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EFFECT OF SHORT-TERM RAT BLADDER OUTLET OBSTRUCTION ON INNERVATION

Hypothesis / aims of study

Bladder outlet obstruction (BOO) occurs during benign prostatic hyperplasia or urethral strictures and is frequently accompanied by irritative bladder symptoms. Studies in animal models of partial BOO or patients have yielded inconsistent results in regard to the aetiology of irritative obstructive symptoms (1). Altered efferent innervation of the bladder is one possible explanation of irritative symptoms during chronic BOO. To test this hypothesis, we have performed early time course experiments in a rat model of BOO.

Study design, materials and methods

Partial BOO was induced in male Sprague-Dawley rats (250-275 g; n=5 for each group) by placing a ligature snugly around the bladder outlet and a 19-g (Ø 1.1 mm) blunted needle. The needle was then carefully removed. Sham operated rats were included. After 1, 3 and 7 days the rats were sacrificed and bladders were excised. Bladder weights were measured and used in organ bath or immunohistochemical studies. The in vitro bladder function in the organ bath was tested using electrical field stimulation (2, 8 and 32 Hz) to release endogenous agonist and the muscarinic agonist carbachol (20 μM), the purinergic agonist ATP (2 mM) and the receptor-independent stimulator KCl (120 mM). The bladder innervation was determined immunohistochemically by staining for neurofilaments and counting of number of nerves per square mm based upon 6 random high power fields (400 x magnification) along each transverse bladder section.

Results

Partial BOO increased bladder weight by 75%, 85% and 90% after 1, 3 and 7 days, respectively, relative to sham-operated animals. Histology of bladders on day 7 showed clear signs of hypertrophy in the obstructed rats. The contractile response to carbachol, ATP and KCl was markedly reduced on day 1 ($p < 0.05$), but showed slight and full recovery on days 3 and 7 respectively. In contrast, the contractile response to field stimulation was also markedly reduced on day 1 ($p < 0.05$) but showed only poor recovery on days 3 and 7. The immunohistochemical experiments showed no alteration of neurofilament density on day 1, but a significant reduction on day 3 ($p < 0.05$) and an even greater reduction on day 7.

Interpretation of results

The impaired contractile response to all stimuli in the absence of alterations of neurofilament staining suggests that the impairment on day 1 is largely due to an acute hyporesponsiveness of the bladder smooth muscle cells, possibly due to acute tissue edema. The recovered contractile responses to exogenous agonists and the reduced neurofilament staining indicate that the impaired response to field stimulation on day 7 results largely from an impaired neuronal transmitter release rather than a reduced smooth muscle cell responsiveness.

Concluding message

The early response to BOO consists of a rapid but reversible impairment of smooth muscle function, followed by a later impairment of innervation. This may explain why in vitro studies on bladder responsiveness in animals or patients with chronic BOO have not consistently observed alterations in tissue responses to exogenous agonists.

References

(1) Urinary bladder contraction and relaxation: physiology and pathophysiology. *Physiol Rev* 2004: **84**(3):935-986.

Figures

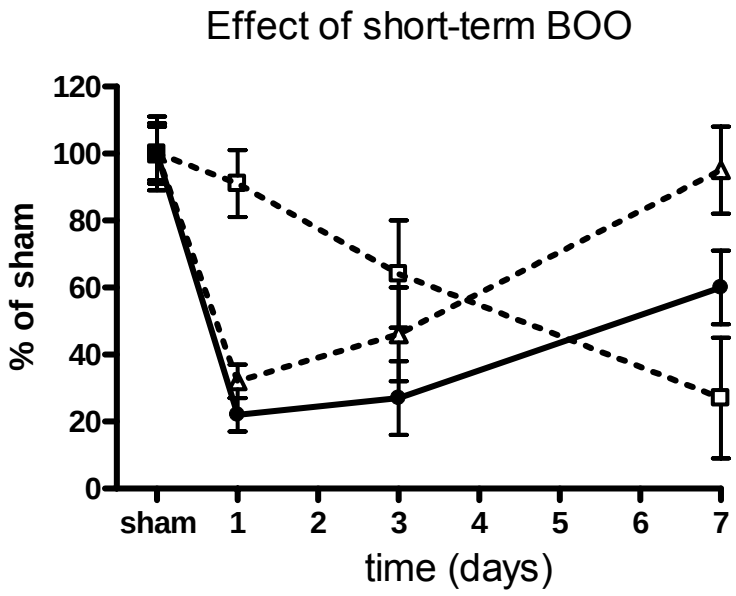

Fig. 1. The early response to BOO consists of a rapid but reversible impairment of smooth muscle function (Δ; muscarinic receptor agonist carbachol), followed by a later impairment of innervation (□; nerve density) leading to an impaired response to field stimulation (●; FS 32 Hz).