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Original Research Article

A comparative study of efficacy of tadalafil and alfuzosin regimens in patients of benign prostate hyperplasia

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ABSTRACT

Background: Aim of the study was to compare efficacy of Tadalafil and Alfuzosin regimens in patients of Benign Prostate Hyperplasia.
Methods: It was a comparative, prospective, observational, non-invasive, parallel and randomised study conducted at the Outpatient Department of Urology, Rajindra Hospital, Patiala. 60 patients diagnosed with Benign Prostate Hyperplasia along with Lower Urinary Tract Symptoms, out which, 30 patients, consuming Tadalafil and 30 patients consuming Alfuzosin were considered. History regarding the concerned disease and the compliance of treatment was taken. Symptom scores were assessed with the help of International Prostate Symptom Score, Quality of Lifestyle Score and Erectile Dysfunction Score. Physical examination consisting of Focused Neurological Examination along with Digital Rectal Examination were conducted. Parameters like Renal Function Test, Urine analysis, Ultrasound of Prostate and uroflowmetry were also considered.
Results: The mean age selected for study was 64 years for Tadalafil and Alfuzosin group. The mean level of IPS Score, Qol Score and ED Score at the first day of inclusion of patients were 23.96±4.49, 4±0.78, and 25.33±4.02 respectively for Tadalafil group and regarding Alfuzosin group they were 25.23±4.84, 3.56±0.81, and 26.1±4.04 respectively. Follow ups were conducted at 15 days, 1 month and 3 months for both the groups which were found to be statistically significant after 3 months and Alfuzosin showed a favourable result.
Conclusions: Alfuzosin 10mg given at daily dose was found to have higher efficacy than Tadalafil (5mg).

Keywords: Alfuzosin, Alpha blockers, Benign prostate hyperplasia, Erectile dysfunction, International Prostate Symptom Score, Phosphodiesterase inhibitors, Tadalafil

INTRODUCTION

Benign Prostate Hyperplasia (BPH) is a condition which is progressive in nature, showing abnormal enlargement of Prostate gland. This ailment is also accompanied with Lower Urinary Tract Symptom (LUTS) and for this, BPH acts as a contributor. It is a well-known fact that BPH and the LUTS is very common in elderly men and has a significant impact on the patients' quality of life. For male population it was observed on Autopsy that the Histological prevalence of BPH alongwith LUTS was found to be 50% in men aged 50-60 years and of 90% over 80 years was seen. 75% of men above 50 years old had symptoms arising from BPH, and 20-30% of men reaching 80 years old required surgery.

BPH being one of the commonest diseases to be managed by Urologists, its aetiology and pathophysiology are still unclear.[1]

Along with being highly prevalent conditions in case of aged male population, they are also associated with a significant negative impact on patients' quality of life.[2,3]

Etiology

Benign prostatic hyperplasia occurs mainly due to proliferation of smooth muscle and epithelial cells in prostatic tissue resulting in lower urinary tract symptom.[4,5] However, various other etiological factors or risk factors have also been pointed out:

Tissue remodelling

According to Mc Neal, BPH first develops in the periurethral transition zone of the prostate and all the BPH nodules develop either in the transition zone or in the periurethral region.[6-8] These nodules have a decreased epithelium-to-stroma ratio, along with disrupted growth and death programmes of stromal cells, leading to increased and an abnormal final stromal volume.[9-11] The underlying mechanism may be due to the involvement of excessive activation of anti-apoptotic cell death mechanisms in the human prostate, resulting in an abnormal growth in favour of cell proliferation that might ultimately induce hyperplasia.[12,13]

Hormonal factors

The development of BPH requires the action of testicular androgens.

Although, serum level of testosterone declines with increasing age, the levels of dihydrotestosterone (DHT) and androgen receptor (AR) remain high at intraprostatic region.

Dihyhydrotestosterone is also stimulated by prostatic 5-alpha reductase. This enzyme is present in fibroblasts of the stroma and in basal epithelial cells of the Prostate gland.[14-16]

Inflammation

According to studies by the 'Reduction by Dutasteride of Prostate Cancer Events' (REDUCE) trial and the 'Medical Therapy of Prostate Symptoms Study' (MTOPS) It was seen that prostate inflammtion led to injury of prostate tissues, and it stimulated cytokines from inflammatory cells which led to local growth factor production and angiogenesis in the tissue as a wound healing process, leading to tissue growth.[17,18]

