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Time-dependent changes in bladder function and plantar sensitivity in a rat model of fibromyalgia induced by hydrochloric acid injection into the gluteus

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INTRODUCTION

Bladder pain syndrome/interstitial cystitis (BPS/IC) was defined as chronic (6 months or more) pelvic pain, pressure, or discomfort perceived to be related to the bladder accompanied by at least one other urinary symptoms such as persistent urge to void or frequency [1]. It is well known that there is a significant association of BPS/IC with other chronic pelvic pain conditions such as irritable bowel syndrome and endometriosis as well as more systemic pain conditions such as fibromyalgia syndrome (FMS) [2–4]. It has been reported that 12–18% of patients diagnosed with BPS/IC also exhibit symptoms and fulfill diagnostic criteria for FMS [4,5] and that 23–27% of FMS patients have BPS/IC-like symptoms such as bladder fullness, urgency and pelvic pain [5]. However, while the pathogenesis of BPS/IC, irritable bowel syndrome, FMS and other chronic pelvic pain disorders have been studied mostly independently, few investigators have examined multi-organ mechanisms in the development of chronic pain disorders despite their striking clinical overlap [6].

The high concurrence rate of chronic pelvic pain disorders further supports a role of sensitized convergent afferent pathways, which may occur due to infectious, idiopathic, inflammatory, neurogenic, metabolic, or other neuropathic mechanisms [7]. A rat model of neural cross-talk and sensitization in the pelvis developed by Pezzone et al. [8] revealed that acute cystitis induced by intravesical infusion of protamine sulfate combined with potassium chloride to produce a BPS/IC-like model lowered distal colonic sensory thresholds to colorectal distention, and that acute intracolonic irritation with trinitrobenzene sulfonic acid (TNBS) to produce an irritable bowel syndrome-like model led to the development of bladder hypersensitivity. In addition, a rat model with surgically induced endometriosis had reduced micturition thresholds and increased Evans Blue dye extravasation in the bladder [9].

A FMS-like rat model induced by hydrochloric acid (HCl) injection (pH4.0) into the unilateral gastrocnemius muscle that could produce mechanical hyperalgesia of the bilateral plantar without evidence of tissue damage has been developed by Sluka et al. [10]. Although colonic hyperalgesia has been shown in a FMS-like rat model induced by HCl injection to the hindlimb muscle [11], it is not known whether muscular pain can induce bladder

hypersensitivity. Thus, we examined time-dependent changes in bladder function and plantar sensitivity in a rat model with FMS induced by HCl injection (pH4.0) into the bilateral gluteus. In addition, we determined whether lidocaine injection into the same area of the gluteus can recover bladder function because it has been reported that pretreatment with intravesical instillation of lidocaine attenuated mechanical hyperalgesia of the plantar induced by intravesically instilled acrolein [12].

MATERIALS AND METHODS

Under isoflurane (Mylan, Canonsburg, PA, USA) anesthesia, 0.2 ml of HCl (Sigma, St. Louis, MO, USA) solution (pH4.0) was injected into the bilateral gluteus muscles of twenty-four female Sprague-Dawley rats weighting 220–280g (FMS rats) because the afferent nerves innervating to the bladder and this area of the gluteus arise from the same L6 level of the spinal cord (FIG.1.) [13], and the gluteus muscle is one of the specific tender points in FMS patients [14]. Control rats (n=24) received 0.2ml of saline injection. All experiments were conducted in accordance with institutional guidelines and approved by Institutional Animal Care and Use Committee of Jikei University.

FMS (n=6) and control (n=6) rats were placed individually in a small acrylic cage with a wire mesh floor 1, 2 and 3 weeks after the HCl or saline injection. After all rats had adapted to the environment for about 1 hour, a 2.0 g von Frey filament (Stoelting, Wood Dale, IL, USA) was pressed vertically against the mid-plantar surface of the right and left hindlimbs through the mesh floor for 3 sec. until the filament slightly buckled. The mean number of bilateral hindlimb withdrawals per ten times at 5 sec. intervals was measured as a data point of mechanical sensitivity in the plantar 1, 2 and 3 weeks after the injection. In our preliminary experiments, the hindlimb withdrawal response occurred in about 10% when a 2.0g von Frey filament was applied ten times to the right or left plantar in control rats, so that this tactile stimulation with a 2.0 g von Frey filament was thought to be suitable for the assessment of mechanical hypersensitivity in the plantar.

