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OVERACTIVE BLADDER IS A DYNAMIC SYNDROME -- A FIVE-YEAR LONGITUDINAL FOLLOW-UP OF THE CHANGES OF OVERACTIVE BLADDER SYMPTOMS, URODYNAMIC STUDY AND THE URINARY NERVE GROWTH FACTOR LEVELS

Hypothesis / aims of study

Overactive bladder (OAB) is a condition of urinary urgency with or without urge incontinence (UI), and is usually accompanied by frequency and nocturia. OAB symptoms could be due to psychological factors, increased urine production, uninhibited urge to void due to central nervous system lesions or having detrusor overactivity (DO). Patients with increased bladder sensation are often misdiagnosed as having OAB. Previous study showed the incidence of UI and OAB increased in a 16 years span with a certain percentage of women having symptoms regression and progression. The overall prevalence of OAB significantly increased from 17% to 26% during the 16 year period. Measurement of urinary NGF levels in patients with OAB and at different conditions provided an insight to the underlying pathophysiology of this sensory disorder. Recent evidence have suggested that urinary NGF level is a promising biomarker for the diagnosis of OAB. Measurement of urine NGF levels may serve as a useful objective test to evaluate idiopathic DO and treatment outcome. The purpose of this study was to evaluate patients who have been diagnosed to have OAB more than 5 years ago and had urinary NGF test at that time. We compared their present urinary NGF levels with their previous urinary NGF levels to realize how the relationship between the changes of urinary NGF levels and clinical OAB symptoms.

Study design, materials and methods

A total of more than 300 patients who have been diagnosed as OAB more than 5 years ago were reviewed from chart. The patients were not regularly treated for their OAB symptoms. We tried to contact with them and assess their current bladder conditions by symptom questionnaires and urodynamic study. The OAB syndrome was classified as OAB-wet, OAB-dry, or hypersensitive bladder (HSB) and urgency severity score (USS) from 0-4 was used to further classify the urgency and UI conditions. Urodynamic study (UDS) at baseline and 5 years later were evaluated and classified as DO, HSB and normal according to UDS findings. A total of 30ml urine sample at full bladder was obtained for laboratory testing of urinary NGF levels. Urinary NGF levels were measured by the ELISA method. Total urinary NGF levels were normalized to the concentration of urinary creatinine (NGF/Cr level). Data on current urinary NGF/Cr levels were compared with the data 5 years ago in available OAB patients. Differences in urinary NGF/Cr levels were compared between baseline and 5 years later by the paired t-test. Furthermore, the changes of bladder conditions (OAB-wet, OAB-dry, HSB/normal) and the changes of USS and UDS findings were classified as improved, stationary or exacerbated and the changes of urinary NGF/Cr levels were compared between baseline and 5 years later according to the changes of bladder conditions. A p-value < 0.05 was considered to indicate statistical significance.

Results

A total of 95 patients including 32 women and 63 men were eligible to follow-up 5 years after the baseline assessment. The mean age was 72.6 ± 11.7 (39 to 96) years old. At baseline, OAB-wet was noted in 31, OAB-dry in 44 and HSB in 20 patients. After 5 years, OAB-wet was noted in 29, OAB-dry in 33 and HSB/normal in 33 patients. The changes of bladder conditions are shown in Table 1. Table 2 and Table 3 show the changes of USS and UDS findings at baseline and 5 years later, respectively. The urinary NGF/Cr levels showed no significant difference in the patients with improved, stationary, or exacerbated bladder conditions based on OAB subtypes or USS classifications. However, the urinary NGF/Cr levels were significantly decreased in patients with improved UDS findings, significantly increased in patients with exacerbated UDS findings and showed no change in those remained stationary UDS findings. (Table 4)

Interpretation of results

OAB symptoms change with time. Patients initially diagnosed as OAB or DO may change to other bladder conditions such as HSB or normal. The severity of OAB may change with or without medical treatment. Urinary NGF levels remain elevated in patients who have OAB and high USS score but cannot reflect the changes of bladder conditions based on subjective OAB symptoms. However, the urinary NGF levels can reflect the changes of bladder conditions according to the UDS findings.

Concluding message

OAB is a dynamic syndrome. Patients who were diagnosed as OAB may change their bladder conditions after 5 years. Although urinary NGF levels are elevated in OAB patients, the changes of urinary NGF levels can only reflect bladder conditions based on the changes of UDS findings. This result suggests OAB symptoms might not be reliable, only UDS findings can provide objective evidence for the bladder conditions of OAB. Urinary NGF levels can serve as biomarker to assess the severity of OAB.

Table 1. Changes of OAB types between baseline and after 5-year follow up

Baseline	After 5 years		
	Normal/HSB	OAB Dry	OAB Wet
HSB	11	8	1

OAB Dry	18	15	11
OAB Wet	4	10	17

Improvement Stable Exacerbation

Table 2. Changes of USS score between baseline and after 5 years follow up

Baseline	After 5 years				
	0	1	2	3	4
0	0	2	0	2	0
1	5	4	3	2	1
2	3	10	5	2	8
3	1	4	1	8	3
4	3	1	8	2	17

Improvement Stable Exacerbation

Table 3. Changes of UDS diagnosis between baseline and after 5 years follow up

Baseline	After 5 years		
	Normal	HSB	DO
Normal	21	4	3
HSB	11	11	8
DO	9	7	21

Improvement Stable Exacerbation

Table 4. Expression of urinary NGF/Cr in OAB patients with different clinical symptom changes or UDS diagnosis after 5 years

OAB symptoms	OAB subtypes			USS Score			UDS diagnosis		
	Baseline	After	*P*	Baseline	After	*P*	Baseline	After	*P*
Improvement	0.75±0.24	0.92±0.38	0.97	1.07±0.22	0.85±0.39	0.46	0.97±0.28	0.22±0.04 *	0.04
Stationary	0.96±0.36	1.07±0.35	0.96	0.75±0.22	1.20±0.39	0.51	0.91±0.29	1.34±0.35	0.69
Exacerbation	0.85±0.27	1.48±0.51	0.30	0.78±0.24	1.31±0.45	0.38	0.51±0.23	2.10±0.75 *	0.01

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