

Temperature Analysis on Clinical Diagnosis and Treatment Characteristics of Hemospermia with Traditional Chinese Medicine

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Keywords: Hemospermia, Literature review, Diagnosis and treatment characteristics, Prescription law

Abstract: The characteristics of tcm clinical diagnosis and treatment of hemospermia were analyzed retrospectively. Methods: The relevant literature concerning the treatment of hemospermia with traditional Chinese medicine in CNKI, WanFang data, VIP and database were retrieved electronically, and the included literature was analyzed. The intervention measures, characteristics of disease debate and treatment, characteristics of commonly used prescriptions and drugs, efficacy evaluation, follow-up and safety-related information in the treatment of hemospermia with traditional Chinese medicine were summarized. Results: A total of 17 articles were included, and the most commonly used intervention measure in the treatment of hemospermia with TCM was oral administration of TCM decoction, 14 articles (82.5%); Regarding the type of disease differentiation, eight articles (47.06%) were devoted to seminal vesiculitis, with 12 articles (70.59%) on hemostasis, 11 articles (64.70%) on heat clearing, 9 articles (52.94%) on nourishing yin, 8 articles (47.06%) on cooling blood, and 4 articles (23.53%) on activating blood circulation being the top five treatments. There were five pieces (29.41%) of Six-Ingredient Dihuang Decoction prescriptions as the main prescription types, and the frequency of use of single Chinese medicine from high to low was: Cortex Moutan, Poria, Cortex phellodendri, and Radix Rehmanniae. The proportions of Chinese herbs in the four qi from more to less were cold, even, warm, cold and hot in sequence. The proportions of meridian tropism were successively liver, kidney, heart, lung, stomach, etc. The proportions of the five herbs from more to less were as follows: sweet, bitter, pungent, sour, pale, unsmooth and salty. The disappearance of spermatorrhea under the microscope was more common for therapeutic evaluation criteria (88.24%), and the effective rate was 77.00%–100%. 52.94% of the articles included follow-up; Only five articles covered mild adverse reactions during treatment. Conclusion: The curative effect of traditional Chinese medicine (TCM) in the treatment of hemospermia is exact, and adverse reactions are rare. However, the specific mechanism is still unclear. In the future, the effective mechanism of TCM should be further clarified on the basis of clarifying the clinical advantages of TCM in the treatment of hemospermia.

1. Introduction

The modern medical definition of hemospermia is the discharge of semen mixed with blood⁰, in clinical according to the severity of the disease, can be divided into naked eye hemospermia and mirror hemospermia. It is one of the common clinical symptoms in modern urology and andrology, accounting for about 1% of all symptoms⁰, mostly accidental or repeated attack, can occur in any stage after adolescence, but still in young adults, sexual activity is more active. The repeated attack of hematospermia, or even the case that cannot be cured after a long period of treatment, or even the severe case that can affect the mental health of patients, should arouse the attention of urologists and andrologists. The treatment methods in modern medicine mainly include medication and surgery. However, in the process of clinical practice, two problems are often faced. On the one hand, during medication, oral antibiotics have poor effect on some refractory hematospermia with repeated attacks. On the other hand, seminal vesicle endoscopy surgery not only has high technical requirements on surgery, but also belongs to invasive treatment, which is difficult for some patients to accept. In contrast, traditional Chinese medicine has a long history in the treatment of hemospermia, which has a good inheritance and curative effect and is more acceptable to patients. Therefore, the author specially searches the literature related to the treatment of hemospermia with traditional Chinese medicine in the past 20 years, and tries to summarize and analyze them as follows, in order to offer food to fellow practitioners.

2. Information and Methods

2.1 Literature Sources and Retrieval Methods

Literature retrieval methods: Advanced retrieval was performed on China Knowledge Network (CNKI), WanFang data Service Platform (Wanfang Data) and Chinese Science and Technology Journal Service Platform (VIP) with hemospermia and hematospermia disease as search terms, and the discipline was limited to traditional Chinese medicine. The retrieval results were subjected to secondary retrieval. Set the search time limit to January 1, 2003 to March 1, 2023.

2.2 Inclusion Criteria

- (1) The research subjects are patients with spermatorrhea;
- (2) Articles from core journals of science and technology of China, core journals of Peking University, and core journals of CSCD;
- (3) The literature types were clinical research literature, including randomized controlled trials and non-randomized controlled clinical efficacy evaluation literature.

