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Original Research Article

Therapeutic Effects of Y10 Capsule on Male Patients with Semen Quality Impairment

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ABSTRACT

Traditional medicine has been effectively used in treating male infertility and other diseases of men. The purpose of the study is to evaluate the safety and effectiveness of Y10 capsules used in improving spermatogenesis in male patients with semen quality impairment. The composition of the capsule includes Velvet antler (*Cornu cervi parvum*) and *Cordyceps militaris* (*Ophiocordyceps sinensis*) in a ratio of 5: 3. Thirty patients with impaired semen quality were recruited for this study from the Embryology Research and Training Center, Military Medical Academy, Vietnam, from October 2017 to December 2017. Each patient participating in the study used four Y10 capsules/day, two hours after meals, continuously for two months. The study results reveal that Y10 capsules effectively regulated LH and FSH secretion, increased serum testosterone levels, sperm count and quality in patients with semen quality impairment. Also, Y10 capsules did not cause unwanted effects nor changes in the biochemical and haematological parameters of the patients surveyed. This study concluded that treatment with Y10 capsules improved semen quality in the study group and could therefore be used to manage patients with semen quality impairment in Vietnam.

***Keywords*:** Semen quality impairment, Cornu cervi parvum, Cordyceps militaris, Vietnam.

Introduction

Infertility is defined as not getting pregnant despite having frequent, unprotected sex for at least a year for most couples. About 15% of couples experienced infertility related problems. Among infertile couples, male infertility accounts for about 50%.[1,2] Between 1990 and 2017, the age-standardized prevalence rate of infertility increased by 0.29% per year for men worldwide. Male infertility tends to increase in countries with low socio-demographic indexes.[3] It is currently estimated that around 30 million men are infertile worldwide, with the highest prevalence regions being Africa and Eastern Europe.[4] Male infertility usually appears between the ages of 18–50, with an average age of 36.[5]

Epididymal obstruction (1%), azoospermia (14%), and abnormalities in sperm production or function (85%) have been implicated in male infertility.[6, 7]Previous studies showed that men's sperm quality and quantity were trending down significantly.[8,9] The risk factors associated with infertility were found to be testicular damage, history of mumps, hereditary factors, smoking, alcohol, recreational drugs, psychological stress, obesity, advanced paternal age (APA), and other factors.[10]

Traditional medicine has a long history of being effectively used in treating male infertility.[11-15] Therefore, traditional medicine is considered a useful option for treating infertility in men. The use of traditional herbs to treat male infertility is gaining popularity. However, the evidence of their effectiveness is still limited. Previous studies indicate that herbal medicines can modulate the hypothalamic-pituitary-testicular axis and enhance Sertoli and Leydig cells' function. In addition, herbal medicines can also reduce inflammation, prevent oxidative stress, reduce DNA fragmentation index, regulate proliferation and death of germ cells,[15,16] and increase the number, motility, forms of sperm.[17-20]

The Military Medical Academy of Vietnam researched and formulated Y10 capsules (Cornu Cervi parvum and Cordyceps militaris as ingredients) to manage reproductive health-related conditions for male soldiers and the Vietnamese people. A study by Wang et al. showed that *Cordyceps militaris* extract was effective against bisphenol A-induced reproductive damage.[21] According to a study by Xiao *et al*.,Velvet antlercan strengthen the liver and kidneys and boost energy. It is used to treat arrhythmia, ischemic heart disease, and heart failure.[22]These are two essential natural products used by Vietnamese traditional medical practitioners to treat infertility and symptoms of male reproductive dysfunction. The results of our previous studies showed that Y10 capsules were safe and effective in improving spermatogenesis in experimental animals.[23] To the best of our knowledge, studies on the effects of these two medicinal herbs on patients (humans) with low sperm count are limited. Therefore, this study was carried out to evaluate the safety and effectiveness of Y10 capsules in improving spermatogenesis in male patients with semen quality impairment.

