EVALUUATION OF ERECTILE DYSFUNCTION AND RETROGRADE EJACULATION IN PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA RECEIVING COMBINED DRUG THERAPY

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ABSTRACT

Objective: To determine the frequency of erectile dysfunction and retrograde ejaculation in patients with benign prostatic hyperplasia (BPH) receiving combined pharmacotherapy with dutasteride and tamsulosin

Methodology: This cross sectional study was conducted on 205 patients enrolled from outpatient department (OPD) of Institute of Kidney Diseases (IKD) Peshawar from September 2017 to March 2018. The International Prostate Symptom Scores (IPSS) score and ultrasound were used to select patients of BPH suitable for medical management rather than surgery. The International Index Erectile Function scoring (IIEFS) was used to measure erectile dysfunction, prior to and after treatment with dutasteride and tamsulosin. Retrograde ejaculation was recorded from history after two months follow-up.

Results: The mean age was 60 years with SD ± 2.16. IIEF score for all patients was ≥ 25, which reflected normal erectile function prior to treatment. But after 2 months of follow up 17% patients had IIEF score < 11 (severe dysfunction) and 83% patients had IIEF score ≥ 22 (mild to moderate dysfunction). Thirty seven (37%) patients had retrograde ejaculation.

Conclusion: Retrograde ejaculation and erectile dysfunction are important adverse effects of combined drug regimen for the treatment of symptoms of benign prostatic hyperplasia.

Key Words: Erectile dysfunction, Dutasteride and tamsulosin, Retrograde ejaculation, Benign prostatic hyperplasi, International Index of erectile function (IIEF), international prostatic symptoms score (IPSS).

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INTRODUCTION

Lower urinary tract symptoms (LUTs) are one of the most common complaints in men above 50 years of xage[1]. Benign prostatic hyperplasia (BPH) is the common cause leading to LUTs and affects quality of life[2]. By the age of 85 years, 90% of men have histologically evident BPH[3]. Current estimates suggest that the number of people of 80 years of age or older in the United States will increase from 3.9 million in 2000 to 19.5 million in 2030, an increase of over 100%[4].

The incidence of BPH is similar in white and African-American men[5], but BPH is more progressive and severe in African-Americans. This is because of higher testosterone levels, androgen receptor expression,[5]-alpha reductase activity and growth factor presentation in this people[6]. The enlargement of prostate is restricted by the capsule around it which ultimately results in the compression of urethra. However, obstruction-induced bladder dysfunction contributes significantly to LUTS[7, 8]. It is postulated that detrusor over activity increases with age and then small volumes of urine will lead to increased frequency and other LUTs. The bladder weakens with time and loses the ability to empty completely. It leads to increased post-void residual volumes and may cause acute on chronic urinary retension[9]. The symptoms that appear are; Urinary frequency, urgency, nocturia, hesitancy, intermittency, straining with micturition and incomplete emptying of the urinary bladder[10]. The diagnosis of BPH is made by history of lower urinary tract symptoms, digital rectal examination and ultrasonography of the urinary tract[11, 3]. IPSS is used for the symptoms index of the patients and endoscopy can also

be used for the definitive diagnosis[12]. IPSS is the most common severity index and is divided into mild, moderate and severe according to the point scoring from 0-35. Alpha blockers, 5α-reductase inhibitors or combined drug therapy is used to treat patients with mild to moderate symptoms of BPH[14, 15, 16]. Surgical interventions like Transurethral resection of the prostate (TURP) and other minimally invasive techniques are being used for more severe cases[17, 18]. Dutasteride and tamsulosin are very effective drugs used for the treatment of BPH. Dutasteride inhibits both iso-enzymes of 5 α- reductase and thus reduces the size of prostate by reducing dihydrotestosterone (DHT) levels in blood, a hormone required for normal erection and maintaining libido in men[19]. According to two international studies the incidence of erectile dysfunction is 7% with dutasteride therapy[20]. Tamsulosin is prostate selective α-antagonist and is the first line drug for the medical management of BPH. It causes retrograde ejaculation in 20 to 35% of patients[21]. Various studies have been done to compare combined drug therapy with single drug and have reached to the conclusion that combined therapy is superior to mono therapy[20, 21].

