CSDH [21]. Therefore, it further confirms that CSDH is a neurological disease with abnormal angiogenesis and inflammatory nature [22]. From this, the theory of collaterals plays a pivotal role in the diagnosis and treatment of neurological diseases, which is evident.

In the state of aging, after the head is traumatized, the meridians are damaged, and blood overflows outside the brain collaterals, leading to a deficiency of qi and blood, and the meridian stasis caused by the weak state. The meridian stasis further exacerbates the weak state, and the two interact with each other, eventually forming a hematoma. Or due to insufficient kidney function, it will lead to a lack of internal energy in the body, thereby affecting the smoothness of the meridians, leading to the occurrence of CSDH. Some studies have shown that using the method of replenishing qi and resolving blood stasis can also promote the absorption of intracerebral hematomas to a certain extent. It can effectively promote vasodilation, combat coagulopathy, and improve blood rheology. Therefore, it is confirmed that maintaining vascular patency and improving vascular stability also have important diagnostic and therapeutic significance for CSDH [23]. In summary, both traditional medicine and modern medicine have demonstrated the scientific connotation of the "Kidney Generates Marrow" theory and the "collateral" theory, as well as their close relationship with the occurrence of CSDH. They also confirm the reference value of the "kidney-marrow-collateral-brain" axis and the close relationship between "kidney deficiency, marrow reduction, and collateral damage" and the pathogenesis of CSDH.

4. Clinical Research on the Treatment of Chronic Subdural Hematoma (CSDH) from the Perspective of "Kidney Deficiency, Marrow Reduction, and Collateral Injury"

Traditional Chinese Medicine (TCM) considers "kidney deficiency, marrow reduction, and collateral injury" as the main etiology of Chronic Subdural Hematoma (CSDH), and treatment should primarily focus on "nourishing the kidney to generate marrow, and unblocking and consolidating the collaterals." The phrase "if the kidney does not generate, then the marrow cannot be full" is mentioned in the "Huangdi Neijing" (Yellow Emperor's Classic of Medicine). Furthermore, in the "Suwen · Wuzang Shengcheng" (Basic Questions · Generation and Transformation of the Five Viscera), it is stated: "All marrows belong to the brain." "Ling Shu Xie Qi Zang Bing Xing" (Spiritual Pivot · Pathogenic Qi and Disease Manifestation of the Viscera) mentions: "The twelve meridians and three hundred and sixty-five collaterals, their blood and qi all rise to the face and flow through the empty orifices." This highlights the close relationship between tonifying the kidney, generating marrow, unblocking collaterals, and benefiting the brain. Guided by TCM's "Kidney Generates Marrow" theory and "Collateral" doctrine, along with the active summarization of clinical physicians through the ages, effective compound prescriptions for treating CSDH have been formed in clinical practice, such as Di Huang Yin Zi, Yi Qi Hua Yu Fang, Shen Nao Fu Yuan Tang, Niu Xi Wan, Bu Gu Zhi Wan, and numerous clinical experience prescriptions.

Based on the "Kidney Generates Marrow" theory, Professor Fan Xiaoxuan's [24] team used their self-devised formula, Pei Yuan Hua Yu Fang, which mainly serves to nourish the kidney and essence, disperse blood stasis, and unblock collaterals. The formula includes Astragalus 40g, Angelica 20g, Rehmannia 20g, Cooked Rehmannia 20g, Codonopsis 10g, Carthamus 5g, Dioscorea 10g, Goji Berry 10g, Schisandra 10g, and Licorice 10g. A treatment group of 16 patients received Pei Yuan Hua Yu Fang treatment, while a control group of 15 patients received the same conditions. After treatment, the hematoma was significantly reduced, and the recurrence rate of CSDH was also markedly lower compared to the control group. The experiment proved that Pei Yuan Hua Yu Fang can reduce brain hematomas or effusions, alleviating symptoms in CSDH patients. Modern medical research indicates that Pei Yuan Hua Yu Fang can effectively prevent and treat chronic subdural hematoma (CSDH) by reducing the expression of VEGF in the hematoma outer membrane and decreasing pathological angiogenesis [25]. Chen Xu [26] and others used their self-devised formula for nourishing the kidney and essence (Angelica 10g, Astragalus 30g, Ophiopogon 10g, Atractylodes Macrocephala 20g, Cornus 10g, Albizia 10g,

Chuanxiong 6g, Bupleurum 10g, Poria 12g, Rehmannia 10g, Paeonia 10g, Dioscorea 15g, and Shanyao 10g) to treat CSDH patients. The control group maintained Western medicine treatment, while the treatment group was given the nourishing kidney and essence formula. The results after 2 months showed that the total effectiveness and daily living ability ($P<0.05$) of the patients treated with the Chinese medicine group were superior to those treated with Western medicine alone. Yao Zhongping [27] and others randomly divided 94 CSDH postoperative patients into 52 treatment groups and 42 control groups. The treatment group was treated with Di Huang Yin Zi plus Danshen and Honghua Jia Jian, with the rest of the conditions being the same as the control group. After observing the treatment effect of the patients one month later, it was found that the cure rate of the treatment group was 86.5%. However, the recovery rate of the control group patients was 64.3%, and there was a statistically significant difference in the recovery rate between the two groups ($\chi^2=6.418$, $P<0.05$). The treatment group with Di Huang Yin Zi plus Danshen and Honghua could significantly alleviate the clinical symptoms of CSDH patients, which pointed out that kidney-tonifying Chinese medicine can affect brain nerve function by changing the microenvironment of neural stem cells.

