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Survey of urologists over the management of benign prostatic hyperplasia in India

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ABSTRACT

Background: The benign enlargement of the prostate gland is known as benign prostatic hyperplasia (BPH). It refers to stromal and glandular epithelial hyperplasia that develops in the region of the prostate that surrounds the urethra known as the periurethral transition zone. **Aims and Objectives:** The aim of the study was to perform a survey of urologists over the management of BPH in India. **Materials and Methods:** A survey questionnaire was e-mailed to a random sample of 57 urologists of India through surveymonkey.com. The enrolled questionnaires were statistically analyzed. Of the 57 questionnaires sent, nine were returned, and 48 of those were included in the final analysis (response rate of 84.21%). **Results:** Majority of urologists' opinion is that USG-KUB with uroflowmetry is the most reliable investigation for diagnosis of BPH. Tamsulosin (tamsulosin 0.4 mg) was the most preferred α-1 selective blocker drug in BPH patients across all the age groups, whereas silodosin was the most preferred α-1 selective blocker drug in cardiac patients having BPH. The preferred 5-alpha reductase inhibiting drug and dose was recorded as dutasteride 0.5 mg/day. Solifenacin is the preferred anti-cholinergic drug for urinary urgency and incontinence. The IPSS score of the patient improved usually within 1–6 weeks of treatment with alpha blockers/5-alpha reductase inhibitor. As per Indian urologists, the drug therapy with alpha blockers gave the fastest symptomatic improvement in BPH patients. **Conclusion:** In our conclusion, there is no uniformity in the treatment of acute urinary retention; however, the overall care must be individualized for the patient. Lack of understanding of the population's history of BPH hinders advancement in appropriate care.

Key words: Benign prostatic hyperplasia; Questionnaire; Urologists

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INTRODUCTION

The non-cancerous enlargement of the prostate gland is known as benign prostatic hyperplasia (BPH). It refers to stromal and glandular epithelial hyperplasia that develops in the prostate's periurethral transition zone, which encircles the urethra. Lower urinary tract symptoms (LUTSs) caused by irritable (urgency, frequency, and nocturia) and obstructive symptoms are a clinical manifestation of BPH (hesitancy, a weak and interrupted urinary stream, straining to initiate urination, a sensation of incomplete bladder emptying).[1] Prolonged blockages may eventually result in renal insufficiency, hematuria, bladder calculi, acute urine retention, and recurrent urinary tract infection.[2] As people get older, LUTS caused by BPH are more common. After the ages of 60 and 80, respectively, 40% and 80% of men experience moderate-to-severe symptoms. By the age of 90, microscopic BPH affects almost all males.[3] It is also referred to as a quality-of-life disorder that makes it difficult for a man to start or stop the flow of urine (the symptoms interfere with daily activities) and lowers his sense of well-being. Although the exact origins of BPH are unknown, a number of factors, including ageing, late cell growth activation, genetics, and hormone changes,

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have been linked to the enlargement of smooth muscle and glandular epithelial tissue.[4,5]

It is unclear exactly how BPH and urologic malignancies are related. According to several research, hormones, inflammation, and metabolic syndrome may all be factors in BPH and prostate cancer.[6] One explanation for the relationship between bladder cancer and BPH is that people with BPH may have reduced urinary tract damage because to the leftover urine in their bladders, and that BPH may lengthen that the amount of time their urothelium is exposed to urinary discharged carcinogens.[7]

Prostate cancer, one of the most prevalent malignancies globally and the leading cause of cancer death for men in developed nations, has been the subject of numerous epidemiological studies that have examined the relationship between BPH and this disease.[8] Similar studies examining the likelihood of bladder cancer in BPH patients also produced mixed results.[9-12] The data linking BPH to an increased risk of urologic malignancies besides prostate and bladder cancer is weak and is rarely properly addressed. Investigation of their relationship is very important for both clinical and public health reasons, given the high frequency of both BPH and urologic malignancies. Understanding this connection would help doctors adopt common preventative measures for BPH and urologic malignancies, enhance the efficacy of cancer screening, and possibly cure cancer at an earlier stage.[13] As far as we know, our topic has not been the subject of a systematic review.

