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Multidimensional Treatment Strategies and Future Prospects of Benign Prostatic Hyperplasia

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Abstract. Objective: Benign prostatic hyperplasia (BPH) is a high-risk disease in elderly men, and its incidence continues to rise with aging. Traditional western medicine treatment has a bottleneck in efficacy and a risk of adverse reactions. This article systematically reviews the pathogenesis and clinical treatment of BPH, focusing on the combination of Chinese and Western medicine treatment strategies. Results: The pathogenesis is the imbalance of sex hormones and the abnormal activation of growth factors, which jointly drive the proliferation of prostate cells. In the treatment of western medicine, although α-receptor blockers can quickly improve symptoms, they can easily cause dizziness and hypotension. 5-α reductase inhibitors reduce prostate volume, but there are limitations such as insufficient short-term efficacy and increased nocturia. In terms of combined treatment of traditional Chinese and Western medicine, the clinical effective rate of Huang 'e capsule combined with tamsulosin/dutasteride increased to 68.13 %. Qianlie Shutong capsule combined with western medicine, can improve bladder function, which is better than single western medicine treatment. Conclusion: The combination of Chinese and Western medicine provides a new path for BPH to enhance efficacy and reduce toxicity. In the future, it is necessary to deeply analyze the targets of active components of traditional Chinese medicine (TCM) and establish a standardized joint program.

Keywords: Benign prostatic hyperplasia, hormonal imbalance, integrated Chinese and Western medicine therapy.

1. Introduction

Benign prostatic hyperplasia (BPH) is a kind of adenoma of the prostate, which can cause severe obstruction of the bladder outlet, block the prostate urethra, and ultimately cause great damage to the bladder and even the kidney [1]. Epidemiological studies have shown that BPH has become a high incidence of disease in elderly men around the world, and its incidence is significantly positively correlated with age. In the United States, 4.5 % of men over 30 years of age have BPH; in China, the prevalence rate of adult males over 40 years old can reach 36.6 %. This trend is synchronized with the aging process of the population, posing a serious challenge to the public health system [2]. Although BPH has been studied for decades, its etiology has not been fully elucidated. At present, aging and functional testis (maintaining androgen secretion) are considered to be necessary for the pathogenesis. The core mechanism involves the combined effects of sex hormone imbalance, such

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as dihydrotestosterone (DHT) accumulation, abnormal activation of growth factors, such as transforming growth factor-β (TGF-β), insulin-like growth factor (IGF-1), and chronic inflammatory microenvironment. At the therapeutic level, although traditional drugs such as anticholinergic drugs can alleviate the symptoms of urinary storage, long-term use may increase the risk of Alzheimer 's disease [3]. Nowadays, drug therapy is not limited to single drug therapy, and therapeutic drugs are not limited to traditional western medicine (TWM) treatment, such as α-receptor blockers and 5-α reductase inhibitors (5ARI). In terms of treatment methods, the treatment system of Chinese patent medicine combined with western medicine has gradually emerged, such as the combined application of Huang 'e capsule with tamsulosin hydrochloride and dutasteride. Relevant clinical data have proved that the indicators of BPH patients under this treatment system, including IPSS, prostate volume, sex hormone levels, etc., are better than single drug treatment. At the same time, Chinese patent medicine as an adjuvant therapy can effectively improve the life problems of BPH patients, such as frequent urination and urgency, so as to improve the personal life of patients [4]. This article aims to systematically review the pathogenesis of BPH, compare the efficacy and safety of traditional and emerging therapeutic drugs, and provide a theoretical basis for optimizing clinical practice and future research directions.

2. Symptoms and pathogenesis of BPH

At the cellular level, BPH is a significant change in the size and structure of the prostate caused by excessive proliferation of stromal cells, glandular cells and other cells [5]. However, histologically, the enlargement of the prostate in BPH patients is a product of cell proliferation, and the cell size has not changed [6]. At present, the imbalance of androgen / estrogen ratio is considered to be a key cause of BPH [7]. Among them, estrogen and androgen not only play a common role because of the imbalance of ratio, but their respective individual effects are also related to the occurrence of BPH: testosterone is transformed into dihydrotestosterone (DHT) through 5α-reductase, which binds to androgen receptor (AR) in prostate cells, activates downstream proliferation signaling pathways (such as IGF-1, FGF), and promotes matrix and epithelial cell proliferation [8]. Estrogen, mediated by estrogen receptor α (Erα), up-regulates TGF-β, IL-6 and other factors, drives the transformation of interstitial fibroblasts into myofibroblasts, thereby promoting adverse symptoms such as benign prostatic hyperplasia. There is also evidence that there is a correlation between BPH and higher serum estrogen levels or estrogen / androgen (E/T) ratios. In older men, estrogen is relatively stable due to a decrease in testosterone levels, resulting in an increase in E / T values, and this ratio is significantly positively correlated with prostate volume [9]. In addition, epidemiological data show that the risk of BPH is also significantly associated with a variety of lifestyle factors that can be intervened, including but not limited to smoking, drinking, and dietary structure [10].

