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DOXAZOSIN VERSUS FINASTERIDE FOR THE TREATMENT OF LARGE SYMPTOMATIZING BENIGN PROSTATIC HYPERPLASIA: A QUESTIONNAIRE AND URODYNAMIC-BASED STUDY

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Objectives: To evaluate and compare the efficacy of both Finasteride and Doxazosin in the treatment of moderately symptomatizing large-sized benign prostatic hyperplasia (BPH) and to correlate symptomatic changes with alterations in the urodynamic values using the Schäfer nomogram and the obstruction coefficient (OCO) values.

Patients and Methods: Fifty male patients with moderately symptomatizing BPH (prostate size > 40 grams) as assessed by ultrasound were randomized to receive either Finasteride (5 mg/day) or Doxazosin (1-4 mg/ day) for 12 months.

Results: Both Finasteride and Doxazosin significantly improved the urinary flow rates. Pressure-flow studies confirmed that both Doxazosin and Finasteride were effective in decreasing the opening detrusor pressure, the detrusor pressure at maximum flow (PdetQmax) and the detrusor pressure at least flow (Pdet least). The OCO values were found to have improved in both treatment groups. There was, however, a significant difference between the groups with respect to the OCO values denoting a greater improvement of the degree of obstruction in patients treated with Finasteride.

Conclusion: The use of a compatible numerical format for grading the degree of bladder outlet obstruction would maximize the usefulness of pressure-flow studies in the evaluation of obstructed patients. Using the OCO value revealed that Finasteride was superior to Doxazosin regarding the degree of improvement in obstruction caused by benign prostatic hyperplasia.

Key Words: benign prostatic hyperplasia, medical treatment, urodynamics

INTRODUCTION

Lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) are common among aged men. Nearly 25% of all men above 40 years of age have such symptoms.[1] Men with moderately symptomatizing BPH can be treated with alpha 1-adrenergic antagonist drugs, such as Doxazosin, that relax the prostatic smooth muscle, or with drugs inhibiting 5 alpha-reductase, such as Finasteride, which reduce tissue androgen concentrations and, hence, the prostate size.

Urodynamic investigations provide an objective, quantitative evaluation of urinary function in patients with BPH. Uroflowmetry and pressure-flow studies are among the best methods for the evaluation of the effects of different drugs used for the treatment of BPH. Several formats and nomograms have been developed to interpret the outcome of pressure-flow studies. The Schäfer nomogram and the Obstruction Coefficient (OCO) have been used as a compatible numerical format for grading bladder outflow conditions on a continuous scale. The OCO normally ranges between 0.3 and 0.9 with a mean of 0.57. The cut-off value for obstruction is >1. The upper range of "normal outflow conditions" is OCO= 0.71. The mean OCO value after surgery of prostate obstruction from various studies is 0.56.[2-4]

Various concepts have been suggested for grading detrusor contractility, such as maximum isometric pressure (Piso), the power factor (Wf), the Schäfer nomogram and the

Table 1: Age and Baseline Values of the Studied Patients

	Age		Baseline IPSS*		Baseline Qmax**	
	mean	range	mean	range	mean	range
Doxazosin Group (n=25)	58.2	49 – 62	15.1	11 – 18	8.6	6.5 – 10.3
Finasteride Group (n=25)	60.3	47 – 65	15.7	12 – 19	8.3	6.3 – 10.9

* IPSS = International Prostate Symptom Score; ** Qmax = maximum flow rate

Detrusor Coefficient (DECO). The mean value for DECO in normal volunteers is 1.33 (±0.20). It ranges between 0.8 and 2.1. The mean value for symptomatic older men is between 0.68 and 1.15.[2-4]

All these objective parameters are helpful in the evaluation of the effects of any drug used in the treatment of BPH as regards both the change in outflow obstruction and detrusor contractility.

The aim of this study was to evaluate and compare the efficacy of Finasteride and Doxazosin in the treatment of moderately symptomatizing large-sized BPH and to correlate symptomatic changes with alterations in urodynamic measures using the OCO and DECO values.

PATIENTS AND METHODS

Fifty male patients with moderately symptomatizing BPH were randomized to receive either Finasteride (5 mg/day) or Doxazosin (1-4 mg/day) for 12 months. The two groups (25 patients each) were similar with respect to patient age, base-line International Prostate Symptom Score (IPSS) and maximum flow rate (Qmax) (Table 1). The patients were initially evaluated subjectively using an IPSS questionnaire that was translated into Arabic. Investigations included routine blood tests, plain X-ray and abdominal and pelvic ultrasound. Only patients with an IPSS equal to or <18 and an estimated prostate size > 40 grams were included in this study.