This study was designed to assess the frequency of erectile dysfunction and retrograde ejaculation in patients on combined medical treatment for BPH in our local population which has not been conducted in target population before. This will provide us frequency of erectile dysfunction and retrograde ejaculation in patients subjected to dutasteride and tamsulosin combined therapy for BPH.

METHODOLOGY

This cross sectional study was conducted on 205 patients enrolled from outpatient department (OPD) of IKD Peshawar from September 2017 to March 2018. Sample size was calculated with Rao State sample size calculator with 95% confidence level, 3.5 % margin of error and prevalence of erectile dysfunction of 17%[10]. Non-probability consecutive sampling technique was used to collect the data.

Inclusion Criteria was patients presenting with lower urinary symptoms, BPH on ultra sound (≥ 60 grams) and IPSS score of ≤ 17, IIEF score of ≥ 25. Exclusion Criteria included diabetes, patients with ischemic heart disease on past medical records, other urinary tract disorders, patients taking drugs like cimetidine, spironolactone, beta blockers, Thiazide diuretics, antidepressants and alcohol. Patients scheduled for surgical management of BPH were also excluded from the study. Study was started after approval from hospital ethical and research committee. Patients matching the inclusion criteria were subjected to IIEF and scores recorded as severe, moderate, mild to moderate, mild or no dysfunction.[22, 23] All patients were started on dutasteride (0.5mg daily) and Tamsulosin (0.4mg daily) combined drug therapy by urologist after informed consent. Erectile dysfunction was assessed for all patients before starting combined therapy and after two months. While retrograde ejaculation was assessed by taking history from the patient about first void urine after ejaculation. The data was collected in a designed proforma. Calculations were done for numerical variables like age, baseline IIEF score and follow up IIEF score. Frequencies and percentages were calculated for categorical variables like erectile dysfunction and retrograde ejaculation with stratification among age.

RESULTS

The mean age of 205 patients was 60 years with SD ±2.16. It showed that majority of patients with symptomatic LUTs due to BPH reported during 60-65 years (n=92, 45%). (Table 1). IIEF score before commencing drug treatment was ≥ 25 revealing mild erectile dysfunction (table 2). After 2 months of starting therapy, 35(17%) patients had IIEF score <11 showing severe erectile dysfunction, while 170 (83%) patients had IIEF score ≥ 22 with mild erectile dysfunction. (Table 3). Retrograde ejaculation was found in 76 patients (37%) (Table 4). Erectile dysfunction was found in total 35 patients with increasing frequency in older age group. Sixteen patients were in the age range of 61-65 years. Retrograde ejaculation was also found in higher number in the age range of 61-65. (Table 5).

Table 1: Age of the patients

Age	Frequency	Percentage
50-55 yrs	41	20%
56-60 yrs	72	35%
61-65 yrs	92	45%
Total	205	100%

Table 2: IIEF Score before drug administration (n=205)

IIEF score	Frequency	Percentage
1-11	0	0
26-30	205	100%
Total	205	100%
Total	205	100%

Table 3: IIEF score 2 months after starting therapy (n=205)

IIEF score after 2 months	Frequency	Percentage
1-11	35	17%
22-25	170	83%
Total	205	100%

Table 4: Frequency of erectile dysfunction and retrograde ejaculation (n=205)

Outcome		Frequency	Percentage
Erectile Dysfunction	<11 IIEF	35	17%
	≥ 22 IIEF	170	83%
Retrograde Ejaculation	Yes	76	37%
	No	129	63%

Table 5: Stratification of erectile dysfunction and retrograde ejaculation with age distribution

Outcome		50-55 yrs	56-60 yrs	61-65 yrs	Total	P Value
Erectile Dysfunction	Yes	8	11	16	35	0.471
	No	33	61	76	170	
Total	41	72	92			
Retrograde Ejaculation	Yes	17	27	32	76	0.501
	No	24	45	60	129	
Total	41	72	92			