Materials and Methods

Patients and procedures

A prospective, open clinical, controlled before-after study was conducted on 30 male patients diagnosed with semen quality impairment. The study patients were recruited from Embryology Research and Training Center, Military Medical Academy, Vietnam, from October 2017 to December 2017.

This research is a part of the Ministry of National Defense of Vietnam Project approved by the Scientific and Ethical Council of the Military Medical Academy, Vietnam (Reference code: 247/2016/HD-NCKHCN). Participants were selected voluntarily. All participants gave informed consent before participating in the study.

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Criteria for selection of patients included (i) patients aged (between 18 and 56); (ii) diagnosed with semen quality impairment using standard WHO criteria 2010,[24] presented in Table 1; (iii) has stopped using drugs affecting sperm count and quality for at least 75 days.

Exclusion criteria included (i) patients with existing infectious diseases; (ii) patients taking treatment or drugs affecting sperm production; (iii) infertile patients due to vas deferens, malformations, varicose veins who did not have surgery; (iv) infertile patients due to elevated prolactin or estradiol; (v) patients that have no sperm.

Each patient participating in the study takes four Y10 capsules/day, two hours after meals, continuously for two months. The Y10 capsules were manufactured at the Drug Research and Production Center, Military Medical Academy, Vietnam, and met the required drug quality standards. The composition of the capsule includes Velvet antler (Cornu cervi parvum), purchased in Huong Son, Ha Tinh, and Cordyceps militaris (Ophiocordyceps sinensis), cultured at the Military Medical Academy, with a ratio of 5:3.

Variables such as age (18–32, 33–40, and 41–56), infertility classification (primary and secondary) were used to characterize the surveyed patients. The history of a patient whose wife has never been pregnant was considered primary infertility. In secondary infertility, the patient's wife has had at least one pregnancy or miscarriage or planned abortion but failed to have conception after more than a year; despite regular mating. Indicators to evaluate before and after treatment were hormone (serum testosterone, LH, and FSH), parameters of semen (volume, pH, and white blood cell count), sperm (density, total count, vitality, progressive motility, and total motility), haematological tests, biochemical tests of liver and kidney function, and monitoring unwanted drug effects. Serum testosterone ranged 7.63–27.74 nmol/L, LH of 1.5–20 UI/L, FSH of 2–10 UI/L are considered a normal level. [25,26]

In this study, the efficacy of Y10 capsules after treatment was classified as follows: (i) very good – semen parameters returned to normal according to WHO 2010 or wife is pregnant, (ii) good – there is an increase in sperm count and quality, (iii) moderate – only increased sperm count or quality, (iv) poor – no increase or decrease in sperm count or quality.

Table 1: Some parameters used to diagnose semen quality impairment according to WHO 2010

Parameters	Reference limit
Total sperm number	<39 x 10^6/mL
Sperm density	< 15 x 10^6/mL
Progressive motility (PR)	< 32%
Total motility*	< 40%
Normal sperm morphology	< 4%
Sperm vitality	< 58%
Non-sperm cells	<10^6/mL

*Total motility = Progressive motility (PR) + non-progressive motility (NP).

Statistical analysis

The research data were analyzed by statistical software SPSS version 17.0. Descriptive Statistics, including frequency (percentage), mean (standard deviation [SD]), were used to present categorical and continuous variables. Wilcoxon tests were used to compare the mean values of two groups of patients. A statistically significant difference was observed when $p < 0.05$.

Results and Discussion

Out of a total of 30 patients enrolled in this study, 16 were aged between 33–40 (53.3%), eight patients were aged 41–56 (26.7%), and six patients aged 18–32 (20.0%). Thus, most of the patients belonged to the group of primary infertility (83.3%). According to the results of the evaluation of serum testosterone, LH, and FSH levels, shown in Table 2, the proportion of patients with LH-related hormonal disorders (> 9.8 IU/L), FSH (>5 IU/L), and testosterone (<9.8 nmol/L) was 16.67%, 56.67%, and 26.67%, respectively.