Aims and objectives

The aim of this study was to perform a survey of urologists over the management of BPH in India.

MATERIALS AND METHODS

A survey questionnaire was e-mailed to a random sample of 57 urologists of India through surveymonkey.com. Selected physicians received an e-mail which consisted of a cover letter describing the purpose of the survey, non-disclosure of identity clause, and the survey itself. The letter indicated that our department was conducting a study on practice patterns in the treatment of BPH in Indian scenario. Patient-related data from the urologists were collected and archived by surveymonkey.com. Of the 57 questionnaires sent, nine were returned, and 48 of those were included in the final analysis (response rate of 84.21%).

Statistical analysis

Statistical analysis was achieved using the SPSS statistical software, version 20.0. Independent samples Student's t-test and Pearson's correlation analysis for the assessment of mean differences between patients and control groups were performed with considered $P<0.05$ to be significant.

RESULTS

Maximum BPH patient visits to the study urologists per month were within the range of 1–25 (16 response), which is followed by 26–50 (14 response) and 51–75 (10 response). The least BPH patient visit to the study urologists per month is within the range of 76–100 (only 8 responses). Hence, an average of around 11.75 BPH patients per month can considered a general figure for BPH patient visit to the study urologists per month. Obstructive complaints (58.33%) were the most common reason for patient visits to urologist followed by increased urine frequency (35.41%). According to the study urologists, the most reliable investigation for diagnosis of BPH was USG-KUB+Uroflowmetry (79.17%) (Table 1).

According to the study urologists, the most preferred α-1 selective blocker drug in BPH patients of <60 years age and >60 years age was tamsulosin, whereas the most preferred α-1 selective blocker drug in cardiac patients having BPH was silodosin. Tamsulosin at 0.4 mg was rated as the preferred dose to prescribe adjoining α-1 selective blocker drugs in BPH patients. This was followed by silodosin 8 mg and alfuzosin 10 mg (Table 2).

The most common adverse drug reaction (ADR) associated with the drug alfuzosin, tamsulosin, silodosin, and 5-alpha reductase inhibiting drugs was recorded as dizziness (39.58%), retrograde ejaculation (39.58%), retrograde ejaculation (50%), and loss of libido (43.75%), respectively. The most preferred 5-alpha reductase inhibiting drug and dose was dutasteride 0.5 mg/day (72.92%). According to the study urologists, the prostate size is >30 g and patients not having improvement using monotherapy were the major indication for putting them directly on fixed-dose combination (FDC) of alpha 1-selective blockers and 5-alpha reductase inhibitors. Monotherapy with alpha blocker and FDC therapy of alpha blocker and 5-ARI is the conservative treatment pattern preferred by study urologists to start in their patients having prostate size <30 and >30 g, respectively (Table 3).

Solifenacin is the preferred (54.16%) anti-cholinergic drug for urinary urgency and incontinence, whereas the preferred FDC for BPH patients and patients of BPH having irritable bladder symptoms is Dutasteride+Tamsulosin

Table 1: Baseline information regarding the management of BPH

Parameters	Questionnaire choices	Number of responses (n=48)	Percentage
Number of patients suffering from BPH treated per month	1–25	16	33.33
	26–50	14	29.16
	51–75	10	20.83
	76–100	8	16.66
The most common reason for which patient come to you for treatment	Obstructive complaints	28	58.33
	Increased urine frequency	17	35.41
	Lower abdominal discomfort	1	2.08
	Urinary tract infection	2	4.16
The most reliable investigation for diagnosis of BPH	PSA	2	4.16
	USG- KUB	6	12.5
	Uroflowmetry	2	4.17
	USG-KUB+Uroflowmetry	38	79.17