In a separate group of FMS (n=18) and control (n=18) rats, under isoflurane anesthesia, the bladder was exposed through a lower midline abdominal incision and a polyethylene (PE-50) catheter (Clay Adams, Parsippany, NJ, USA) was implanted into the bladder through the bladder dome. The intravesical catheter was passed through the abdominal wall when the wound was closed with sutures, and a local anesthetic (EMLA cream, AstraZeneca, Wilmington, DE, USA) was applied to the abdominal wound. The animals were then placed into a sling-suit harness (Lomir Biomedical, Malone, NY, USA) and allowed to recover from the anesthesia for about 1 hour, so that cystometry was performed in an awake condition. The intravesical catheter was connected via a three-way stopcock to a pressure transducer (ADI Instruments, Castle Hill NSW, Australia) and a syringe pump (KD Scientific, Holliston, MA, USA). Saline solution was infused at 0.06 ml/min. for about 1 hour until rhythmic bladder contractions became stable. Cystometric parameters were then measured for 1 hour before and after 1% lidocaine (Sigma) injection (0.2 ml) into the bilateral gluteus at 1, and 3 weeks in FMS or control rats (n=6, respectively). Intercontraction interval (ICI), baseline pressure (BP), voiding threshold pressure (TP) and maximal voiding pressure (MVP) were recorded using a data-acquisition software (sampling at 10Hz, Chart, ADI Instruments) on a computer system equipped with an analog-to-digital converter (PowerLab, ADI Instruments). Saline voided from the urethral orifice was also collected and measured to determine voided volume (VV). After constant voided volumes were collected the infusion was stopped and post-voided residual urine volume (PVR) was measured by dropping the catheter and withdrawing intravesical fluid through the catheter by gravity. Voiding efficiency (VE) was calculated with the formula, $VV / (VV + PVR) \times 100$. All animals were sacrificed at the end of cystometric evaluation.

All data were represented as mean values $\pm$ standard error of the mean (SEM). Statistical analysis software (Prism, GraphPad Software, San Diego, CA, USA) was used to compare the results in each group. Changes in cystometric parameters before and after 1% lidocaine injection at 1, 2 and 3 weeks in FMS or control rats were analyzed using paired Student t-test. The other measurements in comparison of FMS and control rats at 1, 2 and 3 weeks were analyzed using unpaired Student t-test. $P < 0.05$ was regarded as statistically significant.

RESULTS

The mean number of bilateral hindlimb withdrawals was significantly increased in FMS rats compared with controls at 1 week (FMS: 3.0 ± 0.5 / 10 trials versus control: 1.2 ± 0.1 / 10 trials) and 2 weeks (FMS: 2.1 ± 0.2 / 10 trials versus control: 1.0 ± 0.1 / 10 trials). However, there was no significant difference in the mean number of hindlimb withdrawals between FMS and control rats at 3 weeks (FMS: 1.3 ± 0.1 / 10 trials versus control: 1.1 ± 0.1 / 10 trials) (FIG.2.).

The results of cystometry in FMS and control rats with or without 1% lidocaine injection at 1, 2 and 3 weeks were shown in Table 1 in addition to the representative cystometrograms (FIG.3). ICI was significantly decreased in FMS rats compared with controls at 1 week (FMS: 517.4 ± 45.5 sec. versus control: 785.3 ± 90.4 sec.) and weeks (FMS: 524.6 ± 50.3 sec. versus control: 755.9 ± 86.7 sec.). VV was also significantly decreased in FMS rats compared with controls at 1 week (FMS: 0.47 ± 0.05 ml versus control: 0.75 ± 0.09 ml) and 2 weeks (FMS: 0.48 ± 0.06 ml versus control: 0.71 ± 0.08 ml). However, the significant difference in ICI and VV between FMS and control rats was not seen at 3 weeks. In addition, there was no significant difference in the other cystometric parameters such as BP, TP, MVP, PVR or VE between FMS and control rats without lidocaine injection at 1, 2 and 3 weeks.

