

The real-world study of Qian Lie Shu Tong Jiao Nang combined with finasteride tablets in the treatment of benign prostatic hyperplasia

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Abstract: With the rapid development of traditional Chinese medicine, the combination of Chinese and Western medicine for treating Benign Prostatic Hyperplasia (BPH) has been gradually promoted in clinical medical practice in China. Both Qian Lie Shu Tong Jiao Nang and Finasteride tablets are effective in treating BPH. However, there is a lack of reports on their combined use, so their efficacy and safety still need to be verified. This study explored the clinical effectiveness and safety of Qian Lie Shu Tong Jiao Nang combined with Finasteride tablets for BPH based on real-world data. Results showed that this combination significantly improved the total treatment efficiency ($P < 0.05$) and reduced the International Prostate Symptom Score (IPSS), Chronic Prostatitis Symptom Index (NIH-CPSI), residual urine volume (RUV), tumor necrosis factor (TNF- α) and serum estradiol (E2) levels (all $P < 0.05$). Prostate volume (PV) was notably decreased, while interleukin-10 (IL-10), serum testosterone (T) and maximum urinary flow rate (Qmax) were significantly increased (all $P < 0.05$). The incidence of adverse reactions did not increase with the combination treatment. These observations suggest that the combined use of Qian Lie Shu Tong Jiao Nang and Finasteride tablets may more effectively alleviate BPH symptoms, improve urination functions and have a high safety profile.

Keywords: Qian Lie Shu Tong Jiao Nang, finasteride tablets, benign prostatic hyperplasia, real-world study.

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INTRODUCTION

The non-malignant enlargement of the prostate gland known as benign prostatic hyperplasia (BPH) is brought on by cellular hyperplasia of the glandular and stromal components, similar to the nodular hyperplasia of breast fibroadenoma (De Nunzio *et al.*, 2020). In adult men, BPH is usually characterized by lower urinary tract symptoms associated with voiding dysfunction, which in severe cases can cause secondary symptoms such as acute urinary retention or upper urinary tract lesions (Devlin *et al.*, 2021; Choi JB and Min SK, 2021). Currently, there are three major classes of drugs commonly used in clinical practice to treat BPH: 5α -reductase inhibitors, α -blockers, and traditional Chinese medicines (TCMs) and usually a combination of the two classes of drugs is used for treatment (Plochocki and King, 2022). Finasteride is a 5α -reductase inhibitor, which is the clinically preferred drug that can inhibit the proliferation of prostate cells to induce apoptosis, reduce the volume of prostate tissue, and effectively relieve the disease. Qian Lie Shu Tong Jiao Nang is a Chinese medicine preparation, that has the functions of warming the kidney and promoting qi circulation, clearing heat and facilitating urination, activating blood circulation and removing blood stasis, dispersing knots and relieving pain and has shown better efficacy in the treatment of BPH (Liu *et al.*, 2019; Zhang *et al.*, 2021). With the fast advancement of traditional Chinese medicine in recent years, the application of Qian Lie Shu Tong Jiao Nang combined with Finasteride tablets for the treatment of BPH has been gradually

popularized in Chinese clinical medicine. However, there is still a lack of relevant reports on the combination of the two in the treatment of BPH, and most of the existing studies have obtained data through clinical randomized controlled trials (Yin *et al.*, 2022; LI *et al.*, 2023), which lacked real-world studies, and the efficacy and safety of the two remain to be tested. Real-world study (RWS), refers to the non-randomized selection of therapeutic measures to carry out long-term evaluations based on a broad subject population and a large sample, focusing on clinically meaningful outcome metrics, based on the actual conditions and wishes of the subjects, to further evaluate the external validity and safety under real-world conditions (Andrade, 2023). This protocol will use the RWS method to examine the safety and effectiveness of Qian Lie Shu Tong Jiao Nang in conjunction with Finasteride tablets in the treatment of BPH patients, to obtain more comprehensive and realistic clinical data.