Urodynamic studies including uroflowmetry and pressure-flow studies were done. A base-line pressure-flow study was performed with estimation of OCO and DECO values as objective predictors of changes in the outlet resistance and detrusor power, respectively.

Doxazosin was used in a dose of 2 mg once daily in 18 patients, while 7 patients continued the study on 4 mg/day. Finasteride was used in a dose of 5 mg daily in 25 patients. The study was continued for one year in 47 patients, since three patients (two on Doxazosin and one on Finasteride) discontinued the treatment due to retention.

Uroflowmetry, IPSS and pressure-flow studies were done at follow-up after 12 months.

RESULTS

Both Finasteride and Doxazosin yielded a significant and durable improvement in the symptom score. The treatment with Finasteride resulted in a mean reduction of the IPSS score by 48% in comparison to 40% reduction after the administration of Doxazosin.

Both Finasteride and Doxazosin significantly improved the urinary flow rates. Uroflowmetry revealed a mean improvement of Qmax of 1.5 ml/sec with Doxazosin, while Finasteride yielded an improvement of 4.0 ml/sec (p=0.02). The treatment with Finasteride also resulted in a greater improvement of the mean flow rate as compared to the treatment with Doxazosin (1.7 ml/sec versus 0.7 ml/sec). Pressure-flow studies confirmed that both Doxazosin and Finasteride were effective in decreasing the opening detrusor pressure as well as the detrusor pressure at maximum flow (Pdet Qmax) and at least flow (Pdet least).

Also, the Schäfer nomogram was applied, and the OCO values were found to have improved in both groups, while the DECO values were not much changed.

Table 2: Effects of Finasteride

	Before Treatment	After Treatment	P-Value
International Prostate Symptom Score (IPSS)	15.7	8.1	<0.01
Maximum flow rate (Qmax)	8.3	12.3	<0.01
Opening detrusor pressure (Pdet opening)	59.1	46.4	<0.01
Detrusor pressure at maximum flow (Pdet Qmax)	80.2	61.0	<0.01
Detrusor pressure at least flow (Pdet least)	48.9	40.1	<0.01

Table 3: Effects of Doxazosin

	Before Treatment	After Treatment	P-Value
International Prostate Symptom Score (IPSS)	15.1	9.0	<0.01
Maximum flow rate (Qmax)	9.2	10.7	<0.01
Opening detrusor pressure (Pdet opening)	58.5	52.0	0.02
Detrusor pressure at maximum flow (Pdet Qmax)	78.4	71.4	0.02
Detrusor pressure at least flow (Pdet least)	49.9	49.0	0.34

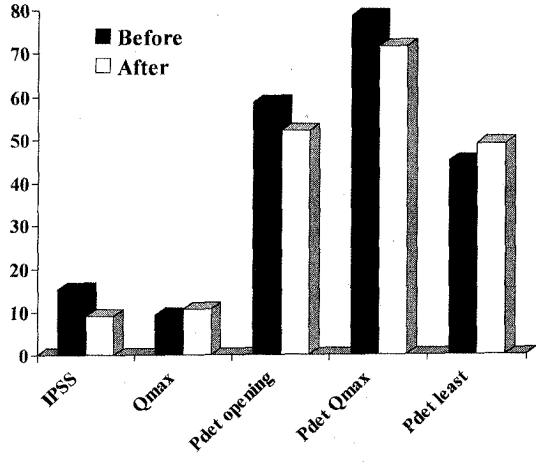

Fig. 1: Diagram illustrating the effects of Doxazosin on patients with moderate obstructive symptoms

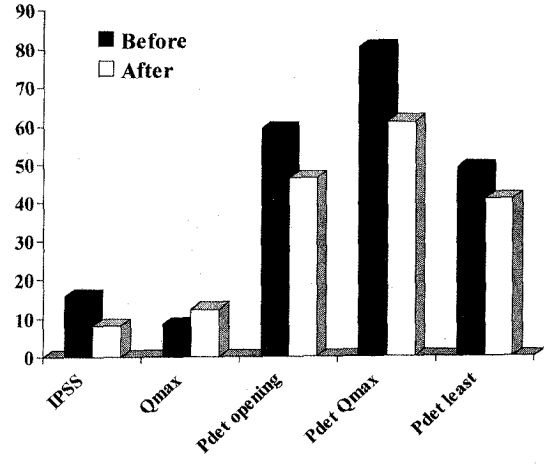

Fig. 2: Diagram illustrating the effects of Finasteride on patients with moderate obstructive symptoms