On the other hand, in FMS rats following lidocaine injection, TP was significantly increased from 7.1 ± 0.3 cmH₂O to 8.4 ± 0.3 cmH₂O at 1 week and from 6.5 ± 0.7 cmH₂O to 7.6 ± 0.8 cmH₂O at 2 weeks. In addition, ICI was significantly increased from 517.4 ± 45.5 sec. to 867.2 ± 64.3 sec. at 1 week and from 524.6 ± 50.3 sec. to 761.9 ± 94.0 sec. at 2 weeks, with VV being significantly increased from 0.47 ± 0.05 ml to 0.82 ± 0.06 ml at 1 week and from 0.48 ± 0.06 ml to 0.72 ± 0.09 ml at 2 weeks. However, cystometric parameters before and after lidocaine injection were not different in FMS rats at 3 weeks or in control rats at 1, 2, and 3 weeks

DISCUSSION

Although there are no perfect animal models of BPS/IC except for a naturally occurring model in cats [15], rodents with intraperitoneal injection of cyclophosphamide [16,17], or with intravesical instillation of mustard oil [18], HCl [19], acetone [20] and protamine sulfate [8,21] have often been used to study the disease process of BPS/IC. Recently, in a rat model of irritable bowel syndrome induced by intracolonic injection of TNBS, colonic irritation can induce BPS/IC-like changes in the bladder [8,22]; therefore it has been proposed as a new model of BPS/IC due to colon-to-bladder cross-sensitization. Although there is a FMS-like animal model which is characterized by muscular pain induced by HCl injection (pH4.0) into the gastrocnemius muscle [10], it is not known whether muscular pain can induce bladder hypersensitivity. This study has demonstrated that HCl injection (pH4.0) into the bilateral gluteus muscles can induce both plantar hypersensitivity and urinary frequency (i.e., reduction of voided volume and intercontraction interval) up to 2 weeks, suggesting that somatic (gluteus)-to-visceral (bladder) cross-sensitization might underlie bladder hypersensitivity in patients with FMS. Our results showed that bladder

hypersensitivity was observed in FMS rats for 2 weeks and that decreased threshold pressure, which indicates the activation of afferent inputs from the bladder [23], was significantly increased to the level of controls following the lidocaine injection in FMS rats.

Recently, three different but interconnected neural mechanisms have been proposed to underlie organ cross-sensitization [24]. The first mechanism considers the presence of dorsal root ganglion (DRG) neurons with branching or multiple axons, which could serve as direct neuronal connections among different organ domains. Previous studies using dual retrograde labeling in DRG sections have demonstrated that convergent DRG neurons receiving afferent inputs from the distal colon and bladder are identified in 14–17% of the total labeled cells [22,25] although there is no evidence showing the existence of axons that branch to supply the bladder and hindlimb muscle. The second mechanism is that afferent inputs from a flamed structure and from other inflamed structures converge on the same interneuron located in the dorsal horn of the spinal cord. Previous studies in female rats have demonstrated that the bladder, cervix and distal colon are innervated by the lumbosacral parasympathetic nerve (the pelvic nerve) derived from L6-S2 and the thoracolumbar sympathetic nerve (the hypogastric nerve) derived from T13-L1 [7,26,27]. The dorsal horns of the T13-L1 and L6-S2 segments were searched for neurons responsive to gentle mechanical stimulation of the cervix and skin areas at the perineum and hindlimbs, and to distention of the colon [28]. The cervix-responsive neurons in T13-L1 and L6-S2 responded to the skin stimulation (34% and 38%, respectively), as well as to the colonic distention (59% and 51%, respectively), suggesting that afferent inputs from the pelvic organ (i.e., the cervix and distal colon) and from the skin at the perineum and hindlimb regions converge in the dorsal horn of the spinal cord [28]. The third mechanism underlying organ cross-sensitization appears to involve higher centers of the brain. It is well known that Barrington's nucleus is the primary component of the pontine micturition center. The divergent projections of Barrington's nucleus neurons to the parasympathetic preganglionic neurons innervating to the bladder and colon have showed that individual neurons within Barrington's nucleus are poised to integrate signals from distal pelvic viscera [29]. In addition, the study of medullary reticular formation in the brain stem has demonstrated a significant degree of convergence from the distal colon, rectum and skin at the hindlimbs [30]. In this study, we have found that HCl stimulation at the gluteus muscle area, which is innervated by the L6 level of the spinal cord, can induce not only frequent micturition, but also referral pain (i.e., mechanical hyperalgesia) in the plantar area, which is innervated by the L3-5 level of the spinal cord [13]. Taken together, these results led us to the hypothesis that plantar hypersensitivity and urinary frequency induced by HCl injection (pH4) into the gluteus might be due to somatic (gluteus)-to-visceral (bladder) and somatic (gluteus)-to-somatic (plantar) cross-sensitization in the DRG, spinal cord and/or brain levels. Further studies are needed to clarify which neural pathways are important for these cross-sensitization mechanisms.