MATERIALS AND METHODS

General information

A retrospective analysis was done on the clinical records of patients with BPH who were admitted to Ankang City Central Hospital between February 2022 and February 2024 and who were prescribed to be treated with Finasteride tablets or Qian Lie Shu Tong Jiao Nang combined with Finasteride tablets. Inclusion criteria: (1) meeting the relevant diagnostic and treatment standards issued by the American Urological Association (AUA) regarding BPH (Lerner *et al.*, 2021; Sandhu *et al.*, 2023); (2) containing ≥ 12 cycles of target drug therapy; (3) normal indicators of all basic vital signs and laboratory

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tests, without major diseases such as malignant tumors; (4) complete clinical data, including basic data, diagnostic and treatment data, biochemical index data, medication follow-up data etc. Exclusion criteria: (1) those who suffered from serious mental diseases and did not cooperate with the treatment; (2) those who did not have the efficacy assessment; (3) those who had urinary disorders caused by other diseases such as neurological, bladder, prostate cancer and urethral stenosis; (4) those who suffered from acute urinary tract infections and blood system diseases. Our hospital's Medical Ethics Committee examined and approved this study [2024No.083].

Subgroups and specific treatment programs

According to the actual treatment plan, i.e., whether Finasteride tablets are combined with the application of Qian Lie Shu Tong Jiao Nang to treat BPH is divided into two groups: Combined treatment group as well as Monotherapy group. The Monotherapy group took Finasteride tablets (State Drug License H20051921, Hangzhou Kang En Bei Pharmaceutical Co. The Combined treatment group was given Qian Lie Shu Tong Jiao Nang (Guoyu Z20027140, Baoding Tianhao Pharmaceutical Co., Ltd., Specification: 0.4g/capsule) based on the Monotherapy group, with each dose of 1.2g, 3 times/d. The main ingredients of Qian Lie Shu Tong Jiao Nang include 13 traditional Chinese medicinal herbs such as Huang Bai, Chi Shao, Dang Gui, Chuan Xiong, Tu Fu Ling, San Ling, Ze Xie, Ma Chi Xian, Ma Bian Cao, Hu Er Cao, Chai Hu, Chuan Niu Xi and Gan Cao; The manufacturing process generally includes the following steps: (1) Extraction of herbs: The required traditional Chinese medicinal herbs are mixed in a certain ratio and extracted with water or ethanol to fully extract the effective components of the herbs; (2) Filtration: The extracted liquid is filtered to remove herbal residues and precipitates, resulting in a clear medicinal liquid; (3) Concentration: The medicinal liquid is concentrated to evaporate the water content and increase the concentration of the liquid; (4) Drying: The concentrated liquid is dried to remove excess water and obtain dried medicinal powder; (5) Granulation: The dried powder is granulated to facilitate subsequent capsule filling; (6) Filling: The granulated powder is filled into capsules to complete the production of Qian Lie Shu Tong capsules. Its specific drug composition ratio was not disclosed in detail in the public information.

This study did not limit any medications for the treatment of the disease, underlying disease, or complications, but all concomitant medications used during treatment should be recorded in detail.

Data collection

The electronic medical record system was used to gather the following patient data: (1) general data, such as body mass index (BMI), age, and Duration of disease. (2) laboratory test results before medication and after 12

weeks of treatment, including inflammatory factors such as interleukin-10 (IL-10) and tumor necrosis factor (TNF- α), as well as serum testosterone (T) and serum estradiol (E₂). IL-10 is an anti-inflammatory cytokine, and TNF- α is a pro-inflammatory cytokine; changes in their levels are associated with inflammation and tissue damage. The gradual development of inflammation is an important cause leading to symptomatic BPH. Therefore, in BPH patients, a decrease in TNF- α levels and an increase in IL-10 levels may be correlated with symptom improvement and therapeutic outcomes. (3) the International Prostate Symptom Score (IPSS) both before and following a 12-week course of therapy (Choi *et al.*, 2015). the IPSS is a widely used scoring system for assessing the severity of symptoms in patients with BPH and it contains 7 symptoms on a 6-point scale of 0-5, with a total score of 35, with a score of 8 or less as mild, 8-20 as moderate, and 21 or more as severe, more severe symptoms are indicated by higher ratings. (4) Chronic Prostatitis Symptom Index (NIH-CPSI) (Litwin, 2002) before treatment and after 12 weeks of treatment. The NIH-CPSI is a scoring system used to assess the severity of symptoms of chronic prostatitis. In patients with BPH, especially those with prostatitis symptoms, the reduction in NIH-CPSI indicates improvement in symptoms. (5) maximum urinary flow rate (Q_{max}), residual urine volume (RUV) and prostate volume [PV, 0.52 × (product of upper and lower, anterior and posterior, and left and right diameters)] before medication and after 12 weeks of treatment; BPH can affect urine flow and bladder function and Q_{max} and RUV are important indicators for assessing these functions. A characteristic of BPH is the enlargement of the prostate volume, and changes in PV may be related to the expression of symptoms. (6) telephone or outpatient follow-up information, which included the patient's medication use, the incidence of adverse effects during medication, and the endpoint of follow up as the final goal of Medication.

