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MEASUREMENT OF BLADDER TISSUE LEVELS OF ISOPROSTANE 8-ISO-PGF2A IN HUMANS – PRELIMINARY RESULTS

Hypothesis / aims of study

Isoprostanes, prostaglandin-like end products of arachidonic acid peroxidation, are produced by a free-radical catalyzed mechanism, and represent the only markers of oxidative stress. Isoprostanes are synthesized locally in both bladder muscle and mucosa and their synthesis is initiated by various physiologic and pathologic stimuli, such as stretching of the detrusor muscle, injury to the vesical mucosa and stimulation of the nerves. Isoprostane 8-iso-$PGF_{2\alpha}$ has been widely investigated in animals because of its potent constrictor effect on smooth muscle. (1) It is found significantly increased in the urine of spinal cord injury patients with detrusor overactivity and in patients with hypocontractile bladder. (2)
At today, no data are available about the production of 8-iso-$PGF_{2\alpha}$ into the bladder wall of patients affected by different voiding dysfunction.
The aim of the present study was to determine bladder tissue levels of 8-iso-$PGF_{2\alpha}$ in patients affected by bladder outlet obstruction (BOO) related to different conditions and to compare the results with those obtained from patients with bladder inflammation.

Study design, materials and methods

We included in the study 30 patients (20 men and 10 women). 12 patients were affected by non neurogenic BOO (NNBOO), 10 were affected by neurogenic BOO (NBOO) and 8 patients presented with hypersensitive bladder. At the beginning of the study all patients had a negative urinalysis and urine colture. In all cases an informed consent was stated. Patients underwent cystoscopy with bladder wall biopsy specimens. At least 1 bioptic specimen was taken deeply from the lateral or the posterior wall of the bladder. Samples were weighted and lysed by EIA buffer containing Triton-100. 8-iso-$PGF_{2\alpha}$. EIA kit from Cayman Chemicals, detection limit of EIA assay was 5 pg/ml. The results were expressed as 8-iso-$PGF_{2\alpha}$ pg/mg bladder tissue.
We compared bladder tissue levels of 8-iso-$PGF_{2\alpha}$ obtained from the three different above mentioned conditions. Statistical analysis was performed by test T of Student, at the level of 0.05 the two means were statistically different.

Results

In the NNBOO group mean level of 8-iso-$PGF_{2\alpha}$ was 56.303 pg/mg ± 67.6; in the NBOO group it was 7.784 pg/mg ± 7.41. Mean concentration of 8-iso-$PGF_{2\alpha}$ in patients affected by hypersensitive bladder was 0.414 pg/mg ± 0.41. We could detect a significant difference between 8-iso-$PGF_{2\alpha}$ concentration in the NNBOO group as compared to the hypersensitive bladder group ($p<0.05$). Furthermore we recorded a significant difference between 8-iso-$PGF_{2\alpha}$ in the NNBOO as compared to the NBOO group ($p<0.05$). Finally, in the NBOO group bladder tissue levels of 8-iso-$PGF_{2\alpha}$ were not significantly higher than those in the hypersensitive bladder group ($p>0.05$).

Interpretation of results

Isoprostanes are used clinically and experimentally as markers for many diseases in which oxidative stress is a prominent feature. Since the production of 8-iso-$PGF_{2\alpha}$ depends on a free radical cathalyzed mechanism it has been suggested that excreted concentrations can be used as a novel marker to monitor or diagnose oxidative stress related disease. It has been observed that urinary levels of 8-iso-$PGF_{2\alpha}$ increase without a concomitant increase in plasma malondialdehyde. This is indicative for a local oxidative stress in patients with hyperactive bladder.
To our knowledge, the present study is the first reporting data about bladder tissue levels of isoprostane 8-iso-$PGF_{2\alpha}$ in humans. The significantly higher bladder tissue levels of 8-iso-$PGF_{2\alpha}$ in patients affected by NNBOO as compared to those affected by NBOO or hypersensitive bladder can indicate that in these patients the oxidative stress related to BOO is more intensive and prolonged. The difference between patients affected by NBOO and patients with hyperactive bladder, even if not significant, can be explained by the lack of obstruction in patients with hypersensitive bladder.

Concluding message

It is possible to measure tissue levels of 8-iso-$PGF_{2\alpha}$ in human bladder. These levels are related to BOO and to the consequent oxidative stress. It is possible to hypothesize its use as a reliable marker in the diagnosis and in the follow up of voiding dysfunction with high level of oxidative stress.

References

1 - Clinica Chimica Acta 339 (2004) 43-47
2 - Trends Pharmacol Sci 2002; 23:360-6

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