ORIGINAL RESEARCH



Clinical efficacy of integrated traditional Chinese and western medicine in the treatment of oligoasthenospermia in male infertility of kidney-yang deficiency type

Chuchu Gao¹, Xinxin Hu¹, Ting Li¹, Huijun Zheng^{1,*}, Xi Zhou¹, Peng Li¹

¹Department of gynecology, Wenzhou TCM Hospital of Zhejiang Chinese Medical University, 325000 Wenzhou, Zhejiang, China

*Correspondence zhenghuijun212@163.com (Huijun Zheng)

Abstract

This study examines the clinically comprehensive effects of Wuzi Shenqi Decoction, an acupoint application that combines traditional Chinese medicine with western medicine on male infertility with oligoasthenospermia of kidney-yang deficiency type. A total of 184 male infertiles with oligoasthenospermia who came to our hospital from April 2022 to June 2023 were randomly assigned to a study group (n = 92) and an experimental group (n = 92). The experimental group was treated with L-carnitine oral solution, while the study group was treated with Wuzi Shenqi Decoction combined with acupoint application based on the experimental group. Before and after treatment, clinical efficacy, semen parameters (semen volume, sperm density, sperm survival rate, sperm motility), sexual hormone parameters (follicle stimulating hormone (FSH), luteinizing hormone (LH), testosterone (T), prolactin (PRL), estradiol), and TCM (Traditional Chinese Medicine) syndrome scores were observed and compared between both groups. Before treatment, there was no significant difference in semen parameter index, sexual hormone index and TCM syndrome score between both groups (p > 0.05); after treatment, the semen parameter index and sexual hormone index in both groups were higher than before treatment, and the TCM syndrome score was diminished with a significant difference (p < 0.05). The overall response rate of the study group was 92.39%, which was significantly higher than that of the experimental group (72.83%) (p < 0.05). For male infertility patients with oligoasthenospermia of kidney-yang deficiency type, the use of Wuzi Shenqi Decoction combined with traditional Chinese medicine acupoint application plus L-carnitine oral solution can effectively improve the clinical symptoms of patients, improve semen quality, regulate sex hormone levels, which is worthy of clinical application.

Keywords

Wuzi Shenqi Decoction; Acupoint application; Kidney-yang deficiency type; Oligoasthenospermia

1. Introduction

Considering the "comprehensive of the second-child and thirdchild" policy now, many elderly couples need fertility treatment as well. According to survey statistics [1], infertility incidence in China is increasing year over year. Among the causes, to men's infertility accounts for half. Male infertility triggers are complex, with oligoasthenospermia being the most common cause in clinical practice. At present, this disease is treated mainly by western medicine; commonly used drugs include testosterone, clomiphene, chorionic gonadotropin and other hormone drugs. Long-term use will damage liver and kidney function with less clinical application [2]. One of these drugs, L-carnitine, is a commonly used drug in Western medicine, has been clinically demonstrated to improve sperm motility and epididymal function, and treat male infertility [3]. However, there are some controversies regarding the administration method and the course of treatment. Clinical treatment of oligoasthenospermia should use multi-channel, multi-way treatment strategies to enhance men's quality of life and improve the cure rate of the disease.

