

Clinical efficacy of Chinese traditional herbal medicine (Fufang Xuanju capsule) on males of late-onset hypogonadism presenting with sexual dysfunction

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Abstract

This study aimed to assess the efficacy and safety of Fufang Xuanju capsule in males with late-onset hypogonadism (LOH) complaining of sexual dysfunction during 3 months period. We identified the patients through questionnaires and laboratory examinations. Patients in the treatment group ($n = 57$) and placebo group ($n = 50$) received Fufang Xuanju capsules (3.78 g) or placebo capsules daily for 3 months, respectively. After treatment, the plasma total testosterone of both groups sustained, however, libido and erectile dysfunction in patients of the treatment group but not placebo group were significantly improved, measured by elevated scores of International Index of Erectile Function-5. The overall efficacy rate of Fufang Xuanju capsule for LOH was 71.9%. The most striking clinical effects were observed in patients exhibiting mild and moderate erectile dysfunction. No severe adverse effects were observed during the period of study. The remaining parameters such as total prostate-specific antigen, prostate volume and uroflow rate remained stable. Fufang Xuanju capsule proves to be an effective and safe treatment in a short time to alleviate symptoms of sexual dysfunction in LOH patients, especially in those exhibiting mild and moderate erectile dysfunction. Little effect on the level of total testosterone makes it well suitable for LOH patients which have contraindications of testosterone replacement therapy.

Abbreviations: ADAM = androgen deficiency in aging male, ED = erectile dysfunction, IIEF-5 = International Index of Erectile Function-5, LOH = late-onset hypogonadism, TPSA = total prostate-specific antigen, TRT = testosterone replacement therapy, TT = total testosterone levels.

Keywords: Fufang Xuanju capsule, late-onset hypogonadism, sexual dysfunction, treatment

1. Introduction

Late-onset hypogonadism (LOH) is defined as a clinical and biochemical syndrome associated with advancing age and characterized by typical symptoms and a deficiency in serum testosterone levels (below range value of the healthy adult male).^[1] It may significantly reduce quality of life and adversely affects the function of multiple organ systems. Sexual dysfunction is a common complain in patients of LOH.^[2] At present, testosterone replacement therapy (TRT) has been applied to alleviate the symptoms of sexual dysfunction in LOH patients. Several studies have reported clinical

and laboratorial improvement when they are submitted to TRT, contributing to their quality of life, libido, and erectile dysfunction (ED).^[3–5] Nevertheless, TRT has the risks of therapy. These concerns are primarily in regards to liver, prostate, lipid profile and cardiovascular system, hematological changes, sleep patterns, social behavior, and emotional state.^[6] Prostate disease, particularly prostate cancer, and cardiovascular disease are the main safety concerns.^[7] Thus, there is a need to explore alternative effective pharmacotherapy for LOH patients, especially for those who have contraindications of TRT contraindication.

This study was supported by the Research and Reform Project of Hospital Administration of University of South China (No. 2021YYGL10), the Scientific Project of Health Commission of Hunan Province (No. B202304055928) and Promotion Project of health suitable technology of Health Commission of Hunan Province (No. 202319016258).

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

This study was carried out in compliance with the 1964 Helsinki Declaration. All experimental protocols and methods were carried out in accordance with relevant guidelines and regulations and approved by the Ethic Committee of the First Affiliated Hospital of University of South China (No. 2010114). Written informed consent to participate was obtained from all individual participants included in this study.

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How to cite this article: Zhang H, Deng S, Liu L, Wang Y, Fei K. Clinical efficacy of Chinese traditional herbal medicine (Fufang Xuanju capsule) on males of late-onset hypogonadism presenting with sexual dysfunction. *Medicine* 2025;104:1(e41160).

