Bladder Pain Syndrome/Interstitial cystitis: aspects on outcome after intravesical and surgical treatment

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Göteborgs Universitet kommer att offentligen försvaras i Aulan, Sahlgrenska Universitetssjukhuset torsdagen den 25 november 2010, kl. 13.00

av

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Avhandlingen baseras på följande delarbeten:

I. Rössberger, J. ; Fall, M. ; Peeker, R.
   Critical appraisal of dimethyl sulfoxide treatment for interstitial cystitis: discomfort, side-effects and treatment outcome.
   *Scand J Urol Nephrol*. 2005; 39 (1) s. 73-77.

II. Rössberger, J. ; Fall, M. ; Jonsson, O. ; Peeker, R.
   Long-term results of reconstructive surgery in patients with bladder pain syndrome/interstitial cystitis: subtyping is imperative.
   *Urology*. 2007; 70 (4) s. 638-42.

III. Rössberger, J. ; Fall, M. ; Kåbjörn-Gustafsson, C. ; Peeker, R.
   Does mast cell density predict the outcome after transurethral resection of Hunner’s lesions in patients with type 3C bladder pain syndrome/interstitial cystitis?

IV. Rössberger, J. ; Fall, M. ; Kåbjörn-Gustafsson, C. ; Peeker, R.
   TURB and bladder contracture in BPS/IC. Does myofibroblast activity play a role?
   *In manuscript.*
Abstract

Background
BPS/IC is a chronic syndrome with bladder pain, divided into two main types: one with so called Hunter’s lesions (classic type) and one without (nonulcer type). In the recently presented ESSIC classification system the classic type, in focus of the present work, has the designation Type 3C BPS/IC. Symptoms are characterized by bladder pain, urgency, frequency and nocturia. The etiology and pathophysiology of BPS/IC remain obscure and treatment is directed towards symptom relief. Intravesical instillation of dimethyl sulfoxide, DMSO, is an established treatment for BPS/IC and can be proposed as first-line treatment for patients with nonulcer BPS/IC. For patients with Type 3C, transurethral resection of lesions in the bladder, TURB, may render satisfactory symptomatic effect. Myofibroblasts might have a role in the evolution towards bladder contracture in patients with Type 3C BPS/IC and high levels of cytoplasmatic α-smooth muscle actin, α-SMA, are consistent with a typical myofibroblast phenotype. In patients with Type 3C, fibrosis of the bladder may represent end-stage disease. At this stage conservative treatment is often no longer effective and reconstructive surgery may be necessary.

Aim and methods
The aims of this thesis were to investigate side-effects and outcome with first-line treatments for BPS/IC, especially in Type 3C BPS/IC. Data on patients were obtained from medical records and by telephone interviews. Immunohistochemical techniques were employed to visualize mast cells and possible myofibroblasts.

Results
I. Side-effects after instillations of DMSO were common but transitory. Maintenance treatment with DMSO may offer long-term symptom improvement.

II. For patients with end-stage Type 3C BPS/IC, the initial major surgical procedure resulted in complete symptom resolution in 82 per cent, in contrast to only 23 per cent of the patients with nonulcer BPS/IC.

III. No statistically significant correlation between mast cell density in the lamina propria, urothelium or the detrusor and duration of symptom amelioration could be seen after the first, second or third TURB. There was a positive correlation between a high mast cell number in the urothelium at the third TURB and the risk of developing end-stage disease.

IV. No statistically significant increase or decrease in α-SMA positive or α-SMA negative fibroblast-like cells could be seen with increased number of TURB. An overweight of α-SMA positive fibroblast-like cells compared to α-SMA negative fibroblast-like cells was identified at the third TURB, but only reaching a statistical significance in the group with patients who had not yet reached end-stage.

Conclusions
Intravesical instillation with DMSO appears to be associated with a reasonable degree of discomfort, when considering the potential benefit of the treatment in both subtypes of BPS/IC. For patients with Type 3C BPS/IC, TURB is potentially quite an effective treatment option. However, mast cell density does not appear to predict the duration of symptom amelioration after complete transurethral resection of Hunter’s lesions, neither in the lamina propria nor in the urothelium or the detrusor. The findings of an overweight of α-SMA positive fibroblast-like cells in patients with signs of active disease, expressed by repeated TURB’s, might represent a time dependent factor of myofibroblast activation eventually resulting in a contracted bladder. When conventional therapies no longer offer any symptom amelioration, in the patient with bladder contracture and/or intolerable symptoms, reconstructive surgery can be an appropriate last resort, however only in patients with Type 3C BPS/IC. The most important determinant in the decision to embark upon major reconstructive surgery is the assessment of subtype and stage of the disease.

Keywords: interstitial cystitis, bladder pain syndrome, dimethyl sulphoxide, mast cells, myofibroblasts, transurethral resection, bladder substitution

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