Western medical research suggests that the incidence of oligoasthenospermia is related to infectious diseases, endocrine diseases, hereditary diseases, reproductive organ dysplasia, physical and chemical factors. In addition, bad living habits such as smoking, alcoholism, staying up late also always threaten male fertility. TCM attributes oligoasthenospermia to the category of "infertility" and "extinction" together, and has unique advantages for the differentiation and treatment of the disease. According to TCM, kidney is always the root of syndrome differentiation and treatment of male infertility. In China, Traditional Chinese medicine (TCM) has accumulated extensive experience treating male infertility [4]. Patients with kidney-yang deficiency oligoasthenospermia (Infertility after marriage, low sperm motility, lack of energy, fear of cold limbs, or low libido, impotence, spermatorrhea, premature ejaculation, clear abundant urine, frequent urination, pale tongue with tooth prints, whitish fur and deep and thin pulse) often experience with male dysfunction such as impotence and premature ejaculation, and treatment is difficult. Providing prenatal and postnatal care that improves sperm quality and reduces sperm malformation rates has become one of the keys to treating male infertility [5]. Wuzi Shenqi Decoction [6] warms the kidney and nourish essence, strengthens the thoroughfare and conception channels, supplements yin and nourishes qi, and warms and replenishes kidney-yang, which has a significant effect on improving male function and sperm quality; acupoint application warms and replenishes kidney-yang and enhances male reproductive function. To further improve the comprehensive clinical efficacy, we took the integrated traditional Chinese and western medicine treatment as the idea, fully combined the advantages of both traditional Chinese and western medicine treatment, and put forward a scheme of oral administration of Wuzi Shenqi Decoction, acupoint application of traditional Chinese medicine combined with western medicine treatment. This study aims to investigate the clinically comprehensive efficacy and safety of Wuzi Shenqi Decoction, acupoint application of traditional Chinese medicine combined with western medicine, in treating male infertility and oligoasthenozoospermia of kidney-yang deficiency type. 184 male infertility patients with oligoasthenozoospermia who visited to the outpatient department of Wenzhou TCM Hospital of Zhejiang Chinese Medical University from April 2022 to June 2023 were selected. Clinical treatment was studied and analyzed.

2. Materials and methods

2.1 Clinical data

184 male infertile patients with oligoasthenospermia who visited our clinic from April 2022 to June 2023 were included in this study. Patients were randomly assigned to a study group (n = 92) and an experimental group (n = 92).

2.1.1 Inclusion criteria

(1) Patients who met the diagnostic criteria of male infertility and asthenospermia under western medicine; (2) TCM syndrome differentiation belongs to the kidney-yang deficiency type; (3) Patients who age <40 years.

2.1.2 Exclusion criteria

(1) Patients with combined syndrome (Combined with endocrine and immune, genetic diseases, mental illness and other conditions that affect fertility); (2) Patients with Azoospermia, retrograde ejaculation or no ejaculation; (3) Patients with bacterial prostatitis; (4) Patients with cardiovascular, liver, kidney and hematopoietic system dysfunction; (5) Age >55 years.

2.2 Criteria for diagnosis

2.2.1 Western diagnostic criteria

According to the relevant criteria for the diagnosis of male infertility in the World Health Organization (WHO) Manual for Standardized Investigation and Diagnosis of Infertile Couples (2021 edition): couples of childbearing ages should have a normal and regular sexual life for at least 1 year, avoid contraceptives and conceive. When female problems are excluded, male infertility may be diagnosed.

Oligozoospermia: sperm density less than 15×10^6 /mL; asthenozoospermia: <32% sperm with progressive motility in semen within 60 min after ejaculation, or total sperm motility <40% (refer to the WHO Laboratory Manual for the examination of human semen and sperm-cervical mucus interaction, 4th edition) [7]. Often, the two are combined clinically.

2.2.2 TCM diagnostic criteria

In accordance with the Guidelines for Clinical Research in New Drugs of Traditional Chinese Medicine formulated by the State Administration of Traditional Chinese Medicine, the following diagnostic criteria apply to kidney-yang deficiency types. The main symptoms include soreness and weakness in the waist and knees, loss of libido, and fear of cold and cold limbs. Minor symptoms, including apathy, frequent urination at night, lower limb edema, shortness of breath, tooth shaking, pale tongue with white fur, slow and sunken pulse, and ulnar weakness. It is possible to diagnose kidney-yang deficiency syndrome based on these two main symptoms and two secondary symptoms [8].

2.3 Treatment methods

2.3.1 Experimental group

Patients were given L-carnitine oral solution (Northeast Pharmaceutical Group Co., State medical permit number: H19990372, Shenyang, Liaoning, China, strength 10 mL/vial), 5 mL each time, half a vial each time, twice daily for three months.