2.3 Exclusions

- (1) Non-traditional Chinese medicine articles concerning treatment of hematospermia;
- (2) Case reports and basic experimental research articles;
- (3) Two contributions in one draft or articles with identical contents, and the article with relatively complete materials shall be selected;
- (4) The full-text literature is not available;
- (5) Articles in which the prescription information could not be clarified in the Chinese patent medicine;
- (6) Types of disease differentiation included prostate cancer, seminal vesicle cancer, hypertension, diabetes, and hematospermia of unknown cause.

2.4 Information Extraction and Data Processing

After a detailed reading of the literature, relevant information including intervention measures, disease differentiation characteristics and treatment, commonly used prescriptions and drug characteristics, efficacy evaluation, follow-up and safety were extracted. According to the national standards of People's Republic of China (PRC) Chinese medicine with reference to the "Chinese medicine"⁰Unified specification of drug names was conducted in textbooks, and the obtained data were entered into Excel for systematic analysis.

3. Results

3.1 Search Results

A total of 2603 articles were obtained. After re-examination and re-examination with literature management software, 190 articles were initially screened, the abstracts or full texts were read, and the articles were screened against the inclusion criteria and exclusion criteria. Finally 17 Chinese articles were included. Among them, 14 were treated with oral Chinese medicinal decoction, 2 with Chinese patent medicine, and 1 with oral Chinese medicine combined with Chinese herbal enema. 15 articles in the random control group and 2 articles in the non-random control group.

3.2 Interventions

Literature analysis showed that the commonly used intervention measures for TCM treatment included oral administration of TCM decoction, oral administration of Chinese patent medicine, and oral administration of Chinese medicine combined with drug enema. The largest number of them were oral Chinese medicinal decoction, 14 (82.35%, 14/17); The second most obvious choice was oral Chinese patent medicine (11.77%,2/17), and one oral Chinese patent medicine combined with Chinese herbal enema (5.88%,1/17).

3.3 Treatment Plan

3.3.1 Characteristics of Disease Differentiation and Treatment

Among them, eight cases (47.06%) of seminal vesicle inflammation, six cases (35.29%) of chronic seminal vesicle inflammation, two cases (11.76%) of prostatitis, two cases (11.76%) of intractable spermatorrhea, and one case (5.88%) of seminal vesicle dilatation were covered for all the diseases identified. Related therapies include nourishing yin (nourishing yin and benefiting yin belong to the same), clearing heat, cooling blood, hemostasis, replenishing qi (tonifying qi belongs to the same), activating blood, breaking blood stasis (breaking blood belongs to the same), removing dampness, tonifying liver, tonifying kidney, detoxification, dredging stagnation, eliminating symptoms, dissipating mass, diuresis, stranguria, essence fixation and strengthening vital qi. The top five treatments were hemostasis (12 articles, 70.59%), heat clearing (11 articles, 64.70%), nourishing yin (9 articles, 52.94%), cooling blood (8 articles, 47.06%) and activating blood (4 articles, 23.53%).

3.3.2 Commonly Used Prescriptions and Drug Characteristics

The main types of prescriptions covered in the literature included Six-flavored Dihuang Decoction-like prescriptions, Guizhi Fuling Pill-like prescriptions, Taohong Siwu Decoction-like prescriptions, Xigen Powder-like prescriptions, and Buyang Huanwu Decoction-combined

with Dang Decoction-like prescriptions. Six-flavored Dihuang Decoction-like prescriptions occupied the first place, with five chapters accounting for 29.41%.

The drugs involved included 68 drugs, with the total frequency of 172 times. Among them, the most frequently used drug was Cortex Moutan 10 times, followed by Poria 9 times, Cortex phellodendri and Radix Rehmanniae 7 times, panax pseudo-ginseng, Ecliptae Herba and Radix Paeoniae Rubra 6 times, Fructus Gardeniae, Rhizoma Imperatae, Fructus Corni, Rhizoma Anemarrhenae and Rhizoma Dioscoreae 5 times, Alismatis Rhizoma, Semen Persicae, Fructus Ligustri Lucidi and Herba Patriniae 4 times, Radix Astragali seu Hedysari, Radix Rehmanniae Preparata, Flos Carthami, Ramulus Cinnamomi, Radix Glycyrrhizae, Radix Angelicae Sinensis, Rhizoma Ligustici Chuanxiong and Semen Plantaginis 3 times. Ramie root, agrimony, leech, rhizoma sparganii, radix rubiae, pollen typhae, achyranthis radix, curcumae rhizoma, radix sangisorbae, squama manis, cacumen platycladi, and colla corii asini were all used twice, and the remaining drugs were only used once, so detailed description is not required.