In the process of follow-up data collection, recall bias and reporting bias may lead to information bias. For example, patients may not accurately recall medication use or the occurrence of adverse effects. All adverse events that were reported spontaneously or detected by inquiry or observation were analyzed and medication use was recorded according to patient reports.

Observation indicators

The main observational index was the clinical efficacy of drug treatment, which was categorized as Clinical Control, Conspicuous Effect, Effective and void of effect, and they were defined as (1) Resolution of clinical symptoms of associated BPH and $\geq 60\%$ reduction in IPSS score is considered clinical control; (2) Substantial disappearance of relevant BPH clinical symptoms and a 45%-59% reduction in IPSS score were considered conspicuous effect; (3) Improvement in clinical symptoms of associated BPH and a 30%-44% reduction in IPSS

score were considered effective; (4) No significant regression of symptoms and clinical indicators or even aggravation after treatment is considered void of effect. Overall Effectiveness Rate = (Clinical Control + +Conspicuous Effect + Effective)/Total Sample Size. Secondary observations were urinary function (Qmax, RUV, PV), NIH-CPSI, levels of inflammatory factors (IL-10, TNF- α), levels of sex hormones (T, E₂) and adverse reactions during drug therapy in the treated patients.

Ethical approval

This study was approved by Ankang City Central Hospital [2024No.083].

STATISTICAL ANALYSIS

The statistical program SPSS 20.0 was used to examine the data. Data on measurements that followed a normal distribution were reported as mean \pm standard deviation ($\bar{x} \pm s$), and group comparisons were made using the independent samples t-test to assess the differences between Combination therapy and Monotherapy groups, intragroup comparisons before and after treatment were conducted using the paired samples t-test. Data on counts were presented as n (%) and group comparisons were made using the χ^2 test. Considering $P < 0.05$ to indicate the statistical significance of the difference.

RESULTS

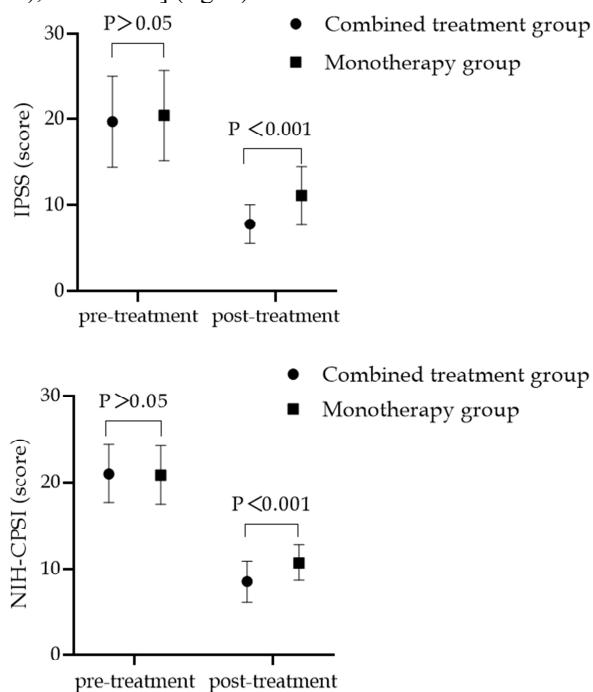
A comparison of the two groups' fundamental information

