Hung S<sup>1</sup>, Chung S<sup>1</sup>, Kuo H<sup>2</sup>

**1.** Department of Urology, Far Eastern Memorial Hospital, New Taipei City, Taiwan,, **2.** Department of Urology, Buddhist Tzu Chi General Hospital and Tzu Chi University, Hualien, Taiwan

# INCREASED SERUM C-REACTIVE PROTEIN LEVEL IS ASSOCIATED WITH INCREASED STORAGE LOWER URINARY TRACT SYMPTOMS SUGGESTING THE PRESENCE OF CHRONIC INFLAMMATION IN MEN WITH BENIGN PROSTATIC HYPERPLASIA

# Hypothesis / aims of study

Serum C-reactive protein (CRP) level is considered as the surrogate of the chronic inflammation and lower urinary tract symptoms (LUTS) are the presenting of many urologic diseases, such as benign prostatic hyperplasia (BPH) and erectile dysfunction (ED). Previous reports revealed the serum CRP level is associated with BPH and ED. This study investigated the association between serum CRP levels and LUTS, and the role of chronic inflammation in men with BPH and LUTS.

#### Study design, materials and methods

A total f 612 men visited the urologic clinic for LUTS were enrolled in this study. All patients completed the International Prostate Symptoms Score (IPSS) questionnaire and urological examinations. The parameters of uroflowmetry (maximum flow rate, Qmax; voided volume, VV), post-void residual (PVR) volume, total prostate volume (TPV) and transition zone index (TZI) measured by transrectal ultrasound, serum prostate specific antigen (PSA), and serum CRP levels were obtained at the initial visit. Exclusion criteria included known urological malignancy, neurogenic bladder dysfunction and those taking non-steroid anti-inflammatory drugs or aspirin. All patients underwent the adequate medical treatment for 3 months according to the clinical diagnosis of voiding dysfunction (IPSS voiding/storage (V/S) ratio >1) or bladder disorders (V/S≤1). The patients were divided into three groups according to the severity of LUTS as mild (IPSS <8), moderate (8≤ IPSS<20) and severe (IPSS ≥20) LUTS groups. Serum CRP levels were correlated with age, PSA, TPV, TZI, Qmax, PVR, VV, and between baseline and post treatment based on The Pearson correlation analysis test was used for statistical analysis with p <0.05 considered significant.

### Results

The mean age was  $66.5 \pm 12.1$  years old and the mean serum CRP level was  $0.56 \pm 1.52$  mg/dl. In overall patients, CRP levels were significantly correlated with age (p=0.002). CRP levels were also positively correlated with serum PSA levels (p=0.024) and negatively correlated with VV (p=0.024) (Fig.1). However, CRP levels were not significantly correlated with TPV (p=0.763), Qmax (p=0.129), or PVR (p=0.845). The mean IPSS was  $13.6 \pm 7.2$  in overall patients, CRP levels were positively correlated with storage IPSS (p=0.004) and negatively correlated with IPSS V/S ratio (p=0.048), but not with total IPSS (p=0.136) or voiding IPSS (p=0.851). (Fig.2) Severe LUTS was noted in 141 patients (23%), moderate LUTS in 340 (55.6 %), and mild LUTS in 131(21.4%). The mean serum CRP level was significantly higher in severe LUTS group (0.79  $\pm 1.59$  mg/dl) than the moderate LUTS group (0.4  $\pm 1.1$  mg/dl, P=0.009). After treatment with doxazosin for patients with IPSS V/S>1, the IPSS parameters, uroflow parameters, and PSA levels all improved, but serum CRP levels did not change significantly. However, patients with IPSS V/S $\leq 1$  and treated with tolterodine showed significant improvement in IPSS and Qmax, serum CRP levels also showed significant decreased (Table 1).