2.3.2 Study groups

This group was treated with Wuzi Shenqi Decoction and acupoint application of traditional Chinese medicine in accordance with the experimental group. Wuzi Shenqi Decoction is a combination of Wuzi Yanzong Pills in Introduction to Medicine and Shenqi Pills in Treatise on Febrile Diseases. It consists of Wuzi Yanzong Pills and Shenqi Pills. Raspberry 15 g, Lycium barbarum 15 g, Cuscuta chinensis 15 g, Plantago asiatica 15 g, Schisandra chinensis 9 g, Cinnamomum cassia 6 g, Aconite 10 g, Rehmannia glutinosa 15 g, Yam 10 g, Fructus Corni 10 g, Cortex Moutan 9 g, Rhizoma Alismatis 10 g, and Poria cocos 10 g were uniformly purchased by our hospital pharmacy. After soaking for half an hour, the 13 were decocted for 20 minutes. A dose of 100 mL was taken twice daily for three months. As a result, it can either be added to or subtracted from the syndrome depending on the circumstances. For patients combined with dampness, Atractylodes lancea 9 g, Phellodendron amurense 1 g were added to clear away heat and dampness; For patients combined with blood stasis, Salvia miltiorrhiza 9 g and Achyranthes bidentata 30 g were added to activate blood and resolve stasis; For patients combined with Qi stagnation, Muxiang 10 g and Litchi seed 10 g were added to regulate Qi and remove stagnation.

Acupoint application: grind powder in an equal proportion of traditional Chinese medicine (white mustard seed, asarum, evodia rutaecarpa, aconite root), take an appropriate amount of ginger juice and mix, apply 1×1 cm of medical application to 6 acupoints, including double Shenshu, Zusanli, Guanyuan and Qihai, and remove after 8 hours. The patients received weekly treatment for three months in a row.

2.4 Outcome measures

2.4.1 Semen parameter indicators

Semen volume, semen density, sperm survival rate, and sperm motility (total motility).

Specimens were collected from patients within 2-7 days of abstinence and submitted for examination within half an hour of heat preservation, which could not be collected using condoms, and all semen had to be obtained. Each liquefied semen was processed using density gradient centrifugation and the Swim-up method were. A density gradient centrifugation method was performed using 1.5 mL of Pureception upper and lower sperm separation solution was added to the centrifuge tube first, which was allowed to stand and layer. Next, 2-3 mL of liquefied semen was pipetted to cover the liquid level of the upper separation solution (if the semen was too thick or not liquefied, it could be mixed with the culture medium in a 1:2 volume and then processed) and centrifuged at $600 \times g$ for 15 min. The supernatant was discarded. The aspirated pellet was added to 2 mL of sperm washing medium and mixed well. It was then centrifuged at $200 \times g$ for 5 min. The supernatant was discarded twice, as required. The pellet was aspirated for the next step. Swim-up method: the pellet was added to the bottom of 1 mL of fertilization medium. The tube was inclined 45° and placed in a 37 °C, 5% carbon dioxide incubator, upstream 1 h. 0.5 mL of the upper nebulous liquid was aspirated for future use.

Sperm motility parameters were determined by drawing the initial semen and semen separated by density gradient centrifugation and the Swim-up method. The chamber was filled with counting plates, and various motility parameters were detected by a computer-assisted sperm detection system at a constant temperature of 35 °C. A minimum of 10 fields and 400 sperm were collected randomly from each specimen for analysis of semen parameters. Generally, it consists of three variables: semen density, sperm survival rate, and sperm motility (total motility).

2.4.2 Sexual hormone parameters

The levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), testosterone (T), prolactin (PRL), and estradiol (E2) were compared.

2.4.3 TCM symptom score

In each group, the main symptoms of decreased libido, soreness and weakness of the waist and knee, and fear of cold and limb cold were scored, with scores of 0–6 points for each dimension, resulting in a total score of 18 points. Higher scores indicate more severe symptoms.

2.4.4 Spouse pregnancy rate

Vaginal ultrasonography was done 5 weeks after menopause in the spouse. Clinical pregnancy was diagnosed in those with a fetal sac, fetal bud and fetal heartbeat.

2.4.5 Clinical efficacy [7, 8]

Recovered: the symptoms and signs of kidney yang deficiency disappear; the score is reduced by \geq 95%; marked response: the symptoms and signs of kidney yang deficiency are significantly improved, and the score is reduced by \geq 70%; moderate response: the symptoms and signs of kidney yang deficiency are improved, and the score is reduced by \geq 30%; no response: recovery, marked response and moderate response were not achieved. Response = recovery + marked response.