Among patients with BPH treated in Ankang City Central Hospital from February 2022 to February 2024, 252 patients were treated with the regimen containing the target drug (Finasteride tablets / Qian Lie Shu Tong Jiao Nang combined with Finasteride tablets). Seventeen patients were excluded from the analysis, of whom 5 did not reach the 12-week endpoint, 4 had other conditions that led to other treatment during the observation period, and 8 were lost to follow-up with incomplete data. Finally, 235 valid cases were available for evaluation; 157 patients received Qian Lie Shu Tong Jiao Nang in addition to Finasteride tablets, making up the Combination treatment group; 78 patients received Finasteride tablets alone, making up the Monotherapy group. The results of the comparison of the general information suggest that the differences in age, duration of disease and BMI between the two groups were not significant (all $P > 0.05$) (table 1).

A comparison of the two groups' NIH-CPSI and IPSS scores

Before treatment, the difference in IPSS scores and NIH-CPSI between the two groups was not statistically significant ($P > 0.05$). Following treatment, IPSS scores as well as NIH-CPSI scores were significantly lower in the two groups ($P < 0.05$) and as compared to the Monotherapy

group, the Combination treatment group's IPSS and NIH-CPSI scores were lower [IPSS scores: (7.77 \pm 2.23 vs. 11.06 \pm 3.40); NIH-CPSI scores: (8.51 \pm 2.41 vs. 10.72 \pm 2.06); all $P < 0.05$] (fig. 1).



IPSS: International Prostate Symptom Score; NIH-CPSI: Chronic Prostatitis Symptom Index.

Fig. 1: Comparison of IPSS and NIH-CPSI in the two groups.

Inflammatory factor comparison in both groups

Before treatment, no significant disparity was observed in the levels of IL-10 and TNF- α in the two groups ($P > 0.05$). After treatment, IL-10 levels increased significantly and TNF- α levels decreased significantly in both groups (both $P < 0.05$); in the Combination therapy group, TNF- α levels were lower and IL-10 levels were greater than in the Monotherapy group ($P < 0.001$) (fig. 2).

Serum T and E₂ level comparison between the two groups

Before receiving therapy, patients in the two groups' serum T and E₂ levels did not differ statistically significantly (all $P > 0.05$). Following therapy, individuals in both groups showed significantly higher serum T levels and significantly lower serum E₂ levels ($P < 0.05$) and The serum T and E₂ levels improved more in the Combined treatment group than in the Monotherapy group ($P < 0.05$) (table 2).

Comparison of Qmax, RUV and PV between the two groups

Before treatment, there were no major differences in Qmax, RUV and PV levels in the two groups (all $P > 0.05$). After treatment, Qmax levels, as well as RUV and PV, were significantly improved in both groups (all $P <$

0.05); And relative to the Monotherapy group, the Combination treatment group had markedly higher Qmax level (16.83±2.91 vs 14.72±2.32), significantly less RUV (22.41±6.85 vs 27.78±7.04) and significantly smaller PV (27.27±7.44 vs 31.86±7.05), the differences all reached the level of statistical significance. (all P<0.05). For details, refer to table 3.

