Urinary Nerve Growth Factor Level Is a Potential Biomarker of Overactive Bladder and Detrusor Overactivity

Hsin-Tzu Liu, M.S., Hann-Chorng Kuo, M.D.
Department of Urology, Buddhist Tzu Chi General Hospital and Tzu Chi University, Hualien, Taiwan; E-mail: hck@tzuchi.com.tw

Clinical diagnosis of overactive bladder (OAB) is based on subjective symptoms. This study is designed to measure the urinary nerve growth factor (NGF) levels in patients with different types of bladder dysfunction and to evaluate whether urinary NGF is be a biomarker for diagnosis of OAB and detrusor overactivity (DO).

NERVE GROWTH FACTOR

Urinary tract nerve growth factor (NGF) is produced by urothelium and smooth muscle [1]. Clinical and experimental data indicate a direct link between increased levels of NGF in the bladder tissue and urine and painful inflammatory conditions in the lower urinary tract, such as interstitial cystitis and chronic prostatitis [2-4]. Intravesical instillation of NGF has been shown to induce bladder hyperactivity in rats [5]. Increased levels of NGF have also been reported in the bladder tissue and urine of patients with sensory urgency and DO [6-8].

Evidence has shown that visceral epithelia are a major source of NGF production and that NGF may regulate the function of adult visceral sensory and motor neurons [9]. The level of NGF in urine could increase bladder sensation or cause DO through some unknown pathways [10]. If the urinary levels of NGF differ between normal controls, patients with OAB and patients with DO, then urinary NGF level could be a biomarker for diagnosis of these types of bladder dysfunction. Furthermore, if urinary NGF levels can be reduced after successful treatment of OAB or DO, then measurement of urinary NGF might be a useful objective tool to assess the therapeutic outcome of specific treatment modalities that do not involve invasive urodynamic assessment. This study aims to measure the urinary NGF levels in patients with different types of bladder dysfunction and to compare the urinary NGF levels in patients after treatment for OAB and DO symptoms.

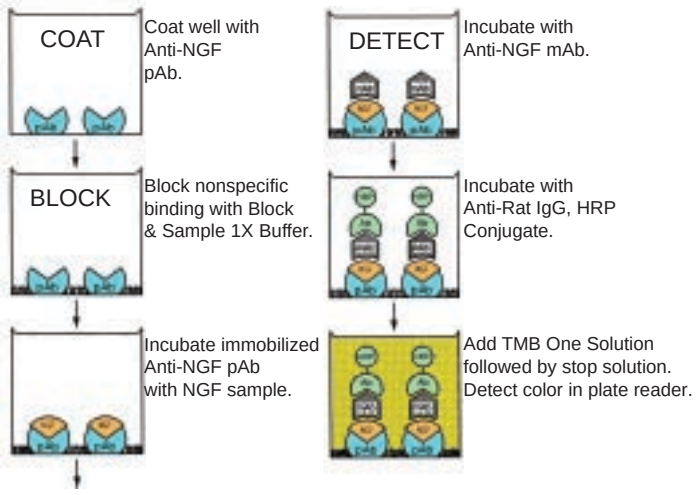

Fig. 1. Principle of the double sandwich ELISA- NGF Emax immunoassay System (PROMEGA).

Table 1. The levels of urinary nerve growth factor in different groups of patients

Bladder dysfunction		Urine samples	Urinary total NGF (pg/mL)	Urinary NGF/Cr	Statistics*
Normal control		40	3.26 ± 13.50	0.0400 ± 0.16	
	at first sensation	21	0.08 ± 0.32	0.0005 ± 0.0022	
	at urge sensation	21	9.80 ± 12.56	0.2100 ± 0.30	P= 0.003#
OAB	untreated	43	42.80 ± 55.60	0.8700 ± 1.40	P= 0.000
	well treated OAB	46	10.80 ± 23.60	0.1200 ± 0.24	P= 0.070
	failed treated OAB	4	15.00 ± 22.90	0.1600 ± 0.26	P= 0.204
IDO	untreated	103	53.70 ± 82.60	1.1800 ± 2.05	P= 0.000
	well treated IDO	19	15.10 ± 22.90	0.1900 ± 0.42	P= 0.050
	failed treated IDO	12	51.40 ± 71.50	0.6400 ± 0.86	P= 0.000
BOO	non-OAB	61	1.80 ± 4.00	0.0290 ± 0.07	P= 0.612
	with OAB	25	40.90 ± 54.60	0.8100 ± 1.53	P= 0.002
	with IDO	47	50.20 ± 60.40	0.8000 ± 0.89	P= 0.000
NDO	CVA	18	35.00 ± 45.00	0.6600 ± 0.96	P= 0.000
	SCI	32	28.00 ± 67.80	0.4300 ± 0.88	P= 0.007
Hypersensitive bladder		10	1.36 ± 2.90	0.0280 ± 0.06	P= 0.811
Detrusor underactivity		10	0.67 ± 2.10	0.0230 ± 0.07	P= 0.741

*: comparison of urinary NGF/Cr level between control and bladder dysfunction; #: comparison between first sensation and urge sensation

MEASUREMENT OF NGF IN LUTD

Urinary NGF levels were measured in patients with different types of bladder dysfunction causing LUTS and in the control subjects without LUTS. A total of 502 urine samples were collected. Urinary NGF levels were measured by the ELISA method (Fig.1). The total urinary NGF levels were then normalized to the concentration of urinary creatinine (NGF/Cr level). The total urinary NGF levels of subgroups and the NGF/Cr levels are listed in Fig. 2. The NGF/Cr level was compared among the control and all patient groups (Table 1).

