Use of PR-2000, a Herbal Formulation in the Medical Management of Benign Prostatic Hyperplasia

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ABSTRACT

Benign prostatic hyperplasia (BPH) is one of the most common processes affecting elderly men. This study was undertaken to evaluate the efficacy of PR-2000, an herbal preparation in the treatment of patients with benign prostatic hyperplasia. The trial included 68 patients who were diagnosed with BPH and graded accordingly using the American Urological Association (AUA) symptom score, uroflowmetric study and pelvic ultrasonography to determine the sonographic size of prostate. PR-2000 was administered orally at a dose of 2 tablets thrice daily for six months. All the patients were periodically evaluated for the entire study period. Following six months of treatment, the patients showed encouraging improvement in the AUA score along with an increase in peak flow rate and a subsequent decrease in sonographic size of prostate. The average AUA score showed an improvement from an initial 21.6 to 11.46 at the end of 6 months. Uroflowmetry measured at the first month showed an average of 10.6 ml/sec and increased to an average of 15.06 by the end of six months. Pelvic ultrasonography revealed that the average size of prostate decreased from 33.30g at the first month to 26.11g by 6 months. No change in biochemical markers were observed and no untoward side effects were noticed during the trial. The results conclude that PR-2000 is an effective, safe, and well-tolerated therapy in the treatment of BPH.

INTRODUCTION

The term benign prostatic hyperplasia (BPH) has very different connotations for the pathologist, radiologist, urodynamicist, urologist and patient. BPH to the pathologist is a microscopic diagnosis characterized by cellular proliferation of the stromal and epithelial elements of the prostate. The radiologist makes the diagnosis of BPH in the presence of bladder base elevation on the cystogram phase of the intravenous pyelogram, or an enlarged prostate on diagnostic imaging studies of the male pelvis. The hallmark of BPH to the urodynamicist is the synchronous observation of elevated voiding pressure and a low urinary flow rate in the absence of other disease processes that cause bladder outlet obstruction. To the practicing urologist, BPH represents a constellation of signs and symptoms that develop in the male population in association with aging and prostatic enlargement presumably due to bladder outlet obstruction. The patient is typically concerned about the impact of BPH on quality of life rather than the presence of cellular proliferation, prostatic enlargement or elevated voiding pressures.
The symptoms associated with BPH are common and increase frequency with age\(^1\). The incidence of BPH can be as high as 50% by the age of 60, and 90% by the age of 85 years\(^2\). It is estimated that in men 80 years old or older, 90% show histologic evidence of the condition, 81% have BPH-related symptoms and 10% suffer urinary retention\(^3\).

Although BPH is one of the most common disease processes affecting the aging male, surprisingly little is known about its etiology and pathophysiology. Despite intense research efforts in the last three decades to elucidate the underlying aetiology of prostatic growth in older men, cause and effect relationships have not been established\(^4\).

Due to the intimate anatomic relationship between the prostate, urethra, and bladder neck, any enlargement of the prostate can cause some degree of outflow urinary obstruction. This phenomenon can produce obstructive voiding symptoms and potentially lead to significant bladder and kidney pathology, ultimately causing impairment in renal function. All forms of treatment are aimed to prevent this impairment from occurring. The late-stage complications of chronic retention caused by BPH include hydrourere ter, hydronephrosis and renal failure, which are rare\(^5\).

The standard line of treatment for BPH is surgery, however, the expense and complications associated with surgical treatment for BPH have led to a search for safe and effective medical therapies\(^6\).

Until recently, prostatectomy and watchful waiting were the widely accepted options to treat BPH. However, recent studies have reported that 5α-reductase inhibitors are effective in reducing the size of prostate, however these patients have to bear with long-term side effects such as ejaculation disorders, loss of libido and impotence\(^7\).

More selective and long-acting α1-adrenoceptor antagonists have also produced statistically and clinically significant improvements in signs and symptoms of BPH, however, these are also associated with side effects such as dizziness, asthenia, peripheral oedema, postural hypotension, somnolence and syncope\(^8\).

In view of the limitations of 5 α-reductase and α1-adrenoceptor antagonists, naturally occurring plant extracts have come into the forefront of research to treat various disorders of the prostate\(^9\).

In this study, the effect of PR-2000, a herbal compound containing various plant extracts was used to evaluate the efficacy in the treatment of patients with BPH.

**MATERIAL AND METHODS**
Sixty eight patients diagnosed with symptomatic BPH were selected in the study after a thorough physical examination at the Urology Department of Shri Sayaji General Hospital, Vadodara, India. Majority of the patients were between 50-60 years of age with symptoms varying from mild thinning of the urine stream to dysuria, urgency, hesitancy, pain, discomfort and heaviness in the groin. Grossly debilitated patients and patients with renal failure and major cardiovascular and respiratory disorders were excluded from the trial.
PR-2000 was administered at a dose of 2 tablets, 3 times daily for 6 months. The assessment and follow-up analysis was done on a regular basis by taking the history, along with regular assessment of AUA symptom score, digital rectal examination, pelvic ultrasonography of the prostate and uroflowmetry. Research studies often refer to the current standard for symptom evaluation, the AUA symptom score. This tool rates 7 symptoms from 0-5, yielding a combined score of 0-35. The patient answers 7 questions related to common symptoms of BPH listed in the AUA symptom score questionnaire. How frequently the patient experiences each symptom is rated on a scale of 1-5. These numbers added together provide a score that is used to evaluate the condition. Scores from 0 to 7 are considered "mild", 8 to 20 "moderate", and 21 to 35 "severe". Uroflowmetry determines the bladder obstruction, an important indication of abnormal urinary symptoms. The speed of urine flow is measured electronically. The flow rate is calculated as milliliters of urine passed per second. The peak flow rate is generally used as the basis to determine the severity of obstruction and also used as an objective standard to judge the success of treatment, although it does not necessarily coincide with a patient's perceptions of the severity of his own symptoms.