2.5 Calculation of sample size

PASS15.0 (NCSS LLC, Armonk, New York, UT, USA) software was used to calculate the sample size, with a test level of $\alpha = 0.05$ and a power of $1-\beta = 0.80$. In the previous study, 93.3% of the study group responded, whereas 76.7% of the experimental group responded. In total, 166 cases were studied, 83 cases in each group. Considering sample dropout, the sample size was increased by 10%. As a result, 184 patients were collected.

2.6 Statistical methods

Data were analyzed and processed using SPSS 27.0 (International Business Machines Corporation, Armonk, NY, USA). Measurement data conforming to the normal distribution were described as ($\bar{x} \pm s$), while in the case of measurement data that did not comply with the normal distribution were presented as the median (upper and lower quartiles) (M (Q1, Q3)). *t*-test (normal distribution) or rank sum test (non-normal distribution) was used. Enumeration data were described as the number of cases and percentage (n (%)), and χ^2 test was used to compare enumeration data between groups. p < 0.05 indicated significant differences.

3. Results

3.1 Comparison of clinical data between both groups

With study comparability, there is no statistically significant difference between both groups in clinical data, as shown in Table 1.

3.2 Comparison of semen parameters between both groups

There is no significant difference in semen parameter indicators between the two groups before treatment (p > 0.05); the

TABLE 1. Comparison of chincal data between both groups.					
Index	Study group $(n = 92)$	Experimental group $(n = 92)$	t/χ^2 value	<i>p</i> value	
Age (yr)	35.35 ± 3.15	35.38 ± 3.09	-0.071	0.944	
Duration of infertility (yr)	4.58 ± 0.50	4.61 ± 0.51	-0.438	0.662	
Type of infertility (n, %)					
Oligozoospermia	48, 52.17	46, 50.00	0.087	0 768	
Asthenozoospermia	44, 47.83	46, 50.00	0.007	0.700	

TABLE 1. Comparison of clinical data between both groups.

TABLE 2. Comparison of semen parameters between both groups ($\bar{x} \pm s$).

Index	Study group $(n = 92)$	Experimental group $(n = 92)$	<i>t</i> value	<i>p</i> value		
Semen volume (mL)						
Before treatment	2.22 ± 0.12	2.23 ± 0.11	0.589	0.557		
After treatment	2.99 ± 0.28	2.75 ± 0.21	6.577	< 0.001		
t value	24.244	21.039				
<i>p</i> value	< 0.001	< 0.001				
Sperm density (×10 ⁶ /mL	L)					
Before treatment	11.31 ± 1.29	11.29 ± 1.30	0.106	0.916		
After treatment	18.24 ± 1.34	16.35 ± 1.94	7.711	< 0.001		
<i>t</i> value	-34.146	-19.817				
<i>p</i> value	< 0.001	< 0.001				
Sperm survival rate (%)	Sperm survival rate (%)					
Before treatment	30.06 ± 3.58	29.98 ± 3.79	0.148	0.883		
After treatment	38.54 ± 3.04	35.24 ± 3.31	7.054	< 0.001		
<i>t</i> value	-17.189	-10.151				
<i>p</i> value	< 0.001	< 0.001				
Sperm motility (total motility) (%)						
Before treatment	32.85 ± 1.39	32.89 ± 1.53	0.186	0.853		
After treatment	57.96 ± 2.64	40.31 ± 2.98	42.523	< 0.001		
t value	80.724	21.246				
<i>p</i> value	< 0.001	< 0.001				

semen parameter indicators of both groups are significantly higher after treatment (p < 0.05); where the study group is higher than the experimental group (p < 0.05). The results are presented in Table 2.

3.3 Comparison of sexual hormone parameters between the two groups

In the two groups, levels of FSH, LH, T, PRL and E2 are not significantly different before treatment (p > 0.05); subsequently, FSH, LH, T, PRL and E2 in both groups are significantly higher after treatment (p < 0.05); FSH, LH, T, PRL and E2 in the study group are higher than in the experimental group, with a notable difference (p < 0.05). The results are demonstrated in Table 3.

3.4 Comparison of TCM symptom scores between the two groups

The TCM symptom scores of both groups show little difference before treatment (p > 0.05); The TCM symptom scores of both groups decrease after treatment, with a significant difference (p < 0.05); the study group scores are lower than the experimental group scores, with differences indicating significance (p < 0.05). The results are shown in Table 4.