In the Finasteride group, Pdet at opening pressure decreased from 59.9 cm/H_20 to 46.4 cm/H_20 ($p<0.01$), PdetQmax decreased from 80.2 cm/H_20 to 61 cm/H_20 ($p<0.01$) and Pdet at least pressure decreased from 48.9 cm/H_20 to 40.6 cm/H_20 ($p<0.01$) (Table 2). OCO decreased from 1.1 to 0.7 ($p<0.01$), while DECO improved from 1.02 to 1.12 ($p=0.04$) (Fig.1).

In the Doxazosin group, Pdet at opening pressure decreased from 61.5 cm/H_20 to 52.7 cm/H_20 ($p= 0.02$), PdetQmax decreased from 71.4 cm/H_20 to 62.1 cm/H_20 ($p= 0.02$) and Pdet at least pressure decreased from 54.4 cm/H_20 to 49.3 cm/H_20 ($p=0.34$) (Table 3). OCO decreased from 1.25 to 0.95 ($p<0.01$), while DECO improved from 1.23 to 1.25 ($p= 0.42$) (Fig.2).

Table 4: Comparison of the Results Achieved Using Doxazosin and Finasteride

	Finasteride	Doxazosin	P-Value
International Prostate Symptom Score (IPSS)	8.1	9.0	0.22
Maximum flow rate (Qmax)	12.3	10.7	0.02
Opening detrusor pressure (Pdet opening)	46.4	52.0	<0.01
Detrusor pressure at maximum flow (Pdet Qmax)	61.0	71.4	<0.01
Detrusor pressure at least flow (Pdet least)	40.1	49.0	<0.01

Table 5: Effects of Both Drugs on the Obstruction Coefficient (OCO)

	Before Treatment	After Treatment	P-Value
Doxazosin	1.25	0.95	<0.01
Finasteride	1.1	0.7	<0.01

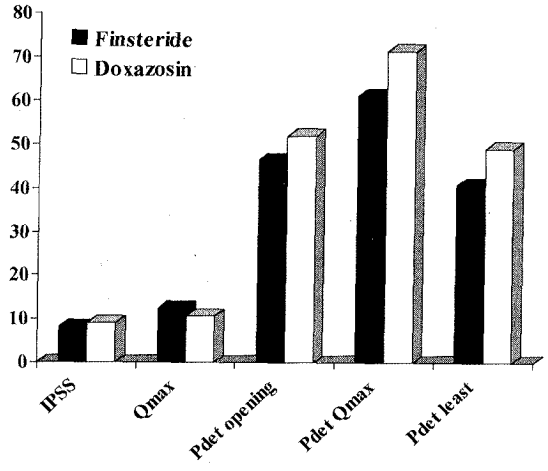

Fig. 3: Diagram illustrating the comparison of the effects of Doxazosin and Finasteride on patients with moderately obstructive symptoms

No significant differences regarding the detrusor pressure at the different phases of the study were found between the two groups (Table 4) (Fig.3). However, there was a significant difference in OCO between the groups denoting a greater improvement in the degree of obstruction in the patients treated with Finasteride (Table 5). DECO was not significantly changed in either treatment group (Fig. 3-5).

DISCUSSION

Medical treatment of BPH is indicated in patients reporting mild to moderate symptoms by means of questionnaires dealing with the subjective evaluation of the symptoms. An IPSS equal to or less than 18 is suggestive of mild to moderate symptoms.

The Finasteride Urodynamic Study Group has shown that men with prostates larger than 40 cc show more significant improvements in the urodynamic parameters compared to those with prostate sizes of 40 cc or less when treated with Finasteride[5]. Similarly, the authors of the Pless Study confirmed that treatment with Finasteride was mainly successful in large prostates[6]. For this reason, we decided to compare the efficacy of Doxazosin and Finasteride only in patients with large prostate sizes. Without such selection, the comparison would not have been valid.

The follow-up period in this study was 12 months, since a short duration of treatment would be in favour of alpha-blockers which are faster acting than Finasteride. On the other hand, longer follow-up periods were not required because the long-term effects of both drugs have been previously evaluated in the work of several authors[7-11].

