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Progress in Clinical Research of Early Pregnancy Chorionic Hematoma in Traditional Chinese and Western Medicine

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Abstract: Subchorionic hematoma is a common cause of vaginal bleeding in early pregnancy, closely related to adverse outcomes such as miscarriage and premature birth. Its onset involves multiple factors such as coagulation abnormalities, immune imbalance, and placental vascular rupture. Western medicine mainly relies on progesterone supplementation and anticoagulant therapy, while traditional Chinese medicine improves the maternal and fetal environment through overall adjustments such as tonifying the kidneys, promoting blood circulation, and stabilizing the fetus. The combination of the two has synergistic advantages in regulating immunity, improving coagulation, and increasing the success rate of fetal preservation. However, existing research has problems such as a lack of standardization in syndrome differentiation and insufficient evidence of long-term efficacy, and there is an urgent need to integrate clinical evidence to optimize diagnosis and treatment strategies. This article provides a systematic review of the etiology, mechanism, and treatment progress of SCH in both traditional Chinese and Western medicine. It emphasizes the potential of combining traditional Chinese and Western medicine to reduce hematoma and improve pregnancy outcomes through the synergistic use of compounds such as progesterone, low molecular weight heparin, and Shou Tai Wan. The purpose of writing this review is to sort out controversies, propose the need for future multi-center large sample studies, establish a biomarker-based syndrome differentiation system, and develop targeted anticoagulant and immunomodulatory Chinese and Western compound preparations. Through interdisciplinary collaboration and technological innovation, we aim to promote the standardized and precise development of SCH diagnosis and treatment, ultimately improving the health level of mothers and infants.

Keywords: Subcystic hematoma; Integrated Traditional Chinese and Western Medicine Therapy; Etiology and pathogenesis; Review

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1. Introduction

Subchorionic hematoma refers to bleeding caused by the separation between the chorionic plate and the decidua, which appears as a dark area between the uterine wall and the gestational sac on ultrasound. The incidence rate of

SCH varies greatly in various studies. Threatened miscarriage refers to a clinical and pathological condition that occurs in early pregnancy, characterized by paroxysmal lower abdominal pain, slight irregular vaginal bleeding, and discomfort in the lumbar and sacral regions. Its clinical features include cervical canal closure and absence of embryonic tissue discharge [1]. Vaginal bleeding in early pregnancy is a common complication of pregnancy, with an incidence rate of 16% to 25% [2]. SCH is the most common cause of vaginal bleeding in patients between 10 and 20 weeks of pregnancy, accounting for approximately 11% of cases [3]. SCH is mainly characterized by vaginal bleeding and lower abdominal pain, and is closely related to adverse pregnancy outcomes such as placental abruption, premature birth, early and late miscarriage [4]. Other studies have shown that the widespread use of assisted reproductive technology has become an important risk factor for SCH [5]. At the same time, the clinical promotion of early pregnancy ultrasound technology has led to a significant increase in the detection rate of asymptomatic SCH. Pan *et al.* found that the presence, size, and duration of asymptomatic submucosal hematoma in early pregnancy may be related to adverse pregnancy outcomes in later pregnancy [6]. Asymptomatic SCH in the first trimester of singleton pregnancy is significantly associated with a variety of pregnancy complications. Its adverse outcomes include diabetes in pregnancy, thrombocytopenia in pregnancy, placental adhesion, fetal growth restriction, macrosomia, and preterm delivery in the third trimester. The presence, size, and duration of asymptomatic submucosal hematoma detected at 5–10 weeks of gestational age are associated with several adverse obstetric outcomes, such as full-term premature rupture of membranes and fetal growth restriction. Although the diagnosis of SCH relies on ultrasound examination, its etiology is complex, involving multiple factors such as maternal coagulation dysfunction, immune imbalance, and rupture of placental chorionic blood vessels [7].