Metabolic symptom

It is defined as abdominal obesity associated with hyperinsulinaemia, insulin resistance and cardiovascular risk factors. Recent studies have shown BPH and Metabolic Symptom to be interlinked.[19]

The size of the prostate rises with the progression of BPH, thus resulting in the obstruction of the urine flow, leading to LUTS. However, the pathopysiology of this disease is rather complex. Prostatic hyperplasia produces an increase in urethral resistance, leading to compensatory changes in the function of urinary bladder. The obstruction-induced changes in detrusor function, accompanied by age-related changes in both bladder and nervous system function, lead to urinary frequency urgency and nocturia. Neal et al, showed prostatectomy could resolve the emptying problem of LUTS but not the storage problem.[20]

It is thought that the enlarged prostate showed obstruction via both dynamic and static mechanisms.[1] The static component was due to enlarged prostate obstructing the urine stream within the prostatic urethra and the dynamic obstruction was thought to be the result of smooth muscle hyperplasia and contraction and was induced by alpha 1 adrenoceptor subtype.[21]

Before early 1990s, symptomatic BPH was most commonly treated with transurethral prostatectomy. At that time only, medical therapy using α-blockers lead to decline of transurethral prostatectomy.[22]

Table 1: Various properties of both the drugs are given in brief.

Properties	Tadalafil	Alfuzosin
Mechanism of action	Eliminates the action of Phosphodiesterase 5 enzyme leading to persistent smooth muscle relaxing action of cGMP induced by Nitric Oxide[26] Increased c GMP causes smooth muscle relaxation by reducing Calcium and via dephosphorylation of myosin light chain phosphate which leads to smooth muscle relaxation[27]	Non selective α1 blocker[28]
Doses prescribed	5mg once daily[29]	Once daily dose of 10mg[23]
Pharmacokinetics	It has a longer half-life than other drugs, with a duration of action of 36 hours[30] It is metabolised by CYP3A4[31]	Shows extensive first pass metabolism, 60% bioavailability. Plasma half life is 3- 5 hrs[32]
Adverse effects	Headache, Dyspepsia, back pain,nasal congestion. Not for patients consuming nitrates[33]	Priapism, Postural Hypotension, Vertigo, Floppy Iris Symptom[34]

Alfuzosin is an inhibitor of alpha-1 adrenoreceptor in the urogenital system and has been used in the treatment of dysuria caused by BPH. Clinical research also showed that PDE5 inhibitors are also beneficial for the treatment of LUTS. Here only tadalafil 5mg once daily has been approved for the treatment of BPH with LUTS.[23] Tadalafil was approved for daily use in the treatment of BPH in October 2011 by US Food and Drug Administration (FDA) and represents a novel mechanism of action for treatment of the signs and symptoms of BPH.[24]

Tadalafil is Phosphodiesterase 5 inhibitor, stimulating Nitric oxide, which diffuses into smooth muscle cells and stimulates guanylyl cyclase. The increase in cGMP mediates vasodilatation via activation of protein kinase Phosphodiesterase enzymes eliminate the effect of cGMP induced by Nitric Oxide.[25]

Tadalafil (dose 5mg OD), retards the effect of Phosphodiesterase 5 enzyme, thus leading to persistent cGMP actions which is induced by Nitric Oxide.[26]

Alfuzosin

It is a competitive α 1 antagonist, having 60% bioavailability and a half-life of 3-5 hours. It shows extensive first pass metabolism. Alfuzosin shows non selective affinity for α1 receptors. These receptors are present at the smooth muscles. Thus, Alfuzosin has greater potency in inhibiting contraction in prostate smooth muscle. As prostate smooth muscle relaxes, it also relieves the compressed lumen of Ureter, thus providing free passage of obstructed urine.

Alfuzosin may lead to postural Hypotension with/without dizziness which is transient in nature. Patients consuming oral Alfuzosin and undergoing cataract surgery are at increased risk of the intraoperative floppy iris symptom (IFIS), consisting of billowing of a flaccid iris, propensity for iris prolapse, and progressive intraoperative pupillary constriction. These effects increase the risk of cataract surgery, and complications are seen within14 days of taking these agents.[34]

Tadalafil

Effects of cGMP induced by Nitric Oxide (NO) are terminated by phosphodiesterase enzymes. Tadalafil is the inhibitor of phosphodiesterase type V that potentiates NO actions.[35]

Nitrergic nerves release nitric oxide, which is a simple signalling molecule of gaseous nature, which diffuses into smooth muscle cells, thus activating guanylyl cyclase. The Amino acid, which acts as a precursor for production of Nitric Oxide is L-Arginine.[36] Nitric oxide, released either in free form or in combination with a thiol compound interacts with the haem moiety of Guanyl Cyclase enzyme. This interaction occurs in cytoplasm of cell leading to conversion of GTP to c GMP.[27]

The resulting increase in cytoplasmic cGMP mediates vasodilatation via activation of protein kinase G. Consequently, inhibition of phosphodiesterase V potentiates the effect of endothelium-derived nitric oxide and of nitrergic nerves.

