INNERVATION INDUCED BY CYSTITIS. COMPARISON OF EXPERIMENTAL CYSTITIS MODEL IN PIGS VERSUS INTERSTITIAL CYSTITIS IN HUMANS

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INTRODUCTION & OBJECTIVES: The etiology of interstitial cystitis (IC) is still far from being understood. The disease has different clinical manifestations and different treatment modalities are tried to treat it. The main problem with studying pathogenesis of IC is the lack of an appropriate animal model. Therefore in our present study we wanted to compare innervation changes induced by IC in humans with that observed in a recently established by us animal model of bladder inflammation.

MATERIAL & METHODS: In our studies we included n=5 female patients suffering from interstitial cystitis. During the cystoscopy, cold-cup bladder biopsies from the posterior bladder wall were collected. Control tissue samples n=7 were obtained during cystectomy performed for invasive transitional cell carcinoma. Samples were collected from unchanged region of the posterior bladder wall and processed for immunohistofluorescence.
In sexually immature female pigs (n=4) cystitis was achieved by combining acute bladder overdistension (pressure 100 cm H_2O) and 30 min chemical irritation with 50% acetone solution (7 days after overdistension). Afterwards animals were kept on normal chow conditions for 30 days and then sacrificed. Bladder scraps from the ventral bladder wall were processed for immunohistofluorescence. Antisera against following putative neurotransmitters were used: SP-substance P, CGRP- calcitonine gene related peptide, VIP-vasoactive intestinal polypeptide, PACAP-27-pituitary adenylate cyclase polypetide 27, NPY-neuropeptide Y, 5-HT-serotonine, DbH-dopamine-β-hydroxylase.

RESULTS: Mean patients age was 63.8 years$\pm$6.3, mean disease duration was 3.3 years$\pm$2.1. No neoplasmatic cells were found in the obtained specimens. In patients with IC an increase in the expression of CGRP immunoreactive (IR) nerve fibers, NPY-IR nerve fibers and PACAP-IR nerve fibers was observed, while fibers being SP-IR, VIP-IR and DbH-IR remained unchanged and 5-HT-IR nerve fibers were wanished. Similar findings were observed in specimen from experimental animals, however no increase in PACAP-IR nerve fibers was observed. Details are presented in Tab. 1

Substance	Human		Pig	
	Control	IC	Control	Cystitis
SP	+	+	+	+
CGRP	+	++	+	+ +
VIP	++	++	++	++
PACAP-27	+	+++	+	+
DbH	++	++	++	++
5-HT	+	-	+	-
NPY	++	+++	++	+++

Expression of neuropeptides within the urothelium. -: no nerve fibers; +: few fibres; ++: moderate number of fibres; +++: numerous nerve terminals

CONCLUSIONS: Our findings demonstrate that the population of CGRP and SP-IR nerve fibers underwent same changes in IC and experimentally induced cystitis in pigs. This makes the proposed model and interesting option to study interstitial cystitis.