3. Clinical treatment and molecular mechanism of BPH

The current clinical treatment of BPH is mainly western medicine. The specific mechanism of action of α-receptor blockers is to effectively relax the prostate and bladder neck smooth muscle by inhibiting sympathetic nerve activity. Compared with other drugs, this type of drug can produce better effects in a shorter time [11]. There are three specific types of drugs, including non-selective alpha antagonists, selective short-acting alpha 1 blockers, and long-acting selective alpha 1 blockers. The long-acting selective α1 blockers approved by the US Food and Drug Administration (FDA) include alfuzosin, doxazosin, tamsulosin, and terazosin, which can relieve symptoms, but the common adverse reaction is vertigo [12]. In addition, alfuzosin is prone to upper respiratory tract

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infection and dizziness and headache. Doxazosin can cause fatigue, hypotension, edema and other symptoms. Tamsulosin can increase the risk of ejaculation disorder and amblyopia, while terazosin is associated with postural hypotension and weakness [12]. Although the efficacy of these drugs is similar, long-term use has different risks.

5ARI mainly contains two drugs, finasteride and dutasteride. As the first BPH treatment drug approved by FDA, finasteride has two differences from dutasteride. One is that the effect of finasteride is slightly inferior to that of dutasteride. The other is that dutasteride acts by inhibiting type I and type II 5α reductase, while finasteride cannot act on type I [11]. Specifically, finasteride can reduce the size of the prostate by blocking the conversion of testosterone to dihydrotestosterone, thereby reducing the symptoms of BPH [13]. Studies have shown that finasteride can improve urodynamics well, so that the patient 's symptoms are greatly reduced. The results of clinical studies showed that 80 BPH patients aged 50 to 80 years old were treated with oral finasteride tablets (5 mg / d) for more than 5 years. The residual urine volume of bladder decreased from 33.9 ± 7.1 mL to 9.6 ± 6.3 mL, and the maximum urinary flow rate increased from 9.4 ± 3.1 mL / s to 13.4 ± 2.2 mL / s. The difference was statistically significant [14]. Nevertheless, experiments have shown that finasteride does not produce better therapeutic effects than placebo in a short period of treatment. In the same experiment, the incidence of adverse reactions such as dizziness was significantly reduced when finasteride was used alone compared with doxazosin or terazosin alone [13]. However, it is still necessary to pay attention to the occurrence of adverse reactions such as increased frequency of nocturia [14]. In general, the symptomatic effect of western medicine is limited, and the side effects suggest that new strategies need to be explored.

4. Chinese medicine treatment of BPH and Chinese medicine theory

From the perspective of traditional Chinese medicine (TCM) theory, the symptoms of BPH can be described as 'longbi ' (dysuria) and 'zhengjia ' (benign tumor) [15]. The theory of TCM believes that its core pathogenesis lies in kidney yang deficiency and blood stasis block. Therefore, the focus of TCM in the treatment of BPH is to adjust kidney Qi and promote blood circulation and remove blood stasis. At present, the integration of traditional Chinese and Western medicine treatment of BPH has obvious advantages, this view is gradually recognized [16]. Qianlie Shutong Capsule is a drug that can effectively treat BPH based on the principle of TCM. Its specific drug composition is 13 TCMs such as Phellodendri Chinensis Cortex, Paeoniae Radix Rubra and Angelicae Sinensis Radix. These 13 drugs all follow the rules of the use of TCM. Among them, Phellodendri Chinensis Cortex and Paeoniae Radix Rubra, as the most important monarch drugs, can effectively remove blood stasis in the body; as the ministerial medicine, Chuanxiong, Smilax glabra, Sparganium stoloniferum, Alisma orientalis, play a more biased role in eliminating dampness and heat; purslane, Verbena officinalis, Saxifraga stolonifera, Bupleuri Radix, Angelicae Sinensis Radix, Cyathulae Radix these six adjuvants, can effectively promote blood circulation, promote the monarch drug ministers play a better role; as the most commonly used TCM, licorice is used to reconcile various drugs and make the drug more peaceful [17]. In addition to the TCM theory, related modern medical experiments have proved that improving the bladder state is a significant mechanism of action of the drug [18]. In the experiment, Ren Junguo and Wang Jianye divided normal rats into five groups, in addition to the control group, including high (0.6 g / kg), medium (0.3 g / kg) and low (0.15 g / kg) doses of Qianlie Shutong Capsule group and Terazosin Hydrochloride (0.2 mg / kg) group. After administration of the five groups, the physiological saline was instilled into the bladder to observe the specific data such as bladder pressure and capacity. The experimental results showed that the increase of bladder volume in each dose group of Qianlieshutong was equivalent to that of terazosin,