As the meridian tropism of five drugs is not supported by widely recognized official data, they are excluded from the data statistics here, and the rest drugs are referred to the Chinese medicine textbooks.⁰ And the China pharmacopoeia 2020 edition⁰ And record its nature and taste meridian tropism. The proportions of Chinese medicinals in the four qi from more to less were cold (94 times, 54.65%), moderate (36 times, 20.93%), warm (35 times, 20.35%), cold (5 times, 2.90%) and heat (1 time, 0.58%). From more to less, the proportions of using Chinese medicine in the five herbs were as follows: sweet (91 times, 52.90%), bitter (87 times, 50.58%), pungent (38 times, 22.09%), sour (16 times, 9.30%), pale (15 times, 8.72%), unsmooth (14 times, 8.13%) and salty (10 times, 5.81%). The descending order of the frequency of drug use for meridian tropism was liver > kidney = heart > lung > stomach > spleen > bladder > large intestine > small intestine > gallbladder = pericardium = triple energizer.

3.4 Efficacy Evaluation

According to whether or not to include the efficacy evaluation under the microscope of hemospermia, it can be mainly divided into two categories. A total of two articles (2/17, 11.76%) evaluated the efficacy based on the disappearance of only gross spermatorrhea. The standard classifications of therapeutic effects included: Cure: After treatment, the naked eye hemospermia disappeared, accompanied by the disappearance of symptoms, and no recurrence was observed during follow-up; Improvement: After treatment, the color of spermatorrhea becomes lighter and the accompanying symptoms decrease. No effect: After treatment, the color of hemospermia does not change or deepens. The remaining 15 articles (15/17, 88.24%) included the disappearance or decrease of hemospermia under the microscope as the basis of efficacy evaluation except for the disappearance of hemospermia by the naked eye. The standard classification of efficacy in this large category included: Cure: disappearance of clinical symptoms and signs, and laboratory examination: no red blood cells were found under the microscope examination of semen. Effective: The clinical symptoms were alleviated, and the red blood cells under semen microscope were reduced. Ineffective: The symptoms were not significantly improved or even worsened. In three of these articles, the curative standard was the complete disappearance of red blood cells and white blood cells at least two times under the semen microscope, and no naked eye sperm was observed after 10 consecutive sperm discharges to evaluate the therapeutic effect in a more precise and detailed manner. Another three included imaging measures for multi-angle evaluation in the evaluation criteria.

According to the above efficacy criteria, there are differences in the efficacy of different treatment methods. According to the effective rate records in the literature, the effective rate of pure

Chinese medicine oral treatment fluctuates in 83.3%⁰~100.00%⁰Meanwhile, the effective rate of oral administration of traditional Chinese medicine combined with enema fluctuated by 90.30%⁰, Chinese patent medicine treatment fluctuation in 77.00%⁰Left and right. In one article, the cure rate was only counted as 70.77%⁰, the effective rate and the ineffective rate are not included in the discussion.

3.5 Follow-up

Among the included articles, 52.94%(9/17) were followed up, and whether there was recurrence after follow-up was included in the cure criteria in seven articles, so the recurrence rate could not be accurately counted. There were two articles that did not include the recurrence rate after follow-up in the efficacy evaluation criteria. The recurrence rate of Chinese patent medicine Ningmitai was 8.20%, and that of Chinese patent medicine Huangbai Bawei Tablets was 5.13%.

3.6 Safety Evaluation

Seven articles (7/17,41.18%) evaluated the safety of treatment and observed the side effects during treatment. There were two articles^{0,0}There was no adverse reaction in the control group and the treatment group. Other adverse reactions recorded in the literature were mainly gastrointestinal adverse reactions, such as nausea and vomiting, and some manifested as dizziness, lethargy, and rash⁰And so on, all of the above reactions were mild and had a short duration, and the adverse reactions of all patients could disappear after symptomatic treatment in a short time, without affecting the subsequent research and treatment.

4. Analysis and Discussion

Hemospermia refers to the clinical symptom that the discharged semen is mixed with blood. At present, in the mainstream studies, the bleeding sites of hemospermia mostly involve seminal vesicles and paramesonephric duct cysts.⁰, some researchers also put forward the urethra prostate lesions can also cause spermatorrhea. In this study, we also specially screened the blood sperm caused by seminal vesicle and prostate lesions.

