INVESTIGATIVE UROLOGY

Detrusor Quantitative Morphometry in Obstructed Males and Controls

Collado A, Batista E, Gelabert-Mas A, Corominas JM, Arano P, Villavicencio H
Urology Service, Instituto Valenciano de Oncologia, Valencia, Spain
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Purpose: We studied the usefulness of computer assisted morphometry for measuring detrusor muscle cell diameter and the connective tissue-to-smooth muscle ratio in patients with bladder outlet obstruction, acute urinary retention and a nonobstructed control group.
Materials and Methods: A prospective study was done in patients with bladder outlet obstruction undergoing transurethral prostate resection. Patients were divided into 33 with obstruction and 14 in acute urinary retention. A total of 15 males without obstruction undergoing transurethral prostate resection for bladder tumor formed the control group. Detrusor specimens were obtained during transurethral prostate resection. Detrusor muscle cell diameter was measured using light microscopy and a semiautomatic image analysis system. The connective tissue-to-smooth muscle ratio was automatically determined with computer assisted image analysis. Symptoms and urodynamic assessment were performed preoperatively and 6 months postoperatively.
Results: A total of 62 patients were included. The obstruction and acute urinary retention groups had a statistically higher detrusor muscle cell diameter and more fibrosis than the control group. Patients in acute urinary retention had more intrafascicular fibrosis (higher connective tissue-to-smooth muscle ratio at 40x magnification) than patients with obstruction. There were no differences in detrusor muscle cell diameter or interfascicular fibrosis (connective tissue-to-smooth muscle ratio at 10x magnification) between the obstruction and acute urinary retention groups. Detrusor muscle cell diameter correlated with symptom duration and functional recovery after transurethral prostate resection. Detrusor fibrosis correlated with preoperative detrusor pressure at maximum flow and postoperative compliance. Patients in acute urinary retention had fewer symptoms and higher residual volume. Other urodynamic parameters and their improvement after surgery were similar in the acute urinary retention and obstruction groups.
Conclusions: Morphometric differences in detrusor muscle cell diameter and the connective tissue-to-smooth muscle ratio were observed between controls and patients with obstruction. There is an increase in detrusor muscle cell diameter and fibrosis in bladder outlet obstruction and more intense intrafascicular collagen deposition in patients in acute urinary retention.

Editorial Comment

Previous studies suggested that bladder outlet obstruction could produce histological changes in detrusor muscle and extracellular matrix; nevertheless, the results have been contradictory, with some authors reporting increase in smooth muscle and collagen decrease, while others reported collagen increase.

The authors studied 33 patients with bladder outlet obstruction (BOO) due to benign prostatic hypertrophy (BPH) and 14 patients in acute urinary retention (AUR). A total of 15 males without obstruction undergoing transurethral prostate resection for bladder tumor composed the control group. The present paper reported that the detrusor muscle cell diameter correlated with symptoms. It was found a positive correlation between the increase in cellular diameter and symptoms duration. The authors also studied the urodynamic parameters and found that there was no correlation in the obstructed and acute urinary retention groups with the detrusor muscle cell diameter. The authors found hypertrophy and an increase in fibrosis in patients with BOO. In patients with obstruction, there were slightly morphometric differences between those with an episode of AUR, that is higher intrafascicular fibrosis. There were no urodynamic differences preoperatively and postoperatively.

In a recent study (1), we analyzed the detrusor extracellular matrix in samples taken from bladders of 10 patients who underwent transvesical prostatectomy for treatment of BPH. Control material was composed of 10 vesical specimens, removed during autopsies performed in cadavers of accident victims, with ages between 18 and 35 years (mean = 26 years). We found that the components of connective tissue (collagen and elastic system fibers) are increased in the detrusor muscle of patients with infravesical obstruction, when compared to controls.

Reference

1. Rubinstein M, Sampaio FJ, Costa WS: Stereological study of collagen and elastic system fibers in the detrusor muscle of bladders from controls and patients with infravesical obstruction. Int Braz J Urol. 2007; 33 (1), In Press.

