Overactive Bladder Changes with Time: A 5-Year Longitudinal Followup of Changes in Overactive Bladder Symptoms, Urodynamic Studies and Urinary Nerve Growth Factor Levels

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Abbreviations and Acronyms

Cr = creatinine
DO = detrusor overactivity
IBS = increased bladder sensation
LUTS = lower urinary tract symptoms
NGF = nerve growth factor
OAB = overactive bladder
UDS = urodynamics
USS = urgency severity score
UI = urinary incontinence
UUI = urgency urinary incontinence

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Purpose: We compared clinical symptoms, urodynamic diagnoses and urinary nerve growth factor levels at baseline and 5 years later in patients with overactive bladder.

Materials and Methods: Patients diagnosed with overactive bladder at a tertiary teaching hospital who underwent urinary nerve growth factor tests 5 years previously were identified by chart review. Patients were invited to return for symptom evaluation, urodynamic studies and a repeat urinary nerve growth factor test. Changes in overactive bladder subtype, urgency severity score and urodynamic diagnosis were classified as improved, stable or worse. Changes in urinary nerve growth factor/creatinine were compared between baseline and 5 years later according to changes in bladder conditions.

Results: A total of 30 women and 45 men completed the study. Mean ± SD age was 73.5 ± 10.3 years. Urinary nerve growth factor/creatinine showed no significant difference among patients with improved, stable or worse bladder conditions based on overactive bladder or urgency severity score subtypes. However, urinary nerve growth factor/creatinine was significantly decreased in patients with an improved urodynamic diagnosis (mean 0.94 ± 1.36 vs 0.17 ± 0.19 pg/mg, $p = 0.02$), significantly increased in patients with a worse urodynamic diagnosis (0.55 ± 0.85 vs 2.08 ± 2.81 pg/mg, $p = 0.04$) and showed no change in those with a stable urodynamic diagnosis. Multiple linear regression analysis revealed that the change in urodynamic diagnosis was still predictive of the change in urinary nerve growth factor/creatinine after adjusting for age, gender, overactive bladder and urgency severity score subtypes ($p = 0.001$).

Conclusions: Urinary nerve growth factor/creatinine did not reflect the changes in bladder conditions based on subjective symptoms. However, the levels reflected dynamic changes in bladder pathophysiology according to urodynamic findings.

Key Words: urinary bladder, overactive; urodynamics; nerve growth factor; creatinine; muscle hypertonia

OAB, characterized by urinary urgency with or without UUI, is usually accompanied by frequency and nocturia.[1] OAB symptoms can be due to peripheral or central nervous system dysfunction, neuromuscular disorders, urothelial dysfunction, medical disease such as diabetes or congestive heart failure, bladder outlet obstruction, depression, inflammation or

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debilitative symptoms caused by aging.[2] Patients with IBS and a strong urge to void are often misdiagnosed with OAB.[3] A longitudinal, population based study of UI, OAB and other LUTS showed that a certain percent of women experienced symptom regression and progression.[4]

Measuring urinary NGF in patients with OAB provides possible insight into the underlying pathophysiology. For example, patients with OAB wet had significantly higher urinary NGF than those with OAB dry.[5,6] However, systematic review did not support the notion that urinary NGF could be recommended for use in current clinical practice.[7]

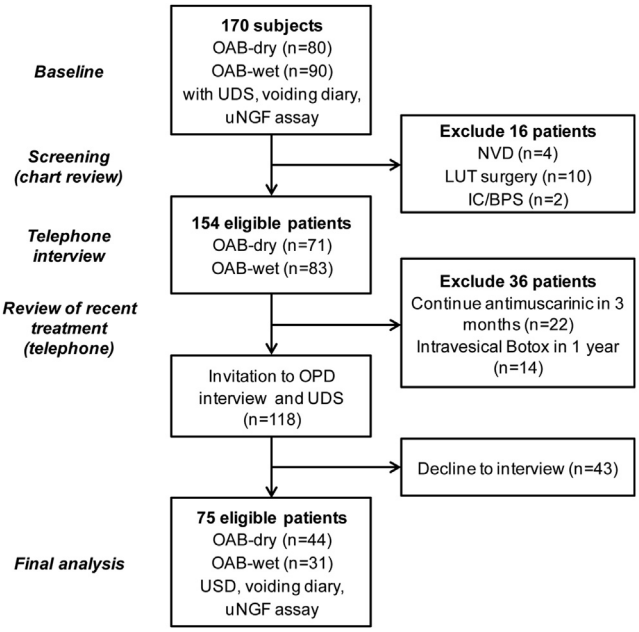
We evaluated the current bladder condition of patients diagnosed with OAB who underwent urinary NGF tests 5 or more years earlier. We compared current urinary NGF levels with previous levels to determine the relationships of changes in urinary NGF with clinical OAB symptoms and UDS findings.