Based on its clinical manifestations, the earliest literature record of hemospermia in traditional Chinese medicine can be seen in the book Syndrome of Various Diseases and Syndrome of consumptive disease and blood outflow from essence. At the same time, hemospermia disease is located in the essence room. It belongs to male cell, and is closely related to liver and kidney, involving the heart, lung, and spleen. It is also stated in Ming Huang-fu's Ming physician's palm that “a lecherous man is diligent in governing his daughter, and has limited refinement but infinite desires. blood is like fire, and he cannot convert it into essence. as a result, his color is red and he depends on blood”. Later generations of physicians mostly attributed it to the diseases such as “red, white and turbid”, “bleeding from sexual intercourse”, and “Jingxue”, which is also followed by modern TCM.

It has been discovered in the present study that the commonly used intervention measures for the clinical treatment of hemospermia with TCM include oral administration of Chinese medicinal decoction or powder, oral administration of Chinese patent medicine, and oral administration of Chinese medicine combined with TCM enema. Oral Chinese medicinal decoction or powder was the most. The common disease differentiation was seminal vesiculitis (47.06%, 8/17); The therapeutic methods were usually applied to stop bleeding (70.59%,12/17), clear heat (64.70%,11/17), and nourish yin (52.94%,9/17). The Liuwei Dihuang Decoction was the first among the main prescriptions mentioned in the literature (29.41%,5/17).

The most criteria for efficacy evaluation were improvement of clinical symptoms, disappearance or reduction of spermatorrhea under the naked eye and microscope (88.24%,15/17). Literatures about follow-up visit indicated that the recurrence rate of Chinese patent medicine in the treatment of hemospermia fluctuated between 5.13% and 8.20%, and whether or not there was recurrence at follow-up visit was taken as one of the efficacy criteria in some literatures, so the recurrence rate could not be accurately counted. A total of seven articles (7/17,41.18%) reviewed and evaluated the adverse reactions in clinical treatment, and all of them disappeared in a short period of time, indicating that the safety of traditional Chinese medicine in the treatment of hematuria was good.

Hemostasis, heat clearing, and nourishing yin are the most commonly used therapeutic methods of traditional Chinese medicine for the treatment of hemospermia, indicating that from the perspective of clinical syndrome differentiation, the pathogenesis of the patients with hemospermia diseases that we most often face are kidney-yin deficiency, mutual exuberant fire, and blood rash, which is consistent with the understanding of hemospermia by national famous traditional Chinese medicine. If professor zeng qingqi thinks⁰, of blood and essence, the responsibility to the spleen and kidney two dirty, cover because of excessive discharge of kidney essence, phase fire Kang Sheng did not make, spleen deficiency can not be taken, no lean outside the blood vessels, and cause the essence chamber loss, blood collateral burning, red and white out, in the treatment should be zi kidney Yin, discharge phase fire, healthy temper, blood taken behavior main treatment. Such as professor Xu Fusong in his decades of testimony also accumulated rich experience⁰, think that kidney Yin deficiency is the root of the hemospermia, sex is not section, day long kidney injury, kidney Yin deficiency, cause deficiency fire from inflammation, very desire fire is more prosperous, disturbance essence room, forced blood line in error, blood overflow outside the pulse, so into hemospermia; Or young people fire exuberant, sex brimming with essence, and blood collateral damage, red white turbidity with the essence of the room, often lead to blood. In summary, the key to such pathogenesis in clinic is to grasp it, which can best affect the diagnosis and treatment effect.

In the prescription medication, Liuwei Dihuang Decoction is the most widely used prescription. *Rehmannia Radix* in the prescription mainly enters the liver and kidney meridians, has mild nature and sweet taste, and is good at tonifying the yin of liver and kidney. *Fructus Corni* is sour and astringent in taste, capable of astringing essence. *Rhizoma Dioscoreae* enters the spleen and kidney meridians together, which are the three supplements for harmonizing nature, invigorating spleen and reinforcing kidney, as well as tonifying deficiency and nourishing source. *Alismatis Rhizoma* is capable of draining dampness and turbidity, *Moutan Cortex* is capable of clearing away the pathogenic fire, and *Poria* is weak in infiltrating spleen dampness, which not only assists *Alisma Rhizoma* in draining kidney and turbidity, but also assists *Rhizoma Dioscoreae* in tonifying spleen. These are the three drainage processes. Its formula of three reinforcing and three reducing is specially used for the treatment of kidney-yin deficiency with exuberant fire. Just as it is stated in the *Commentary on Medical Prescriptions* that “herbs can stop six flavors, and there are both opening and closing herbs, as well as the treatment of the three yin meridians in combination, which can alone and supplement the original prescription.” These six drugs appeared in high-frequency drugs.