#### Interpretation of results

Serum CRP levels are found increased with ageing, higher PSA levels, severe LUTS, smaller voided volume and higher storage IPSS and smaller IPSS-V/S ratio. In patients with IPSS-V/S >1 and treated with doxazosin, serum CRP levels did not change although other measured parameters improved after treatment. However, serum CRP levels showed significantly decreased in patients with IPSS-V/S ratio
1 and treated with tolterodine and improved storage IPSS. The serum CRP levels do not have significant correlation with prostate volume and total or voiding IPSS. These findings suggest serum CRP is more closely associated with bladder disorders rather with bladder outlet conditions such as BPH or outlet obstruction in men with LUTS.

## Concluding message

Serum CRP levels is associated with storage LUTS and bladder disorders rather than voiding LUTS and outlet obstruction. CRP levels could be reduced after 3-month tolterodine treatment for patients with predominant storage LUTS, suggesting chronic inflammation might play a role in the patients with BPH and predominant storage LUTS.

Fig.1. Serum CRP levels significantly correlated with (A) age, (B) serum PSA levels, and (C) voided volume.

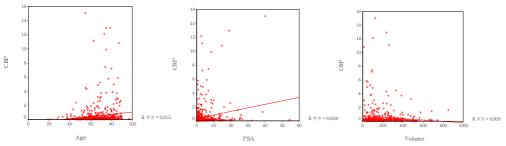


Fig.2. The serum CRP levels significantly correlated with (A) storage IPSS and (B) IPSS V/S ratio, but not with (C) total IPSS.

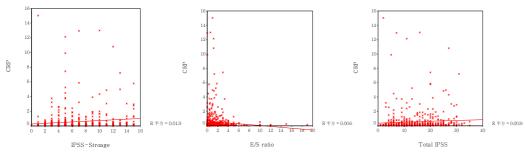


Table 1. The changes of measured parameters at baseline and 3 months after medical treatment in patients with IPSS V/S>1 and V/S≤1

|               | V/S>1 baseline | V/S>1 3 months  | V/S<1 baseline  | V/S<1 3 months  |
|---------------|----------------|-----------------|-----------------|-----------------|
|               | (n=64)         | (n=64)          | (n=61)          | (n=61)          |
| IPSS-total    | 17.8 ± 7.19    | 8.80 ± 6.12 *   | 9.84 ± .92      | 7.20 ± 4.7 *    |
| IPSS-voiding  | 11.96 ± 4.80   | 4.79 ± 4.76 *   | $3.71 \pm 3.06$ | $3.09 \pm 3.75$ |
| IPSS-storage  | 5.74 ± 3.13    | 3.90 ± 2.25 *   | 6.51 ± 3.57     | 4.18 ± 2.40 *   |
| Qmax          | 9.75 ± 5.15    | 11.5 ± 5.88 *   | 11.3 ± 7.15     | 13.1 ± 6.4 *    |
| Voided volume | 200.0 ± 120.   | 266.0 ± 145.9 * | 224.0 ± 15.4    | 246.6 ± 131.6   |
| PVR (ml)      | 72.8 ± 69.2    | 60.7 ±71.2      | 51.3 ± 60.0     | 50.2 ± 52.      |
| TPV (ml)      | 48.6 ± 23.8    | 48.5 ± 23.8     | 52.9 ± 32.6     | 51.6 ± 33.2     |
| TZI (%)       | 38.3 ± 14.1    | 35.8 ± 13.4 *   | 39.2 ± 11.1     | 0.411 ± 0.134   |
| PSA (ng/ml)   | 3.41 ± 4.51    | 2.56 ± 2.96 *   | 6.37 ± 8.32     | 4.59 ± 4.90 *   |
| CRP (mg/dl)   | 0.506 ± 1.20   | 0.341 ± 0.724   | 0.768 ± 1.773   | 0.212 ± 0.218 * |

Data are presented as mean ± standard deviation, \* indicates p<0.05 compared between baseline and 3 months after treatment

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