Table 2 also describes the results of changes in serum testosterone, LH, and FSH levels before and after treatment. In the groups of patients with normal serum LH, FSH, and testosterone levels before treatment, LH and FSH levels decreased slightly, and testosterone levels increased slightly after treatment. But the difference between before and after treatment was not statistically significant ($p > 0.05$). On the other hand, evaluation of pre-treatment group of patients who had serum LH and FSH levels above the normal limit (LH > 9.8 IU/L; FSH > 5 IU/L) and testosterone levels below the limit of normal showed that the levels of these hormones changed statistically ($p < 0.01$). The changes were close to the normal level after treatment.

In a normal adult male, the plasma concentration of LH is 1.5–20 IU/L, FSH is 2–10 IU/L, and testosterone is 7.63–27.74 nmol/L. The concentration of LH, FSH decreased or increased compared with the normal range, and testosterone below the normal range is considered abnormal. This change in testosterone may be due to the impaired function of the pituitary gland and testicles.[25,26] The results of the evaluation of serum testosterone, LH, and FSH levels showed that Y10 capsules have the effect of stimulating the body to increase the production of serum testosterone and regulate the secretion of LH and FSH, possibly by acting on the hypothalamic-pituitary-testicular axis. This result is consistent with our previous study on experimental animals.[27]

In the semen analysis results, all patients had improved semen parameters after the treatment period. Out of the 30 patients, five (16.67%) had normal semen parameters after the treatment. The results of the comparison of semen parameters before and after treatment are presented in Table 3. The results show that compared with before treatment, semen volume increased after treatment ($p < 0.05$) and white blood cell count decreased after treatment ($p < 0.05$). In addition, the sperm density, the percentage of sperm vitality, the percentage of progressive motility, the percentage of total motility after treatment increased compared to before treatment; the differences were statistically significant ($p < 0.01$).

Table 2: Changes in serum testosterone, LH, and FSH levels before and after treatment (n = 30)

Parameters		n (%)	Mean (SD)		p-value
			Before treatment	After treatment	
LH (IU/L)	Above normal limit (> 9.80)	5 (16.67)	10.26 (0.45)	7.09 (1.06)	**< 0.01**
	Normal limit (2.50-9.80)	25 (83.33)	5.22 (1.07)	4.68 (1.98)	> 0.05
	Overall	30 (100)	6.02 (2.14)	5.08 (2.06)	**< 0.05**
FSH (IU/L)	Above normal limit (> 5)	17 (56.67)	10.98 (3.09)	8.86 (3.92)	**< 0.01**
	Normal limit (1.20-5.00)	13 (43.33)	4.49 (0.60)	4.37 (1.27)	> 0.05
	Overall	30 (100)	8.16 (4.01)	6.85 (3.69)	**< 0.05**
Testosterone (nmol/L)	Below normal limit (< 9.80)	8 (26.67)	6.12 (2.32)	12.68 (5.62)	**< 0.01**
	Normal limit (≥ 9.80)	22 (73.33)	17.76 (3.82)	18.43 (6.09)	> 0.05
	Overall	30 (100)	14.65 (6.27)	16.89 (6.42)	**< 0.05**

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Table 3: Comparison of parameters of semen and sperm before and after treatment (n = 30)

Parameters	Mean (SD) Before treatment	After treatment	p-value
Semen volume (mL)	2.00 (1.05)	2.34 (1.02)	**<0.05**
Semen pH	7.42 (1.35)	7.51 (0.27)	>0.05
White blood cell count	6.79 (1.26)	6.34 (1.49)	**<0.05**
Sperm density (10^6/mL)	13.54 (10.62)	22.96 (12.65)	**< 0.01**
Total sperm count (10^6)	31.05 (33.89)	58.20 (49.01)	**< 0.01**
Sperm vitality (%)	24.05 (12.94)	31.94 (18.26)	**< 0.01**
Progressive motility (%)	8.26 (5.86)	14.03 (6.98)	**< 0.01**
Total motility (%)	25.01 (11.24)	34.12 (12.93)	**< 0.01**