AUA scoring and peak urinary flow by uroflowmetry were evaluated and recorded at the beginning of the trial, at three months, and at the end of the trial. Abdominal pelvic ultrasonography was done before and after completing the study to estimate the approximate prostate weight and size.

RESULTS AND ANALYSIS
All the patients were analysed at regular intervals during the six-month trial period involving treatment with PR-2000. Almost all the patients began to show symptomatic relief by the end of 3 months. Further improvement in parameters was evident by the end of 6 months with a significant alleviation in symptoms. Results revealed a significant improvement in the AUA score from an average of 21.6 in the first month to an average of 16.9 in the third month, and a further improvement in the score at the end of 6 months when it was recorded at 11.6 (Table 1). In 28 patients, burning micturition was completely relieved following 1 month of therapy. The flow rate showed better results in severe cases of enlargement of prostate and it also showed that long-term treatment increased the response rate. Uroflowmetry at the first month showed an average of 10.6ml/sec, increasing to 13.5ml/sec by the third month and an average of 15.06ml/sec by the end of the sixth month of the trial (Table 2). In addition to the above findings, there was also a comparatively marked decrease in the size of prostate after 6 months of treatment with PR-2000. Pelvic ultrasonography done at the first month showed the average size of the prostate to be 33.30g and decreased to an average size of 26.11g by the end of six months (Table 3). No gross change in biochemical markers were observed and no untoward side effects were noticed during the trial.

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<th>Table 1: Average improvement of AUA score</th>
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<td>First month</td>
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<td>21.60</td>
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AUA Score: Mild <7; Moderate 8-20 and Severe >21-35

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<th>Table 2: Average improvement in peak flow rate</th>
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<td>First month (ml/sec)</td>
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<td>10.60</td>
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<th>Table 3: Average size of prostate (ultrasonography)</th>
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<td>First month (g)</td>
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<td>33.30</td>
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DISCUSSION

Benign prostatic hyperplasia is a common condition among older men, causing morbidity primarily through lower urinary tract symptoms. The primary physician should attempt to distinguish BPH from the other causes of such symptoms, objectively determine symptom severity, and, when the symptoms are bothersome enough, design a therapeutic approach that offers symptomatic improvement. The constellation of cellular pathologies that give rise to the symptoms of BPH are far more complex than we realise. The treatment of BPH has changed substantially in recent years, with increasing emphasis on non-surgical approaches. For patients who elect a course of "watchful waiting" or medical therapy, a strategy of regular follow-up visits should be instituted to monitor for symptom changes or BPH complications. Improvement in urinary symptoms and the quality of life are important issues for decision-making in the treatment of patients with BPH. The clinically relevant end-points of therapy have been to decrease bladder outlet obstruction, thereby relieving symptoms, improving bladder emptying, reversing renal insufficiency, and preventing future episodes of urinary tract infection and urinary retention.

The main constituents of PR-2000 are Tribulus terrestris, Caesalpinia bonducella, Asparagus racemosus, Areca catechu, and Crataeva nurvala. Tribulus terrestris has analgesic, antibacterial, diuretic and smooth muscle relaxant properties. The diuretic, analgesic and antibacterial properties found in Tribulus terrestris are utilised and found beneficial in treating the symptoms of prostatic enlargement such as haematuria, painful micturition and dysuria\textsuperscript{11,12}.

Caesalpinia bonducella, which acts as an anti-inflammatory, also has urinary antiseptic and diuretic properties.

Asparagus racemosus, which is a potent diuretic and antispasmodic also has an immunomodulatory effect on the prostate\textsuperscript{13}.

Areca catechu possesses anti-microbial properties and is useful in the treatment of urinary disorders\textsuperscript{14}.

Crataeva nurvala is useful in the treatment of urinary disorders caused by enlarged prostate. It has anti-inflammatory, diuretic, lithontriptic, demulcent and tonic properties useful in disorders of urinary organs, urinary tract infections, pain and burning micturition.

Almost all the patients began to show symptomatic relief by the third month of treatment with PR-2000. Further improvement in all the parameters was evident by the end of 6 months along with a noticeable alleviation in symptoms. The data from the study coincided with the findings and indicated that the effect of drug depended on the duration of therapy with PR-2000. Most of the patients graded as “severe” according to the AUA symptom score, may however require longer duration of therapy with PR-2000. The AUA symptom index is a self-assessment test that is used to rank the severity of symptoms. The score on this test gives a highly accurate assessment of the effect on the quality of life and a reasonable basis from which the physician can discuss treatment options. The index is also often used to gauge treatment outcomes and maybe a better indicator than objective tests. Thus, AUA symptom index is useful only as a gauge of symptom severity and is not used as a diagnostic tool for benign prostatic hyperplasia.
It was also noticed that there was better response in those patients who had a more advanced form of BPH. Further improvement of the disease beyond six months of therapy however was not evaluated under the current study.

From the above results it can be stated that PR-2000 is a very effective mode of conservative therapy in patients suffering from benign prostatic hyperplasia. The study also demonstrated that in patients with symptomatic BPH, treatment with PR-2000 is safe since there were no adverse effects.

REFERENCES