The clinical treatment of SCH is mainly based on Western medicine intervention, including progesterone supplementation and hemostasis and anticoagulation. Progesterone, such as progesterone, can reduce the risk of miscarriage by maintaining endometrial receptivity. Chen *et al.* found that progesterone has clinical value in patients with early pregnancy complicated with SCH by regulating progesterone levels and adjusting Th1/Th2 cytokine balance [8]. Its mechanism of action may involve the reconstruction of the immune microenvironment, significantly improving the effectiveness of fetal protection treatment and maternal-fetal prognosis. Low molecular weight heparin is suitable for patients with SCH and a hypercoagulable state [9], but the long-term thrombotic risk of its use still needs to be carefully evaluated. Traditional Chinese medicine treatment emphasizes overall adjustment, such as Fang *et al.* using modified Shou Tai Wan formulas to improve the maternal fetal microenvironment by tonifying the kidneys, consolidating the Chong, nourishing Qi and blood, while tonifying the kidneys, promoting blood circulation, and stabilizing the fetus formula can regulate coagulation function and improve pregnancy success rate [10,11]. Luo focuses on tonifying the kidneys and strengthening the spleen, and uses the method of promoting blood circulation and removing blood stasis to eliminate pathological factors. He has selected Pinghe products to promote blood circulation and remove blood stasis, which have shown significant therapeutic effects in treating SCH [12].

Based on the theory of traditional Chinese medicine pathogenesis of "Yin deficiency, blood heat, and insufficient flushing and retention," Li added raw *Rehmannia glutinosa* to nourish Yin and cool blood, Di Gu Pi to clear and eliminate deficiency heat, Xuan Shen to nourish Yin and detoxify, Fu Ling to invigorate the spleen and calm the heart, Huang Qin to clear heat and stabilize the fetus, Di Yu Charcoal to converge and stop bleeding, and ramie root to solidify flushing and stop leakage to nourish kidney Yin, clear blood heat, and solidify fetal essence [13]. In addition, extensive clinical studies have been conducted on the treatment of SCH during pregnancy using a combination of traditional Chinese medicine and Western medicine. Wang *et al.* found that the combination of

traditional Chinese medicine tonifying the kidney, activating blood circulation, and stabilizing the fetus formula with progesterone significantly increased the levels of Ps and Pc in early pregnancy SCH patients, while the levels of coagulation factor VIII, D-dimer (D-D), and NK cells were significantly reduced [11]. The improvement in coagulation function in the integrated Chinese and Western medicine treatment group was significantly better than that in the single Chinese medicine/Western medicine intervention group, indicating that the combination of Chinese and Western medicine has a synergistic effect in correcting coagulation dysfunction, inhibiting pathological thrombosis, and promoting fibrinolysis activation. However, there are still controversies surrounding existing treatment plans, such as a lack of standardization in syndrome differentiation and insufficient evidence of long-term efficacy [14].

This article systematically reviews the pathogenesis, treatment progress, and synergistic effects of traditional Chinese and Western medicine in SCH in recent years, aiming to integrate clinical evidence and explore potential directions for optimizing treatment strategies. By analyzing the limitations of existing research, this article further proposes that future research should focus on standardized diagnosis and treatment guidelines, interdisciplinary collaboration, and the development of new compound formulations, in order to provide the scientific basis for improving pregnancy success rates and maternal and infant safety.