3.5 Comparison of clinical efficacy between the two groups

The overall response rate of the study group is 92.39%, higher than 72.83% in the experimental group, with statistical significance (p < 0.05). The results are presented in Table 5 and Fig. 1.

Index	Study group $(n = 92)$	Experimental group $(n = 92)$	<i>t</i> value	<i>p</i> value
FSH (mU/mL)				
Before treatment	4.21 ± 0.46	4.20 ± 0.46	0.147	0.883
After treatment	4.72 ± 0.42	4.58 ± 0.45	2.206	0.029
t value	-7.671	-5.520		
<i>p</i> value	< 0.001	< 0.001		
LH (mU/mL)				
Before treatment	3.79 ± 0.39	3.77 ± 0.38	0.350	0.726
After treatment	4.21 ± 0.35	3.99 ± 0.33	4.388	< 0.001
t value	-7.224	-4.111		
<i>p</i> value	< 0.001	< 0.001		
T (ng/mL)				
Before treatment	4.65 ± 0.44	4.66 ± 0.46	-0.150	0.881
After treatment	5.12 ± 0.39	4.81 ± 0.42	5.084	< 0.001
t value	-7.709	-2.329		
<i>p</i> value	< 0.001	< 0.001		
PRL (ug/L)				
Before treatment	8.92 ± 0.91	8.96 ± 0.93	-0.293	0.770
After treatment	12.92 ± 1.06	11.75 ± 1.09	7.409	< 0.001
t value	-25.487	-17.482		
<i>p</i> value	< 0.001	< 0.001		
E2 (pg/mL)				
Before treatment	22.93 ± 2.31	22.89 ± 2.09	0.123	0.902
After treatment	26.95 ± 2.29	24.55 ± 2.33	7.046	< 0.001
<i>t</i> value	-12.174	-5.282		
<i>p</i> value	< 0.001	< 0.001		

TABLE 3. Comparison of FSH, LH, T, PRL and E2 between the two groups ($\bar{x} \pm$	± s)
---	------

FSH: follicle stimulating hormone; LH: luteinizing hormone; T: testosterone; PRL: prolactin; E2: estradiol.

TABLE 4. Comparison	of TCM symptom scores	between the two groups	$(\bar{x} \pm s)$), point
---------------------	-----------------------	------------------------	-------------------	----------

TABLE 4. Comparison of TCM symptom scores between the two groups ($ar{x}\pm s$), point.				
Index	Study group $(n = 92)$	Experimental group $(n = 92)$	<i>t</i> value	<i>p</i> value
Libido decreased				
Before treatment	5.21 ± 0.46	5.20 ± 0.45	0.162	0.871
After treatment	1.62 ± 0.50	3.08 ± 0.45	-21.032	< 0.001
t value	53.029	31.592		
<i>p</i> value	< 0.001	< 0.001		
Soreness and weakness	of waist and knee			
Before treatment	5.23 ± 0.54	5.21 ± 0.55	0.272	0.786
After treatment	1.58 ± 0.50	3.15 ± 0.51	-21.185	< 0.001
t value	47.802	26.928		
<i>p</i> value	< 0.001	< 0.001		
Intolerance of cold and	cold limbs			
Before treatment	5.15 ± 0.55	5.16 ± 0.56	-0.132	0.895
After treatment	1.62 ± 0.49	3.50 ± 0.54	-24.659	< 0.001
t value	40.755	20.234		
<i>p</i> value	< 0.001	< 0.001		
Total score				
Before treatment	15.59 ± 0.89	15.57 ± 0.96	0.159	0.874
After treatment	4.82 ± 0.89	9.73 ± 0.84	-38.538	< 0.001
t value	77.868	41.889		
<i>p</i> value	< 0.001	< 0.001		



TABLE 5. Comparison of clinical efficacy between the two groups (n, %).



FIGURE 1. Comparison of clinical efficacy between both groups.

3.6 Adverse reactions

There is no significant damage to liver and kidney function in both groups.