Dr. Francisco Sampaio
Full-Professor and Chair, Urogenital Research Unit
State University of Rio de Janeiro
Rio de Janeiro, Brazil

Dynamic Contrast Enhanced Magnetic Resonance Imaging as a Biological Marker to Noninvasively Assess the effect of Finasteride on Prostatic Suburethral Microcirculation

Jia G, Heverhagen JT, Polzer H, Jacko RV, Liang J, Zhang J, Levine AL, Rosol TJ, Knopp MV
Department of Radiology, Ohio State University, Columbus, Ohio, USA
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Purpose: We assessed dynamic contrast enhanced magnetic resonance imaging as a biological marker of in vivo changes in microcirculation in the prostatic suburethral region.
Materials and Methods: A total of 12 male beagle dogs with spontaneous benign prostatic hyperplasia were randomly allocated to 1 control group and 1 finasteride (Merck and Co., Whitehouse Station, New Jersey) treated group. Two baseline dynamic contrast enhanced magnetic resonance imaging examinations and 3 followups were performed to assess prostate microcirculation. Treatment duration was 3 months. The pharmacokinetic parameters evaluated in prostatic suburethral areas were the maximum enhancement ratio in AU, time to maximum signal enhancement in minutes, amplitude in AU and the exchange rate constant in minutes(-1).
Results: After completion of the therapeutic regimen time to maximum signal enhancement was significantly longer in the finasteride group than in controls ($p < 0.01$). Amplitude and the exchange rate constant decreased 39% and 34%, respectively, in the finasteride group at the end of treatment, which significantly differed from results in the control group ($p < 0.05$).
Conclusions: Dynamic contrast enhanced magnetic resonance imaging is capable of noninvasively assessing the prostatic microcirculation changes induced by finasteride. Pharmacokinetic parameters show considerable promise to be biomarkers for the development of benign prostatic hyperplasia drugs such as 5alpha-reductase inhibitors by the in vivo monitoring of microvascular changes. A relevant clinical application could be the pretreatment assessment of finasteride effectiveness to decrease perioperative bleeding at transurethral prostate resection and in treatment for hematuria.

Editorial Comment

During the last years we learned that finasteride could decrease prostatic bleeding, both in benign prostatic hyperplasia (BPH) and in transurethral resection of the prostate (TURP), and we have been using finasteride in

the clinical setting for these proposes. Nevertheless, the mechanism of finasteride action in stopping bleeding is still unknown.

The authors of the present paper used male beagle dogs to assess dynamic contrast enhanced magnetic resonance imaging as a biological marker of in vivo changes in microcirculation in the prostatic suburethral region. They found that subjects in the finasteride group had decreased microcirculation, as expressed by lower and slower contrast enhancement, and as quantified by increased Tmax, and decreased A and kep in the prostatic suburethral area. They concluded that finasteride would decrease the prostatic microcirculation and therefore diminish prostatic bleeding in BPH and TURP.

In a recent experimental paper, Canda et al. (1) evaluated the effects of finasteride on the vascular surface density (VSD), number of microvessels (NVES) and vascular endothelial growth factor (VEGF) expression of the rat prostate. After studying 19 adult rats, the authors found that the mean prostatic weights were decreased significantly in rats given finasteride ($p=0.0001$). On the other hand, finasteride does not seem to decrease VSD, NVES and VEGF expression at the level of the rat prostate. The effect of reduction of bleeding in BPH is more likely to be due to its effect on shrinking glandular hyperplasia, which might enhance vessel wall stability, rather than decreasing overall vascularity (1).

From these two papers, we can infer that the exact mechanism of action of finasteride on the prostatic vessels is still open to research and discussion.

Reference

1. Canda AE, Mungan MU, Yilmaz O, Yorukoglu K, Tuzel E, Kirkali Z: Effects of finasteride on the vascular surface density, number of microvessels and vascular endothelial growth factor expression of the rat prostate. Int Urol Nephrol. 2006; 38: 275-80.

Dr. Francisco Sampaio
Full-Professor and Chair, Urogenital Research Unit
State University of Rio de Janeiro
Rio de Janeiro, Brazil

RECONSTRUCTIVE UROLOGY

Gender Specific Chronological and Morphometric Sssessment of Fetal Bladder Wall Development

Koerner I, Deibl M, Oswald J, Schwentner C, Lunacek A, Fritsch H, Bartsch G, Radmayr C
Department of Pediatric Urology, Medical University of Innsbruck, Innsbruck, Austria
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Purpose: To enhance our understanding of sonographically visible alterations in bladder wall thickness, we delineated phenotypic changes occurring in developing smooth muscle cells of the fetal and postnatal bladder with respect to gender specific differences.
Materials and Methods: Bladders of 30 male and 18 female fetuses and 4 stillborn infants were immunostained with an alpha-smooth muscle actin antibody. Morphological and morphometric assessment was performed with the assistance of an image analysis system.
Results: Alpha-smooth muscle actin expression in fetal bladder wall was detectable at 9 weeks of gestation. Bladder wall thickness and mean profile area of smooth muscle bundles increased significantly with advancing gestation, mediated by linear growth patterns. Fetal bladder wall development occurred uniformly, unrelated to gender.