Received: 17 January 2024 / Received in final form: 28 November 2024 / Accepted: 12 December 2024

<http://dx.doi.org/10.1097/MD.00000000000041160>

In theory of traditional Chinese medicine, LOH is considered as a disease associated with kidney-yang deficiency.^[8] The corresponding treatment is to tonify the kidney and strengthen Yang. Fufang Xuanju capsule, a traditional Chinese medicine product, has been developed for the treatment of sexual dysfunction. It is organized by 4 Chinese medical herbs: Xuanju, *Epimedium brevicornum* Maxim, *Fructus Cnidii*, *Lycium barbarum* L. All active ingredients have a primary effect on tonifying the kidney and strengthening Yang. Previous researches have demonstrated that Fufang Xuanju capsule can improve the sexual function.^[9,10] But the clinical effects of Fufang Xuanju capsule in patients with LOH remain unknown. The purpose of the present study was to evaluate the short-term effectiveness and safety of Fufang Xuanju capsule for the treatment of patients with LOH.

2. Methods

2.1. Subjects

In the present study, those middle-aged and elderly patients complaining of sexual dysfunction (decreased libido and organic ED) were screened out from our outpatient department. They all received an Androgen Deficiency in Aging Male (ADAM) questionnaire and plasma testosterone detection. Then 111 patients with low serum total testosterone levels ($TT < 11.5 \text{ nmol/mL}$),^[11] and ADAM positive (questions 1 or 7, or other 3 questions, except for questions 1 and 7, are positive)^[12] were diagnosed as LOH and enrolled in this study. They were randomly divided into treatment group ($n = 58$) or placebo group ($n = 53$). Exclusion criteria included pathologies which might be aggravated by testosterone administration, such as male breast cancer, biopsy-confirmed prostate cancer, and elevated plasma levels of total prostate-specific antigen ($TPSA > 4 \text{ ng/mL}$), abnormal findings in digital rectal examination (until prostate cancer was ruled out), severe cardiac disease, diabetes mellitus, severe lower urinary tract obstructive symptoms, polycythemia, severe renal and liver disease. All patients were informed on the purposes of the research and its potential benefits as well as of adverse effects of the drugs, and the study was approved by the Ethics Committee of The First Affiliated Hospital of University of South China (No. 2010114).

2.2. Treatment

All enrolled patients were subjected to the treatment with Fufang Xuanju capsules (Strong pharmaceutical group, Licence No. Z20060462) or placebo capsules as 3 capsules (0.42 g per capsule) in the morning, afternoon and evening, respectively, immediately after meals.

2.3. Measurements

Before and after the treatment, all patients were evaluated by International Index of Erectile Function-5 (IIEF-5), transrectal ultrasound and laboratory tests. The IIEF-5 is a questionnaire for assessing erectile dysfunction.^[13] The higher the scoring in a total of 25 points, the better the sexual function: scores above

22 on are considered normal, without any ED; between 17 and 21, mild ED; between 12 and 16, mild to moderate ED; between 8 and 11, moderate ED; and between 5 and 7, severe ED. Transrectal ultrasound was performed for measurement of prostate volume. Laboratory tests included sexual hormone levels, liver function, blood lipid, blood glucose, hematocrit value, uroflow rate, TPSA. Blood sample for laboratory tests was taken in the early morning between 8:00 and 10:00 AM.

After 3 months of treatment, all patients were followed up within 2 months. In the end, the efficacy of Fufang Xuanju capsule for LOH is defined as follows: excellent response group (excellent), IIEF-5 score were normalized; medium response group (medium), IIEF-5 score was improved and turned to a better grade, but still not normalized; poor response group (poor), IIEF-5 score was improved but did not turn to a better grade. No response group (ineffectiveness), IIEF-5 score was not improved.

2.4. Statistical analysis

Statistical analyses were performed using “paired t test” or chi-square (χ^2) test. P value $< .05$ was considered significant. The values are presented as the mean \pm standard deviation.