Tadalafil is metabolised by CYP3A4. Some unwanted effects of phosphodiesterase type V inhibitors consist of vasodilatation in other vascular beds; which include hypotension, flushing and headache. Visual disturbances have occasionally been reported.[31]

METHODS

The study was conducted at the Outpatient Department of Urology, Government Medical College, Patiala.

Study design

The study was conducted for 3 months. It was a comparative, prospective, observational, non-invasive, parallel and randomised study which comprised of total 60 patients diagnosed with Benign Prostatic Hyperplasia along with Lower Urinary Tract Symptom, out which, 30 patients, consuming Tadalafil and 30 patients consuming Alfuzosin were chosen.

Subjects at the age group of 50 and above were chosen for the study, after they understood the nature of the study, the risks and advantages associated with it with the help of patient information sheet and when they agreed to sign the informed consent forms voluntarily, after understanding the clauses given in them. The patient information sheet and the informed consent form was made in Hindi, English and Punjabi languages.

For each patient, proper history regarding the disease and the consumption of drug was taken. Symptom scores were assessed with the help of International Prostate Symptom Score (IPS Score), Quality of Lifestyle Score (QoL Score) and Erectile Dysfunction Score (ED Score).

Physical examination consisting of Focussed Neurological Examination along with Digital Rectal Examination were also conducted. Other parameters consisting of Renal Function Test, Urine analysis, Ultrasound of Prostate and uroflowmetry were also considered.

The follow up of patients at each group were done at 15 days, 1 month, 3 months.

Inclusion criteria

Inclusion criteria comprised of patients who are already diagnosed with Benign Prostate Hyperplasia (BPH) along with Lower Urinary Tract Symptom (LUTS) and are on either Tadalafil or on Alfuzosin Therapy. They should not suffer from any other diseases like Diabetes mellitus/insipidus or hypertension.

Exclusion criteria

It comprises of following patients:

- Those who are on medication other than Tadalafil or Alfuzosin.
- Those who are suffering from any other diseases like Diabetes Mellitus/Insipidus or Hypertension.
- History or evidence of prostate cancer
- History of previous prostatic surgery or other invasive procedure to treat BPH
- History of acute urinary retention (AUR) within 3 months prior to screening visit,
- Any causes other than BPH.

RESULTS

A total of 60 patients who were diagnosed with Benign Prostatic Hyperplasia and Lower Urinary Tract Symptom were selected for this study, out of which, 30 patients were administered Tadalafil and other 30 were administered Alfuzosin. The mean age group of patients consuming Tadalafil were found to be 64.06±10.4yrs (Mean±Standard deviation) whereas, for Alfuzosin group it was found to be 64.13±9.39 yrs, which was statistically non significant. Also, out of 30 patients who were on Tadalafil, 1 patient had an Erectile Dysfunction score of 21 whereas, 2 patients gave Erectile Dysfunction score of 18 and 1 patient gave Erectile Dysfunction score of 19. All the three scores depicted Moderate Erectile Dysfunction

Mean results regarding International Prostate Symptoms Score Quality of Life Score were calculated at first day of visit and follow up of these scores were conducted at 15 days, 1 month and 3 months. Similarly, Erectile Dysfunction score was also calculated for these patients at first day of visit and also follow up was conducted at 15 days, 1 month and 3 months.

Table 2 shows the baseline values of International Prostate Symptom Score, Quality of Life Score and Erectile dysfunction Score. These values were noted during the first visit and are given in the form of mean± standard deviation.

Table 2: Baseline value of International Symptom score, Quality of Life Score, Erectile Dysfunction Score of the patients involved in this study.

Variables	Tadalafil group	Alfuzosin group
International Prostate Symptom Score	23.96±4.49	25.23±4.84
Quality of Life score	4±0.78	3.56±0.81
Erectile Dysfunction Score	25.33±4.02	26.1±4.04

Table 3: Values of International Prostate Symptom Score given during follow up after 15 days, 1 month and 3 months.

