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PROSTATIC ISCHEMIA AND LOWER URINARY TRACT DYSFUNCTION

Hypothesis / aims of study

Our goal was to investigate the role of pelvic ischemia in lower urinary tract dysfunction. In prior animal studies, we found that chronic ischemia led to increased prostatic fibrosis, decreased smooth muscle content, decreased vascular endothelial growth factor expression, and decreased smooth muscle relaxation in response to electrical stimulation. These findings suggest that prostatic ischemia may lead to bladder outlet obstruction or lower urinary tract symptoms, but this has not been investigated in the clinical setting. The effect of chronic ischemia on the human prostate is unknown.

Study design, materials and methods

Methods: Males presenting for clinically indicated prostate biopsy were prospectively offered participation according to an Institutional Review Board-approved protocol. Clinical information was gathered regarding tobacco, peripheral vascular disease, hypercholesterolemia, hypertension, and diabetes. The International Prostate Symptom Score and International Index of Erectile Function were administered. Serum was drawn for total cholesterol, hemoglobin A1c, total and bioavailable testosterone and dihydrotestosterone. Pressure flow studies, transrectal prostate volume measurements, and duplex doppler assessment of blood flow were performed prior to prostate biopsy. Pathologic examination of the prostate tissue was performed. Masson's trichrome histochemical stain for fibrosis, CD34 immunohistochemical stain for microvessel density and Mouse anti-VEGF (vascular endothelial growth factor) immunohistochemical staining (Santa Cruz Biotechnology, Inc, California) for VEGF expression were performed. Positive controls were tonsil for CD-34 and kidney for VEGF. Omission of the primary antibody was used as negative control. Tissue was assessed in a double-blind fashion by two observers. The fibrosis was reported as a percent. The number of CD34-stained vessels were counted in five 40x fields bilaterally and averaged. VEGF expression was rated on a 0-3 scale of intensity. Because of the effect of cancer on VEGF expression (strong positive correlation), the ten patients with cancer were excluded. Pearson's correlation coefficient was calculated and considered significant at a level of $p<.05$.

Results

Results: 33 men chose to participate all completed the study. The average age was 66.4 years with an average smoking history of 35 pack years. There was no correlation between prostate size and outflow obstruction index ($r=.24$, $P > 0.1$). Smaller glands tended to be more fibrotic (more collagen was represented on trichrome stain). There was a strong inverse correlation between bladder outlet obstruction and VEGF intensity ($p<0.01$) but not with CD34 expression.

Interpretation of results

Decreased VEGF expression is a histologic marker for ischemia in non-cancerous tissue. We found that VEGF expression was diminished in patients demonstrating and increased obstructive index on pressure flow studies. Prostate size did not correlate with obstructive index.

Concluding message

These data suggest a role for ischemia as a determinant of prostatic structure and function. Further studies are underway to expand these observations, including investigating hypoxia-inducible factor–1 alpha expression in fresh human prostatic tissue.