In clinical practice, there is a significant association of BPS/IC with other chronic pain syndromes including FMS [2–5]. The results in this study suggest that the somatic (gluteus)-to-visceral (bladder) cross-sensitization mechanism might be involved in BPS/IC-like bladder symptoms of FMS patients. Because lidocaine injection into the gluteus normalized bladder function in FMS rats in this study, the intervention of specific tender points (e.g., gluteus) outside the bladder might be effective to treat urinary frequency in FMS patients. Furthermore, when patients with BPS/IC exhibit other chronic pelvic pain conditions such as FMS, irritable bowel syndrome and/or endometriosis, the treatment outside the bladder would also be important to control their bladder-related symptoms in addition to focal therapies such as intravesical instillation of dimethyl sulfoxide or hydrodistention of the bladder [31].

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REFERENCES

1. van de Merwe JP, Nordling J, Bouchelouche P, Bouchelouche K, Cervigni M, Daha LK, Elneil S, Fall M, Hohlbrugger G, Irwin P, Mortensen S, van Ophoven A, Osborne JL, Peekers R, Richter B, Riedl C, Sairanen J, Tinzl M, Wyndaele JJ. Diagnostic criteria, classification, and nomenclature for painful bladder syndrome/interstitial cystitis: an ESSIC proposal. *Eur Urol*. 2008; 53:60–67. [PubMed: 17900797]
2. Alagiri M, Chottiner S, Ratner V, Slade D, Hanno PM. Interstitial cystitis: unexplained associations with other chronic disease and pain syndromes. *Urology*. 1997; 49:52–57. [PubMed: 9146002]
3. Warren JW, Howard FM, Cross RK, Good JL, Weissman MM, Wessellmann U, Langenberg P, Greenberg P, Clauw DJ. Antecedent nonbladder syndromes in case-control study of interstitial cystitis/painful bladder syndrome. *Urology*. 2009; 73:52–57. [PubMed: 18995888]
4. Nickel JC, Tripp DA, Pontari M, Moldwin R, Mayer R, Carr LK, Doggweiler R, Yang CC, Mishra N, Nordling J. Interstitial cystitis/painful bladder syndrome and associated medical conditions with an emphasis on irritable bowel syndrome, fibromyalgia and chronic fatigue syndrome. *J Urol*. 2010; 184:1358–1363. [PubMed: 20719340]
5. Clauw DJ, Schmidt M, Radulovic D, Singer A, Katz P, Bresette J. The relationship between fibromyalgia and interstitial cystitis. *J psychiat Res*. 1997; 31:125–131. [PubMed: 9201654]
6. Rodriguez MA, Afari N, Buchwald DS. Evidence for overlap between urological and nonurological unexplained clinical conditions. *J Urol*. 2009; 182:2123–2131. [PubMed: 19758633]
7. Berkley KJ. A life of pelvic pain. *Physiol Behav*. 2005; 86:272–280. [PubMed: 16139851]
8. Pezzone MA, Liang R, Fraser MO. A model of neural cross-talk and irritation in the pelvis: implications for the overlap of chronic pelvic pain disorders. *Gastroenterology*. 2005; 128:1953–1964. [PubMed: 15940629]
9. Morrison TC, Dmitrieva N, Winnard KP, Berkley KJ. Opposing viscerovisceral effects of surgically induced endometriosis and a control abdominal surgery on the rat bladder. *Fertil Steril*. 2006; 86:1067–1073. [PubMed: 16962120]
10. Sluka KA, Kalra A, Moore SA. Unilateral intramuscular injections of acidic saline produce a bilateral, long-lasting hyperalgesia. *Muscle Nerve*. 2001; 24:37–46. [PubMed: 11150964]
11. Miranda A, Peles S, Rudolph C, Shaker R, Sengupta JN. Altered visceral sensation in response to somatic pain in the rat. *Gastroenterology*. 2004; 126:1082–1089. [PubMed: 15057747]
12. Guerios SD, Wang ZY, Boldon K, Bushman W, Bjorling DE. Lidocaine prevents referred hyperalgesia associated with cystitis. *Neurourol Urodyn*. 2009; 28:455–460. [PubMed: 19291783]
13. Takahashi Y, Nakajima Y. Dermatomes in the rat limbs as determined by antidromic stimulation of sensory C-fibers in spinal nerves. *Pain*. 1996; 67:197–202. [PubMed: 8895248]
14. Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Katz RS, Mease P, Russell AS, Russell IJ, Winfield JB, Yunus MB. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. *Arthritis Care Res (Hoboken)*. 2010; 62:600–610. [PubMed: 20461783]
15. Westropp JL, Buffington CA. In vivo models of interstitial cystitis. *J Urol*. 2002; 167:694–702. [PubMed: 11792956]
16. Maggi CA, Lecci A, Santicoli P, Del Bianco E, Giuliani S. Cyclophosphamide cystitis in rats: involvement of capsaicin-sensitive primary afferents. *J Auton Nerv Syst*. 1992; 38:201–208. [PubMed: 1613209]
17. Vizzard MA. Alterations in spinal cord Fos protein expression induced by bladder stimulation following cystitis. *Am J Physiol Regul Integr Comp Physiol*. 2000; 278:R1027–R1039. [PubMed: 10749792]