Mean results	Tadalafil group	Alfuzosin group	p value	Inference
International Prostate Symptom score at first day	23.96±4.49	25.23±4.84	>0.05	Non- significant
International Prostate Symptom score at first follow up (15 days)	21.53±4.53	20.6±5.22	>0.05	Non- significant
International Prostate Symptom score at second follow up (1 month)	19.2±4.03	16.03±5.06	<0.01	Highly significant
International Prostate Symptom score at third follow up (3 month)	16.26±4.84	9.3±3.82	<0.01	Highly significant

Table 3 depicts the mean value of International Prostate Symptom Score (IPSS) for patients on Tadalafil group and Alfuzosin group which was noted on the first day of their visit. The value of IPSS at first day for Tadalafil Group was 23.96±4.49 whereas for Alfuzosin group, it was 25.23±4.84. p value was found to be >0.05 i.e. statistically non significant.

Value of IPSS for Tadalafil group at first follow up (after 15 days), second follow up (after 1 month), and at third follow up (after 3 month) were 21.53±4.53, 19.2±4.03 and 16.26±4.84 respectively whereas those for Alfuzosin group were 20.6±5.22, 16.03±5.06 and 9.3±3.82 respectively. p value for both the groups were found to be >0.05 at first follow up (statistically non significant), <0.01 at second and third follow up (statistically highly significant).

Table 4 depicts the mean value of Quality of Life Score (QoL) for patients on Tadalafil group and Alfuzosin group which was noted on the first day of their visit. The value of QoL Score at first day for Tadalafil Group was 4.00±0.78 whereas for Alfuzosin group, it was 3.56±0.81. p value was found to be >0.05 i.e. statistically non significant.

Table 4: Values of quality of Score given during follow up after 15 days, 1 month and 3 months.

Mean results	Tadalafil group	Alfuzosin group	p value	Inference
Quality of Life score at first day	4.00±0.78	3.56±0.81	>0.05	Non- Significant
Quality of Life score at first follow up (15 days)	3.53±0.73	2.83±0.53	<0.01	Highly significant
Quality of Life score at second follow up (1 month)	3.4±0.56	2.60±0.72	<0.01	Highly significant
Quality of Life score at third follow up (3 months)	3.33±0.54	2.23±0.67	<0.01	Highly significant

Table 5: Values of erectile dysfunction Score given during follow up after 15 days, 1 month and 3 months.

Mean results	Tadalafil group	Alfuzosin group	p value	Inference
Erectile Dysfunction score at first day	25.33± 4.02	26.13± 4.04	>0.05	Non- significant
Erectile Dysfunction score at first follow up (15 days)	26.23± 2.96	26.43± 3.67	>0.05	Non- significant
Erectile Dysfunction score at second follow up (1month)	26.6± 2.58	26.5± 3.56	>0.05	Non-significant
Erectile Dysfunction score at third follow up (3month)	26.96± 2.64	26.73± 3.36	>0.05	Non- significant

Value of QoL Score for Tadalafil group at first follow up (after 15 days), second follow up (after 1 month), and at third follow up (after 3 month) were 3.53±0.73, 3.4±0.56, and 3.33±0.54 respectively whereas those for Alfuzosin group were 2.83±0.53, 2.60±0.72, 2.23± 0.67 respectively. p value for both the groups were found to be <0.01 at first, second and third follow up (statistically highly significant).

Table 5 depicts the mean value of Erectile Dysfunction Score (ED) for patients on Tadalafil group and Alfuzosin group which was noted on the first day of their visit. The value of ED Score at first day for Tadalafil Group was 25.33±4.02 whereas for Alfuzosin group, it was 26.13±4.04. p value was found to be >0.05 i.e. statistically non significant.

Value of ED Score for Tadalafil group at first follow up (after 15 days), second follow up (after 1 month), and at third follow up (after 3 month) were 26.23±2.96, 26.6±2.58, and 26.96±2.64 respectively whereas those for Alfuzosin group were 26.43±3.67, 26.5±3.56, 26.73±3.36 respectively. p value for both the groups were found to be >0.05 at first, second and third follow up (statistically non significant).

A total of 4 patients from a sample size of total 60 patients, who were administered Tadalafil gave an ED Score of moderate Erectile Dysfunction, and by the end of 3rd month, showed considerable improvement, but, on overall comparison with those of Alfuzosin, the p value came out to be >0.05. This shows that no significant difference in this study was observed between Tadalafil and Alfuzosin in terms of improving ED Score.

