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CAN EJACULATORY DYSFUNCTION BE RECOVERED BY LOW DOSE TAMSULOSIN WHILE TREATING SYMPTOMATIC BENIGN PROSTATIC HYPERPLASIA?

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Abstract:

Purpose: *To evaluate the use of low dose Tamsulosin in relieving lower urinary tract symptoms related to benign prostatic symptoms as a trial to increase the drug safety (in terms of reducing the drug full dose side effects especially retrograde ejaculation) while maintaining its efficacy in relieving the patients' symptoms.*

Material and Methods: *This Prospective study was conducted in King Faisal University polyclinic between November 2013 and March 2014. Patients enrolled in this study were suffering from Lower urinary tract symptoms due to benign prostatic hyperplasia and were receiving 0.4 mg Tamsulosin for variable period and was complaining of ejaculatory dysfunction. Base line assessment involved medical history with evaluation of ejaculatory function, IPSS, abdominopelvic ultrasound with estimation of postvoid residual urine (PVR) and quality of life questionnaire. The patients were excluded whenever there is any significant aggravation of their symptom. During the course of this study, 0.2 mg Tamsulosin was given to patients and they were assessed by the same tools of base line assessment at the first and third month of the study. Drug compliance and adverse events were also recorded in all patients.*

Results: *Before we started our treatment with the low dose, twenty one patients had mean IPSS of 7.00 ± 0.948 and mean residual volume of 92.38 ± 20.47 ml. At first month follow up, the mean IPSS and the mean residual volume became 7.47 ± 0.67 and 104.76 ± 21.82 ml respectively with a statistically significant difference as compared with that of the baseline (p-value <0.05). Out of 21 patients, 16 (76.2%) patients reported no ejaculation at all and 5 (23.8%) patients reported low ejaculatory volume. After treatment with low dose Tamsulosin i.e. 0.2 mg, out of 16 patients with no ejaculation, 12 (75%) had recovered and out of the 5 patients who reported low ejaculatory volume, 3 (60%) patients reported increased ejaculatory volume. All patients with improved ejaculatory function **were** fully satisfied as measured by quality of life score and want to continue on the low dose. None of our patients showed adverse effects with the low dose.*

Conclusion: *For patients complaining from LUTS due to BPH, low dose Tamsulosin (0.2 mg/day) shows potential advantage for patients with bothering ejaculatory dysfunction. In spite of the significant change in IPSS after administration of the low-dose, most of patients show higher overall satisfaction rate as compared to the standard dose (0.4mg/day). A prospective study on a large scale is still needed to confirm our result.*

Key words: *Prostate, Prostatic Hyperplasia, Tamsulosin, Ejaculation, Erectile dysfunction, Lower urinary tract symptoms*

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INTRODUCTION:

Benign prostatic hyperplasia (BPH) is a chronic, progressive disease due to a benign enlargement of the transition zone of the prostate gland[1,2,3]. Lower urinary tract symptoms (LUTS) caused by BPH is commonly found among aging patients, with roughly 25% of men over 40 years [4,5].The severity of LUTS including urinary frequency, urgency, nocturia, hesitancy, weak stream, interrupted stream and postmicturetion dribbling, are commonly evaluated by International Prostate Symptom Score (IPSS) [6]. α1-receptors are involved in contraction of the smooth muscle of the prostate gland; contraction of this muscle blocks the urethra at the bladder neck which leads to LUTS [3,4,7,8]. α1-receptors are further subdivided into α1A, α1D and α1B, with α1A being the most common, 70% [4]. When patients present with BPH, α1-Adrenergic antagonist are the first line medication. Tamsulosin is uroselective α1-receptors antagonist as it acts specifically on α1A and α1D [6,7].