2. Traditional Chinese Medicine's understanding of submucosal hematoma

2.1. Etiology and pathogenesis of submucosal hematoma

There is no SCH related disease name in ancient Chinese medicine books, but according to the clinical manifestations of "a small amount of vaginal bleeding and fetal movement and descent" as described in classics such as "The Treatise on the Origins of Various Diseases" [15], the core pathogenesis belongs to the categories of "fetal leakage" and "fetal movement instability". The disease is located in the Chong and Ren meridians, and is essentially caused by Chong and Ren damage and fetal instability. Its etiology and pathogenesis are closely related to kidney deficiency, blood stasis, and Qi and blood imbalance. Traditional Chinese Medicine believes that the kidneys are the foundation of innate nature and play a major role in reproduction. If the kidney Qi is insufficient, it will not be able to maintain a stable circulation of the meridians, and blood will not return to the meridians. This can lead to blood stasis and stagnation in the uterus, resulting in the formation of hematomas [16]. The Blood Syndrome Theory [17] states: "Although it is the blood that deviates from the classics, it is clear blood and fresh blood, but it is also stagnant blood." The article points out that the "blood that deviates from the classics" is called "stasis blood." If the stasis blood does not disappear, new blood will not be born, and the fetus will lose its nourishment, causing fetal instability. The book "Yi Lin Gai Cuo" [18] states: "Without knowing that there is blood stasis occupying the uterus, the fetus grows to three months and there is no place to live inside. Fetal diseases rely on compression, and blood cannot enter the placenta, flowing down from the side. Therefore, blood appears first. Since blood does not enter the placenta, the fetus lacks blood nourishment, resulting in miscarriage. Blood stasis blocks the uterus, causing blood to not follow the meridians and resulting in fetal leakage. Blood stasis blocks the fetus, leading to loss of nourishment and disturbance of the fetal element, resulting in unstable fetal movement and ultimately leading to miscarriage. Modern research has also shown that traditional Chinese medicine's "blood stasis" is associated with microcirculatory disorders and immune disorders [19], which may increase the risk of adverse pregnancy outcomes. In addition, the "Annotation on Women's Good Prescriptions" [20] states: "If the wife strengthens her stomach Qi and promotes harmony, then the fetus will find a place like a fish

in the abyss." In the "Gezhi Yulun" [21], it is said: "Qi and blood deficiency and lack of nourishment will cause the fetus to fall naturally." It can be seen that Qi and blood deficiency are also the main pathological factors leading to fetal leakage. The kidneys are responsible for reproduction and play an important role in it. The abundance of kidney essence depends on the microdistribution of water and grain essence in the middle energizer. The spleen and stomach are the source of blood biochemistry in the postnatal stage. When the spleen and stomach are healthy, blood and Qi are abundant. The spleen and the kidney are always closely related, and the process of reproduction can only proceed smoothly if they complement each other. The spleen and stomach are the organs of the granary, and abnormal transport and transformation of the middle energizer can lead to a lack of sources of kidney essence, which in turn can cause reproductive dysfunction. If the deficiency of spleen and kidney leads to insufficient transformation of essence and blood, and the operation of qi is obstructed, it will form stasis, causing dysfunction of the Chong Ren meridians, leading to the loss of fetal essence, and ultimately causing symptoms such as fetal leakage and fetal instability.

2.2. Traditional Chinese Medicine syndrome differentiation and prescription selection for Subcystic hematoma

In summary, the etiology and pathogenesis of SCH are centered around "deficiency and blood stasis." Fang *et al.* [22] found through clinical investigation that SCH is mainly divided into five syndrome types: kidney deficiency syndrome, spleen kidney deficiency syndrome, blood heat syndrome, kidney deficiency and blood stasis syndrome, and Qi and blood deficiency syndrome. Among them, kidney deficiency and blood stasis are the most common syndrome types. For kidney deficiency and kidney deficiency blood stasis types, the classic formula is Shoutai Wan. Modern pharmacological research has confirmed that Shoutai Wan simulates endogenous hormone function through estrogen-like biological effects, while inhibiting abnormal contractions of uterine smooth muscle, thereby maintaining pregnancy stability and playing a role in preventing miscarriage and leakage [23]. The deficiency of qi and blood can be treated by nourishing Qi and blood. Huangqi, *Codonopsis pilosula*, and other herbs can be used to nourish qi and blood, while *Artemisia argyi* can be used to stop bleeding and improve the patient's deficiency of Qi and blood [24]. For the spleen and kidney deficiency combined with blood stasis type, the formula of tonifying the kidney, promoting blood circulation, and stabilizing the fetus can strengthen the spleen and kidney, remove blood stasis, and generate new blood. Clinical studies have shown that it can significantly reduce D-dimer levels and improve the pregnancy success rate [11]. The treatment of blood heat syndrome should mainly focus on tonifying the kidney and spleen, supplemented with heat-clearing products such as *Scutellaria baicalensis* and *Eclipta alba*, which can nourish the liver and kidneys, cool blood and stop bleeding. Another doctor used modified Huanglian ass hide glue Decoction to treat SCH, and the results showed that the efficacy was significantly better than that of the group only taking didroxyprogesterone [25].

