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Histologic Evaluation in Patients with Benign Prostatic Hyperplasia Treated with Finasteride and Surgery Alone

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Abstract: In this study, we compared stroma, epithelium, glandular lumen, smooth muscle hyperplasia, inflammation and fibrous components in benign prostatic hyperplasia (BPH) tissue between the group undergone surgery only and the group who had taken finasteride (5 alpha-reductase inhibitor) prior to surgical treatment.

Prostate adenomas were obtained from both 12 patients administered finasteride for six months prior to surgical treatment and those of 11 patients undergone only surgical treatment. The histological evaluation were

performed quantitatively by planimetry.

The mean epithelium ratio in the group administered 5 alpha-reductase inhibitor prior to surgery lessened approximately two-fold compared to the other group's.

In conclusion, morphometric analysis may have an indicative role in determining alternative pharmacotherapies for BPH.

Key Words: 5 alpha-reductase inhibitor, morphometric analysis, Histology of benign prostatic hyperplasia.

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Introduction

Benign prostatic hyperplasia (BPH) contains three main components:

1. Epithelial cells (glandular tissue); it contains acini and ducts. There are three major types of cells: Secretory epithelial cells, basal cells and neuroendocrine cells. Epithelial cells surround the periphery of the acini and secrete into the acini, and then secretions are drained into ducti and urethra. In the ablation of androgen, there occur a 90 % decrease in the number of secretory cells, and an 80 % lessening in the volume of cells,

2. Luminal surfaces in acini (glandular lumen),

3. Stroma; stromal tissue composed of smooth muscle, connective tissue, fibroblasts, nerves, lymphatic and blood vessels (1,2).

BPH is a stromal process occurred together with a significant smooth muscle hyperplasia primarily. The stroma/epithelium ratio in BPH is 4/1 and 5/1. The ratio of smooth muscle of hyperplastic stroma is about 40 % (3).

Performing the quantitative morphometric analysis of BPH tissue, the numerical quantities of areas that components cover were determined by various studies (4-8) (Table 1).

In this study, we compared stroma, epithelium, glandular lumen, smooth muscle hyperplasia, inflammation and fibrous components in BPH tissue between the group undergone surgery only and the group who had taken finasteride prior to surgical treatment.

Materials and Methods

Obtaining tissue specimen: Prostate adenomas were obtained from both 12 patients who were administered Finasteride for six months prior to surgical treatment and those of 11 patients undergone only surgical treatment (total 23 patients). All of them were undergone open prostatectomy. Surgical specimens were taken from mid part of adenoma and were evaluated by same pathologist who didn't know which group the patient belonged to. The weights of enucleated prostate adenomas were recorded.

The obstructive and irritative symptoms were investigated according to AUA symptom score questionnaire(9). Maximum urinary flow rates were measured with Storz uroflowmetry. In respect to these parameters, there was no significant difference among patients chosen for the study group. The distribution of so determined patients into two study groups was

done at random. These characteristics of both groups are shown in Table 2.

Tissue Analysis for Quantitative Morphometry: Histologic evaluations were performed quantitatively with planimetry. The measurements were made on projected images in ten different areas and mean per cent values were accounted.

Statistical Analysis: Statistical evaluation of parameters of both groups were performed by unpaired student-t test and statistical software.

Results

Attention was paid to have no statistically significant differences between clinical findings of both groups while open prostatectomy specimens were obtained (Table 2). Thus, we tried to minimize the factors that might have affected the histological components in both groups.

The ages of 23 patients were between 59 and 72. There was no significant difference between two groups in respect to ages (p>0.05).

The weight of enucleated prostate adenomas showed no significant difference between two groups (p>0.05). However, the adenoma weights of the group administered finasteride prior to surgery was lower than that of the other group (64.5±5.1 and 68.9±9.4 respectively). It is known that the weight of prostatic capsule is approximately 15 gm (10). But, this weight has been neglected in all our cases because open prostatectomy was applied to all of the patients included in the study.

The mean AUA symptom score was on the median symptomatic level in both groups (low symptomatic: 0-7, median symptomatic: 8-19, high symptomatic: 20-35). The difference between two groups was statistically insignificant (p>0.05).

The maximum urinary flow rates of patients were between 6.3 ml / sec., and 13.4 ml / sec. Besides, the difference between two groups was of no importance statistically (p>0.05).

