

## URINARY BDNF LEVELS AND BLADDER BIOPSY FINDINGS IN WOMEN WITH LUTS

### Hypothesis / aims of study

Chronic inflammation has been considered a possible underlying mechanism for OAB or interstitial cystitis/bladder pain syndrome (IC/BPS)[1]. These patients often undergo cystoscopy and bladder biopsy as part of their management.

It is possible that BDNF levels could indicate of the extent of inflammation present in the bladder. BDNF has been identified in the peripheral tissues of the bladder, including the urothelium and detrusor muscles and it has been proposed to contribute to bladder overactivity and noxious input in bladder inflammation [2]. In patients with bladder pain syndrome, BDNF levels decreased following treatment with botulinum toxin A as did pain levels [3]. This suggests that in addition to indicating severity of inflammation in OAB, urinary BDNF could also be an indicator of severity in bladder pain syndrome.

The aim of this study was to evaluate whether urinary BDNF is related to the cystoscopic and histological findings of bladder inflammation in women with OAB and IC/BPS.

### Study design, materials and methods

Women attending for rigid cystoscopy and bladder biopsy under general anaesthetic were recruited into the study. Indications for cystoscopy included refractory OAB, botulinum toxin A injection to the bladder and bladder pain.

A mid stream specimen of urine was and immediately refrigerated at 4°C and centrifuged at 3000 rpm for 10 minutes. Supernatant was collected in 1ml aliquots and frozen at -80°C until further processing.

Urinary BDNF levels were measured by ELISA. Urine BDNF content was normalised against the creatinine (Cr) concentration as the BDNF/Cr ratio in pg/mg.

The BDNF data was non parametric therefore median urinary BDNF levels were compared to the asymptomatic control group with the Mann Whitney U test.

### Results

A total of 31 women underwent cystoscopy and provided a urine sample for BDNF analysis. Urinary BDNF was collected from 24 asymptomatic women who served as controls. The average age was 55 yrs (range 25 to 84) and average BMI was 25. Clinically all 31 women had OAB. 12 women with OAB had additional bladder pain.

**Table 1: Cystoscopic findings in women with OAB (n=31)**

Findings	Yes			No	
Trigone squamous metaplasia	30			1	
Trigone increased vascularity	30			1	
Bladder wall increased vascularity	30			1	
Hunners lesions	0			30	
Trabeculations	30			1	
Glomerulations (grade 0-4)	0 (normal mucosa)	1(petechiae in at least 2 quadrants)	2(large submucosal bleeding)	3(diffuse global mucosal bleeding)	4(mucosal disruption, with or without bleeding/oedema)
	22	3	5	1	0

**Table 2: Histological findings from bladder biopsies in women with OAB**

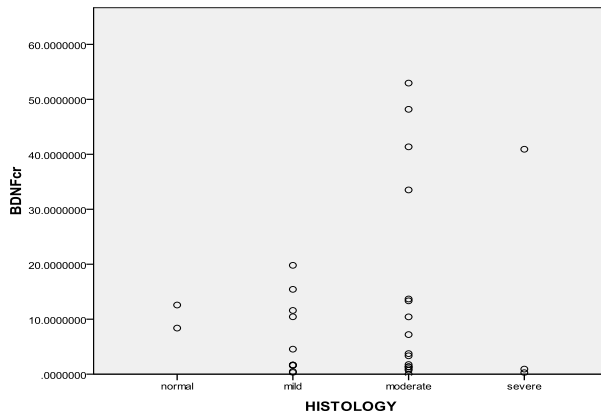
Histology findings	Total number (n=30)	Subgroup- bladder pain (n=12)
Normal	2	1
Mild inflammation	10	4
Moderate inflammation (with congestion and increased vascularity)	15	6
Severe inflammation (with lymphocytes)	3	1

The median urinary BDNF level in women with OAB was 4.54 (IQR 1.33-13.67) compared to 3.75 (IQR 1.62-15.52) in the control group. Although BDNF was higher in the symptomatic group there was no significant difference between the two (p=0.97).

In the OAB group those who had bladder pain (n=12) had a non significantly higher median BDNF compared to those without bladder pain (n=19) (10.43, IQR 1.6-14.90 vs. 3.73, IQR 0.99-13.67, z value -0.649, p=0.535). There was no significant difference in the median BDNF in those with bladder pain compared to controls (p=0.78).

The cystoscopic and histological findings are summarised in table 1 and 2. Squamous metaplasia, increased vascularity and trabeculations were seen in nearly all cases. On examining histology 50% of women with OAB demonstrated inflammation with congestion and increased vascularity. Of those just under half had bladder pain. Patients with a higher degree of inflammation on bladder histology showed a trend towards increased BDNF levels (figure 1)

**Figure 1: Scatter plot showing BDNF values compared to histological findings**



#### Interpretation of results

Our study has firstly demonstrated cystoscopic findings in women with OAB of increased vascularity and trabeculations. In addition bladder histology reveals evidence of inflammatory processes within the bladder in those with OAB and bladder pain.

We found higher levels of BDNF in OAB patients compared to healthy controls and in those with bladder pain compared to those without bladder pain. However these findings were not statistically significant and so the clinical value of BDNF is limited based on this data. In addition BDNF samples showed a high variability in this study.

#### Concluding message

There does seem to be trend towards higher BDNF levels in women with OAB and/or bladder pain syndrome however there is insufficient evidence to say that BDNF can be considered a biomarker of inflammatory processes in the bladder.

#### References

1. Curr Urol Rep 2008 Jul;9(4):314-9.
2. Am J Physiol Renal Physiol 2011 Feb;300(2):F345-F355.
3. Eur Urol 2010 Sep;58(3):360-5.

#### Disclosures

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**Helsinki:** Yes **Informed Consent:** Yes