3. Western medicine's understanding of subdural hematoma

3.1. Pathogenesis and risk factors of submucosal hematoma

The etiology of SCH has not yet reached a consensus. Although its incidence rate is on the rise, the specific pathophysiological process and its impact on pregnancy outcomes are still controversial. At present, the research on the etiology of SCH mainly focuses on several aspects, such as coagulation system dysfunction, autoimmune factors, the widespread use of assisted reproduction, medication during pregnancy and vaginal flora imbalance [26]. A study found that anti cardiolipin antibodies can induce abnormal platelet aggregation on one hand, and on the other hand,

they can bind to phospholipid dependent antigens on the surface of trophoblast cells, interfere with the normal differentiation process of trophoblast cells, and ultimately lead to insufficient synthesis of key hormones that maintain pregnancy in the placenta, thereby significantly increasing the risk of embryonic arrest and spontaneous abortion [27]. Homocysteine is a non-protein-derived sulfur-containing amino acid, and its abnormal increase in serum concentration has been confirmed as an independent risk factor for adverse pregnancy outcomes. It can activate coagulation factors VII and V in the body, promote thromboxane formation, and inhibit the activity of coagulation factors III and IV. This dual effect breaks the dynamic balance between human coagulation and anticoagulation mechanisms, causing blood to show a hypercoagulable tendency and significantly increasing the risk of intravascular thrombosis [28] . Assisted reproductive technology (IVF-ET) is an important risk factor for SCH. A survey of IVF-ET patients showed that the incidence of SCH in pregnant women after IVF-ET was significantly higher than that in the non-IVF group, with an incidence rate of about 22.4% [29]. Yue *et al.* found that there is a correlation between the risk of developing SCH and previous pregnancy history, with patients who undergo IVF-ET having a higher number of pregnancies having a higher incidence of SCH. Other risk factors include advanced pregnancy (≥ 35 years old), multiple pregnancies, and a history of miscarriage [30,31].

3.2. Western medicine treatment of subdural hematoma

In recent years, the strategies for treating SCH in Western medicine have tended towards individualization and multidisciplinary collaboration. Progesterone supplementation is still the preferred option. Dexmedetomidine is a progesterone drug similar to progesterone, which can ensure pregnancy homeostasis through multidimensional mechanisms of action, without male or female hormones or adverse reactions, and has high safety [32]. For SCH patients with a pre-thrombotic state, low molecular weight heparin calcium has strong antithrombotic effects, counteracts the pre-thrombotic state, regulates immunity, maintains maternal-fetal immune tolerance, improves endometrial receptivity, and improves microcirculation at the maternal-fetal interface [33]. Sun used a combination therapy of tranexamic acid and progesterone to treat patients with threatened miscarriage and SCH in early pregnancy, which showed significant therapeutic effects [34]. Studies have shown that tranexamic acid can inhibit inflammatory reactions, reduce vascular permeability, inhibit prostaglandin synthesis, inhibit platelet activation, reduce cervical relaxation and uterine contractions, and have analgesic effects. Therefore, it can be used to treat SCH, alleviate SCH symptoms, reduce related risks, and improve patients' quality of life. Phloroglucinol is a myophilic smooth muscle antispasmodic drug with pharmacological properties that specifically acts on smooth muscle tissue in a spastic state. Its mechanism of action does not rely on the anticholinergic pathway and does not significantly interfere with normal physiological smooth muscle function. It can effectively improve abdominal pain symptoms in patients with threatened miscarriage by accurately relieving abnormal uterine contractions, while significantly reducing the risk of bleeding caused by pathological uterine contractions, inhibiting premature rupture of membranes, and having no effect on embryo and fetal development [35]. Scholars have proposed that the combination of immunoglobulin and low molecular weight heparin has a synergistic effect on the quality of SCH [36]. Through the unique antibody effect exerted by immunoglobulin, the degree of immune disorder in patients is reduced. Then, low molecular weight heparin is used to improve the receptivity of the endometrium and the intrauterine environment in patients, thereby maintaining normal pregnancy. The combined use of low molecular weight heparin and immunoglobulin in the treatment of SCH patients can effectively improve the success rate of fetal preservation while significantly improving the serum progesterone levels of patients, thereby reducing the risk of adverse pregnancy outcomes such as premature birth and miscarriage [37]. Low molecular weight heparin combined with immunoglobulin

therapy can significantly improve the efficacy of treating SCH in pregnancy. While effectively reducing the incidence of adverse events, miscarriage, and premature birth during pregnancy, it can also promote the recovery of pregnancy-related hormones and cytokine expression levels such as IFN-γ and IL-10 in patients [38].