Therefore, blocking the action of α1relaxes the muscle and restores the normal urinary flow in BPH patients. Tamsulosin has advantage over other α-blockers as it has insignificant effects on blood pressure with minimal undesirable effects [8-9]. However, it has some side effects such as sexual dysfunction by causing retrograde ejaculation (RE) i.e. the semen instead of going through the urethra; it goes back into the bladder, due to the relaxed bladder neck [8]. This side effect has stolen the enjoyment of life to a lot of Tamsulosin using-patients. The Tamsulosin Dosage used clinically range from 0.4 to 0.8 mg/day. However, in Koreans and other East Asian countries, several studies have proved that an initial low dose Tamsulosin 0.2 mg to be effective [8,9]. The aim of the present study is to evaluate the use of low dose Tamsulosin in relieving lower urinary tract symptoms related to benign prostatic symptoms as a trail to increase the drug safety (in terms of reducing the drug full dose side effects especially retrograde ejaculation) while maintaining its efficacy in relieving the patients' symptoms.

MATERIAL AND METHODS:

This Prospective study was conducted in King Faisal University polyclinic between November 2013 and March 2014. Patients suffering from LUTS due to BPH and were receiving 0.4 mg Tamsulosin for variable period and complaining of retrograde ejaculation, were enrolled in this study after taking their consent.

The exclusion criteria were residual urine volume of more than 400 ml, previous bladder neck, prostate or pelvic region surgery, renal impairment and diabetes mellitus. In addition, patients on the course of other drugs such as α-adrenoceptor agonist and anticholinergic are also excluded from the study.

Base line assessment involves medical history with evaluation of ejaculatory function, IPSS, physical examination, blood pressure, abdominopelvic ultrasound, postvoid residual urine(PVR) and quality of life. During the course of this study, 0.2 mg Tamsulosin was given to patients and they were assessed by the same tools of base line assessment at the first and third month of the study. The patients were excluded whenever there is any significant aggravation of their symptoms and have been put back to the regular dosage (0.4 mg). The ejaculatory function was assessed in all patients at the same time of the follow up (one and three months).

Data for the IPSS are recorded at the first and third month after low dose administration. Drug compliance and adverse events were also analyzed in all patients. Statistical analysis used on all patients, and included Student t-test is used to compare the outcomes of IPSS before and after changing the dose for those who completed the three month follow up. All statistical analysis was done by IBM SPSS ver. 21.0. Also, a p-value of <0.05 was considered statistically significant.

RESULTS:

We started the study with 24 men with LUTS due to BPH, with a mean age of 54.04 ± 4.9 years. Three patients were excluded from the study, because they did not complete the third month follow up. Twenty-one patients fit the inclusion criteria, and therefore were included in the study.

Before starting the study, the 21 patients had mean IPSS of 7.00 ± 0.948 and mean residual volume of 92.38 ± 20.47 ml. At first month follow up, the mean IPSS was 7.47 ± 0.67 and the mean residual volume was 104.76 ± 21.82 ml. Moreover, at third month follow up, the mean IPSS was 8.47 ± 1.24 and the mean residual volume was 108.57 ± 21.04 ml. The IPSS at first month has a statistically significant difference as compared with that of the baseline (p-value<0.05). None of our patients showed adverse effects with the low dose.

Out of 21 patients, 16 (76.2%) patients reported no ejaculation at all and 5 (23.8%) patients reported low ejaculatory volume. After treatment with low, dose Tamsulosin i.e. 0.2 mg, 12 (75%) patient who reported no ejaculation had recovered, and 4 (25%) patients did not recover. Moreover, out of the 5 patients who reported low ejaculatory volume, 3 (60%) patients reported increased ejaculatory volume, and 2 (40%) patients reported no change in ejaculatory volume. Overall, after treatment with low,

dose Tamsulosin i.e. 0.2 mg, 15 (71.4) patients had recovered from the ejaculatory problems, and 6 (28.6%) did not recover. Furthermore, the 15 (71.4%) patients who had recovered from their ejaculatory problems are fully satisfied as measured by quality of life score and want to continue on the low dose.

