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GAG-REPLENISHMENT: PROTECTING THE UROTHELIUM FROM CHRONIC DAMAGE.

Hypothesis / aims of study

Urothelium has a very low permeability which protects the deep layers of the bladder wall from irritant urine solutes. The first line of defense, the glycosaminoglycans (GAG) layer, is compromised in patients with bladder pain syndrome. This enables substances as urea and potassium to leak into the bladder wall and cause inflammation which leads to irritative symptoms. This is the base for the rationale behind GAG-replenishment therapies such as intravesical instillations with chondroitin sulfate (CS). In this study, for the first time the urothelial barrier function is objectively measured before and after GAG-replenishment. The urothelium was damaged repeatedly in order to simulate a more chronic situation. In addition to functional barrier measurements, the effects were visualized using scanning electron microscopy (SEM).

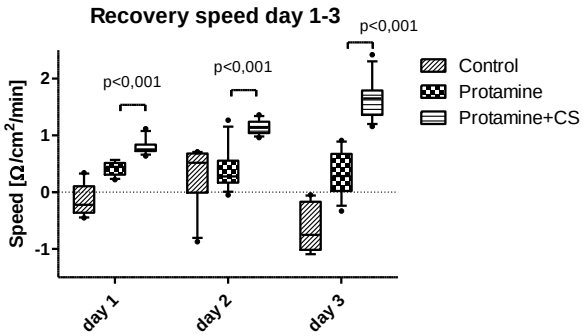
Study design, materials and methods

Primary porcine urothelial cells were cultured on membranes which made it possible to measure the transepithelial electrical resistance (TEER) which is a measure for barrier function. The cells were driven into differentiation using serum and calcium. Through this, the cells formed a tight layer with a high resistance. By using protamine, key barrier components were degraded to simulate the situation as is seen in patients. In this model, CS 0,2% (Gepan®) was instilled for one hour, similar to the treatment of BPS/IC patients. TEER was then measured at several time points over 17 hours. TEER recovery speed was determined at 7 hours post-instillation. This protocol was repeated for three days. The three experimental groups were as follows: negative control (n=10), protamine and protamine & CS with n=12 in the latter groups.

Results

In the group with CS the recovery was increasingly faster on each day (table & figure). Additionally, the differences between protamine and protamine&CS reached P-values of <0,001. Imaging with SEM shows a layer covering the urothelium in the group with CS.

	Recovery speed [Ω/cm2/min]		
Group	Day 1	Day 2	Day 3
Negative control	-,13 ± 0,27	,30 ± 0,52	-,65 ± 0,40
Protamine	,41 ± 0,12	,39 ± 0,37	,33 ± 0,38
Protamine+CS	**,80 ± 0,13**	**1,15 ± 0,63**	**1,64 ± 0,35**



Interpretation of results

The barrier recovered partially in both damaged groups while in the control group TEER remained stable .Nevertheless, the group in which additional CS was instilled showed a significantly faster recovery. SEM showed a different appearance of the urothelium after CS instillation.

Concluding message

BPS/IC is a chronic condition. In this study we have shown that the urothelial barrier is able to recover from repetitive injury which enables the model to be used in a more chronic situation. Moreover it shows that in repeatedly damaged urothelium CS has an advantageous effect on barrier recovery.

Disclosures

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