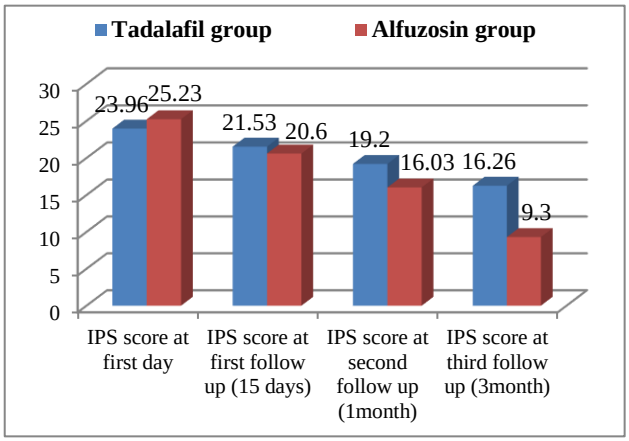

Figure 1: Comparing the efficacy of tadalafil and alfuzosin on the basis of IPS Scores in patients of BPH.

As mentioned in Figure 1, the Y-Axis denotes the level of IPS Score whereas the X-Axis denotes the time period during which, the follow up was conducted i.e. after 15 days, 1 month, 3 months. At the graph, it can be seen that initially, the patient groups for Tadalafil and Alfuzosin, having IPS Score at their first day during their inclusion in the study are also mentioned. The subsequent figures denote the falling level of IPS Scores or improvement in the condition of BPH in both the groups during each follow up time. The Red bar depicting Alfuzosin group show a favourable response as compared to that of Blue bar for Tadalafil group because the Red bar shows a greater improvement in IPS Score than the Blue bar. Thus, showing a favourable response of Alfuzosin over Tadalafil in improving symptoms of BPH.

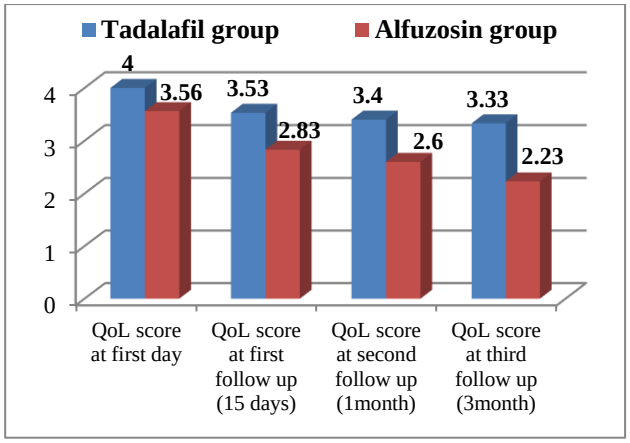

Figure 2: Comparing the efficacy of tadalafil and alfuzosin on the basis of QoL Score in patients of BPH.

As mentioned in Figure 2, the Y-Axis denotes the level of QoL Score whereas the X-Axis denotes the time period during which, the follow up was conducted i.e. after 15 days, 1 month, 3 months. At the graph, it can be seen that initially, the patient groups for Tadalafil and Alfuzosin, having QoL Score at their first day during their inclusion in the study are also mentioned. The subsequent figures denote the falling level of QoL Scores or improvement in Quality of life for BPH patients in both the groups during each follow up time. The Red bar depicting Alfuzosin group show a favourable response as compared to that of Blue bar for Tadalafil group because the Red bar shows a greater improvement in QoL Score than the Blue bar. Thus, showing a favourable response of Alfuzosin over Tadalafil in improving quality of life of BPH patients.

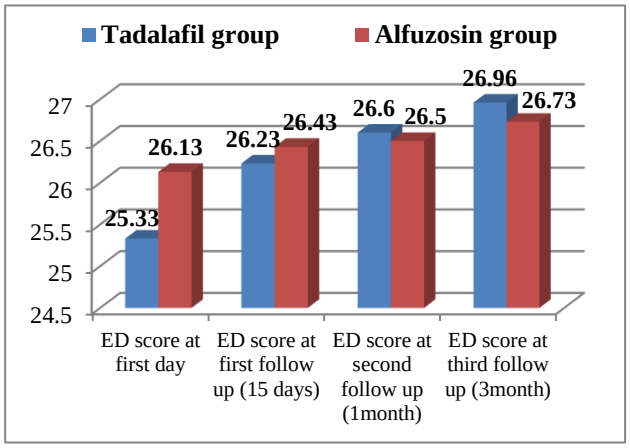

Figure 3: Comparing the efficacy of Tadalafil and Alfuzosin on the basis of ED Score in patients of BPH.

