

ACID-SENSING CHANNELS IN HUMAN BLADDER: EXPRESSION, FUNCTION AND ALTERATIONS DURING BLADDER PAIN SYNDROME

Hypothesis / aims of study

To examine the possible role of H⁺-activated acid-sensing ion channels (ASICs) in pain perception we characterized their expression in bladder dome biopsies of Bladder Pain Syndrome (BPS) patients and controls, in cultured human urothelium and in urothelial TEU-2 cells.

Study design, materials and methods

Cold cut biopsies from the bladder dome were obtained in 8 asymptomatic controls and 28 patients with symptoms of BPS. ASIC expression was analyzed by QPCR and immunofluorescence. The channel function was measured by electrophysiology.

Results

ASIC1a, ASIC2a and ASIC3 mRNAs were detected in human bladder. Similar amounts of ASIC1a and -3 were detected in detrusor smooth muscle, whereas in urothelium ASIC3 levels were higher than -1a. ASIC2a mRNA levels were lower than either -1a or -3 in both layers. ASIC currents were measured in TEU-2 cells and in primary cultures of human urothelium, and ASIC expression was confirmed by QPCR. Differentiation of TEU-2 cells caused an up-regulation of ASIC2a and ASIC3, and a down-regulation of ASIC1a mRNAs. BPS patients showed an up-regulation of ASIC2a and -3 mRNA, whereas ASIC1a remained unchanged. In contrast, the mRNA levels of TRPV1 were down-regulated during BPS. All differences were statistically significant ($p < 0.05$)

Interpretation of results

Several types of ASICs are expressed in human bladder and TEU-2 cells, where their levels are regulated during urothelial differentiation. An up-regulation of ASIC2a and -3 in BPS suggests their involvement in increased pain and hyperalgesia. A down-regulation of TRPV1 mRNA levels might indicate a different regulatory mechanism, controlling its expression in human bladder.

Concluding message

ASICs 2a and 3 may be involved in pain and hyperalgesia in Patients with BPS.

<i>Specify source of funding or grant</i>	Swiss National Fund (SNF)
<i>Is this a clinical trial?</i>	No
<i>What were the subjects in the study?</i>	HUMAN
<i>Was this study approved by an ethics committee?</i>	Yes
<i>Specify Name of Ethics Committee</i>	Kant. Ethikkommission Bern
<i>Was the Declaration of Helsinki followed?</i>	Yes
<i>Was informed consent obtained from the patients?</i>	Yes