In terms of medication frequency, there are also herbs capable of lowering fire, nourishing yin, cooling blood, and activating blood. For example, *Rhizoma Anemarrhenae* and *Cortex Phellodendri* taste bitter but cold in nature, so draining fire and building up Yin can pacify the mutual fire and preserve the real Yin in kidney. Glossy privet fruit tastes sweet and bitter, but it is mild in nature, while *Eclipta prostrata* tastes sweet and sour, but it is cool in nature. The combination of the two can nourish liver and kidney, purge fire in phase, and cool blood heat. Cogongrass rhizome tastes sweet and cold, and is good at clearing the heat in the lower energizer. *Gardenia jasminoides* Ellis has the function of cooling heart and kidney and draining mutual fire. *Notoginseng Radix*, *Radix Paeoniae*

Rubra and Semen Persicae are also good at activating blood and stopping bleeding to remove blood stasis and generate new blood. All of the above herbs are commonly used in clinic for the treatment of hemospermia. Mastering the use and modification of these drugs in clinic is the key to the treatment of hemospermia.

From the perspective of meridian tropism of drugs, the two meridians of liver and kidney are firstly selected, among which the pulse of liver meridian of foot jueyin flows along the femoral yin and into the hair, encircling the yin vessels and reaching the lesser abdomen. It provided the theoretical support for medication from the perspective of meridian running. Then, meridians and collaterals refer to liver and kidney of zang-fu organs, in which the liver controls the storage of blood and the kidney controls the storage of essence. For example, it is mentioned in *Miraculous Pivot to God* that “the liver stores blood, while blood stores soul”. It is stated in *Suwen Liujie Zang Xiang Lun* that “the kidney governs the sting and seals the essence.” Therefore, liver and kidney affect the occurrence of hemospermia from the source, and attention should be paid to the recovery of liver and kidney function in the treatment. Professor Cui Yun, National Famous Veteran Doctor of Traditional Chinese Medicine⁰It is summarized from the clinical experience of essence room disease that the essence room is in the lesser abdomen, located in the liver meridian and prepared by the liver. Since liver and kidney are homologous and essence and blood are mutually changed, the essence chamber is nourished by liver blood and kidney essence, which are physiologically related to each other and inevitably affect each other pathologically. Therefore, from the perspectives of meridians and viscera, the treatment of blood and essence in essence room should start with liver and kidney.

From the perspective of five flavors of drugs, those with sweet taste are good at nourishing and tonifying deficiency, as well as harmonizing and relieving. Those with bitter taste are good at clearing heat and purging fire, as well as being capable of drying and building up. The combination of the two can purge fire and retain Yin, strengthen body resistance and drive away pathogenic factors, thus treating both manifestation and root cause of the disease. The choice of sweet and bitter herbs is also the common understanding basis of national famous doctors on syndrome differentiation of hemospermia⁰.

At present, in most clinical literature concerning the treatment of hemospermia with traditional Chinese medicine, the main evaluation criterion for efficacy is the disappearance of hemospermia under the microscope. Although the disappearance of hemospermia under the microscope can reflect the recovery of hemospermia, the red blood cell count of semen under the microscope cannot provide complete feedback and evaluation of the recovery of hemospermia. Sufficient auxiliary examination methods should be supplemented to evaluate the treatment effect of patients. For example, semen leukocyte count under the microscope is used to assess the level of inflammation, and pelvic magnetic resonance imaging and transrectal B-ultrasound of seminal vesicles are used from the imaging perspective to assist in the diagnosis of spermatorrhea and evaluate the therapeutic effect. In addition, apart from the main symptoms of hematuria caused by naked eye and endoscopy, hematuria can also be accompanied by ejaculation pain and lower urinary tract symptoms, which may affect the patients' semen routine or even cause sexual dysfunction. However, the related clinical studies are currently few and further improvement studies are needed.

5. Conclusion

In summary, different treatments with traditional Chinese medicine have good effects on hemospermia. However, there are still some problems in the literature, such as the design of clinical trials is not scientific enough, the inclusion and exclusion criteria are not rigorous enough, the evaluation criteria for efficacy are not standardized enough, and the follow-up visit and safety

evaluation are missing. Therefore, the exact efficacy of traditional Chinese medicine in the treatment of hemospermia needs to be further verified. Although TCM treatment has a good curative effect on hemospermia, the specific mechanism is still unclear. In the future, the effective mechanism of TCM should be further clarified on the basis of clarifying the clinical advantages of TCM in the treatment of hemospermia.

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