4. Discussion

Wuzi Shenqi Decoction is a combination of Wuzi Yanzong Pills in Introduction to Medicine and Shenqi Pills in Treatise on Febrile Diseases. In clinical practice, Wuzi Yanzong Pills, are the basis of various effective prescriptions for male infertility based on traditional Chinese medicine. Research based on the Shengi Pills of Treatise on Febrile Diseases is used widely in andrology as well. Wuzi Shenqi Decoction contains Raspberry 15 g, Lycium barbarum 15 g, Cuscuta chinensis 15 g, Plantago asiatica 15 g, Schisandra chinensis 6 g, Cinnamomum cassia 6 g, Aconite root 6 g, Rehmannia glutinosa 15 g, Yam 15 g, Fructus Corni 9 g, Cortex Moutan 9 g, Rhizoma Alismatis 10 g, and Poria cocos 10 g, which can warm the kidney and nourish the essence, strengthen the thoroughfares and conception channels. High doses of Wuzi Yanzong Pills have been found to promote Catsper1 protein expression and participate in cAMP (Cyclic Adenosine monophosphate)-Ca (calcium ion)²⁺ positive feedback in rat testicular tissue, thereby improving sperm quality [9–13]. Shengi Pills are composed of Gui and Liuwei Dihuang Pills, which balance Yang in Yin and junior fire, supporting vital QI, which nourishes Yin essence and supports kidney Yang.

Modern studies [11, 12] have shown that Shenqi Pills can repair injured spermatogenic cells in mice *via* reducing intracellular Ca²⁺ concentrations by regulating Ry Rs (Ryanodine receptors) and MMP (mitochondrial membrane potential) pathways. They play an essential role in improving male function and sperm quality. Clinically, it can also be added or subtracted according to the actual situation with the syndrome: for dampness, Atractylodes lancea 9 g, Phellodendron amurense 10 g are added to eliminate heat and dampness; for blood stasis, Salvia miltiorrhiza 9 g, Achyranthes bidentata 30 g are added to stimulate blood circulation and remove blood stasis; for those with Qi stagnation, wood incense 10 g and litchi seed 10 g are added to regulate Qi and resolve stagnation.

Acupoint application was applied to Shenshu, Zusanli, Guanyuan, and Qihai points with equal proportions of white mustard seed, asarum, Evodia rutaecarpa and aconite root, which were removed after 8 hours [14–16]. White mustard seed reduces phlegm and resolves masses. Asarum diffuses gases and dredges channels. In addition to warm yang, Evodia rutaecarpa and aconite disperse cold. *Via* acupoints, drugs reach the viscera along meridians from the exterior to the interior. The drug can regulate the liver and kidney, Qi and blood, warm kidney Yang, which can improve male reproductive function and be used in "acupoint therapy". Acupoint application stimulates local skin tissue, dilates capillaries and accelerates blood circulation. Meanwhile, the drug is absorbed into the systemic circulation by the capillaries through the epidermis. This avoids the "first-pass elimination" and "gastrointestinal inactivation" effects of the drug and boosting the drug utilization rate. From the perspective of microscopically and macroscopically, integrating traditional Chinese and western medicine to diagnose and treat male infertility and asthenospermia. This can greatly improve the clinical response rate and cure rate of the disease [17–19]. It is more effectively to administer traditional Chinese medicine compound—Wuzi Shenqi Decoction through acupoint application than L-carnitine oral solution as a treatment on western medicine [20, 21].

The results of this study showed that after treatment, the semen parameter indicators of the two groups were notably higher after treatment, and the difference was significant (p < 0.05); the study group was more significant than the experimental group, and the difference was prominent (p < p0.05). Semen quality, density, survival rate and motility of sperm can all be improved with this regimen. This study showed that after treatment, FSH, LH, T, PRL and E2 in both groups had conspicuously higher levels, and the difference had statistical significance (p < 0.05); the increase of FSH, LH, T, PRL and E2 in the study group was greater than in the experimental group, and the difference had statistical significance (p < 0.05). Interestingly, it appears that this regimen promotes the synthesis and secretion of FSH, LH, T, PRL and E2 and promotes testicular spermatogenesis. In this study, both groups' TCM symptom scores were lower after treatment, and the difference was significant (p < 0.05). It is suggested that this scheme can improve the TCM syndrome score and reduce clinical symptoms. The results of this study indicated that the overall response rate was 94.57% in the study group, higher than 88.04% in the experimental group. The difference had statistical significance (p < 0.05). This result indicated that, given the advantages of the above aspects, the use of Wuzi Shengi Decoction combined with traditional Chinese medicine acupoint application and L-carnitine oral solution effectively improved the clinical efficacy of male infertiles with kidney-yang deficiency oligoasthenospermia.