Figure 1 Analysis of ejaculatory volume after treatment with low dose Tamsulosin i.e. 0.2 mg

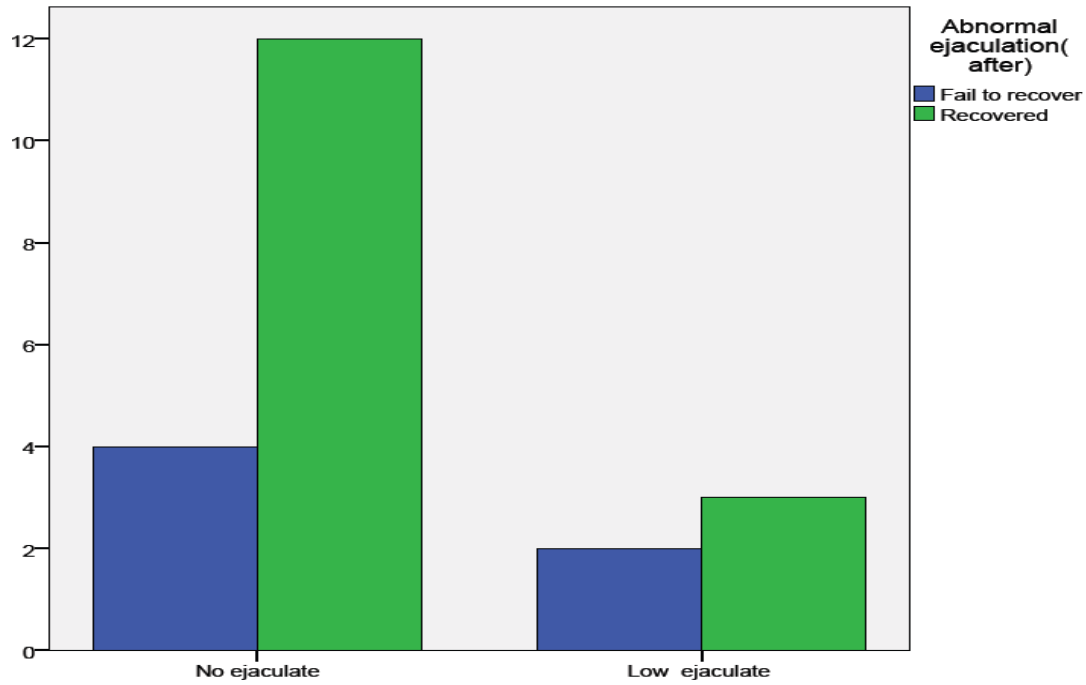

Table 1 Analysis of treatment with normal dose Tamsulosin i.e. 0.4 mg, and low dose Tamsulosin i.e. 0.2 mg

Variable	Normal Dose	Low dose (after 1 month follow up)	Low dose (after 3 months follow up)	P value
IPSS	7.00 ± 0.948	7.47 ± 0.67	8.47 ± 1.24	Normal Dose x 1 month follow up = 0.004
				Normal Dose x 3 months follow up = 0.0001
				1 month follow up x 3 months follow up = 0.0001
Mean residual volume	92.38 ± 20.47 ml	104.76 ± 21.82	108.57 ± 21.04 ml	Normal Dose x 1 month follow up = 0.0001
				Normal Dose x 3 months follow up = 0.0001
				1 month follow up x 3 months follow up = 0.008

Table 2 Analysis of ejaculatory volume after treatment with low dose Tamsulosin i.e. 0.2 mg

Abnormal ejaculation after the Low dose	Fail To Recover	Recovered	Total
No ejaculate	4 (25%)	12 (75%)	16 (76.2%)
Low ejaculate	2 (40%)	3 (60%)	5 (23.8%)
Total	6 (28.6)	15 (71.4)	21 (100%)

DISCUSSION:

Many treatments can be used for BPH in order to relieve the symptoms associated with it. Transurethral prostatectomy represents the gold standard surgical treatment for BPH, but patients prefer the non-invasive medical treatment over surgery[8]. Surgery is usually only recommended for moderate to severe symptoms of prostate enlargement that have failed to respond to medication [2].