BPH: Benign prostatic hyperplasia, PSA: Prostate-specific antigen

Table 2: Preference of study urologists toward drug management of BPH

Parameters	Questionnaire choices	Number of responses (n=48)	Percentage
The most preferred α-1 selective blocker drug in BPH patients of <60 years age	Doxazosin	0	0
	Alfuzosin	19	39.58
	Tamsulosin	25	52.08
	Silodosin	4	8.33
The most preferred α-1 selective blocker drug in BPH patients of >60 years age	Doxazosin	0	0
	Alfuzosin	7	14.58
	Tamsulosin	22	45.83
	Silodosin	19	39.58
The most preferred α-1 selective blocker drug in cardiac patients having BPH	Doxazosin	4	8.33
	Alfuzosin	6	12.5
	Tamsulosin	14	29.16
	Silodosin	24	50
Preferred dose to prescribe adjoining α-1 selective blocker drugs in BPH patients (drug dose in mg) (n=48)	Doxazosin 1 mg	0	0
	Doxazosin 2 mg	0	0
	Doxazosin 4 mg	3	6.25
	Doxazosin – not prescribed	9	18.75
	Alfuzosin 5 mg	3	6.25
	Alfuzosin 10 mg	21	43.75
	Tamsulosin 0.2 mg	2	4.17
	Tamsulosin 0.4 mg	41	85.42
	Tamsulosin 0.8 mg	1	2.08
	Silodosin 4 mg	7	14.58
	Silodosin 8 mg	28	58.33

BPH: Benign prostatic hyperplasia

(56.25%) and Solifenacin+Tamsulosin (62.5%), respectively (Table 4).

Tadalafil was the preferred PDE inhibitor for patients experiencing erectile dysfunction. The maximum entries (54.16%) were recorded for 1–6 weeks for patient's treatment with alpha blockers/5-alpha reductase inhibitors, the IPSS score of the patient improves usually. Alpha blockers gave the fastest symptomatic improvement in BPH patients. Study urologists believed that around 1–25% of their patients were non-compliant with the medical treatment due to financial issues. Study urologists recorded that in around 1–25% of their patients, surgery is required because of failure of conservative treatment. Several study urologists believe that the estimated cost of drug/drugs for BPH given per day was 10–25 INR. Study urologists suggested that the duration of medical management before you advise them surgery was less than 6 months. Finally, according to the opinion of the study urologists, the drug therapy plus surgery was the most cost-effective strategy for BPH patients (Table 5).

DISCUSSION

The biological basis for androgen ablation therapy is the discovery that androgen dihydrotestosterone is necessary for the prostate's embryonic development (DHT). In addition, prostatic hypertrophy regressed among individuals who had been castrated before to reaching puberty.[14] The prostatic volume decrease brought on by androgen deprivation is thought to lessen the static component

Table 3: Opinion of urologists toward adverse drug reaction profile for BPH patients

Parameters	Questionnaire choices	Number of responses (n=48)	Percentage
The most common ADR associated with the drug alfuzosin	Dizziness	19	39.58
	Postural hypotension	13	27.08
	Retrograde ejaculation	11	22.92
	Psychosexual distress	5	10.42
The most common ADR associated with the drug tamsulosin	Dizziness	12	25
	Postural hypotension	15	31.25
	Retrograde ejaculation	19	39.58
	Psychosexual distress	2	4.16
The most common ADR associated with the drug silodosin	Dizziness	13	27.08
	Postural hypotension	2	4.17
	Retrograde ejaculation	24	50
	Psychosexual distress	9	18.75
The most common ADR occurring in patients receiving 5-alpha reductase inhibiting drugs	Loss of libido	21	43.75
	Erectile dysfunction	15	31.25
	Decreased volume of ejaculation	6	12.5
	Gynecomastia	6	12.5
The most preferred 5-alpha reductase inhibiting drug and dose	Finasteride 5 mg/day	9	18.75
	Finasteride 10 mg/day	0	0
	Dutasteride 0.5 mg/day	35	72.92
	Dutasteride 1.0 mg/day	4	8.33
What is the major indication for putting them directly on FDC of alpha 1-selective blockers and 5-alpha reductase inhibitors	Prostate size is >30 g	19	39.58
	International Prostate Symptom Score (IPSS) >8	5	10.42
	Patient refusing surgery	5	10.42
	Patients not having improvement using monotherapy	19	39.58
Which conservative treatment pattern do you prefer to start in your patients having prostate size <30 g?	Monotherapy with alpha blocker	40	83.33
	Monotherapy with 5-alpha reductase inhibitor	2	4.16
	Fixed-dose combination therapy of alpha blocker and 5-ARI	3	6.25
	Alpha blocker monotherapy before adding 5-ARI	3	6.25
Which conservative treatment pattern do you prefer to start in your patients having prostate size >30 g?	Monotherapy with alpha blocker	8	16.66
	Monotherapy with 5-alpha reductase inhibitor	3	6.25
	Fixed-dose combination therapy of alpha blocker and 5-ARI	31	64.58
	Alpha blocker monotherapy before adding 5-ARI	6	12.5