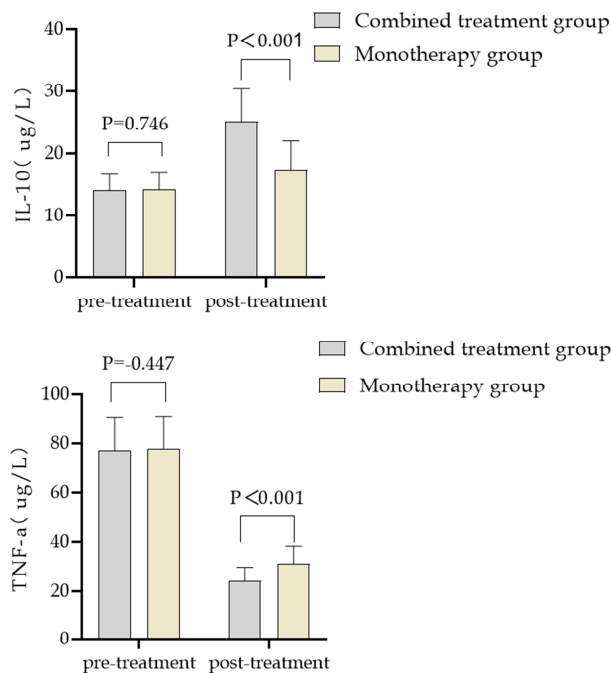
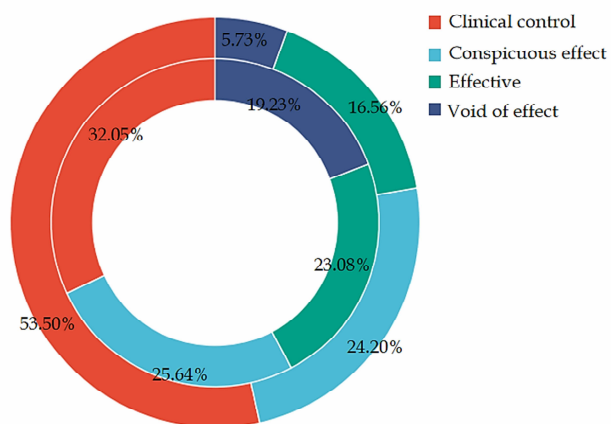


Fig. 2: Inflammatory factor comparison in both groups (IL-10: interleukin-10; TNF-a: tumour necrosis factor)

Evaluation of the clinical efficacy of the two groups

Following pharmacological treatment, the combination therapy group's overall effective rate was 94.27% (148/157), substantially higher than the Monotherapy group's 80.77% (63/78) and the disparity achieved statistical significance (P = 0.001). For details, refer to fig. 3.



(outer circle pie chart: Combination treatment group; inner circle pie chart: Monotherapy group)

Fig. 3: A comparison of the two groups' clinical efficacy.

Safety evaluation

During the treatment period, the incidence of adverse reactions was 6.41% (5/78) in the Monotherapy group and 8.28% (13/157) in the combination therapy group, and the difference in the incidence of adverse reactions in both groups was small (P>0.05) (table 4).

DISCUSSION

The American Urological Association defines BPH as a diagnosis based on histological evidence, characterized primarily by the proliferation of smooth muscle and epithelial tissue in the transition area of the prostate. BPH is one of the most common diseases of the male urinary system, and its incidence increases significantly with the increase of age. It is a disease affected by many factors (Liedtke *et al.*, 2024). With age, serum T levels decrease and the T/E₂ ratio decreases, leading to increased E₂ activity, which may promote prostate cell proliferation (Hata *et al.*, 2023). In addition, there is a theory focusing on serum T being converted to dihydrotestosterone (DHT) by the action of 5α-reductase and that DHT promotes prostate epithelial cell proliferation (Joseph *et al.*, 2022; Zheng *et al.*, 2024). Therefore, 5α-reductase inhibitors that block DHT formation are beneficial in attenuating prostate tissue proliferation.

Finasteride is a 5α-reductase inhibitor, which inhibits 5α-reductase, blocks T conversion, reduces DHT levels, and contributes to an increase in T levels, thereby inhibiting disease progression and contributing to improvements in RUV, PV and Qmax (Inamura S and Terada N, 2024). However, clinical treatment of BPH with finasteride alone is sometimes difficult to achieve the desired therapeutic effect.

A prospective clinical study showed that the additional use of curcumin was superior to finasteride alone in improving IPSS and QoL scores and controlling urinary tract infections in patients with BPH (Ledda *et al.*, 2012). Qiao *et al.* also showed that finasteride combined with tamsulosin and curcumin in the treatment of BPH could significantly improve IPSS-S score and urinary retention symptoms (Qiao *et al.*, 2021). All these studies suggest that finasteride combined with other drugs is a more effective strategy for the treatment of BPH. In recent years, the comprehensive treatment programs of Chinese and Western medicine have achieved remarkable results in treating a variety of complicated diseases, which makes the use of combined Chinese and Western medicine in the treatment of BPH also gradually become a new option for doctors to consider.

