

## URINARY HB-EGF VARIATION WITH SYMPTOM SEVERITY AND MENSTRUAL CYCLE IN PATIENTS WITH PAINFUL BLADDER SYNDROME

### Hypothesis / aims of study

Urinary heparin-binding epidermal growth factor-like growth factor (HBEGF) has been suggested as a promising marker for the presence of interstitial cystitis.<sup>1</sup> Our objectives were to determine whether similar findings were present in patients with symptomatically diagnosed painful bladder syndrome (PBS) and to explore whether HBEGF levels varied within PBS patients according to symptom severity or with menstrual cycle phase.

### Study design, materials and methods

Ten patients were included in the menstruating PBS arm of this study if they had bladder pain and urinary frequency, and had approximately monthly menses. Ten patients with neither symptoms of bladder pain nor abnormal urinary frequency and with approximately normal monthly menses were included in the asymptomatic control arm of the study. Ten patients were included in the nonmenstruating PBS arm of this study based on the presence of bladder pain and abnormal urinary frequency and did not have menstrual cycles. Consenting subjects donated midstream clean-catch urine samples weekly during a menstrual cycle. Samples were refrigerated overnight, centrifuged and stored in aliquots at -80°C. HB-EGF concentration was determined by a direct capture method utilizing triplicate urine samples in an Immulon 4 HB Elisa plate, incubated overnight at 40°C. HB-EGF signal was revealed with a monoclonal antibody to HB-EGF (1:250, R&D) followed by goat anti-mouse IgG horseradish peroxidase (Santa Cruz). The signal was developed with an ABTS kit from KPL and measured spectrophotometrically at 405nm. HB-EGF concentration was determined by linear regression using a standard curve generated with carrier-free HB-EGF (R&D). Data were analyzed to determine the effect of cycle week and diagnosis across the three patient populations by repeated measures ANOVA, controlling for age.

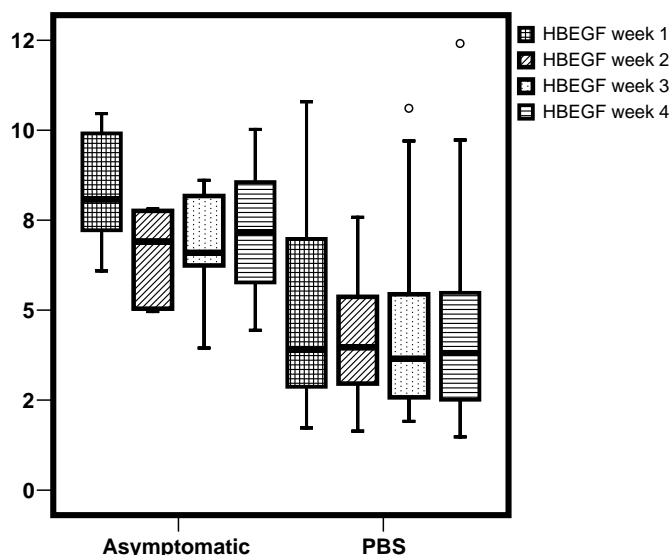
### Results

Patients in the non-menstruating PBS arm were significantly older (median 58 years, range 47-75) than patients in the asymptomatic group.

There was considerable variability in HBEGF values during repetitive testing of individual patients, but mean HBEGF values were significantly lower in both PBS groups (median 29, range 24-51ng/mL) than in asymptomatic controls (median 36, range 27-47ng/mL;  $p=0.045$ ). HBEGF did not vary significantly with age or with the week of menstrual cycle. HBEGF values did not correlate with symptom ratings.

### Interpretation of results

We confirm that HBEGF levels are lower among patients with PBS. We found no consistent variation of HBEGF with symptom severity and/or menstrual cycle phase, implying that there is no 'optimal' time at which such testing should be carried out.



### Concluding message

Our study supports and extends the findings of others concerning HBEGF as a possible marker for IC/PBS. In view of the considerable variability seen within some patients, the mean of more than one urinary HBEGF value may prove to be a more discriminatory tool than the use of single HBEGF values.

### References

1. J Urol 1997;158:1983.

**FUNDING:** United States National Institutes of Health:National Institute Diabetes & Digestive & Kidney Diseases.

**HUMAN SUBJECTS:** This study was approved by the Loyola University Medical Center Institutional Review Board and followed the Declaration of Helsinki Informed consent was obtained from the patients.