Urinary NGF levels were low in the control groups but increased slightly when the bladder was extremely urge to void. Patients with idiopathic DO with or without bladder outlet obstruction (BOO) had the highest urinary NGF levels. Patients with OAB symptoms also had significantly higher urinary NGF levels compared to controls. The urinary NGF levels reduced to normal levels after treatment in patients with OAB and in those with DO. Urinary NGF levels increased in patients with neurogenic DO due to spinal cord lesions or cerebrovascular accidents.

RESULTS AND DISCUSSION

This study has shown that urinary NGF levels were significantly high in patients with OAB and in patients with IDO. Patients with OAB

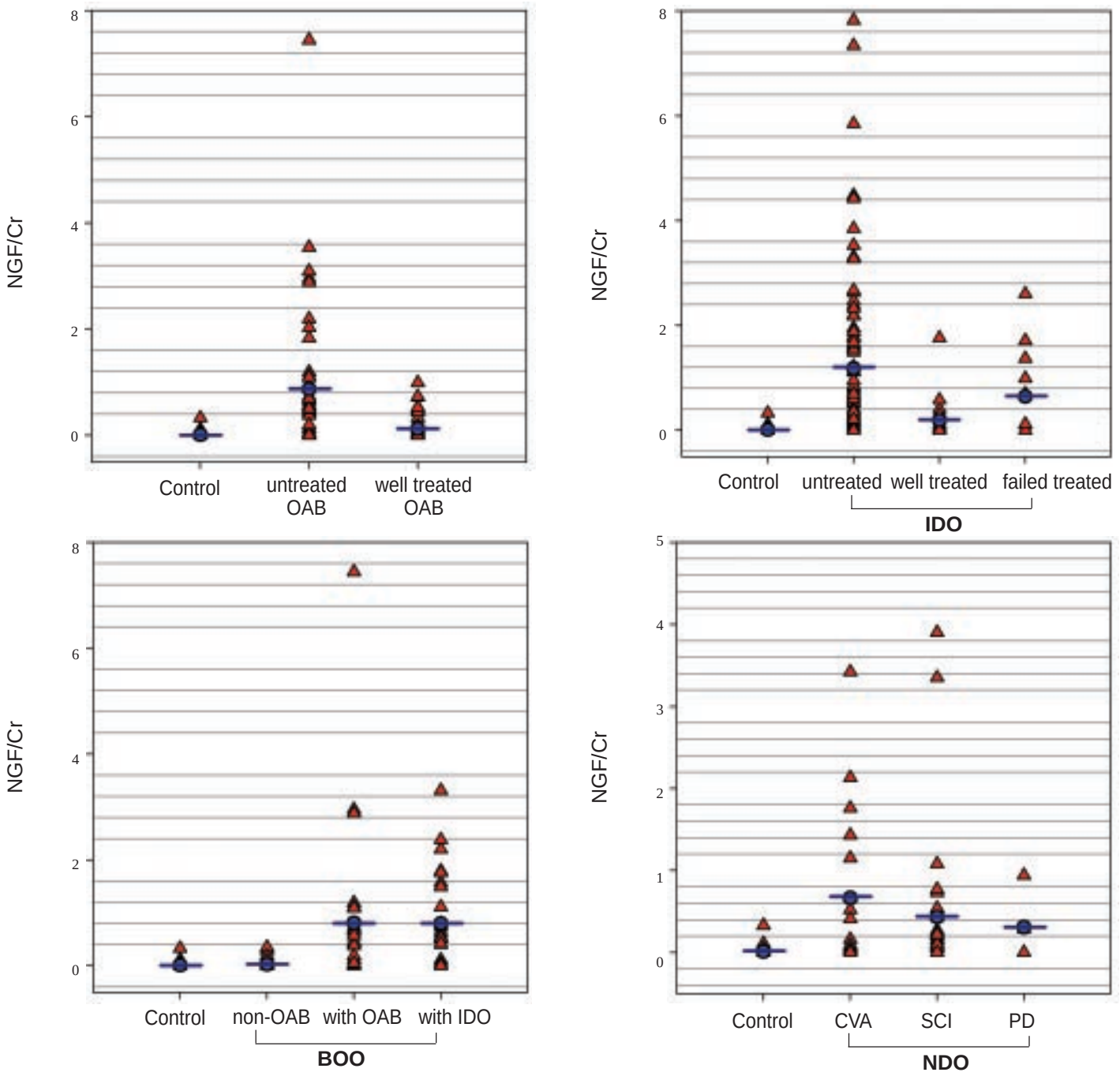

Fig. 2. The distribution of NGF/Cr levels in various bladder dysfunctions.

and those with IDO who were successfully treated with antimuscarinics or intravesical botulinum toxin injections had significantly reduced NGF levels. Urinary NGF levels in patients with OAB and in patients with IDO for whom treatment failed were significantly higher than those in controls and patients with well treated OAB or IDO. Urinary NGF levels in patients with NDO, regardless of whether they had concomitant SCI or CVA, were also significantly higher than those in controls and were similar to the NGF level in patients with OAB. These results suggest that urinary NGF levels are a potential biomarker for diagnosis of OAB and DO and can be used in assessing the therapeutic effects of OAB and DO.

CONCLUSION

The level of urinary NGF is a potential biomarker of OAB and DO. Patients with OAB and IDO had a significantly higher urinary NGF level compared to the controls. Patients with OAB and those with DO who were successfully treated had reduced urinary NGF levels.

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