MATERIAL AND METHODS

A total of 170 patients diagnosed with OAB more than 5 years earlier were identified in the medical records. After chart review we excluded from analysis 16 patients in whom neurogenic voiding dysfunction developed, lower urinary tract surgery was done or interstitial cystitis was proved. We contacted the remaining 154 patients by telephone to ask whether they would participate in interviews. Of those patients 22 had received antimuscarinic treatment in the last 3 months, 14 had received intravesical Botox® injection during the last year and 43 refused the outpatient clinic interview. Thus, only 75 patients were eligible for interview and investigation who had not been treated for LUTS in the last 3 months (see figure).

We assessed the bladder conditions of patients who consented to participate. If the patient agreed to return to the urological outpatient clinic, physical examination, urinalysis, uroflowmetry, post-void residual volume measurement and bladder condition evaluation were performed. Current bladder conditions were evaluated using a 3-day voiding diary, USS and UDS. This study was approved by the hospital research ethics committee. Informed consent was obtained from patients during the urological outpatient clinic interview. Patients with a current or previous urinary tract infection in the last 3 months, interstitial cystitis proven by cystoscopic hydrodistention or new onset neurogenic bladder were excluded from study.

All patients were assessed by a validated Chinese USS questionnaire and completed a 3-day voiding diary regarding urgency and UUI episodes. The validated Chinese USS questionnaire, which was linguistically translated from the validated PPIUS (Patient Perception of Intensity of Urgency Scale),[8] was scored as 0—no feeling of urgency, 1—mild feeling, 2—moderate feeling, 3—severe feeling and 4—unable to hold urine.[9] We used the validated Chinese version of USS to distinguish true urgency from a strong urge to void (USS 2 to 4) for patient selection.



Patient flow chart. *NVD,* neurogenic voiding dysfunction. *LUT,* lower urinary tract. *IC/BPS,* interstitial cystitis/bladder pain syndrome. *uNGF,* urinary NGF. *OPD,* outpatient clinic.

The 3-day voiding diary record was obtained and UDS were performed to assess bladder conditions. OAB wet was considered at least 1 UI episode in the 3-day voiding diary. OAB dry was considered no UI episode but at least 1 urgency episode in the voiding diary. IBS was considered no urgency episode in the voiding diary but functional bladder capacity less than 350 ml. Average voiding frequency less than 8 times per day, no urgency or UUI episode and functional bladder capacity more than 350 ml were considered normal bladder conditions. The UDS diagnosis was classified as normal, IBS or DO if UDS showed characteristic findings.[4] Patients were considered to improve during the 5-year interval if symptoms changed from OAB wet to OAB dry, from OAB dry to IBS or normal, USS decreased, or the UDS diagnosis changed from DO to IBS or from IBS to normal. The bladder condition was considered to have worsened if the change in clinical symptoms, USS or UDS diagnosis was reversed.

Urinary NGF Measurement

A 30 ml urine sample with a full bladder was obtained at the outpatient clinic interview for laboratory testing of urinary NGF. Levels were measured by enzyme-linked immunosorbent assay using undiluted urine samples using a previously reported standard procedure.[10] At the same time 3 ml urine were obtained to measure urinary Cr. The NGF concentration was determined using the Emax® ImmunoAssay System with a specific and highly sensitive enzyme-linked immunosorbent assay kit with a minimum sensitivity of 7.8 pg/ml. The amount of NGF in each urine sample was determined from a standard curve. All samples were run in triplicate and values were