3. Results

No severe adverse events were observed in this treatment period. Well-tolerated mild inappetence or nausea was found in 3 patients. However, another 4 patients needed to be excluded from the study for discontinued treatment. Therefore, finally 57 patients of treatment group and 50 patients of placebo group were included for analysis in our study. The characteristics of them are listed in Table 1.

Through clinical assessment of the IIEF-5 questionnaire scores in the present study, the general sexual function of LOH men improved significantly as the total score increased from 11.2 ± 5.6 to 17.9 ± 6.3 after 3 months of treatment with Fufang Xuanju capsule (Table 2). In detail, it might be most beneficial to erection firmness, maintaining erection frequency and intercourse satisfaction ($P < .01$), followed by erection confidence and maintaining erection ability ($P < .05$). Moreover, increased libido was reflected in more than 90% patients. However, No improved erectile function was found in patients of placebo group.

Among the 57 patients with LOH who received Fufang Xuanju capsule, 8 (14.0%) achieved normalized IIEF-5 scores, 20 (35.1%) achieved improved IIEF-5 scores and turned to a better grade, and 13 (22.8%) achieved improved IIEF-5 scores but did not turn to a better grade. Thus, the overall efficacy rate of Fufang Xuanju capsule for LOH was 71.9% (excellent + medium + poor) (Table 3).

No significant changes in TT, serum TPSA, prostate volume, and uroflow rate were noticed while receiving Fufang Xuanju capsules and placebo capsules ($P > .05$) (Table 4). Blood lipid, blood glucose, blood pressure, and body mass index were all stable as before.

Table 1
Characteristics of placebo group and treatment group patients presented with ED.

Characteristics	Mean age (years)	Age range (years)	Duration of ED (months)	ED severity (n)			
				Mild	Mild to moderate	Moderate	Severe
Placebo group (50)*	58	45–72	15	15	5	20	10
Treatment group (57)*	56	41–69	16	16	7	23	11

ED = erectile dysfunction.

*Number of patients.

Table 2
Erectile functions of placebo group and treatment group patients before and after treatment with Fufang Xuanju capsule being evaluated by IIEF-5.

IIEF-5	Placebo group		Treatment group	
	Baseline	After treatment	Baseline	After treatment
Q1, erection confidence	1.6 ± 0.5	1.8 ± 0.4	1.8 ± 0.5	3.3 ± 0.9*
Q2, erection firmness	2.2 ± 1.2	2.0 ± 1.5	2.0 ± 1.1	3.6 ± 1.5†
Q3, maintain erection frequency	1.9 ± 1.5	2.5 ± 1.2	2.3 ± 1.0	3.7 ± 1.2†
Q4, maintain erection ability	2.5 ± 1.3	3.3 ± 1.3	2.4 ± 1.5	3.5 ± 1.4*
Q5, intercourse satisfaction	2.8 ± 1.4	3.0 ± 1.1	2.7 ± 1.2	3.8 ± 1.3†
Total score	11.0 ± 5.3	12.6 ± 4.9	11.2 ± 5.6	17.9 ± 6.7†

Q, question. Values are presented as mean ± SD.
IIEF-5 = International Index of Erectile Function-5.
*P < .05, baseline versus after treatment for treatment group.
†P < .01, baseline versus after treatment for treatment group, paired t test. No significant differences were found in the placebo group.

Table 3
The efficacy rate of Fufang Xuanju capsule for 57 LOH patients presented with ED.

ED severity	Excellent	Medium	Poor	Ineffectiveness	Efficacy rate (%)
Mild	4	6	3	3	13/16 (81.3)*
Mild to moderate	1	4	1	1	6/7 (85.7)*
Moderate	3	9	6	5	18/23 (78.3)*
Severe	0	1	3	7	4/11 (36.4)
Total	8	20	13	16	41/57 (71.9)

ED = erectile dysfunction, LOH = late-onset hypogonadism.
*P < .05, versus severe ED group, chi-square (χ²) test.