One of the most commonly used medications for BPH related LUTS;α-blockers have a great use in treating these symptoms [8,10]. Of these α-blockers, terazosin, doxazosin, alfuzosinrepresent non-selective α1-adrenoreceptors subtypes [8,10].Because α1-adrenoreceptors are also present in the peripheral vessels, using above-mentioned drugs can also cause vasodilator effects, such as orthostatic hypotension, syncope, headache, and dizziness [5]. On the other hand, Tamsulosin represents one of the most commonly used uroselective α1A-adrenoreceptors antagonists, so it offers a great advantagein terms of cardiovascular adverse events [1,6,7]. In agreement with this fact, in our series, no cardiovascular adverse events were reported using this drug. However with the previous advantage, Tamsulosin can also cause undesirable side effects such as retrograde ejaculation and decreased ejaculate volume in great proportion of patients [10]. In our series of 21 patients using 0.4 mg Tamsulosin, 16 (76.2%) of our patients reported no ejaculation at all, and 5 (23.8%) patients reported low ejaculatory volume.

Several studies have reported that Tamsulosin at doses of 0.2 to 0.8 mg is clinically effective in patients with symptomatic BPH [5, 8]. However, mostof the previous reports on the efficacy of Tamsulosin were based on a dose of 0.4 mg/day and they all reported that IPSS improved significantly compared with the baseline. Based on these reports, 0.4mg/day is commonly the recommended dose which show long-term high efficacy.

Kim J. H. et al reported that a low dose Tamsulosin would show aclinical effectiveness and symptomatic improvement[8].However, in our study with 24 patients, there was a significant change in IPSS and residual urine volume in 21 patients when shifted from the standard dose (0.4 mg) to the low dose (0.2 mg) with exclusion of three patients who showed sever deterioration of their symptoms.

Ejaculatory dysfunction is one of the most common conditions in aging men who use Tamsulosin as treatment for BPH [11]. This problem has a significant negative effect on quality of life. In a placebo controlled study, it was found that the incidence of ejaculatory dysfunction is dose-related. This means that when increasing the dose, the incidence of ejaculatory dysfunction will also increase. So, the incidence of ejaculatory dysfunction in patients taking 0.4 mg is higher than among low dose Tamsulosin-patients [10, 12-13]. In Kim et al study, low-dose Tamsulosin does not have any significant negative impacts on ejaculation[5].On the other hand, the present study reported that after treatment with low dose Tamsulosin i.e. 0.2 mg, 12 (75%) patients who reported no ejaculation had recovered. Moreover, out of the 5 patients who had low ejaculatory volume, 3 (60%) patients reported an increase in ejaculatory volume, with overall 71.4% recovery of their ejaculation.

Using other treatment protocol to overcome the problem of ejaculatory dysfunction in Tamsulosin-patients, Goktas et al reported animprovement of 63.3% from abnormal ejaculatory function during

intermittent Tamsulosin (0.4 mg) treatment i.e. every other day [14].

In terms of patients' satisfaction, in Kim J. H. et al series, 63.4% of their patients were satisfied with the low dose Tamsulosin based on the drug efficacy to relieve their symptoms. However, in our study, 71.4% of our patients show overall satisfaction with the low-dose based on both drug efficacy and recovery of their ejaculatory dysfunction.

CONCLUSION:

For patients complaining from LUTS due to BPH, low dose Tamsulosin (0.2 mg/day) shows a potential advantage for patients with bothering ejaculatory dysfunction. In spite of the significant change in IPSS after administration of the low-dose Tamsulosin, most of patients show higher overall satisfaction rate as compared to the standard dose (0.4mg/day). A prospective study on a large scale is still needed to confirm our results.

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