As mentioned in Figure 3, the Y-Axis denotes the level of ED Score whereas the X-Axis denotes the time period during which, the follow up was conducted i.e. after 15 days, 1 month, 3 months. At the graph, it can be seen that initially, the patient groups for Tadalafil and Alfuzosin, having ED Score at their first day during their inclusion in the study are also mentioned. The subsequent figures denote the improving level of ED Scores for BPH patients in both the groups during each follow up time. As the time duration of follow up progressed, the blue bar depicting Tadalafil group show favourable response in curbing Erectile dysfunction in BPH patients, but on overall comparison with Alfuzosin group (red bar), there no significant differences.

Out of 60 patients, enrolled for this study, 4 BPH patients were also having moderate Erectile Dysfunction, with an ED score of 21 given by 1 patient, 19 given by 1 patient whereas, 18 given by 2 patients. All these patients were administered Tadalafil. During subsequent follow ups it was seen that ED Score levels started improving. Although, on comparison with Alfuzosin, there was no significant difference between them on basis of improving ED Score, but overall improvement of ED Score was shown by Tadalafil.

Adverse effects

Out of 60 patients enrolled for the Comparative study between Tadalafil and Alfuzosin, 2 patients complained of mild dizziness and 1 patient complained of mild nasal congestion.

DISCUSSION

Benign Prostatic Hyperplasia and Erectile dysfunction had increased incidence and prevalence with increasing age. Earlier they were looked upon as two different diseases and separate treatments were administered. Generally erectile dysfunction part is neglected both by patient and physician as they relate this as normal part of ageing and hence, untreatable. Treatment used for BPH and LUTS also has negative impact on sexual function of male patient.[37]

Several mechanisms are present to establish relationship between BPH and ED, which consist of reduction in nitric oxide synthase or nitric oxide and induction of autonomic nervous system over activity. Abnormal induction of Rho A/ Rho kinase pathway, leads to smooth muscle contraction at prostate, urethra, bladder neck, and penis. Upregulation of this pathway has also been associated with ischemia or atherosclerosis of blood vessels supplying pelvic organs which is further associated with ED. Altered androgen environment and inflammation represent additional pathophysiologic risk factors for BPH, LUTS and ED.[38]

Tadalafil is a Phosphodiesterase 5 Inhibitor which is a popular modality for treatment of Erectile Dysfunction. Phosphodiesrerase 5 inhibitors upregulate NO/cGMP activity. This drug has also been approved by FDA with an aim to treat Benign Prostatic Hyperplasia along with Lower Urinary Tract Symptom.[39,40]

Selective α1-blockers like Alfuzosin act as first line of treatment. It is considered as the most effective medical therapy for benign prostate enlargement. These drugs block α1-adrenergic receptors abundant in the bladder neck, prostate capsule, and stroma.[41]

In this study total of 60 patients were selected out of which 30 patients were provided Tadalafil and 30 patients were provided Alfuzosin. Average age group for Tadalafil group and Alfuzosin group was 64.06±10.4 yrs and 64.13±9.39 yrs respectively. The level of IPS Score, Qol Score and ED Score at the first day of inclusion of patients were 23.96±4.49, 4±0.78, and 25.33±4.02 respectively for Tadalafil group and regarding Alfuzosin group they were 25.23±4.84, 3.56±0.81, and 26.1±4.04 respectively. Tadalafil was provided at dose of 5mg and Alfuzosin was provided at dose of 10mg.

In this study, it was seen that patients on Alfuzosin had shown a favourable improvement in IPS Score, and QoL score in the long run as compared to that of Tadalafil. As far as ED score was concerned it was found that although Tadalafil was effective in improving ED Score in patients of BPH with Erectile Dysfunction, it did not show any significant role in case of patients showing normal ED Score. Also, on comparing the overall effect of Tadalafil with Alfuzosin in terms of improving ED Score, there was also no significant differences observed between the 2 drugs. Regarding IPS Score and Qol Score, the difference between two drugs were found to be both statistically significant and clinically meaningful after the end of 3 months ($p < 0.01$).