According to this study, the combination of Wuzi Shenqi Decoction, traditional Chinese medicine acupoint application, and oral L-carnitine solution significantly improved the quality and quantity of semen in patients with kidney-yang deficiency asthenospermia and oligospermia. Its response rate and various semen parameters were superior to those of L-carnitine oral solution alone.

5. Research limitations and future perspectives

This study limits the number and source of cases, as well as its methodology limits. There is insufficient research on the mechanism of Yuwuzi Shenqi Decoction combined with traditional Chinese medicine sticking plus L-carnitine oral solution on male infertility with asthenospermia of kidneyyang deficiency type. For further comparative study, the Wuzi Shenqi Decoction combined with traditional Chinese medicine applications was not included as an experimental group. As such, the future study should broaden its scope and connotation so that a more comprehensive and objective conclusion can be drawn and then provide a reference for the diagnosis and treatment of male infertility and asthenospermia of the kidneyyang deficiency type.

6. Conclusions

For male infertility patients with oligoasthenospermia of kidney-yang deficiency type, the use of Wuzi Shenqi Decoction combined with traditional Chinese medicine acupoint application plus L-carnitine oral solution can effectively improve the clinical symptoms of patients, improve semen quality, regulate sex hormone levels, which is worthy of clinical application.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

CCG, XXH, TL and HJZ—designed the study and carried them out; CCG, XXH, TL, HJZ, XZ and PL—supervised the data collection, analyzed the data, interpreted the data; prepared the manuscript for publication and reviewed the draft of the manuscript. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of Wenzhou TCM Hospital of Zhejiang Chinese Medical University (Approval no. IEC-SW-A25). Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

ACKNOWLEDGMENT

Not applicable.

FUNDING

This work was supported by University-level Research Project Affiliated Hospital of Zhejiang Chinese Medicine University (Natural Sciences) (Grant No. 2022FSYYZQ23).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

- [1] Dougherty GW, Mizuno K, Nöthe-Menchen T, Ikawa Y, Boldt K, Ta-Shma A, et al. CFAP45 deficiency causes situs abnormalities and asthenospermia by disrupting an axonemal adenine nucleotide homeostasis module. Nature Communications. 2020; 11: 5520.
- ^[2] Jiao J, Xu P, Wang X, Xing Z, Dong S, Li G, et al. Enterotypes

in asthenospermia patients with obesity. Scientific Reports. 2022; 12: 16993.

- [3] Liang G, Wang Q, Zhang G, Li Z, Wang Q. Differentially expressed miR-NAs and potential therapeutic targets for asthenospermia. Andrologia. 2022; 54: e14265.
- [4] Zhao Y, Yang J, Lu D, Zhu Y, Liao K, Tian Y, *et al.* The loss-function of KNL1 causes oligospermia and asthenospermia in mice by affecting the assembly and separation of the spindle through flow cytometry and immunofluorescence. Sensors. 2023; 23: 2571.
- [5] Zhou S, Wu H, Zhang J, He X, Liu S, Zhou P, *et al.* Bi-allelic variants in human TCTE1/DRC5 cause asthenospermia and male infertility. European Journal of Human Genetics. 2022; 30: 721–729.
- [6] Zhimin C, Mingyue AO, Yujiao L, Lingying YU, Zhuo Y, Lin HU, *et al.* Wuzi Yanzong prescription from traditional Chinese medicine for male infertility: a narrative review. Journal of Traditional Chinese Medicine. 2023; 43: 416–428.
- [7] Chen WQ, Ding CF, Yu J, Wang CY, Wan LY, Hu HM, et al. Wuzi Yanzong pill-based on network pharmacology and *in vivo* evidenceprotects against spermatogenesis disorder via the regulation of the apoptosis pathway. Frontiers in Pharmacology. 2020; 11: 592827.
- [8] Pan T, Xiao Q, Fan H, Xu L, Qin S, Yang L, et al. Wuzi Yanzong pill relieves MPTP-induced motor dysfunction and neuron loss by inhibiting NLRP3 inflammasome-mediated neuroinflammation. Metabolic Brain Disease. 2023; 38: 2211–2222.
- [9] Xu Y, Li Y, Hu S, Li C, Liu D, Hu K, et al. Effect of Wuzi Yanzong pills on sertoli cells and blood–testis barrier in heat-stressed rats based on Akt signalling pathway. Andrologia. 2021; 53: e14169.
- [10] Hang W, Fan H, Li Y, Xiao Q, Jia L, Song L, et al. Wuzi Yanzong pill attenuates MPTP-induced Parkinson's Disease via PI3K/Akt signaling pathway. Metabolic Brain Disease. 2022; 37: 1435–1450.
- [11] Chen WQ, Wang B, Ding CF, Wan LY, Hu HM, Lv BD, et al. In vivo and in vitro protective effects of the Wuzi Yanzong pill against experimental spermatogenesis disorder by promoting germ cell proliferation and suppressing apoptosis. Journal of Ethnopharmacology. 2021; 280: 114443.
- [12] Li Y, Sun M, Hang W, Xiao Q, Fan H, Jia L, et al. Wuzi Yanzong pill relieves CPZ-induced demyelination by improving the microenvironment in the brain. Heliyon. 2022; 8: e12277.
- [13] Wang X, Yang C, Ru Y, Xie L, Xiao B, Jin X, et al. An optimal combination of five main monomer components in Wuzi Yanzong pill that prevents neural tube defects and reduces apoptosis and oxidative stress.