A semen analysis is one of the most basic tests used to assess a man's fertility. This is the first test that should be done for all couples who come to the infertility clinic. Most medical facilities in the world and the region perform semen analysis using WHO standards. Currently, the new WHO 2010 standard is widely applied in medical facilities in Vietnam. Therefore, in this study, we evaluated semen according to this standard.[28] The study results showed that Y10 capsules increased semen volume, sperm density, sperm count, sperm vitality, and progressive motility while decreasing white blood cell count. This is important because these indicators play a decisive role in the conception process, ensuring healthy embryo formation. This result is consistent with our experimental study with animals [27]and the study of Doan Minh Thuy, which evaluated the effect of 'Hoi xuan hoan' in infertile patients with reduced sperm quality.[29]

The results of clinical safety evaluation of Y10 capsules during treatment showed that patients did not experience any undesirable effects. In addition, the haematological indexes tests and biochemical assessment of renal and liver function after treatment were not statistically different from before treatment ($p > 0.05$) (Table 4). The treatment results with Y10 capsules showed that over 80% of patients had good and very good treatment effects (Table 5).

Previous studies showed that Velvet antler and Cordyceps militaris of Y10 capsules contain amino acids, fats, sugars, vitamins, etc. These are necessary substances for the proliferation of sperm epithelium and sperm formation.[30,31]In addition, the trace elements (Ca, P, Fe, Zn) of Velvet antler and Cordyceps militaris were shown to promote enzymes that increase protein synthesis, especially zinc, which increases the number and quality of sperm.[32,33,34]

After taking Y10 capsules, the serum AST and ALT in the study patients did not change statistically and were always within the normal physiological limits. This proves that Y10 does not affect liver function. Serum urea and creatinine levels after treatment did not differ from those before treatment. Thus, Y10 capsules did not cause adverse effects on the function and morphology of the liver and kidneys. This result is consistent with the evaluation results of the safety of Y10 on experimental animals.[23]

This study has some limitations. Firstly, the study sample size was small. This is explained by the limited number of patients visiting the Embryology Research and Training Center, Military Medical Academy, during the study period. Secondly, patients were recruited using convenience sampling. Finally, there are no comparison groups to evaluate the effects of Y10 capsules as this study was a non-interventional trial.

Table 4: Results of haematological and biochemical tests of liver and kidney function before and after treatment (n = 30)

Parameters	Mean (SD) Before treatment	After treatment	p-value
Haematological tests			
Red blood cell count (T/L)	5.49(0.64)	5.38(0.56)	>0.05
Hemoglobin (g/dL)	13.20 (2.37)	14.04 (3.99)	>0.05
Hematocrit (%)	38.96 (4.63)	40.10(4.18)	>0.05
Mean corpuscular volume (fl)	85.80(1.99)	86.10(4.25)	>0.05
White blood cell count (G/L)	6.16 (3.86)	6.25 (3.92)	>0.05
Platelet count (G/L)	326.86 (82.32)	341.02 (91.36)	>0.05
Biochemical tests of liver and kidney function			
AST (UI/L)	31.28 (6.46)	29.86 (8.21)	>0.05
ALT(UI/L)	38.42 (11.63)	36.95 (11.74)	>0.05
Urea (mmol/L)	4.36 (1.02)	4.43 (0.98)	>0.05
Creatinin (μmol/L)	86.29 (12.63)	85.03 (12.61)	>0.05

Table 5: The efficacy of Y10 capsules after treatment (n = 30)

Classification	n	%
Very good	5	16.67
Good	20	66.67
Moderate	5	16.67
Poor	0	0%

Very good – semen parameters returned to a normal or pregnant wife.
Good – an increase in sperm count and quality.
Moderate – only increased sperm count or quality.
Poor – no increase or decrease in sperm count or quality.