CONCLUSION

In this study, it was observed that Alfuzosin was responsible for improving the level of IPS Score and QoL much more efficiently Tadalafil. Both treatment groups had patients of Benign Prostatic Hyperplasia and Lower Urinary Tract Symptom whose scores of IPS, QoL and ED were measured. After 15 days of providing treatment, the patients were followed up and the same was performed after 1 month and 3months of providing treatment. In case of IPS Sore and QoL Score, the difference between two drugs were found to be both statistically significant and clinically meaningful after the end of 3 months ($p < 0.01$). Regarding ED, Tadalafil was effective in improving ED Score in patients of BPH with Erectile Dysfunction, but, no significant role was seen in case of patients showing normal ED Score. Also, on comparing the overall effect of Tadalafil with Alfuzosin in terms of improving ED Score, no significant differences were observed between the 2 drugs.

Thus in this study it was observed, that although Alfuzosin played a favourable role than Tadalafil in improving the symptoms of Benign Prostatic Hyperplasia and Lower Urinary Tract Symptom, there was no significant difference between the 2 drugs in altering ED Score. Although, Tadalafil improved the ED Score of 4 BPH patients suffering from Erectile Dysfunction, no significant changes in ED Score was seen in patients having normal ED Score.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Chan SWH. Pathology and Medical Therapy of Benign Prostatic Hyperplasia. The Hong Kong Medical Diary. 2011;16(6):4-8.
2. Robertson C, Link C, Onel E, Mazzetta C, Keech M, Hobbs R, et al. The impact of lower urinary tract symptoms and comorbidities on quality of life: the BACH and UREPIK studies. BJU Int. 2007;99:347-54.
3. Rosen R, Altwein J, Boyle P, Kirby R, Lukacs B, Meuleman E, et al. Lower urinary tract symptoms and male sexual dysfunction: The Multinational Survey of the Aging Male (MSAM-7). Eur Urol. 2003;44:637-49.
4. Auffenberg GB, Helfand BT, McVary KT. Established medical therapy for benign prostatic hyperplasia. Urol Clin North Am. 2009;36:443-59.
5. Lee C, Kozlowski JM, Grayhack JT. Intrinsic and extrinsic factors controlling benign prostatic growth. Prostate. 1997; 31:131-8.
6. McNeal JE. Origin and evolution of bening prostatic enlargement. Invest Urol. 1978;15:340.
7. Price H, McNeal JE, Stamey TA. Evolving patterns of tissue composition in benign prostatic hyperplasia asa a function of specimen size. Human Pathology. 1990;21:578-85.
8. Lee KL, Peehl DM. Molecular and cellular pathogenesis of benign prostatic hyperplasia. J of Urol. 2004;172:1784-91.
9. Ishigooka M, Hayami S, Hashimoto T, Suzuki Y, Katoh T, Nakada T. Relative and total volume of histological components in benign prostatic hyperplasia: relationships between histological components and clinical findings. The Prostate. 1996 Aug;29(2):77-82.
10. Claus S, Berges R, Senge T, Schulze H. Cell kinetic in epithelium and stroma of benign prostatic hyperplasia. The Journal of urology. 1997 Jul 1;158(1):217-21.
11. Lin VK, Wang D, Lee IL. Myosin heavy chain gene expression in normal and hyperplastic human prostate tissue. Prostate. 2000;44:193-203.
12. Thomphson TC, Yang G. Regulation of apoptosis in prostatic disease. Prostate Suppl. 2000;9:25-8.
13. Kyprianuou N, Tu H, Jacobs SC. Apoptotic versus proliferative activities in human benign prostatic hyperplasia. Hum Pathol. 1996;27:668-75.
14. Siiteri PK, Wilson JD, Dihydrotestosterone in prostatic hypertrophy. I. The formation and content of dihydrotestosterone in the hypertrophic prostate of man. J Clin Invest. 1970;49:1737-45.