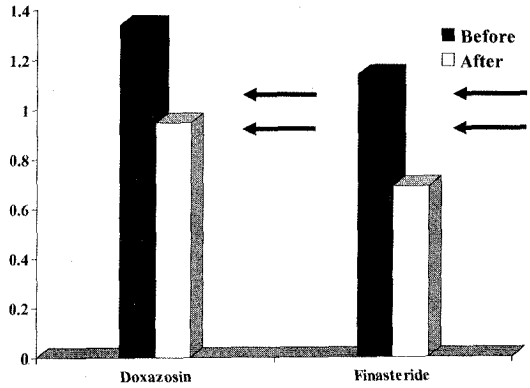

Fig. 4: Diagram illustrating the effect of both drugs on the obstruction coefficient

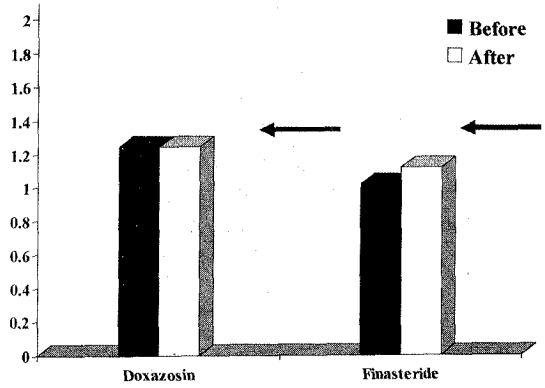

Fig. 5: Diagram illustrating the effect of both drugs on the detrusor coefficient

Both drugs have been shown to be effective in relieving the symptoms of BPH as confirmed by the patients' answers to the IPSS questionnaire. No significant difference between both drugs was found with respect to the improvement of symptoms.

Uroflowmetry also showed a significant improvement of the urinary flow in both groups of patients without a statistically significant difference between the groups. The improvement of 1.5 ml/sec in the Qmax of the Doxazosin group was similar to that found by McDiarmid et al.[12]. Still, several studies showed a greater improvement in Qmax, up to 3.2 ml/sec, when an 8 mg dose was used, although this was associated with a higher rate of side effects[12-14]. As for the Finasteride group, the Qmax improved by 4 ml/sec which is slightly better than the values reported in previous studies[6,15,16]. This may be due to the use of the drug in patients with large-sized prostates for at least one year.

Urodynamic studies give a strict standard testing result of the effects of drugs. They are objective and do not depend on the patient's or doctor's bias. However, their main draw-back is that they are invasive tests.

In the present study, a good correlation was found between the urodynamic studies and the answers to the IPSS questionnaire. Both measures proved the effectiveness of the two study drugs. Still, the pressure-flow studies showed a more favourable result in the Finasteride group. The improvements in pressure-flow studies reported by the Finasteride Urodynamics Study Group[5,9] for Finasteride and by Abrams[17] for Doxazosin are similar to our results.

As seen in our study, urodynamics are useful for a more accurate evaluation of the effect of drugs on BPH. In cases of clinical studies, this tool allows the investigator an extra measure of evaluation. However, we do not recommend it as a routine test in patients on medical treatment for BPH.

The use of a compatible numerical format for the grading of the degree of bladder outlet obstruction would even maximize the usefulness of pressure-flow studies because it allows the comparison of every single numerical value with the pre-operative one. This would facilitate a simple interpretation of urodynamic studies. In spite of the improvement in the IPSS score by 40% and the Qmax by 16% in the Doxazosin group, OCO proved that the patients were marginally improved, with a mean value of 0.95, just below the cut-off value of obstruction (OCO < 1). On the other hand, Finasteride resulted in an OCO value of 0.7, well bellow that level. This shows that Finasteride yielded a better result regarding the degree of improvement of bladder outlet obstruction.

The two drugs were equal in their effects on the detrusor contractility; the DECO values did not show any significant change of the detrusor

contractility in either group. Such marginal change is expected from drugs acting mainly on bladder outlet obstruction and prostatic size.

In conclusion, both Doxazosin and Finasteride, achieve a significant improvement in patients with moderately symptomatizing BPH. Subjective evaluation using the IPSS questionnaire revealed that the two drugs were equivalent. Objective evaluation using uroflowmetry and pressure-flow studies showed that both drugs significantly improved the patients' condition. The use of the OCO value revealed, however, that Finasteride yielded a significantly better result regarding the degree of improvement in obstruction caused by BPH.

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RESUME

The translation of the abstract will be published in the next issue of the *African Journal of Urology*.

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