The percentages of stroma, epithelium (Figure 1) and glandular lumen (Figure 2) of both groups were summarized in Table 3. A stromal dominance was observed in both groups. But the percentages of glandular lumen and stroma of both groups didn't show a significant statistical difference. Whereas no significant difference was found in the ratio of smooth muscle tissue (Figure 3), one of elements forming stroma, fibrotic and inflammatory areas (Figure 4) in finasteride group showed a significant increase compared to the group undergone only surgery (p<0.05, p<0.01 respectively) (Table 4). Epithelium percentage in finasteride group decreased significantly compared to the epithelium ratio of the group undergone only surgery. The mean epithelium ratios in both groups were 9.2 ±5 and 20.7±13.2 respectively (p<0.05).

Parallel to the decrease in ratio of epithelium in finasteride group, there was an increase in the ratio of stroma relatively. This can clearly be seen in stroma / epithelium ratio (Table 5). This ratio was found as 2.5±1.6 in the group undergone only surgery whereas it was 4.3 ± 1.7 in finasteride group. The difference between two groups was statistically significant (p<0.05).

Studies	Stroma	Epithelium	Glandular lumen
Bartsch et al. (4,5)	60 %	12 %	28 %
Shapiro et al. (6)	62 %	15 %	23 %
Shapiro et al. (7)	76 %*	16 %	9 %
Jonler et al. (8)	68.7 %	15.4 %	15.9 %

Table 1. Quantitative morphometric analysis of BPH tissue

* smooth muscle: 22 %
Fibrous tissue: 54 %

Groups	n	Ages	Prostatic weights (gr.)	AUA	Q max. (ml./sec.)
Finast.+Surg.	12	66.3± 4.1	64.5±5.1	13.5±6.0	9.7±2.0
Surgery	11	68.6±2.4	68.9±9.4	15.4±6.6	9.8±2.0

Table 2. Clinical findings of both groups

Unpaired student-t test: The difference between two groups are not significant (p>0.05).

Groups	n	Stroma %	Epithelium	Glandular lumen %
Finast.+Surg.	12	66.3± 14.2	9.2±5.2*	24.5±14.2
Surgery	11	49.4±22.6	20.7±13.2*	29.9±15.0

Table 3. Ratios of stroma, epithelium and glandular lumen

Unpaired student-t test: Statistically significant difference (p<0.05).

Groups	n	Smooth muscle tissue %	Fibrous tissue %	Inflammation %
Finasteride Surgery	12	44.4± 21.1	9.9±8.4*	12.3±6.4**
Surgery	11	42.0±20.1	3.2±4.6*	4.2±3.4**

Table 4. Ratios of stromal elements

Unpaired student-t test:

* Statistically significant difference (p<.05).

** Statistically highly significant difference (p<0.01).

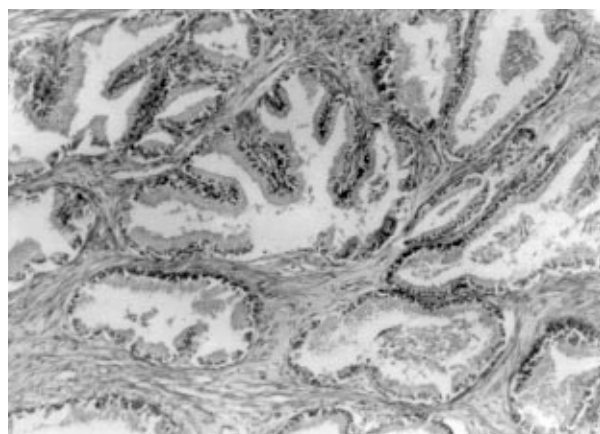


Figure 1. Glandular hyperplasia forming papillary structures toward lumen (H&Ex100)

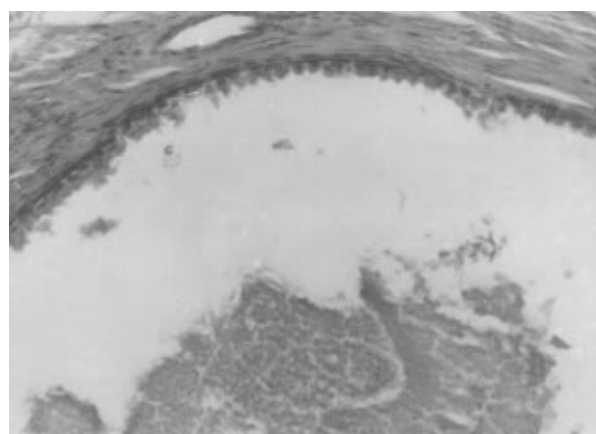


Figure 2. Cystic glandular structure having secretion in the lumen (H&Ex200)

Discussion

New invasive and clinical pharmacologic attempts as alternatives for the treatment of BPH have been on agenda for the last ten years(1). At present, clinical pharmacologic attempts are made as the alpha blockage of prostate smooth muscle contraction with alpha receptor blockers and lessening in the size of prostate through the inhibition of 5 alpha reductase enzyme.