15. Geller J, Albert J, Lopez D. Comparison of androgen metabolites in benign prostatic hypertrophy (BPH) and normal prostate. J Clin Endocrinol Metab. 1976;43:686-8.
16. O'Malley KJ, Dhir R, Nelson JB. The expression of androgen-responsive gene is up-regulated in the epidthelia of benign prostatic hyperplasia. Prostate. 2009;69:1716-23.
17. Nickel JC, Roehrborn CG, O'Leary MP. Examination of the relationship between symptoms of prostatitis and histological inflammation: baseline data from the REDUCE chemoprevention trial. J Urol. 2007;178:896-900.
18. Kramer G, Mitteregger M. Is benign prostatic hyperplasia (BPH) an immune inflammatory disease? Eur Urol. 2007;51:1202-16.
19. Balkau B, Charles MA. Comment on the provisional report from the WHO consultation. European Group for the Study of Insulin Resistance (EGIR). Diabetes Me. 1999;16:442-3.
20. Neal DE, Ramsden PD, Sharples L. Outcome of elective prostatectomy. BMJ. 1989;299:762-7.
21. Caine M, Raz S, Ziegler M. Adrenergic and cholinergic receptors in the human prostate, prostatic capsule and bladder neck. Br J Urol. 1975;27:193-202.
22. McConnell JD, Roehrborn CG, Bautista OM, Andriole Jr GL, Dixon CM, Kusek JW, et al. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. New England Journal of Medicine. 2003 Dec 18;349(25):2387-98.
23. Roni MA, Kibria G, Jalil R. Formulation and in vitro Evaluation of Alfuzosin Extended Release Tablets Using Directly Compressible Eudragit. Indian J. Pharm. Sci. 2009;71(3):252-8.
24. Hatzimouratidis K. A review of the use of tadalafil in the treatment of benign prostatic hyperplasia in men with and without erectile dysfunction. Ther Adv Urol. 2014;6(4):135-47.
25. Sharma HL, Sharma KK. Principles of Pharmacology: Vasoactive Peptides and Nitric Oxide. 2nd ed. Hyderabad: Paras Medical Publisher; 2013.
26. Sharma HL, Sharma KK. Principles of Pharmacology: Androgens and Drug Treatment of Erectile Dysfunction. 2nd ed. Hyderabad: Paras Medical Publisher; 2013.
27. Sharma HL, Sharma KK. Principles of Pharmacology: Drugs acting on smooth muscles. 2nd ed. Hyderabad: Paras Medical Publisher; 2013.
28. Sharma HL, Sharma KK. Principles of Pharmacology: Drugs acting on sympathetic nervous system. 2nd ed. Hyderabad: Paras Medical Publisher; 2013.
29. Oelke M, Giuliano F, Mirone V, Xu L, Cox D, Viktrup L. Monotherapy with Tadalafil or Tamsulosin Similarly Improved Lower Urinary Tract Symptoms Suggestive of Benign Prostatic Hyperplasia in an International, Randomised, Parallel, Placebo-Controlled Clinical Trial. European Association of Urology. 2012;61:917-25.
30. Porst H, Roehrborn C, Secrest R, Esler A, Viktrup L. Effects of tadalafil on lower urinary tract symptoms secondary to benign prostatic hyperplasia and on erectile dysfunction in sexually active men with both conditions: analyses of pooled data from four randomized, placebo-controlled tadalafil clinical studies. J Sex Med. 2013;10:2044-52.
31. Rang HP, Dale MM, Ritter JM, Flower RJ, Henderson G. Rang and Dale's Pharmacology: Erectile Dysfunction. 7th ed. Livingstone: Churchill Elsevier; 2012.
32. Moffat AC, Osselton MD, Widdop B, Watts J, Eds., Clarke's Analysis of Drugs and Poisons, Pharmaceutical Press, London, UK.
33. Asseldonk BV, Barkin J, Elterman DS. Medical therapy for Benign Prostatic Hyperplasia: a review. Can J Urol. 2015;22(1):7-17.
34. Product monograph including patient medication information. 2017;11:1-42.
35. Rang HP, Dale MM, Ritter JM, Flower RJ, Henderson G. Rang and Dale's Pharmacolgy: Effects of Nitric Oxide. 7th ed. Livingstone: Churchill Elsevier; 2012.
36. Rosselli M, Keller PJ, Dubey RK. Role of nitric oxide in the biology, physiology and pathophysiology of reproduction. Human Reproduction Update. 1998;4(1):3-24.
37. Pawar DS, Kumar A, Singh SK, Singh R, Yadav L, Mittal S. Comparative Study of Tadalafil and Tamsulosin as Monotherapy for Lower Urinary Tract Symptoms Due to Benign Hyperplasia of Prostate. IOSR-JDMS. 2016;15(6):46-50.
38. Reddy SVK, Shaik AB. Combination of alfa blocker with low dose tadalafil in benign prostatic hyperplasia with erectile dysfunction management. International Journal of Medical Science and Clinical Invention. 2017;4(1):2581-7.
39. Kedia G, Uckert S, Kedia M, Kuczyk M. Effects of phosphodiesterase inhibitors on contraction induced by endothelin-1 of isolated human prostatic tissue. Urology. 2009;73:1397-401.
40. Kirby RS. The natural history of benign prostatic hyperplasia: what have we learned in the last decade? Urology. 2000;56(5):3-6.
41. Debruyne FMJ. Alpha blockers: are all created equal? Urology. 2000;56:20-2.

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