The results of the present study analyzing the combination of Qian Lie Shu Tong Jiao Nang and Finasteride tablets in the treatment of BPH showed that in the following treatment, there was a significant reduction in the IPSS

score, E₂ level, RUV and PV value of both groups and the Qmax value and T content were significantly improved, while the Combination treatment group demonstrated a greater improvement of the above scores and indexes compared to the Monotherapy group, with statistically significant differences seen (P<0.05); moreover, the Combination therapy group's overall effective rate substantially higher than the Monotherapy group (P<0.05). The above results indicate that Qian Lie Shu Tong Jiao Nang combined with Finasteride tablets can better inhibit disease progression, improve clinical efficacy and improve urinary function by blocking the formation of DHT compared with single Finasteride tablets. Prostatic hyperplasia falls into the "stranguria" and "retention of urine" categories in traditional Chinese medicine, which is mainly formed under the combined effect of kidney deficiency, blood stasis and phlegm-phlegm conjugation and the treatment is mainly based on activating blood circulation and removing blood stasis, and tonifying the kidney and transforming qi (Zhang *et al.*, 2023). Qian Lie Shu Tong Jiao Nang is a commonly used Chinese medicinal preparation, which is composed of 13 traditional Chinese medicines, including Huang Bai, Chi Shao, Dang Gui, Chuan Xiong, Tu Fu Ling, San Ling, Ze Xie, Ma Chi Xian, Ma Bian Cao, Hu Er Cao, Chai Hu, Chuan Niu Xi and Gan Cao, with the effects of clearing heat and promoting diuresis, as well as resolving stasis and dispersing swelling (Liu *et al.*, 2019). In the formula, Huang Bai and Chi Shao are used together as the principal herbs, to clear the damp heat in the lower jiao and eliminate blood stasis; Tu Fu Ling, Chuan Xiong, San Ling, and Ze Xie are used together to strengthen the effect of the monarch in removing damp-heat and dispersing stasis and stagnation and are used as the ministerial herbs; Ma Chi Xian, Hu Er Cao, Chai Hu, Dang Gui, Chuan Niu Xi, Ma Bian Cao are used together as the adjuvant drugs to exert the effects of detoxification, swelling dispersion, and blood-activating; Chuan Niu Xi and Gan Cao are used together as the ambulatory herbs (ZHANG, 2021). Qian Lie Shu Tong Jiao Nang is the recommended medication for the treatment of damp-heat stasis-type BPH guideline, which is widely used in the clinic and it can promote prostate cell apoptosis by decreasing the expression of vascular endothelial growth factor in prostate tissues, apoptosis inhibiting factor (bcl-2) and fibroblast growth factor, which in turn can achieve the effect of inhibiting the proliferation of prostate tissues (LI *et al.*, 2023).

Some clinical studies have found that most patients with BPH have chronic inflammation and the gradual development of inflammation is an important cause of eventual symptomatic BPH (Tsunemori *et al.*, 2021; Naiyila *et al.*, 2023). Therefore, reducing the inflammatory response is also an important mechanism in the pharmacologic treatment of BPH. The study's findings demonstrated that compared with the pre-treatment, the

levels of NIH-CPS and TNF- α were considerably reduced while the levels of IL-10 were substantially greater in the two groups, and the Combined therapy group exhibited reduced levels of NIH-CPS and TNF- α compared to the Monotherapy group while showing an increase in IL-10 levels (P<0.05). This indicates that the combination of Qian Lie Shu Tong Jiao Nang and Finasteride tablets is more effective than Finasteride tablets alone in reducing the inflammatory response in patients with BPH. Analysis of the reasons for this show that Finasteride tablets are a synthetic steroidal compound that inhibits the formation of micro vessels in prostate tissue to improve the inflammatory microenvironment of the body (Lee *et al.*, 2024); however, it lacks a direct anti-inflammatory effect. While the Chai Hu in Qian Lie Shu Tong Jiao Nang contains Chaihu saponin, which has the effect of reducing the inflammatory response of the human body (Wang and Li, 2023); Dang Gui contains a large amount of volatile oil, which can reduce the damage suffered by the human body, thus inhibiting the inflammatory response (Li *et al.*, 2021). Therefore, the direct anti-inflammatory effect of Qian Lie Shu Tong Jiao Nang combined with Finasteride tablets can synergistically enhance the inhibition of the body's inflammatory factor production, further preventing the release of inflammatory factors and reducing the body's inflammatory response.