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suggesting its effectiveness [18]. Huang 'e capsule is also a kind of Chinese patent medicine based on the principle of TCM, and the treatment basis of this drug in the theory of TCM is as a kind of Qi-tonifying and blood-activating drug to solve the problem of blood stasis block in patients. Among them, there are two kinds of monarch drugs that play the most important role, namely astragalus, which have the effect of benefiting Qi; peach kernel can effectively remove stasis and promote blood circulation. From the analysis of modern clinical data, it can also be seen that Huang 'e capsule can play a certain role. In the relevant experiments designed by Cheng Wei, after obtaining the consent of the patients, 100 patients were divided into two groups. The treatment group added Huang 'e capsule as part of the treatment system on the basis of the experimental group using tamsulosin and dutasteride. In the final results, whether it is the patient 's psychological state, physiological state, or patient satisfaction, the relevant scores of the treatment group using Huang 'e capsule are all better than the control group using only western medicine [4].

Network meta-analysis showed that the combination of Chinese and Western medicine, such as Huang 'e capsule combined with Western medicine, was superior to single treatment in controlling prostate volume, improving international prostate symptom score (IPSS) and maximum urinary flow rate [19]. In this study, the researchers were divided into experimental group and control group, both of which were selected from patients identified as BPH. The experimental group was the combination of TCM and western medicine without other treatment methods, while the control group included patients who only used western medicine and patients who added other treatment methods on the basis of the experimental group. The main results of related research, that is, the comparative data of clinical effective rate display, show that the improvement of most experimental groups is significantly better than that of the control group using only western medicine. For example, the clinically effective rate of Huang 'e capsule combined treatment is as high as 68.13 %, and the data of the control group is only 1.57 %. This improvement has also occurred in all of the above-mentioned areas [19]. In related clinical trials, Shenqi Pills combined with western medicine also significantly improved lower urinary tract symptoms (LUTS), especially in dysuria and incomplete emptying symptoms [20]. In the combined use of Qianlieshutong capsule and western medicine, the experimental data show that the combined use of Qianlieshutong capsule and tamsulosin can significantly improve the symptoms of BPH patients. In the experiment designed by Zhang Fan, 116 BPH patients were randomly divided into an observation group and an experimental group. The observation time of the two groups was 3 months. During this period, each patient took one tamsulosin hydrochloride sustained-release capsule every day. On this basis, the observation group took 9 more Qianlieshutong capsules every day, which were taken three times. After the completion of the experiment, the relevant data including IPSS and TCM syndrome scores were compared. The final experimental results showed that the observation group was superior to the control group in clinical treatment results. Although the combination of Chinese and Western medicine is superior in efficacy, long-term safety still needs further study.

5. Conclusion

This article systematically expounds the pathogenesis and clinical treatment progress of BPH. At the mechanism level, factors such as sex hormone imbalance and abnormal activation of growth factors promote the proliferation of prostate matrix and epithelial cells. In terms of treatment, TWMs such as α-blockers can quickly relieve symptoms but are accompanied by adverse reactions such as vertigo and hypotension. 5ARI can reduce the prostate volume, but the short-term effect is limited and may increase the frequency of nocturia. The combined treatment of traditional Chinese and western medicine showed significant advantages. Qianlie Shutong Capsule improved bladder

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function by promoting blood circulation and removing blood stasis. Huang 'e Capsule combined with western medicine significantly improved clinical efficiency, and the effect was better than that of single western medicine treatment. The significance of this paper is to provide a key theoretical basis for the clinical practice of BPH. Firstly, it verifies the core role of hormone imbalance and points out the direction for the development of targeted drugs. Second, it is confirmed that the combination of Chinese and Western medicine can improve the efficacy of TWM and reduce side effects. However, there are still limitations in the current study: the molecular mechanism of multi-component action of TCM compound has not been fully elucidated, and the long-term safety data of combined treatment still need to be verified by large sample follow-up. Future research can focus on three aspects: first, to further explore the specific targets of active components of TCM and promote drug optimization; the second is to establish a standardized scheme for the combination of Chinese and Western medicine; the third is to explore the association mechanism between BPH and lifestyle, and provide new strategies for prevention.

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