Table 4
Observed parameters before and after treatment with Fufang Xuanju capsule.

Parameters	Baseline	After treatment
TT (nmol/L)	8.71 ± 1.51	9.23 ± 1.83*
TPSA (pg/mL)	1.23 ± 0.03	1.18 ± 0.05*
Prostate volume (mL)	38.44 ± 2.01	40.21 ± 2.60*
Uroflow rate (mL/S)	14.58 ± 3.52	15.10 ± 3.13*
Total cholesterol (mmol/L)	4.66 ± 1.25	4.33 ± 1.01*
Triglycerides (mmol/L)	1.58 ± 0.18	1.64 ± 0.15*
HDL-C (mmol/L)	1.20 ± 0.21	1.38 ± 0.16*
Blood glucose (mmol/L)	4.86 ± 0.23	4.71 ± 0.18*
Systolic blood pressure (mm Hg)	150.24 ± 8.57	148.08 ± 9.52*
Diastolic blood pressure (mm Hg)	93.06 ± 3.11	88.89 ± 5.74*
Body mass index (kg/m ²)	25.86 ± 4.27	24.61 ± 3.35*
Waist circumference (cm)	95.82 ± 11.63	96.46 ± 10.17*
Hip circumference (cm)	93.25 ± 8.71	93.99 ± 7.94*

HDL-C = high density lipoprotein cholesterol, LOH = late-onset hypogonadism, TPSA = total prostate-specific antigen, TT = total testosterone levels.
Values are presented as mean ± SD of 57 LOH patients in treatment group.
*P > .05, baseline versus after treatment, paired t test. Values are not statistically significant.

4. Discussion

Aging is characterized by a virtually progressive decline of all physiological functions. The reason is the decreasing secretory capacity of the endocrine glands.^[14] The testosterone concentration in men remains stable until around the age of 40 years, after which the circulating level of TT decreases by 1% to 2% annually and that the biologically active free testosterone decreases by 2% to 3%.^[15] The recommended indications for TRT in LOH include low T levels together with typical symptoms.^[1] According to the guideline,^[16] a total testosterone level below 12 nmol/L is considered pathological. However, abnormal testosterone level is still controversial, due to the uncertainty of different individuals, aged groups, race and laboratory test.

Thus, a lower cutoff value for definition of androgen deficiency from Chinese men is used in our study.^[17] That was defined as TT < 11.5 nmol/L.

The ADAM questionnaire is widely used for screening LOH cases because of its high sensitivity, time saving and easy implement. It has 88% sensitivity and 60% specificity.^[12] The ADAM questionnaire is applicable to the Chinese population. The sensitivity and specificity of ADAM in the Chinese population are basically consistent with the results of most studies abroad. The IIEF-5 was reorganized using IIEF question 15 (erection confidence), question 2 (erection firmness), question 4 (erection frequency), question 5 (ability to maintain an erection), and question 7 (intercourse satisfaction).^[13] The IIEF-5 has been proved to be a reliable test for the diagnosis of the presence and severity of ED. Thus, the ADAM and IIEF-5 were selected to apply in our study accordingly.

It considers in traditional Chinese medicine that LOH belongs to the category of “Yang-insufficiency of the kidney.” Fufang Xuanju capsule is considered as a drug which can nourish the kidney-yang. In our study, Fufang Xuanju capsule also showed satisfying therapeutic effect in LOH patients with sexual dysfunction which was not found in the placebo group. The pretreatment baseline of 57 patients revealed low TT, low libido and low IIEF-5 scores. After 3 months treatment with Fufang Xuanju capsule, low libido and low IIEF-5 scores had significantly improved, though they were not yet within normal range. The overall efficacy rate of Fufang Xuanju capsule for LOH was 71.9% (excellent + medium + poor). The response to LOH treatment is also variable. Compared with the severe subgroup, the moderate and mild group showed more significant efficacy rate. This may be due to insufficient course of treatment or complex etiology existing in these patients. Actually, in contrast to Western medicine, traditional Chinese medicine is often characterized by comparatively mild but long lasting effect. Interestingly, the level of TT did not changed after treatment, although the symptoms had been significantly alleviated.

