

## CHANGES OF URINARY NERVE GROWTH FACTOR AND PROSTAGLANDIN E<sub>2</sub> AFTER ANTICHOLINERGIC TREATMENT IN FEMALE PATIENTS WITH OVERACTIVE BLADDER

### Hypothesis / aims of study

Overactive bladder (OAB) is a syndrome consisting of urgency, with or without urgency urinary incontinence, usually with frequency and nocturia. Nerve growth factor (NGF) plays a critical role in the development of the peripheral nervous system and increased expression of the NGF in the urinary bladder may contribute to irritative symptoms in patients with OAB. Prostaglandins (PGs) affect the micturition reflex and the bladder is a site of PG synthesis. Therefore, NGF and PGs can be related to storage symptom in patients with OAB. This study was performed to investigate urinary NGF and PGE<sub>2</sub> levels in the female OAB patients and the changes of urinary NGF and PGE<sub>2</sub> levels after treatment with anticholinergics.

### Study design, materials and methods

The study group included 50 female OAB patients who had not suffered from any neurological disease and showed no abnormality in their urine analysis. Fifteen females without bladder symptoms and with normal urine analysis were used as control. The initial evaluation included consecutive voiding diaries for 3 days, recording the grade of urgency by urinary sensation scale and urodynamic study in the OAB patients. After a 4-week treatment period with anticholinergics (tolterodine), the follow-up evaluations were done with consecutive voiding diaries for 3 days and urinary sensation scale in the total 50 OAB patients. They were assigned to group 1 (n=23, no interval change in urgency scale), group 2 (n=15, 1 point improvement in urgency scale) and group 3 (n=12, more than 2 points improvements in urgency scale) by the changes in urinary sensation scale after treatment. Voided urine was collected from the OAB patients and control at the first visit. After a 4-week treatment period with anticholinergics (tolterodine), voided urine was collected again from the female with OAB. And then, the urinary NGF and PGE<sub>2</sub> levels in voided urine were analyzed by enzyme linked immunosorbent assay. The urinary NGF and PGE<sub>2</sub> levels in female with OAB were compared with control. And also the urinary NGF and PGE<sub>2</sub> levels were compared among the 3 groups before and after treatment with anticholinergics.

### Results

The mean age was 57.4 (20-85). Urgency grade in group 3 was significantly high compared with Group 1 and Group 2 before treatment with anticholinergics (p<0.05). Only in the group 3, the significant decreases in frequency and nocturia were observed after a 4-week treatment of anticholinergics based on consecutive voiding diaries (p<0.05). The urinary NGF (11.34±1.84 ng/ml) and PGE<sub>2</sub> (0.65±0.08 ng/ml) levels were significantly increased in female with OAB compared with urinary NGF (2.34±0.41 ng/ml) and PGE<sub>2</sub> (0.25±0.07 ng/ml) levels in female without OAB (p<0.05). The urinary NGF and PGE<sub>2</sub> level before and after treatment with anticholinergics were not significantly different in group 1 and group 2. However, the urinary NGF level (5.33±1.38 ng/ml) after a 4-week treatment with anticholinergics was significantly decreased compared with the pre-treatment level (13.07±3.36 ng/ml) in group 3 (p<0.05). The urinary PGE<sub>2</sub> level was not significantly different before and after treatment with anticholinergics in group 3.

### Interpretation of results

After treatment with anticholinergics, the symptoms of OAB were much more improved in patients complaining with more severe symptoms. The significantly increased urinary NGF and PGE<sub>2</sub> levels were observed in female with OAB compared with female without OAB. These results show that the increase of urinary NGF and PGE<sub>2</sub> levels can correlate with development of symptoms of OAB. The significant decrease of urinary NGF level after treatment with anticholinergics was observed in the patients who have improvement of OAB symptoms, which reflect relationship between changes of NGF and OAB symptom. The urinary PGE<sub>2</sub> level may be unrelated with the changes of OAB symptoms before and after treatment with anticholinergics.

### Concluding message

The NGF and PGE<sub>2</sub> can be important factors in the development of OAB symptoms in female. Also, it is considered that the urinary NGF correlates with the changes of OAB symptoms after treatment with anticholinergics in female with OAB.

<b>Specify source of funding or grant</b>	<b>No</b>
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<b>Is this study registered in a public clinical trials registry?</b>	<b>No</b>
<b>What were the subjects in the study?</b>	<b>HUMAN</b>
<b>Was this study approved by an ethics committee?</b>	<b>Yes</b>
<b>Specify Name of Ethics Committee</b>	<b>Institutional Review Board of the Catholic University of Korea</b>
<b>Was the Declaration of Helsinki followed?</b>	<b>Yes</b>
<b>Was informed consent obtained from the patients?</b>	<b>Yes</b>