FDC: Fixed-dose combination, ADR: Adverse drug reaction, BPH: Benign prostatic hyperplasia

Table 4: Opinion of urologists toward fixed-dose combination in BPH patients

Parameters	Questionnaire choices	Number of responses (n=48)	Percentage
For urinary urgency and incontinence, which of the below mentioned anti-cholinergic drug do you prefer to prescribe?	Solifenacin	26	54.16
	Darifenacin	9	18.75
	Tolterodine	5	10.41
	Flavoxate	8	16.66
Which FDC would you prefer in BPH patients?	Finasteride+Tamsulosin	9	18.75
	Dutasteride+Tamsulosin	27	56.25
	Dutasteride+Silodosin	12	25
	Solifenacin+Tamsulosin	0	0
Which FDC would you prefer in patients of BPH having irritable bladder symptoms?	Finasteride+Tamsulosin	2	4.16
	Dutasteride+Tamsulosin	8	16.66
	Dutasteride+Silodosin	8	16.66
	Solifenacin+Tamsulosin	30	62.5

FDC: Fixed-dose combination, BPH: Benign prostatic hyperplasia

of BPH.[15] By suppressing the release of luteinizing hormone, progestational drugs (hydroxyprogesterone acetate and megesterone) can lower serum testosterone levels, resulting in reversible androgen deprivation.[16,17]

Table 5: Patient and BPH management profile

Parameters	Questionnaire choices	Number of responses (n=48)	Percentage
In your patients, if erectile dysfunction occurs, which PDE inhibitor do you prefer to prescribe?	Sildenafil	15	31.25
	Tadalafil	33	68.75
In your patients, after how many weeks of treatment with the above drugs (alpha blockers/5-alpha reductase inhibitors) the IPSS score of the patient improves usually?	1–6 weeks	26	54.16
	7–12 weeks	17	35.42
	13–24 weeks	3	6.25
	>24 weeks	2	4.16
As per your opinion the drug therapy giving fastest symptomatic improvement in BPH patients is?	Alpha blockers	28	58.33
	5-ARI	0	0
	Combination of 5-ARI and alpha blocker	20	41.66
	Anticholinergic	0	0
How many of your patients were non-compliant with the medical treatment?	1–25%	30	62.5
	26–50%	15	31.25
	51–75%	3	6.25
	>75%	0	0
In your patients what is the most common reason for non-compliance to medical treatment?	Adverse drug reactions	8	16.66
	Drug interactions	0	0
	Ineffectiveness	17	35.42
	Financial issues	23	47.92
In what percentage of your patients, surgery is required because of failure of conservative treatment?	1–25%	26	54.16
	26–50%	20	41.66
	51–75%	2	4.16
	76–100%	0	0
In your patients, what is the estimated cost of drug/drugs for BPH given per day?	<10 INR	8	16.66
	10–25 INR	20	41.66
	25–50 INR	16	33.33
	50–100 INR	4	8.33
In your patients, what is the duration of medical management before you advise them surgery?	<6 months	21	43.75
	6–12 months	20	41.66
	12–18 months	2	4.16
	>18 months	5	10.41
In your opinion what is the most cost-effective strategy for BPH patients?	Drug therapy alone	7	14.58
	Drug therapy plus minimal invasive procedure	10	20.83
	Surgery alone	11	22.92
	Drug therapy plus surgery	20	41.67

