

The activity of intravesical hyaluronic acid and chondroitin sulfate administration on urothelial gene expression. Preliminary results on the epidermal growth factor receptor and fibronectin gene expression evaluated in bladder washings of patients affected by non muscle-invasive bladder cancer

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Introduction & Objectives

Hyaluronic acid (HA) and chondroitin sulfate (CS) are two major constituents of the bladder glycosaminoglycan layer. Recent data show that Fibronectin (FN) and Epidermal Growth Factor Receptor (EGFR) gene expression can be measured in bladder washings and could represent potential biomarkers of urothelial damage and tumor aggressiveness, respectively (1,2). The aim of our study was to investigate the interference of a single intravesical instillation of HA-CS solution on the expression of FN and EGFR genes in patients affected by non-muscle-invasive bladder cancer (NMIBC).

Material & Methods

A prospective double-blinded study included patients undergoing adjuvant intravesical therapy for NMIBC and age matched healthy controls. For EGFR evaluation, a single HA-CS solution was administered intravesically 14 days after transurethral resection of high risk NMIBC, before the start of the adjuvant therapy. For FN evaluation, a single HA-CS instillation was administered to patients showing local toxicity secondary to intravesical adjuvant therapy. Samples of bladder washings were collected before and one week after the HA-CS instillation, obtaining a cellular pellet stored at -80 °C. Cellular RNA was isolated by a miRNeasy Mini Kit (Qiagen®) and cDNA, obtained using a “High Capacity cDNA Reverse Transcription Kit” (Life Technologies®) was used to perform a gene expression analysis by a Real Time PCR. EGFR and FN gene expression values were expressed in FOLDS of change compared to healthy controls (FN and EGFR=1).

Results

Thirty-eight patients and 5 controls entered the study. Seventeen and 21 patients were evaluated for FN and EGFR respectively. In 21 patients with high risk NMIBC, the median EGFR expression decreased from 2.4 folds (range: 0.1-39.0) to 1.0 fold (range: 0.05-36.8) showing a statistically significant decrease of 58.3% ($p<0.02$). In patients showing clinically relevant toxicity secondary to intravesical adjuvant therapy (BCG in 9 and Epirubicin in 8 patients) the median FN expression value dropped from 1.8 folds (range: 0.07-8.1) to 0.9 fold (range: 0.1-7.5) after HA-CS administration with a statistically significant decrease of 50% ($p<0.05$).

Conclusions

FN gene expression in bladder washings appears related to the intensity of the urothelial damage, reaching higher expression levels in case of severe toxicity induced by intravesical adjuvant therapy

(2). In our experience the FN gene expression significantly decreases a week after the administration of HA-CS solution with contemporary symptomatic relief. Moreover the urothelial EGFR gene expression resulted significantly lowered one week after the HA-CS intravesical administration. The reduced availability of its receptor could limit the proliferative activity of EGF on the urothelium promoting recurrence and progression.

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References:

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