In this context, the patients whose major component of prostates is stroma are candidates for alpha receptor blockage treatment since prostate smooth muscle is innervated with nerves containing alpha-1 receptor in high concentration, and blockage of these receptors lessen prostatic smooth muscle tone and bladder outlet resistance (11-14). In contrast, the patients

having less stroma are ideal for androgen deprivation and 5 alpha reductase treatment since the blockage of androgen in these patients will cause a reduction in epithelium, prostate size and outlet resistance (15-18).

In our study, we evaluated morphometric components in patients groups administered 5 alpha-reductase inhibitor (finasteride) prior to surgery and patients undergone only surgical treatment. It is known that 5 alpha-reductase inhibitors aim at lessening the epithelial component of prostate. The mean epithelium ratio in the group administered 5 alpha-reductase inhibitor prior to surgery lessened approximately two-fold compared to the other group. Stereological analysis has been demonstrated that BPH is a stromal process(4). In our study, there was no statistically significant difference between two groups

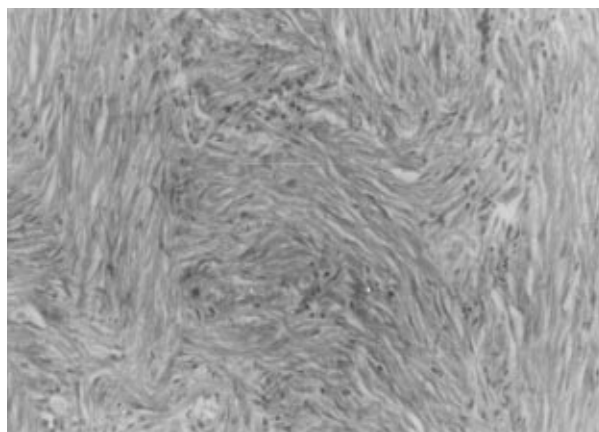


Figure 3. Clear muscle tissue hyperplasia (H&Ex100)

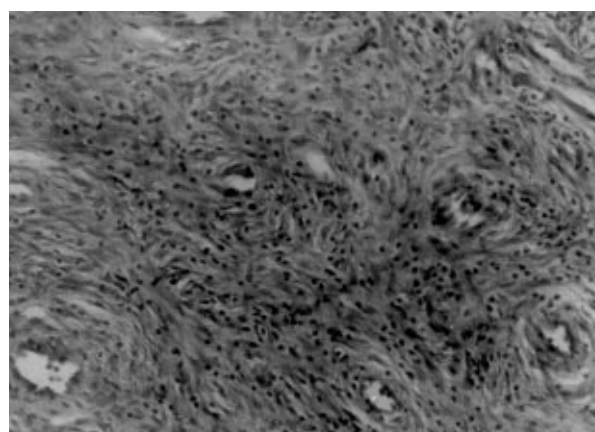


Figure 4. Fibroblastic proliferation, capillary vessel proliferation and inflammatory mononuclear cell infiltration (H&Ex200)

Table 5. Ratio of stroma/epithelium

Groups	n	Ratio of stroma/epithelium
Finasteride+Surgery	12	4.3±1.7*
Surgery	11	2.5±1.6*

Unpaired student-t test: * Statistically significant difference (p<0.05).

in respect to their mean stromal ratios. Yet, mean stroma/epithelium ratio in finasteride group was found to be 1.7 times greater than that of the other group. This is due to the relative increase of stromal ratio because of the decrease in epithelium. Whereas there was no difference in smooth muscle tissue between two groups, the development of fibrosis and inflammation showed a notable increase in finasteride group compared to the other group (p<0.05).

