

## AUTONOMIC DYSFUNCTION IN A RAT MODEL OF IC/PBS IS MEDIATED BY C-FIBER

### Hypothesis / aims of study

Previous studies have demonstrated elevated indices of sympathetic activity and exaggerated autonomic responses during hydrodistention in patients with interstitial cystitis/ painful bladder syndrome (IC/PBS). Animal experiments have shown a vesico-vascular reflex (VVR) in urethane anesthetized spinal cord intact normal rats. We investigated whether this phenomenon is reproducible in a cyclophosphamide (CYP)-induced interstitial cystitis rat model and what mediates the response.

### Study design, materials and methods

**Anesthesia:** Intraperitoneal injection of Zoletil (Tiletamine+Zolazepam) 0.1cc/100g and Rompun (Xylazine) 0.025~0.04/100g.

**CYP dose determination:** Sprague-Dawley female rats (200-250g) were divided into four groups (control, CYP 50, 100 and 200 mg/Kg) after 1 week of acclimation and intraperitoneal injection of CYP dissolved in normal saline (40 mg/ml) was performed. Three days after injection, hydrodistention was performed for 1 minute per each session (total 3 sessions) with intravesical pressure of 140-150mmHg. VVR was confirmed by measuring increased blood pressure (BP) from intra-arterial catheters in the carotid artery during bladder hydrodistention.

**Capsaicin pretreatment:** Seven rats were pretreated with capsaicin (125mg/sc) for 7 days and injected with a CYP dose that evoked a VVR response (100mg/Kg). Blood pressure was monitored during bladder hydrodistention in the same manner

**c-fos expression:** Spinal cord at the T9-11 level were harvested and measured for c-fos expression using Western blot.

### Results

BP did not change during hydrodistention in the control group. BP significantly increased during hydrodistention only in the 100mg CYP group ( $\Delta$  SBP 16.03 $\pm$ 6.86mmH<sub>2</sub>O,  $\Delta$  DBP 14.03 $\pm$ 4.97mmH<sub>2</sub>O,  $p < 0.001$ ). After capsaicin pretreatment, previously observed BP increase was not demonstrated in the 100mg CYP group. The spinal expression of c-fos was significantly increased in the 100mg CYP group compared with control and other CYP groups.

### Interpretation of results

VVR was reproducible in CYP-induced IC/PBS rat model and not in normal controls. Our result in controls when compared to previous studies implies that the type of anesthesia could affect the VVR response in rats but regardless seems to be mediated by c-fiber activation.

### Concluding message

We demonstrated that autonomic dysfunction reported in patients with Hunner's lesion is reproducible in CYP induced IC/PBS rat model. This finding was not observed after pretreatment with capsaicin, which implies that the phenomenon was mediated by c-fiber activation. CYP induced IC/PBS rat model could be used to further study the VVR especially in IC/PBS patients.

**Table 1.** Autonomic response after hydrodistention

	Control (n=5)	50mg CYP (n=5)	100mg CYP (n=7)	200mg CYP (n=5)	Capsaicin-100mg CYP (n=7)	p value
SBP at Baseline (mmH <sub>2</sub> O)	69.20 $\pm$ 6.14	104.33 $\pm$ 17.20	89.43 $\pm$ 42.87	75.20 $\pm$ 47.23	104.14 $\pm$ 39.68	0.341
SBP during HD (mmH <sub>2</sub> O)	70.00 $\pm$ 7.54	106.86 $\pm$ 14.94	105.58 $\pm$ 46.80	76.66 $\pm$ 48.65	105.13 $\pm$ 40.37	0.288
$\Delta$ SBP (mmH <sub>2</sub> O)	0.84 $\pm$ 1.68	2.43 $\pm$ 3.04	16.03 $\pm$ 6.86*	1.31 $\pm$ 3.95	0.79 $\pm$ 2.41	<0.001
DBP at Baseline (mmH <sub>2</sub> O)	67.27 $\pm$ 6.16	95.40 $\pm$ 15.53	83.11 $\pm$ 36.53	72.61 $\pm$ 45.13	100.74 $\pm$ 38.15	0.365
DBP during HD (mmH <sub>2</sub> O)	68.11 $\pm$ 7.36	98.41 $\pm$ 13.42	97.15 $\pm$ 38.91	73.97 $\pm$ 46.59	101.81 $\pm$ 39.04	0.330
$\Delta$ DBP (mmH <sub>2</sub> O)	0.84 $\pm$ 1.61	3.01 $\pm$ 2.53	14.03 $\pm$ 4.97*	1.36 $\pm$ 3.88	1.06 $\pm$ 2.25	<0.001

### References

1. Kobi Stav, Erez Lang, Zacci Fanus, Autonomic Response During Bladder Hydrodistention in Patients with Bladder Pain Syndrome, J Urol 2012; 188, 117-121

### Disclosures

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