International Continence Society August 22-26, 1999 29th Annual Meeting Denver, Colorado USA

Category No. 5 | Video Demonstration | Ref. No. 353

Abstract Reproduction Form B-1

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Title (type in CAPITAL LETTERS): **ACTIVITY OF MATRIX METALLOPROTEINASES 2 AND 9 IN NORMAL URINE AND BLADDER BIOPSIES OF PATIENTS WITH SENSORY URGENCY AND INTERSTITIA CYSTITIS**

Aims of Study Interstitial cystitis (IC) is a chronic inflammatory condition of the bladder of unknown aetiology, characterised by irritative symptoms, sterile urine and the presence of petechial lesions at second-fill cystoscopy. IC tends to run a chronic course. Immunological findings include an increase in mast cells, CD4 and CD8 T cells. Such findings could indicate a similar aetiology for IC and other inflammatory conditions such as rheumatoid arthritis. There has been a suggestion that alterations in the glycosaminoglycan (GAG) lining of the bladder could allow urine to interact with the mucosal surface, leading to symptoms. Matrix metalloproteinase enzymes (MMPS) are implicated in the breakdown of the joints in rheumatoid disease, are responsible for catabolism of extra-cellular connective tissue and could be responsible for alterations in the bladder GAG layer. Also several empirical treatments for interstitial cystitis are MMP inhibitors (steroids, DMSO). We carried out a pilot study to assess MMP levels in urine in a group of asymptomatic male and female volunteers over a one month period (Group 1A) and in a group of patients diagnosed as having interstitial cystitis by NIDDK criteria (Group 1B). We also investigated the level of MMP activity in bladder biopsies taken from patients with sensory urgency (Group 2A) and a group of patients undergoing Burch Colposuspension for genuine stress incontinence (Group 2B).

Methods

- **Group 1A. Normal volunteers over a one month period:** Three males and three females (one post-menopausal, two pre-menopausal) were recruited. They were asymptomatic, (age 26 to 50). A mid-stream specimen of early morning urine was collected for 28 days.
- **Group 1B Interstitial cystitis patients:** Patients were identified on the Departmental database and were asked to provide a single early morning specimen of urine.
  - An aliquot of each urine sample was sent for creatinine level to standardise for fluid intake. The samples were then stored at -20°C until processed.
  - Urine samples were concentrated 100x and gelatinolytic activity of MMPs was determined using a gelatin-degradation ELISA.
- **Group 2A. Bladder biopsies from patients with sensory urgency:** Patients undergoing cystoscopy for sensory urgency had bladder biopsies taken after second fill cystoscopy. Biopsies were stored in culture medium for 24 hours and the supernatant used to assess gelatinolytic activity of MMPs as above.
- **Group 2B. Bladder biopsies from Burch patients** were taken during routine intraoperative cystoscopy and processed as 2A.

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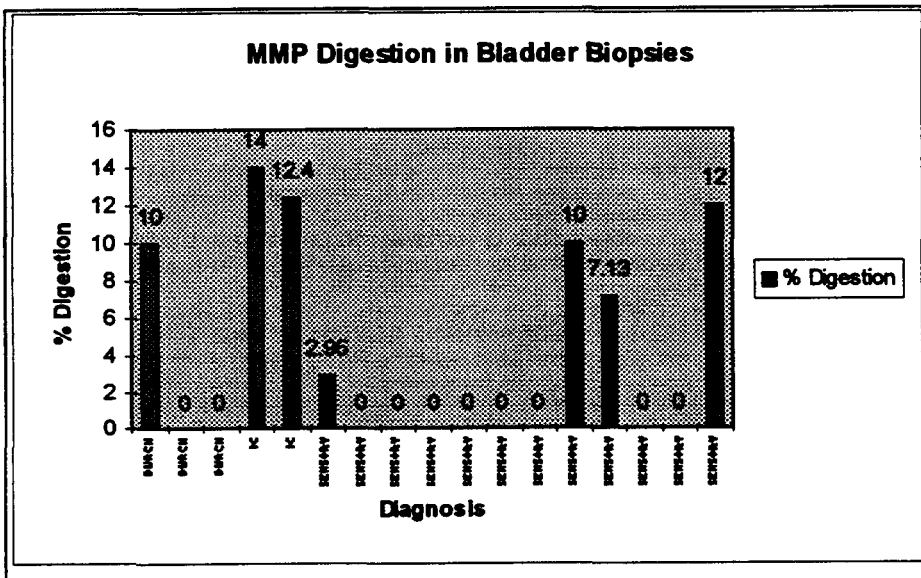
Results

- **Urinary MMP activity:** A range of MMP activity was observed in normal male and female subjects over a month. Peaks of 10-16 units/mm creatinine were observed. Higher levels of enzyme activity were observed in the post-menopausal female compared to pre-menopausal females and we plan to investigate this further. Similar levels of MMP activity were observed in the 'snap-shot' samples obtained from patients with interstitial cystitis.
- **Bladder biopsy MMP activity:** Biopsies were obtained from 14 patients with a urodynamic diagnosis of sensory urgency. Twelve were shown to have chronic inflammatory cell infiltrate only, without evidence of excessive mast cell activity in muscle/epithelial layers and 2 demonstrated high mast cell counts in all layers compatible with a histological diagnosis of IC. 3 patients undergoing Burch colposuspension had biopsies taken. The MMP results are shown in Graph 1.

Conclusions

- There is a range of MMP activity in the normal urine with a range of 0-16 units/mm creatinine. Further investigation of interstitial cystitis patients is planned to correlate MMP levels with disease activity.
- Patients with IC appear to have higher levels of tissue MMP 2 and MMP 9. One Burch [redacted] control [redacted] and 3 sensory urgency patients had increased MMP levels. The question of biopsy stimulation of MMP needs to be addressed as does the histological differentiation between sensory urgency and interstitial cystitis. However, in this pilot study increased MMP activity did seem to correlate with the degree of inflammation/IC.



Graph 1