4. The synergistic advantages of combining traditional Chinese and Western medicine in the treatment of subdural hematoma

The combination of traditional Chinese medicine and Western medicine in the treatment of SCH demonstrates a significant synergistic effect by integrating the holistic treatment of traditional Chinese medicine with precise intervention of Western medicine. Traditional Chinese medicine treatment focuses on syndrome differentiation and treatment, while Western medicine directly improves placental blood flow and maternal-fetal immune microenvironment through methods such as supplementing progesterone and low molecular weight heparin anticoagulation. Clinical studies have shown that the combination of traditional Chinese and Western medicine significantly improves coagulation factors, sex hormones, pregnancy outcomes, and pregnancy complications compared to high single Western medicine and single traditional Chinese medicine treatments [11]. Clinical studies by Xu *et al.* have shown that for early stage SCH patients with cold coagulation and blood stasis type, the use of a combination of traditional Chinese and Western medicine treatment with modified Jiaoai Tang and progesterone can not only significantly promote hematoma absorption, effectively improve cold coagulation and blood stasis symptoms such as lower abdominal pain and vaginal bleeding, but also reduce the incidence of adverse pregnancy outcomes [39]. This therapy has been clinically validated to have high safety and no significant side effects have been observed. According to literature records, the classic formula Shou Tai Wan, as recorded in the "Medical Zhong Zhong Shen Xi Lu," is mainly used in the clinical practice of traditional Chinese medicine for the treatment of pregnancy-related diseases such as kidney deficiency type fetal restlessness, fetal leakage, and fetal developmental delay. Through modern pharmacological research, it has been found that Shoutai Pill can promote the secretion of Th2 cytokines, inhibit the secretion of Th1 cytokines, restore the balance between the two, reduce immune rejection, enhance resistance, and restore normal serum levels [40]. Some studies have shown that for patients with early pregnancy complicated with SCH, the application of a combination of traditional Chinese and Western medicine treatment with modified Shou Tai Wan and Western medicine can achieve multiple therapeutic effects simultaneously. While significantly improving the clinical manifestations of patients, it can effectively reduce the hematoma area, shorten the course of the disease, and significantly improve the stability of embryonic development and pregnancy maintenance rate [9,41,42]. In addition, traditional Chinese medicine characteristics external treatment methods such as ear acupuncture combined with dexamethasone, can improve the clinical efficacy of treating early threatened miscarriage with SCH. In terms of regulating immune factors and promoting hematoma absorption, it has a good synergistic effect with dexamethasone, reducing the risk of Western medicine dose dependence and side effects [43].

5. Summary and prospect

Although the current combination of traditional Chinese and Western medicine has achieved phased results in the treatment of SCH, the following key issues still need to be addressed: firstly, existing studies are mostly single-center center small sample sizes, and it is urgent to conduct multi-center randomized controlled trials to verify the efficacy. Secondly, there is a lack of unified standards for TCM syndrome differentiation and classification, and

an objective evaluation system based on biomarkers needs to be established. Thirdly, the mechanism of action of traditional Chinese medicine formulas has not been fully elucidated, and the molecular pathways regulating the maternal-fetal interface can be analyzed using network pharmacology and metabolomics techniques. Future research should also explore new treatment strategies, such as developing targeted anticoagulation and immune regulation Chinese Western compound preparations, or using scoring to construct SCH risk prediction. In addition, long-term follow-up studies are crucial for evaluating the safety of treatment and the impact on offspring health. Through a systematic review of existing literature, the combination of traditional Chinese and Western medicine therapy is expected to provide more accurate and personalized diagnosis and treatment plans for SCH, to reduce the risk of adverse pregnancy and improve the fetal survival rate.

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Disclosure statement

The authors declare no conflict of interest.

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