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LOWER URINARY NERVE GROWTH FACTOR LEVELS INDICATE LOWER INNATE IMMUNITY AND MIGHT PREDICT RECURRENT URINARY TRACT INFECTION IN WOMEN

Hypothesis / aims of study

Recurrent urinary tract infection (UTI) is frequently occurred in women. Previous studies have revealed that patients with recurrent UTI have elevated urinary nerve growth factor (uNGF) compared with the controls, suggesting chronic inflammation is present in the bladder of these patients after resolution of UTI. We hypothesized that chronic inflammation might reside in the bladder wall, so UTI might be easy to recur in these patients. This study was designed to investigate whether uNGF can be used as a biomarker to monitor the bladder condition and predict recurrence of UTI in women.

Study design, materials and methods

Women with non-complicated, symptomatic and urinary analysis (U/A) proved UTI were enrolled into this study. Cephalexin 500 mg/Q6H was given for 1 week to treat the acute UTI. When UTI episode had been completely resolved and urine analysis showed negative, the women were randomized to receive Baktar 800 mg/HS or Celebrex 200 mg/QD for 3 months. All of them signed inform consent of this study. A total of 30ml urine sample at full bladder was obtained for laboratory testing of urinary NGF levels at baseline (acute UTI), 1 week (after Cephalexin treatment), 4 weeks and 12 weeks (under Baktar or Celebrex treatment). Urinary NGF levels were measured by the ELISA method. The changes of urinary NGF levels were compared between 1 st time UTI and recurrent UTI women, Baktar and Celebrex treated women, non-UTI and UTI occurred during the study period. Recurrent UTI was defined as at least three symptomatic and medically diagnosed UTI in the previous 12 months. We also invited 20 women who were free of UTI to be controls. A p-value < 0.05 was considered to indicate statistical significance.

Results

A total of 159 women were enrolled into this study, including 20 controls, 50 women with 1st time UTI and 89 women with recurrent UTI. The mean age was similar among the three groups (49.4-58.7 years old). At the baseline of acute UTI episode, comparison of uNGF level, OABSS, VAS, Qmax, voided volume and post-void residual urine amount showed no specific difference between 1 st time UTI women and recurrent UTI women (Table 1). Finally, there were 37 women completed the protocol of this study. Table 2 showed recurrent UTI (n=23) women had a trend of lower levels of uNGF than the 1 st time UTI (n= 14) women. However, the comparison of each uNGF level between the two groups showed no specific difference. Baktar or Celebrex was observed to have no superior effect of reducing uNGF levels in each other, showed in Table 3. During the follow-up, there were 9 women had recurrent UTI attack. Seven of them were the victims of recurrent UTI (7/23 30.4%), the ratio of UTI attack was higher than in the women with initial 1st time UTI (2/14, 14.3%). Table 4 presents the serial comparison of uNGF levels between non-UTI and UTI women. The serial uNGF levels of UTI attack women were lower than that of non-UTI women. The uNGF levels of non-UTI and UTI women were 18±31.66 versus 2.98±7.87 pg/mL (P=0.021) at 12 weeks follow-up.

Interpretation of results

The uNGF level was significantly higher in the acute stage of UTI. According the serial follow-up of uNGF levels, we found the reaction of uNGF associated with an episode of acute UTI may declined gradually, but still above the NGF level of controls at 12 weeks. Inconsistent with our hypothesis that uNGF might reflect the more severe residual inflammation in recurrent UTI women, the results showed a trend of lower levels of uNGF in this group. The lower levels of uNGF in women with recurrent UTI and women with UTI attack during the follow-up implied that uNGF may have an innate immunity role in the victims of recurrent UTI.

Concluding message

In addition to the biomarker of inflammation, uNGF seems to represent an innate immunity in response to bacterial infection of the urinary bladder in the victims of recurrent UTI.

Table 1. The baseline parameters among the control, 1 st time UTI and recurrent UTI groups

	Control (n=20)	**1 st time UTI (n=50)**	**Recurrent UTI (n=89)**	**P ***
Age (mean ± SD, range) (year)	49.4 ± 6.5 (41~63)	56.9 ± 18.7 (20~94)	58.7 ± 17.3 (20~89)	0.556
Urine NGF (pg/mL)	1.59 ± 4.91	49.68 ± 84.22	37.59 ± 70.35	0.438
OABSS	2.24 ± 1.09	4.76 ± 2.96	5.16 ± 2.58	0.405
VAS	0.03 ± 0.24	1.55 ± 2.57	1.74 ± 2.46	0.680
Qmax-1 week (mL/s)	----	20.54 ± 10.80	20.99 ± 11.36	0.847
VV-1 week (mL)	----	290.66 ±186.92	257.28 ±159.68	0.336

PVR-1 week (mL)	----	33.36 ±56.30	37.39 ±63.52	0.747

P values indicate statistical difference between 1 st time UTI and recurrent UTI groups. Qmax: maximum flow rate, PVR post-void residual, VV: voided volume;

Table 2. The serial comparison of uNGF levels between the first time UTI and recurrent UTI women

Parameter (pg/mL)	The first time (n=14)	Recurrent UTI (n=23)	P value
uNGF-Baseline	55.47 ± 58.36	27.27 ± 39.56	0.075
uNGF-1 week	42.88 ± 106.26	15.88 ± 27.04	0.367
uNGF-4 weeks	23.96 ± 48.80	13.86 ± 27.38	0.431
uNGF-12 weeks	15.13 ± 24.76*	14.17 ± 29.33	0.919

uNGF-B: baseline

Table 3. The serial comparison of uNGF levels between Baktar and Celebrex treated women

Parameter (pg/mL)	Baktar (n=17)	Celebrex (n=20)	P value
uNGF-Baseline	44.19 ± 56.43	33.48 ± 43.03	0.614
uNGF-1 week	41.96 ± 100.95	13.91 ± 21.20 *	0.291
uNGF-4 weeks	12.04 ± 29.71 *	22.93 ± 42.42	0.384
uNGF-12 weeks	16.19 ± 31.66	13.13 ± 23.82 *	0.739

Table 4. The serial comparison of uNGF levels between women with non-UTI and UTI during follow-up period

Parameter (pg/mL)	Non UTI (n=28)	UTI (n=9)	P value
uNGF-Baseline	43.43 ± 53.09	22.68 ± 31.12	0.308
uNGF-1 week	28.69 ± 78.04	19.46 ± 34.37	0.735
uNGF-4 weeks	21.62 ± 41.85	6.27 ± 7.45	0.078
uNGF-12 weeks	18.0 ±31.66 *	2.98 ± 7.87	0.021 *

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