Conclusion

Y10 capsules had significant treatment effects on the majority of patients surveyed and could be used to treat patients with semen quality impairment in Vietnam. The study results revealed that Y10 capsules had the effect of increasing serum testosterone levels, regulating Leutenizing hormone and Follicle stimulating hormone secretion, and increasing sperm count and quality in patients with semen quality impairment. In addition, Y10 capsules do not cause unwanted effects and do not change the biochemical and haematological parameters of the patient surveyed. Future studies should increase sample size and use random sample and control group to improve the results' reliability. Moreover, the efficacy of Y10 capsules should be further evaluated in female infertility patients to expand the use of Y10 capsules.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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References

1. Rowe PJ, Comhaire FH, Hargreave TB, Mahmoud AM. WHO manual for the standardized investigation and diagnosis of the infertile male: Cambridge university press; 2000.
2. Kamel RM. Management of the infertile couple: an evidence-based protocol. Reprod Biol Endocrinol. 2010;8(1):1-7.
3. Sun H, Gong T-T, Jiang Y-T, Zhang S, Zhao Y-H, Wu Q-J. Global, regional, and national prevalence and disability-adjusted life-years for infertility in 195 countries and territories, 1990–2017: results from a global burden of disease study, 2017. Aging (Albany NY). 2019;11(23):10952.
4. Agarwal A, Mulgund A, Hamada A, Chyatte MR. A unique view on male infertility around the globe. Reprod Biol Endocrinol. 2015;13(1):1-9.
5. Punab M, Poolamets O, Paju P, Vihljajev V, Pomm K, Ladva R, Korrovits P, Laan M. Causes of male infertility: a 9-year prospective monocentre study on 1737 patients with reduced total sperm counts. Hum Reprod. 2017;32(1):18-31.
6. Vuong N TL, Duong DV, Thang BM, Hop TV, Anh TQ,. Fine needle aspiration biopsy of the epididymis in male infertility (Sinh thiết hút kim nhỏ mào tinh trong vô sinh nam). HCMC Med J. 2007;11.
7. Thao NT. Infertility situation in Thanh Hoa province (Thực trạng vô sinh tại tỉnh Thanh Hóa). The 9th Vietnam-France Asia-Pacific Obstetrics and Gynaecology Conference. 2011. 16-23 p.
8. Carlsen E, Giwercman A, Keiding N, Skakkebæk NE. Evidence for decreasing quality of semen during past 50 years. Br Med J. 1992;305(6854):609-613.
9. Öztekin Ü, Caniklioğlu M, Sarı S, Selmi V, Gürel A, Işıkay L. Evaluation of male infertility prevalence with clinical outcomes in middle Anatolian region. Cureus. 2019; 11(7): e5122.
10. Durairajanayagam D. Lifestyle causes of male infertility. Arab J Urol. 2018;16(1):10-20.
11. Jiang D, Coscione A, Li L, Zeng B-Y. Effect of Chinese herbal medicine on male infertility. Int Rev Neurobiol. 2017;135:297-311.
12. Jo J and Jerng UM. The effects of traditional Korean medicine in infertile male patients with poor semen quality: A retrospective study. Eur J Integr Med. 2016;8(1):36-40.
13. Sohrabvand F, Mahroozade S, Bioos S, Nazari SM, Dabaghian FH. Improvement in sperm parameters with traditional Iranian remedy: A case report. J Evid-Based Compl Altern Med. 2017;22(2):223-226.
14. Jaradat N and Zaid AN. Herbal remedies used for the treatment of infertility in males and females by traditional healers in the rural areas of the West Bank/Palestine. BMC Compl Altern Med. 2019;19(1):1-12.
15. Zhou SH, Deng YF, Weng ZW, Weng HW, Liu ZD. Traditional Chinese medicine as a remedy for male infertility: a review. World J Mens Health. 2019;37(2):175-185.
16. Abarikwu SO, Onuah CL, Singh SK. Plants in the management of male infertility. Androl. 2020;52(3):e13509.
17. Amano T, Hirata A, Namiki M. Effects of Chinese herbal medicine on sperm motility and fluorescence spectra parameters. Arch Androl. 1996; 37(3):219-224.
18. Furuya Y, Akashi T, Fuse H. Effect of Bu-zhong-yi-qi-tang on seminal plasma cytokine levels in patients with idiopathic male infertility. Arch Androl. 2004; 50(1):11-14.
19. Ghazeeri GS, Awwad JT, Alameddine M, Younes ZM, Naja F. Prevalence and determinants of complementary and alternative medicine use among infertile patients in Lebanon: a cross sectional study. BMC Compl Altern Med. 2012;12(1):1-9.
20. Park HJ, Choe S, Park NC. Effects of Korean red ginseng on semen parameters in male infertility patients: a randomized, placebo-controlled, double-blind clinical study. Chin J Integr Med. 2016; 22(7):490-495.
21. Wang J, Chen C, Jiang Z, Wang M, Jiang H, Zhang X. Protective effect of Cordyceps militaris extract against bisphenol A induced reproductive damage. Syst Biol Reprod Med. 2016;62(4):249-257.
22. Xiao X, Xu S, Li L, Mao M, Wang J, Li Y, Wang Z, Ye F, Huang L. The effect of velvet antler proteins on cardiac microvascular endothelial cells challenged with ischemia-hypoxia. Front Pharmacol. 2017;8:601.
23. Le MH, Nguyen HN, Pham XP, Nguyen DB. Study of acute toxicity and semi-toxicity of Y10 capsule actor on experimental organisms (Nghiên cứu độc tính cấp và độc tính bán trường diễn của viên nang Y10 trên động vật thực nghiệm). J Vietnam Med (Tạp chí Y học Việt Nam). 2018;456(1):152-158.
24. Cooper TG, Noonan E, von Eckardstein S, Auger J, Baker HW, Behre HM, Haugen TB, Kruger T, Wang C, Mbizvo MT, Vogelsong KM. World Health Organization reference