18. McMahon SB, Abel C. A model for the study of visceral pain states: chronic inflammation of the chronic decerebrate rat urinary bladder by irritant chemicals. *Pain*. 1987; 28:109–127. [PubMed: 3822491]
19. Rivas DA, Chancellor MB, Shupp-Byrne S, Shenot PJ, McHugh K, McCue P. Molecular marker for development of interstitial cystitis in rat model: isoactin gene expression. *J Urol*. 1997; 157:1937–1940. [PubMed: 9112567]
20. Shimizu I, Kawashima K, Hosoki K. Urodynamics in acetone-induced cystitis of anesthetized rats. *Neurourol Urodyn*. 1999; 18:115–127. [PubMed: 10081951]
21. Soler R, Bruschini H, Truzzi JC, Martins JR, Camara NO, Alves MT, Leite KR, Nader HB, Srougi M, Ortiz V. Urinary glycosaminoglycans excretion and the effect of dimethyl sulfoxide in an experimental model of non-bacterial cystitis. *Int Braz J Urol*. 2008; 34:503–511. discussion 11. [PubMed: 18778502]
22. Malykhina AP, Qin C, Greenwood-van Meerveld B, Foreman RD, Lupu F, Akbarali HI. Hyperexcitability of convergent colon and bladder dorsal root ganglion neurons after colonic inflammation: mechanism for pelvic organ cross-talk. *Neurogastroenterol Motil*. 2006; 18:936–948. [PubMed: 16961697]
23. Yoshimura, N.; Chancellor, MB. Physiology and pharmacology of the bladder and urethra, Philadelphia, PA, USA, Chapter 56. In: Wein, AJ., editor. *Cambell-Walsh Urology*. 9th. B. Saunders Elsevier; 2006. p. 1922-1972.
24. Malykhina AP. Neural mechanisms of pelvic organ cross-sensitization. *Neuroscience*. 2007; 149:660–672. [PubMed: 17920206]
25. Christianson JA, Liang R, Ustinova EE, Davis BM, Fraser MO, Pezzone MA. Convergence of bladder and colon sensory innervation occurs at the primary afferent level. *Pain*. 2007; 128:235–243. [PubMed: 17070995]
26. Berkley KJ, Robbins A, Sato Y. Functional differences between afferent fibers in the hypogastric and pelvic nerves innervating female reproductive organs in the rat. *J Neurophysiol*. 1993; 69:533–544. [PubMed: 8459284]
27. De Groat WC. Integrative control of the lower urinary tract: preclinical perspective. *Br J Pharmacol*. 2006; 147 Suppl 2:S25–S40. [PubMed: 16465182]
28. Berkley KJ, Hubscher CH, Wall PD. Neuronal responses to stimulation of the cervix, uterus, colon, and skin in the rat spinal cord. *J Neurophysiol*. 1993; 69:545–556. [PubMed: 8459285]
29. Rouzade-Dominguez ML, Miselis R, Valentino RJ. Central representation of bladder and colon revealed by dual transsynaptic tracing in the rat: substrates for pelvic visceral coordination. *Eur J Neurosci*. 2003; 18:3311–3324. [PubMed: 14686904]
30. Hubscher CH, Kaddumi EG, Johnson RD. Brain stem convergence of pelvic viscerosomatic inputs via spinal and vagal afferents. *Neuroreport*. 2004; 15:1299–1302. [PubMed: 15167553]
31. Hanno P, Lin A, Nordling J, Nyberg L, van Ophoven A, Ueda T, Wein A. Bladder Pain Syndrome Committee of the International Consultation on Incontinence. *Neurourol Urodyn*. 2010; 29:191–198. [PubMed: 20025029]

1. .