Qi-tonifying and collateral-unblocking Bu Yang Huan Wu Tang is a representative formula guided by the "collateral" doctrine. Liu Wenping [28] and others randomly divided 40 CSDH patients into 20 treatment groups and control groups. The treatment group was treated with Bu Yang Huan Wu Tang, with the rest of the conditions being the same as the control group. After observing the cure situation of the patients two months later, it was found that the symptoms of the treatment group patients were significantly improved compared to the control group. During the treatment process, it was found that the hematoma in the treatment group of CSDH patients decreased more quickly, and their daily living ability recovered faster than that of the control group patients. At the same time, the treatment group patients had fewer postoperative recurrences than the control group patients, which was statistically significant ($p<0.05$), thus proving that Bu Yang Huan Wu Tang can accelerate the absorption of hematomas and improve the clinical symptoms of CSDH patients, as well as prevent postoperative recurrence in CSDH patients. At the same time, Yang Ming [29] and others observed the protective effect of the earthworm extract in Bu Yang Huan Wu Tang on cerebral ischemic injury in rabbits and found that earthworms can protect brain function by inhibiting the influx of calcium ions. Modern research has also confirmed that the combination of Western medicine and blood-activating and collateral-unblocking Xue Fu Zhu Yu Tang Jia Jian can play a positive role in promoting the absorption of hematomas in CSDH and preventing hematoma recurrence by improving microcirculation and hemodynamics, improving vascular endothelial function, and promoting angiogenesis, which is worth promoting in clinical use [30]. Therefore, the treatment of CSDH can adopt the basic method of "nourishing the kidney to generate marrow and unblocking and consolidating the collaterals."

5. Discussion

In recent years, the incidence rate of Chronic Subdural Hematoma (CSDH) has gradually increased with the acceleration of population aging and the popularization of imaging technology [31], and its etiology and pathogenesis are not yet fully understood. However, studies have shown [32, 33] that there is a certain correlation between it and various factors such as age, lifestyle, history of head trauma, and medication use. According to literature reports, the total number of CSDH patients aged 70 to 79 is about 76.5 per 100,000 people, while for those aged 80 and above, it is 127.1[31]. The prognosis of CSDH patients aged 75 and above is significantly poorer compared to those under 75, and it has been proven that age is closely related to the prognosis of CSDH patients [34]. Clinically, CSDH is referred to as a "silent" cerebral hemorrhage, and its high incidence and recurrence rates have a profound impact on the physical and mental health of patients, increasing their economic burden. It has now become a social health issue that is a common concern at all levels of society. The urgent problem that the clinic needs to solve now is to actively seek effective and economical treatment and prevention plans for CSDH.

In recent years, with the continuous understanding of CSDH by traditional Chinese medicine (TCM), it has been found that the TCM "Kidney Generates Marrow" theory and "Collateral" doctrine are highly relevant to the occurrence of CSDH. Modern medicine has also confirmed that "kidney deficiency, marrow reduction, and collateral injury" are one of the main causes of its occurrence, and it has also confirmed that the "kidney-marrow-collateral-brain" axis has a certain reference significance. At the same time, TCM has achieved significant clinical diagnostic and treatment effects in preventing and treating CSDH with the principle of "nourishing the kidney to generate marrow, and unblocking and consolidating the collaterals," which also provides a broad range of ideas and a solid theoretical basis for the treatment of CSDH. Under the guidance of the holistic concept and syndrome differentiation and treatment of TCM, the treatment principle of "nourishing the kidney to generate marrow, and unblocking and consolidating the collaterals" can regulate the functions of the nervous, reproductive, endocrine, and other systems at multiple levels and in a multi-faceted manner, thereby effectively playing a role in preventing and treating CSDH.

6. Summary

In summary, there are many and complex studies on the "Kidney Generates Marrow" theory and "Collateral" doctrine and their relationship with CSDH, but their correlation cannot be fully explained. The "Kidney Generates Marrow" theory and the "Collateral" doctrine are closely related to the overall, systematic, vascular, cellular, and genetic aspects of modern medicine. In the future, it is still necessary to strengthen the combination of the "Kidney Generates Marrow" theory and the "Collateral" doctrine with the molecular microfield of modern medicine, to give play to the unique advantages of the holistic concept and syndrome differentiation and treatment of TCM, and to provide more innovative ideas and theoretical support for the treatment of CSDH.

Fund Project

Shaanxi Province "Dual Chain Integration" Young and Middle-aged Scientific Research Innovation Team Project:

Traditional Chinese and Western Medicine Prevention and Treatment Innovation Team for Vascular Aging and Neurodegenerative Diseases Project Number: 2022-SLRH-LJ-015.

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