values for human semen characteristics. Hum Reprod Update. 2010; 16(3):231-245.
25. Pham TMD. Physiology (Sinh lý học): Medical publishing company (Nhà xuất bản Y học); 2011; 475.
26. Nguyen TN. Clinical andrology (Nam khoa lâm sàng): Ho Chi Minh City general publishing company. 2013; 395.
27. Le MH, Nguyen HN, Pham XP, Nguyen DB,. Study on the effect of improving spermatogenesis of Y10 capsules on experimental animals (Nghiên cứu tác dụng cải thiện khả năng sinh tinh của viên nang Y10 trên động vật thực nghiệm). J Trad Mil Med. 2018; 3:6-13.
28. World Health Organization. WHO laboratory manual for the examination and processing of human semen: World Health Organization; 2010.
29. Doan MT. Effect of Hoi xuan hoan on sperm motility in patients with infertility, impaired spermatogenesis (Tác dụng của hồi xuân hoàn trên tinh trùng sống, tinh trùng di động ở bệnh nhân vô sinh suy giảm tinh trùng). J Tradit Mil Med. 2017; 3:39-43.
30. Li N, Liu J, Zhang H. Comparison of chemical constituents of Cordyceps militaris and Cordyceps sinensis (蛹虫草与冬虫夏草化学成分比较). J Jilin Agric Univ. 1995; S1:80-83.
31. Hu T, Tao R, Su F, Zhang J. Overview of research on antler's chemical constituents and medicinal effects. J Econ Zool. 2015;19(3):156-162.
32. Wong WY, Flik G, Groenen PM, Swinkels DW, Thomas CM, Copius-Peereboom JH, Merkus HM, Steegers-Theunissen RP. The impact of calcium, magnesium, zinc, and copper in blood and seminal plasma on semen parameters in men. Reprod Toxicol. 2001;15(2):131-136.
33. Colagar AH, Marzony ET, Chaichi MJ. Zinc levels in seminal plasma are associated with sperm quality in fertile and infertile men. Nutr Res. 2009; 29(2):82-88.
34. Sundaram V, Srinivas M, Gurunathan J, Rao K, Maniyan RP, Balasundaram S. Influence of trace elements and their correlation with semen quality in fertile and infertile subjects. Turk J Med Sci. 2013; 43(6):1000-1007.