A chart showing the site of HCl injection (pH4.0) into the bilateral gluteus muscles. The HCl injection site is shown as double circles (⊙). The afferent nerves innervating to the bladder and this area of the gluteus arise from the same L6 level of the spinal cord. In addition, this area is regarded as one of the specific tender points in FMS patients. HCl; hydrochloric acid, FMS; fibromyalgia syndrome.

Mean number of hindlimb withdrawals /10 trials

2. .

Time-dependent changes in the number of bilateral hindlimb withdrawals in response to tactile stimulation with a 2.0 g von Frey filament. The mean number of bilateral hindlimb withdrawals was significantly increased in FMS rats compared with controls at 1 week (**P<0.01) and 2 weeks (**P<0.01). FMS; fibromyalgia syndrome, N.S.; not significant.

3. .

Representative cystometrograms in FMS and control rats with or without 1% lidocaine injection into the bilateral gluteus muscles. Intercontraction interval (ICI) was significantly decreased in FMS rats compared with controls at 1 and 2 weeks prior to lidocaine injection. The ICI in FMS rats was, however, significantly increased to the same interval of controls at 1 and 2 weeks after lidocaine injection. FMS; fibromyalgia syndrome.

Time-dependent changes in cystometric parameters 1, 2 and 3 weeks after HCl injection (pH4.0) into the bilateral gluteus muscles with or without 1% lidocaine injection.

1W		n	BP (cmH ₂ O)	TP (cmH ₂ O)	MVP (cmH ₂ O)	ICI (sec.)	VV (ml)	PVR (ml)	VE (%)
Control	without lidocaine	6	4.9±0.7	7.8±0.5	20.8±1.3	785.3±90.4	0.75±0.09	0.04±0.01	94.5±1.3
	with lidocaine	6	4.9±0.4	7.8±0.3	20.9±1.0	834.11±92.6	0.80±0.09	0.04±0.01	95.3±0.9
FMS	without lidocaine	6	4.7±0.4	7.1±0.3	20.5±1.0	517.4±45.5 [#]	0.47±0.05 [#]	0.05±0.01	89.9±2.1
	with lidocaine	6	4.6±0.3	8.4±0.3 [*]	22.9±1.1	867.2±64.3 ^{**}	0.82±0.06 ^{**}	0.05±0.01	94.5±0.6
2W		n	BP (cmH ₂ O)	TP (cmH ₂ O)	MVP (cmH ₂ O)	ICI (sec.)	VV (ml)	PVR (ml)	VE (%)
Control	without lidocaine	6	5.0±0.3	8.1±0.4	21.1±1.1	755.9±86.7	0.71±0.08	0.04±0.01	94.4±0.7
	with lidocaine	6	4.9±0.3	8.0±0.2	21.7±1.2	793.3±88.4	0.75±0.09	0.04±0.01	94.9±1.0
FMS	without lidocaine	6	4.6±0.7	6.5±0.7	21.4±0.9	524.6±50.3 [#]	0.48±0.06 [#]	0.05±0.01	90.2±3.0
	with lidocaine	6	4.5±0.6	7.6±0.8 [*]	20.9±0.8	761.9±94.0 [*]	0.72±0.09 [*]	0.04±0.01	94.4±1.4
3W		n	BP (cmH ₂ O)	TP (cmH ₂ O)	MVP (cmH ₂ O)	ICI (sec.)	VV (ml)	PVR (ml)	VE (%)
Control	without lidocaine	6	4.5±0.7	7.1±0.6	20.6±1.6	786.4±68.0	0.76±0.07	0.03±0.01	95.5±0.9
	with lidocaine	6	4.3±0.6	7.3±0.5	22.2±1.6	850.4±84.4	0.82±0.09	0.04±0.01	95.7±0.8
FMS	without lidocaine	6	4.1±0.4	6.5±0.4	21.6±1.5	681.6±103.2	0.65±0.10	0.04±0.01	94.1±1.6
	with lidocaine	6	4.4±0.7	7.1±0.5	20.8±0.8	737.0±86.6	0.70±0.09	0.04±0.01	94.8±1.4

All parameters are represented as mean values ± SEM. BP: baseline pressure, TP: threshold pressure, MVP: maximal voiding pressure, ICI: intercontraction interval, VV: voided volume, PVR: post-voided residual urine volume, VE: voiding efficiency.

[#] p<0.05; FMS rats without lidocaine versus control rats without lidocaine.

^{*} p<0.05 and

^{**} p<0.01; FMS rats with lidocaine versus FMS rats without lidocaine. HCl: hydrochloric acid, FMS: fibromyalgia syndrome.