References

1. Deering Re, Choongkittaworn M, Bigler SA, Aramburu E, King J, Brawer MK. Morphometric quantitation of stroma in human benign prostatic hyperplasia. *Urology* 44:64-7, 1994.
2. DeKlerk DP, Heston WDW, Coffey DS. Studies on the role of macromolecular synthesis in the growth of the prostate. *Benign Prostatic Hyperplasia. Proceedings of a workshop sponsored by the Kidney Disease and Urology Program of the NIAMDD.* (Eds. JT Grayhack, JT Wilson and MJ Scherbenske) US Government Printing Office Washington 1976 pp.43-51.
3. Sant GR, Long JP. *Benign Prostatic Hyperplasia. Pathophysiologic Principles of Urology.* (Ed. Sant GR) Blackwell Scientific Publications Boston 1994 pp. 123-54.
4. Bartsch G, Müller HR, Oberholtzer M, Rohr HP. Light microscopic stereological analysis of the normal human prostate and benign prostatic hyperplasia. *J Urol* 122: 487-90, 1979.
5. Bartsch G, Keen F, Daxenbicher G, Marth c, Margreither R, Brungger A, Sutter T, Rohr HP. Correlation of biochemical (receptors, endogenous tissue hormones) and quantitative morphologic (stereologic) findings in normal and hyperplastic human prostates. *J Urol* 137:559-62, 1987.
6. Shapiro E, Becich MJ, Hartanto V, Lepor H. The relative proportion of stromal and epithelial hyperplasia is related to the development of symptomatic benign prostate hyperplasia is related to the development of symptomatic benign prostate hyperplasia. *J Urol* 147: 1293-5, 1992.

Shapiro et al. reported a correlation between the density of smooth muscle of the prostate tissue obtained with needle biopsies and responsiveness to alpha blockers(19). Besides, Deering et al. showed that stromal components were similar in all 3 sample groups in the quantitative morphometric analysis of prostate specimens obtained with transurethral resection (TUR), open prostatectomy and needle biopsy (1). This shows that all tissues obtained with these procedures can be reliable in the morphometric analysis of prostate.

As a conclusion, our study has shown that finasteride shrank the prostate as it decreased mean epithelium ratio and relatively increased the stroma/ epithelium ratio. Thus, it can be suggested that morphometric studies may have an indicative role in determining alternative pharmacotherapies in BPH treatment. If needle biopsy of prostate can be use for morphometric analysis, this procedure will be much practicable.

7. Shapiro E, Hartonto V, Lepor H. Quantifying the smooth muscle content of the prostate using double-immunoenzymatic staining and color assisted image analysis. *J Urol* 147: 1167-9, 1992.
8. Jonler M, Bruskewits RC. Prostatic histology in secondary transurethral resection of the prostate. *J Urol* 154: 119-22, 1995.
9. Barry MJ, Fowler FJ, O'Leary MP. Correlation of the American Urological Association symptom index with self-administered versions of the Madsen-Iversenn, Boyarsky, and Maine Medical Assesment program symptom index. *J Urol* 136:1-3, 1992.
10. Leissner KH, Tissel LE. The weight of the human prostate. *Scrand J Urol Nephrol* 13:233-6, 1979.
11. Jonler M, Riehmman M, Bruskewitz RC. Benign prostatic hyperplasia. *Current Pharmacological treatment. Drugs* 47:66-8,1994.
12. Khanna OP, Gonick P. Effects of phenoxybenzamine hydrochloride an canine lower urinary tract: clinical implications. *Urology* 6:323-5, 1975.
13. Lepor H. Nonoperative management of henign prostatic hyperplasia. *J Urol* 141:1283-6, 1989.
14. Lepor H. Medical therapy for benign prostatic hyperplasia. *Urology* 42:483-5, 1993.
15. Gomley GJ, Stoner E, Bruskewitz RC, Imperato-McGinley J, Walsh PC, McConnel JD, Andriole GL, Geller J, Bracken BR, Tenover JS. The effect of finasteride in men with benign prostatic hyperplasia. *The Finasteride Study Group. New Engl J Med* 327: 1185-7, 1992.
16. Stoner E. Three-year safety and efficacy data on the use of finasteride in the treatment of benign prostatic hyperplasia. *Urology* 43:284-6, 1994.
17. Lepor H. Efficacy of terazosin, finasteride or both in benign prostatic hyperplasia. *NEJIM* 335 (8): 533-9, 1996.
18. Patrick CW. Treatment of benign prostatic hyperpiasia. *NEJIM* 335(8): 586-7, 1996.
19. Shapiro E, Hartanto V, Lepor H. The response to alpha blockade in benign prostatic hyperplasia is related to the percent area density of prostate muscle. *Prostate* 21: 290-7, 1992.