In our study, the unchanged level of TT was observed after treatment. Thus, it seems that Fufang Xuanju capsule performs in a nonhormonal way. It may directly targets the gonadal tissues, not through effects on the level of testosterone. Although the functional mechanism of Fufang Xuanju capsule in LOH patients remains largely unknown. From the perspective of modern western medicine, several hypotheses or experimental data have been advanced to explain its mechanism and effects. Fufang Xuanju capsule includes 4 Chinese medical herbs: Xuanju, *E brevicornum* Maxim, Fructus Cnidii, *L barbarum* L. In rats treatment with Xuanju, erection function and mating ability were significantly enhanced, with increasing capture rate and mating rate.^[9] Icariinis, the major compound of *E brevicornum* Maxim, has testosterone mimetic properties and biological effects on selectively inhibiting phosphodiesterase-5 (PDE-5), suggesting it a therapeutic potential on erectile dysfunction.^[18,19] As to another component, Fructus Cnidii, active ingredient of which is called osthole. Osthole possesses a relaxing effect on rabbit corpus cavernosum tissues which was attributable to the release of NO from sinusoidal endothelium and to the potentiation of the NO-stimulated cGMP and/or cAMP signal mediating relaxation of cavernosal smooth muscle by inhibition of phosphodiesterase.^[20] These results might confirm further the therapeutic effect of Fufang Xuanju capsule in LOH patients with sexual dysfunction. Despite these, the underlying mechanism need to be further studied.

The adverse reactions of Fufang Xuanju capsule can be neglected. Furthermore, the prostate volume and TPSA did not increase after treatment. The liver function, hematocrit value, blood lipid, blood glucose uroflow rate were not significantly changed.

The present study has suggested that Fufang Xuanju capsule is very beneficial to the libido and erectile function of LOH patients when evaluated using the IIEF-5 questionnaire. However, compared with the results of the clinical trials of the PDE-5 inhibitors, the improvement in erections is not yet optimal. But improvement of libido, few adverse events and considerably cheaper cost made it a good compliance with the treatment in our study. Lack of libido, high cost or the adverse events appeared to be the reasons to discontinue treatment with sildenafil.^[21] Moreover, without elevation of serum testosterone level, worry about side effects of TRT may be precluded, resulting in a good compliance.

5. Conclusion

In conclusion, this is a pilot study and it has shown sexual dysfunction in patients with LOH was alleviated after administration of Fufang Xuanju capsule, without serious adverse reactions. The most striking clinical effects were observed in patients exhibiting mild and moderate ED. Hence, Fufang Xuanju capsule may be a novel candidate for the treatment of LOH patients with sexual dysfunction, especially for cases which are not suitable for TRT, in view of unchanged TT level. Admittedly, this is only a small size and a single-center study, so we recommend a rigorous, randomized controlled, multicentre, long-term study to confirm our results.