Journal of Ethnopharmacology. 2023; 313: 116540.

- ^[14] Wang JS, Gong XF, Feng JL, Li HS, Li X, Deng S, *et al.* Study on the mechanism of Jiawei Shengjiang powder in improving male asthma-induced asthenospermia based on network pharmacology and bioinformatics. Drug Design, Development and Therapy. 2021; 15: 1245–1259.
- [15] Cheraghi E, Sajadi SMS, Soleimani Mehranjani M. The effect of quercetin on the quality of sperm parameters in frozen-thawed semen of patients with asthenospermia. Andrologia. 2021; 53: e14167.
- [16] Zhang S, Xu L, Yu M, Zhang J. Hypomethylation of the DAZ3 promoter in idiopathic asthenospermia: a screening tool for liquid biopsy. Scientific Reports. 2020; 10: 17996.
- [17] Hong G, Zhuang Y, Wang K, Lin H, Zhang R. A case of balanced translocation: 46, XY, t(9;22) (q22;q13) accompanied with oligospermia and asthenospermia. Clinical Laboratory. 2021; 67.
- ^[18] Maghsoumi-Norouzabad L, Zare Javid A, Mansoori A, Dadfar M, Serajian A. Evaluation of the effect of vitamin D supplementation on spermatogram, seminal and serum levels of oxidative stress indices in asthenospermia infertile men: a study protocol for a triple-blind, randomized controlled trial. Nutrition Journal. 2021; 20: 49.
- [19] Liu SM, Yao WL, Li CX, Li HQ, Qin GZ. Er-Xian decoction exhibits protective activity in a rat model of asthenospermia through a mechanism associated with DJ-1 protein upregulation. Canadian Journal of Physiology and Pharmacology. 2021; 72.
- ^[20] Wang J, Bao B, Meng F, Deng S, Dai H, Feng J, *et al.* To study the mechanism of cuscuta chinensis lam. and lycium barbarum L. in the treatment of asthenospermia based on network pharmacology. Journal of Ethnopharmacology. 2021; 270: 113790.
- [21] Meng Z, Meng Q, Gao T, Zhou H, Xue J, Li H, et al. Identification of bi-allelic KIF9 loss-of-function variants contributing to asthenospermia and male infertility in two Chinese families. Frontiers in Endocrinology. 2022; 13: 1091107.

How to cite this article: Chuchu Gao, Xinxin Hu, Ting Li, Huijun Zheng, Xi Zhou, Peng Li. Clinical efficacy of integrated traditional Chinese and western medicine in the treatment of oligoasthenospermia in male infertility of kidney-yang deficiency type. Journal of Men's Health. 2023; 19(12): 99-106. doi: 10.22514/jomh.2023.135.