BPH: Benign prostatic hyperplasia

A well-established method for treating BPH involves blocking gonadotropin release from the anterior pituitary gland using agonistic gonadotropin-releasing hormone (GnRH) analogs (nafarelin acetate and leuprolide), which desensitizes and downregulates the pituitary GnRH receptor.[18-20] In addition, antiandrogens such as cyproterone acetate and flutamide, which are used therapeutically for BPH, competitively reduce the ligand DHT binding to the androgen receptor.[21,22] Multiple lines of evidence point to the involvement of estrogen and androgen in BPH. Men primarily create estrogens through the peripheral conversion of testicular and adrenal androgen into estradiol through aromatase activity. The estrogenic effect probably comprises its stromal and epithelial interaction, which controls the prostate's proliferative activity and changes the prostate's sensitivity to androgens.[23] The pharmaceutical therapy of BPH uses aromatase inhibitors such as atorvastatin and abiraterone that prevent the peripheral conversion.[24,25] Although androgen deprivation therapy has been shown to be an effective treatment, its usage has been constrained due to its potential side effects, including erectile dysfunction and libido loss.[26,27]

BPH has a complex and poorly understood molecular etiology.[28] There have been some recognized potential risk factors for BPH development. Age, genetics, hormones, growth factors, inflammation, and lifestyle factors are some of these.[29] BPH is initially diagnosed with a digital rectal exam, urine test, blood test, and a blood test for prostate-specific antigen. Urologists may advise transrectal ultrasonography, prostate biopsy, urodynamic and pressure flow investigations, or cystoscopy in cases of difficult

conditions and the use of alpha blockers, 5-alpha reductase inhibitors, and combination medication therapy in the treatment of BPH.[30]

In this survey, the most common reason for which patient came to the urologist was for the treatment of obstructive complaints. Majority of urologist's opine that USG-KUB with uroflowmetry is the most reliable investigation for diagnosis of BPH. Tamsulosin (tamsulosin 0.4 mg) was the most preferred α-1 selective blocker drug in BPH patients across all the age groups, whereas silodosin was the most preferred α-1 selective blocker drug in cardiac patients having BPH. These observations are in consistent with the survey of Ku et al., among the Korean urologists.[31]

Recently, Gustafsson et al.,[32] also reported that dizziness was the most common ADR associated with the drug alfuzosin, which is in line with the result obtained from our survey. According to the observations of our survey, Imperatore et al.,[33] found that retrograde ejaculation was the most common ADR associated with the drug tamsulosin and silodosin. Loss of libido was the most common recorded ADR in patients receiving 5-alpha reductase inhibiting drugs. Whereas Hay-Smith et al.,[34] have also suggested that solifenacin is the preferred anticholinergic drug for urinary urgency and incontinence.

According to Emberton et al.,[35] surgical intervention is generally considered to be the endpoint for BPH. In the present survey, study urologists recorded that in around 1–25% of their patients, surgery is required because of failure of conservative treatment. Several study urologists believe that the estimated cost of drug/drugs for BPH given per day was 10–25 INR. Study urologists suggested that the duration of medical management before you advise them surgery was <6 months. The findings are consistent with a prospective, cross-sectional survey carried out by Fitzpatrick et al.,[36] in public and private urology offices in France, Asia, Latin America, Algeria, and the Middle East.

Numerous guidelines exist in the therapeutic fields, which causes a great deal of variation in the suggestions they offer. In addition, some standards do not adequately address the problem of BPH therapy.[37-39] Additional detail is required in this clinical field, and future versions of BPH management guidance should aim to resolve this problem more effectively.

Limitations of the study

There are some possible drawbacks to our analysis that should be taken into consideration. First, our results need to be carefully viewed because our data on the practice habits of urologists are focused on self-reported actions, not real behavior as assessed by audit. Second, the response to the survey was just around 84.21%. Non-response would inevitably lead to some random sampling error rising beyond what would be predicted if most of the questionnaires were returned.

CONCLUSION

Our data provide a description of current practice by urologists in India concerning the management of BPH. There is no uniformity in the treatment of acute urinary retention; however, the overall care must be individualized for the patient. Lack of understanding of the population's history of BPH hinders advancement in appropriate care. Further details on BPH care can continue to advance the feasibility of BPH therapy.

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