Author contributions

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References

- [1] Nieschlag E, Swerdloff R, Behre HM, et al. Investigation, treatment, and monitoring of late-onset hypogonadism in males: ISA, ISSAM, and EAU recommendations. *J Androl*. 2006;27:135–7.
- [2] Travison TG, Morley JE, Araujo AB, O'Donnell AB, McKinlay JB. The relationship between libido and testosterone levels in aging men. *J Clin Endocrinol Metab*. 2006;91:2509–13.
- [3] Andrade ES Jr, Clapauch R, Buksman S. Short term testosterone replacement therapy improves libido and body composition. *Arq Bras Endocrinol Metabol*. 2009;53:996–1004.
- [4] Chiang HS, Cho SL, Lin YC, Hwang TI. Testosterone gel monotherapy improves sexual function of hypogonadal men mainly through restoring erection: evaluation by IIEF score. *Urology*. 2009;73:762–6.
- [5] Yassin AA, Saad F. Improvement of sexual function in men with late-onset hypogonadism treated with testosterone only. *J Sex Med*. 2007;4:497–501.
- [6] Lunenfeld B. Androgen therapy in the aging male. *World J Urol*. 2003;21:292–305.
- [7] Liu PY, Swerdloff RS, Veldhuis JD. Clinical review 171: the rationale, efficacy and safety of androgen therapy in older men: future research and current practice recommendations. *J Clin Endocrinol Metab*. 2004;89:4789–96.
- [8] Zhang CH, Li YF, Zhao HM. Curative effect of Chinese drugs combined with Andriol in the treatment on 30 cases of late onset hypogonadism in males [in Chinese]. *Chin J Androl*. 2007;6:46–7.
- [9] Jiang H, Shang XJ, Guo J, et al. Multi-centered clinical trial of Fufang Xuanju capsule for oligoasthenospermia [in Chinese]. *Zhonghua Nan Ke Xue*. 2008;14:755–8.
- [10] Zhang FB, Tian Y, Du LD. Xuanju compound capsule combined with erogenous focus exercise is effective for premature ejaculation [in Chinese]. *Zhonghua Nan Ke Xue*. 2006;12:1139–40.
- [11] Li JY, Li XY, Li M, et al. Decline of serum levels of free testosterone in aging healthy Chinese men. *Aging Male*. 2005;8:203–6.
- [12] Morley JE, Charlton E, Patrick P, et al. Validation of a screening questionnaire for androgen deficiency in aging males. *Metabolism*. 2000;49:1239–42.
- [13] Rosen RC, Cappelleri JC, Smith MD, Lipsky J, Pena BM. Development and evaluation of an abridged, 5-item version of the international index of erectile function (IIEF-5) as a diagnostic tool for erectile dysfunction. *Int J Impot Res*. 1999;11:319–26.
- [14] Kalinchenko S, Vishnevskiy EL, Koval AN, Mskhalaya GJ, Saad F. Beneficial effects of testosterone administration on symptoms of the lower urinary tract in men with late-onset hypogonadism: a pilot study. *Aging Male*. 2008;11:57–61.
- [15] Feldman HA, Longcope C, Derby CA, et al. Age trends in the level of serum testosterone and other hormones in middle-aged men: longitudinal results from the Massachusetts male aging study. *J Clin Endocrinol Metab*. 2002;87:589–98.
- [16] Wu FC, Tajar A, Pye SR, et al. Hypothalamic-pituitary-testicular axis disruptions in older men are differentially linked to age and modifiable risk factors: the European Male Aging Study. *J Clin Endocrinol Metab*. 2008;93:2737–45.
- [17] Wang C, Nieschlag E, Swerdloff R, et al. Investigation, treatment, and monitoring of late-onset hypogonadism in males: ISA, ISSAM, EAU, EAA, and ASA recommendations. *J Androl*. 2009;55:1–130.
- [18] Liu WJ, Xin ZC, Xin H, Yuan YM, Tian L, Guo YL. Effects of icariin on erectile function and expression of nitric oxide synthase isoforms in castrated rats. *Asian J Androl*. 2005;7:381–8.
- [19] Zhang ZB, Yang QT. The testosterone mimetic properties of icariin. *Asian J Androl*. 2006;8:601–5.
- [20] Chen J, Chiou WF, Chen CC, Chen CF. Effect of the plant-extract osthole on the relaxation of rabbit corpus cavernosum tissue in vitro. *J Urol*. 2000;163:1975–80.
- [21] Klotz T, Mathers M, Klotz R, Sommer F. Why do patients with erectile dysfunction abandon effective therapy with sildenafil (Viagra)? *Int J Impot Res*. 2005;17:2–4.