Safety evaluation results show that the difference in the incidence of adverse reactions in both groups was small (P>0.05), the adverse effects were less severe in both groups, and the adverse reactions disappeared after discontinuation of symptomatic treatment, indicating that the combination of Qian Lie Shu Tong Jiao Nang and Finasteride tablets has a high degree of safety. A meta-analysis that included 18 RCTs showed results consistent with this study, indicating that the combination of Qianlieshu Tong capsules and finasteride tablets for the treatment of BPH did not observe any serious drug-related adverse events or reactions (Liu *et al.*, 2019). Finasteride tablets have high bioavailability and less effect on the digestive system, skin and central nervous system (Salisbury *et al.*, 2024), while Qian Lie Shu Tong Jiao Nang is a common Chinese medicine, mild and well tolerated. Thus, there is no increased risk of adverse reactions while using Finasteride tablets combined with Qian Lie Shu Tong Jiao Nang for the treatment of BPH.

There are some limitations to this study: (1) Due to the poor availability of real-world data, this study is single-center research, and the included subjects may have certain biases; (2) Due to the complexity of real-world medication regimens and treatment protocols, there may be some bias in the evaluation and analysis of relevant data; (3) Bias due to patient loss of visits could not be avoided, although this may have been comparable in the two cohorts.

Table 1: Comparison of the two groups' general information ($\bar{x}\pm s$)

Items	Combined treatment group (n=157)	Monotherapy group (n=78)	t value	P value
Age (years)	57.24±6.83	55.69±6.70	1.640	0.102
Duration of disease (years)	3.31±1.04	3.32±1.06	-0.098	0.922
BMI(kg/m ²)	23.58±1.55	23.43±1.51	0.692	0.489

Table 2: Comparison of the two groups' serum T and E₂ levels ($\bar{x}\pm s$)

Groups	T (ng/ML)		E ₂ (pg/ml)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Combined treatment group (n=157)	808.03±77.69	982.18±79.32*	41.12±8.63	24.03±4.90*
Monotherapy group (n=78)	798.92±84.05	876.10±84.44*	42.39±9.47	27.73±7.29*
t value	0.824	9.448	-1.025	-4.054
P value	0.411	<0.001	0.307	<0.001

Table 3: Comparison of Qmax, RUV and PV levels between the two groups ($\bar{x}\pm s$)

Groups	Qmax(mL)		RUV(mL)		PV(cm ³)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Combined treatment group (n=157)	12.91±2.49	16.83±2.91*	54.37±13.23	22.41±6.85*	36.23±7.52	27.27±7.44*
Monotherapy group (n=78)	12.78±2.29	14.72±2.32*	53.95±15.10	27.78±7.04*	37.52±10.36	31.86±7.05*
t value	0.380	6.020	0.219	-5.609	-0.975	-4.525
P value	0.704	<0.001	0.827	<0.001	0.332	<0.001

Note: *P<0.05 compared to pre-treatment.

Table 4: The occurrence of adverse reactions in both groups [n(%)]

Groups	dizzy	Vomiting	diarrhoea	Fatigue	Urethral burning	Total adverse reactions
Combined treatment group (n=157)	3(1.91)	2(1.27)	3(1.91)	3(1.91)	2(1.27)	13(8.28)
Monotherapy group (n=78)	1(1.28)	1(1.28)	2(2.56)	1(1.28)	0(0)	5(6.41)
χ^2 value						0.258
P value						0.612

CONCLUSION

Qian Lie Shu Tong Jiao Nang has a superior therapeutic impact on BPH when taken with Finasteride tablets, which can inhibit the conversion of DHT, improve the patient's sex hormone level and strengthen the regulation of the level of inflammatory factors of the patient to alleviate the symptoms of the prostate gland of the body, reduce the volume of the prostate gland body, and improve the function of urination, with a high degree of safety.

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