DISCUSSION

Benign prostatic hyperplasia (BPH) is one of the most common diseases of old age people[24] which can be accompanied by LUTS that interferes with daily activities. At 60 years its prevalence is over 50% and at 85 years it is as high as 90%. According to histological evidence, the prevalence of annoying symptoms also increases with age[13]. In this study, the average age of the patients was also 60 years (SD ± 2.16), which is in accordance to the findings of Macvary and his colleagues[13]. The incidence of symptomatic BPH was 20% at the age of 50 years which was increased to 45% at the age of 60 years. In the literature, studies have been performed on the relationship between BPH and erectile dysfunction[25]. Recent knowledge emerged to indicate several potential links in epidemiological, physiological, pathological and treatment aspects of these two pathologies[25, 26]. However, the precise mechanism between these two pathologies has not yet been elucidated. While anatomical factors have been reported, it seems unlikely[26]. BPH treatment may cause the development of erectile dysfunction[27]. Berger et al found no direct relationship between BPH and erectile dysfunction[28]. Gacci et al found no significant association between prostate symptoms and sexual dysfunction[29].

In this study, results were found similar to findings in the literature. IIEF scores before the start of treatment for each patient with symptomatic BPH were greater than 25 meaning no impairment. According to Wu and Kapoor Dutasteride is an effective, safe and well-tolerated treatment both in monotherapy and in combination drug therapy. It improves symptoms, reduces the risk of acute urinary retention and the risk for BPH surgery[32]. In this study, the combined drug regime results strongly correlated with the findings of Wu and Kapoor,[32] nevertheless it relieved all symptoms secondary to enlarged prostate size. However, sexual side effects can occur as erectile dysfunction, ejaculation disorder, decreased libido and breast tenderness. All of these findings were also observed by Roehrborn[33] and Naslund[34]. Similar findings were recorded in this study by scoring IIEF after 2 months follow-up and the score was found ≤ 11 reflecting the severe erectile dysfunction with combined drug therapy. Although combined drug regime is more effective in patients with larger prostate, more severe symptoms and higher PSA values than monotherapy but it causes more severe erectile dysfunction and retrograde ejaculation[35]. Andriole at al also observed erectile dysfunction, impotency, ejaculatory disorders and decreased libido with combined drug therapy in comparison with dutasteride and tamsulosin. He observed these effects after two to four years of treatment[36]. Tamsulosin is very effective drug, strongly recommended by American Urological Association committee causing on average of 4-6 point improvement in AUA score which is noticeable change in the life of patients suffering symptoms due to enlarge prostate[37].

On the other hand adverse effect in the form of sexual dysfunction (retrograde or diminished ejaculation) has been reported with the use of tamsulosin, in the study of Gillen et al[38]. In control trials, exhibited by anderson[39] and Calais,[40] the percentage of patients treated with tamsulosin reported retrograde ejaculation between 4-26% depending on the duration of treatment. In long term study conducted by Lopar[41] and Narayan,[42] 30% patients reported with retrograde ejaculation. Although the follow up of this study is short results are coherent with existing literatures. The recorded value for retrograde ejaculation was 37% after 2 month follow-up, which is higher value when compared to the long term study of Lopar[41] and Narayan[42] but as Narayan concluded that adverse events occurs more frequently in the first two years of use of tamsulosin and decline thereafter.

CONCLUSION

Retrograde ejaculation and erectile dysfunction are the major adverse effects of combined drug therapy with dutasteride and tamsulosin for the treatment of benign prostatic hyperplasia.

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CONTRIBUTORS

SQ conceived the idea, designed the study, wrote initial draft and supervised the project till writing of the final draft. ST helped in searching literature including study tools and finalized the proposal after going through the initial draft and discussion with principle author. FY collected and compiled data after understanding the basic theme of the project and compiled results including statistical analysis. All author contributed significantly to the manuscript.