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BDNF: A POTENTIAL BIOMARKER OF OVERACTIVE BLADDER

Hypothesis / aims of study

Overactive bladder (OAB) is a symptom complex in which urinary urgency must be present in order to establish the diagnosis. Therefore, the necessity of a biomarker to assist OAB diagnosis is doubtful. Nevertheless, OAB may co-exist with stress urinary incontinence (SUI). Mixed urinary incontinence (MUI) is the most prevalent form of urinary incontinence in elderly women (1) and discrimination of OAB wet from SUI remains a challenge to clinicians, with therapeutic decision implications. In this context, a biomarker able to separate OAB wet from SUI could be helpful in such doubtful clinical cases.

In the last few years, urinary neurotrophins (NTs) have emerged as potential biomarkers of OAB. Nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) are the most ubiquitous NTs, exerting their effects via specific tyrosine kinase (Trk) receptors. NGF binds to TrkA and BDNF to TrkB receptor, both expressed in bladder urothelium and primary sensory fibers.

Recent clinical studies have reported high levels of NGF in the urine of OAB patients (2,3), although a significant overlap between healthy individuals and patients' values was noted. Less is known about BDNF. Recently, BDNF was found in high concentration in the urine of OAB patients and appears to be sensitive to lifestyle intervention.

In the present study we assessed the urinary levels of BDNF in healthy female individuals, in OAB wet patients, before and after treatment, and in patients with pure SUI. Urinary BDNF levels were correlated with OAB symptoms severity along treatment.

Study design, materials and methods

Urine samples from 20 patients with SUI and 20 healthy women were collected and adequately stored until further processing.

Thirty-seven female naïve OAB patients (32 OAB wet) were evaluated at baseline. Twenty-five patients were reevaluated at 3 months, after lifestyle intervention (LSI), and 6 months, after 3-month antimuscarinic treatment (AMT) with oxybutynin chloride ER, 10mg/d. Urine samples from OAB patients were collected at each time point of evaluation.

Urine samples were processed for ELISA analysis of BDNF, and urinary content of BDNF was normalized against creatinine concentration.

All OAB patients completed a 7-day bladder diary combined with an Urgency Severity Scale (USS) at baseline, 3 months and 6 months. The bladder condition was assessed using the number of urgency episodes per week (NUE/w). For that matter, urgency events, corresponding to micturitions scored as 3 or 4 in the bladder diary, were counted.

Results

Urinary BDNF/Cr ratio was significantly higher in OAB patients (647.0 ± 584.1), compared to healthy women (110.4 ± 159.5, $p<0.001$) and to SUI patients (160.1 ± 231.4, $p<0.001$). Using receiver-operator characteristic (ROC) analysis, the area under the curve (AUC) for BDNF/Cr was 0.831. A threshold urinary BDNF/Cr value of 200pg/mg provided a sensitivity of 78.4% and a specificity of 73.7% in the diagnosis of OAB.

Twenty-five OAB patients were treated and monitored for 6 months. After LSI, there was a decrease in urinary BDNF/Cr ratio (792±641 to 432±589, $p=0.013$). After AMT, BDNF/Cr had a further reduction to 147±265 (vs. baseline, $p<0.001$).

At baseline, the mean NUE/w, that is micturition preceded by sensations scored as 3 or 4 in USS, was 68±9. After LSI, there was a decrease to 56±9 ($p<0.05$), and, after AMT, there was a further reduction to 35±14 ($p<0.05$). The reduction of NUE/w, brought by treatment, strongly correlated with BDNF/Cr variation ($r=0.607$, $p=0.006$)

Interpretation of results

According to these results, urinary BDNF may constitute a potential biomarker of OAB, with eventual diagnostic and monitoring interest. In diagnosis, it might help the clinician in the diagnosis of MUI, elucidating the preponderant form of UI in these patients, and supporting therapeutic decisions. In monitoring, it could find utility in assessing the dynamic progression of OAB. In fact, a biomarker able to predict the relapse or remission of symptoms would be valuable in this condition.

Concluding message

To our knowledge, this is the first study comparing urinary BDNF levels in OAB and SUI patients.

In OAB patients, urinary BDNF levels were significantly higher, compared to healthy women and SUI patients.

In the OAB group, urinary BDNF levels normalized after LSI plus AMT. This variation significantly correlated with symptoms reduction.

BDNF may constitute a potential biomarker of OAB, with diagnostic and monitoring interest.

References

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