Mechanisms of Pelvic Organ Cross-Talk: Impact of Urethral Ligation on the Inhibitory Rectovesical Reflex

Sara Persyn,* Stefan De Wachter, Michel Wyndaele, Lori Birder† and Jean-Jacques Wyndaele

From the Department of Urology, Antwerp University Hospital and Faculty of Medicine, University of Antwerp, Antwerp (SP, SDW, MW, LB, JJW), Belgium, and Departments of Medicine and Pharmacology, University of Pittsburgh School of Medicine (LB), Pittsburgh, Pennsylvania

Abbreviations and Acronyms

BCF = bladder contraction frequency

CNS = central nervous system

CRD = colorectal distension

CRF = corticotrophin releasing factor

GABA = γ-aminobutyric acid

ICI = intercontraction interval

IRVR = inhibitory rectovesical reflex

LC = locus coeruleus

MTP = micturition threshold pressure

MTV = micturition threshold volume

Accepted for publication May 5, 2014.

Study received University of Antwerp animal ethics committee approval.

* Correspondence: Campus Drie Eiken, S4.51, Antwerp University, Universiteitsplein 1, 2610, Wilrijk, Antwerp, Belgium (telephone: +32(0)32652535; FAX: +32(0)38214479; e-mail: Sara.Persyn@uantwerpen.be).

† Financial interest and/or other relationship with Astellas.

Purpose: The existence of an inhibitory rectovesical reflex elicited by noxious colorectal afferent input was previously documented in an isovolumetric cystometry model with a ligated urethra. We compared the effect of noxious colorectal distension on bladder cystometry with an open and a ligated urethra.

Materials and Methods: We used female Sprague Dawley® rats anesthetized with urethane. The effect of noxious (60 mm Hg) colorectal distension on intermittent and continuous cystometry with an open urethra was studied and then compared to inhibiting isovolumetric bladder contractions in the same rat after ligating the urethra. We evaluated volume, the pressure micturition threshold, the intercontraction interval, bladder contraction frequency and amplitude of micturition contractions.

Results: Noxious colorectal distension at 60 mm Hg did not significantly influence volume or the pressure micturition threshold during intermittent cystometry. It also did not influence the pressure micturition threshold, the intercontraction interval or bladder contraction frequency during continuous cystometry. After urethral ligation 60 mm Hg colorectal distension inhibited isovolumetric bladder contraction frequency in the same rat (mean ± SEM 0.363 ± 0.207 vs 0.886 ± 0.106 contractions per minute, $p < 0.05$). This inhibition persisted a mean of 289.08 ± 91.24 seconds after deflating the rectal balloon.

Conclusions: The inhibitory rectovesical reflex elicited by noxious colorectal distension clearly occurred in an isovolumetric bladder model with a ligated urethra but only to a negligible extent in filling related voiding contractions. Our results suggest that the inhibitory rectovesical reflex, most likely at the level of the lumbosacral spinal cord, is the result of an additive noxious urethral and colonic afferent stimulus.

Key Words: urinary bladder, rectum, reflex, urination, afferent pathways

LOWER urinary tract and colorectal pathologies often coexist. In a community based study the prevalence of combined fecal and urinary incontinence was 6% to 9%.[1] Patients with urinary incontinence experienced more complaints of fecal incontinence and constipation than a control group.[2]

Coordinated activity of the lower urinary tract and colorectum by neural crosstalk is essential for physiological functions in the pelvic region.[3] Micturition and defecation mostly

0022-5347/14/1925-1574/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2014.05.023
Vol. 192, 1574-1579, November 2014
Printed in U.S.A.

alternate[4] and previous clinical studies showed that CRD increases bladder filling sensation.[5] Furthermore, CRD can inhibit bladder activity.[6]

The existence of this IRVR was confirmed in animal studies[7–9] but the exact mechanism is not yet fully understood. CRD and electrical stimulation of the colon inhibit spontaneous bladder contractility and increase the micturition threshold.[7–9] The IRVR is considered to occur in the lumbosacral spinal cord through glycinergic and GABAergic mechanisms, and it persists after spinal cord injury.[8,9]

Previously it was reported that only noxious CRD (40 to 60 mm Hg) inhibits isovolumetric bladder contraction frequency with 67% complete abolishment of bladder contractions during 60 mm Hg CRD.[10] Bladder contraction amplitude and duration, which are parameters of efferent activity, were not affected. These results suggest that the IRVR is only activated by high threshold colonic afferents and it occurs in the afferent limb of the micturition arc or at the spinal level. However, a subsequent study demonstrated that noxious CRD increases afferent bladder activity, indicating that noxious colorectal afferent stimuli may exert an inhibitory effect on the spinal connection between the afferent and efferent limbs of the micturition pathway.[11]

Previous experiments were performed in an isovolumetric model with a ligated urethra, which is considered a noxious stimulus.[8–10,12] Normal storage and voiding function of the bladder require coordinated activity between the bladder and urethra. Stimulating urethral (pelvic and pudendal) afferents during voiding facilitates reflex bladder contractions. Stimulation of somatic afferent pathways projecting in the pudendal nerve (originating from the external urethral sphincter) to the lumbosacral spinal cord can suppress the micturition reflex.[13]

To further explore the IRVR and more specifically the role of the urethra in this reflex we determined the effect of noxious CRD in 2 cystometry models with an open urethra, which occurs naturally. We first evaluated the effect of noxious CRD on the volume threshold of separate individual micturitions obtained by intermittent bladder filling. In the same rat we evaluated the effect of noxious CRD on uninterrupted micturition cycles using continuous cystometry. Finally, the urethra was ligated and we studied the effect of noxious CRD on spontaneous rhythmic isovolumetric bladder contractions.

MATERIALS AND METHODS

Animal Model

The protocol was approved by the University of Antwerp animal ethics committee. A total of 13 female Sprague Dawley rats weighing 200 to 255 gm were kept under standard laboratory conditions with a 12-hour light-12-hour dark cycle and free access to food pellets and tap water. Anesthesia was induced by intraperitoneal injection of urethane (1.5 gm/kg). After the experiments the rats were sacrificed by urethane overdose.

The rat was positioned supine. A flare tipped PE-50 polyethylene catheter (Clay-Adams, Parsippany, New Jersey) was inserted in the bladder through the dome via a lower abdominal incision, secured with a 7-zero Prolene® purse-string suture and externalized via the proximal aspect of the ventral abdominal incision.[11] During catheter implantation we administered extra isoflurane anesthesia (1.5% oxygen at 1 L per minute).

The catheter was connected to a pressure transducer (Emka Technologies, Paris, France) and a NE-1000 syringe pump (New Era Pump Systems, Farmingdale, New York) via 3-way stopcocks. Normal saline was infused in the bladder at a rate of 0.09 ml per minute.

A 3.5 cm latex balloon catheter was made from the little finger of a size 6 Triflex® surgical glove, inserted in the rectum and fixed to the tail 1 cm from the anus. The balloon was connected to a pressure controlled 2PK+ Pressure/Vacuum Generator (ALA Scientific Instruments, Farmingdale, New York) as the distension device to maintain constant pressure during CRD. All data were monitored with time using WinDaq® DI-710 data acquisition.[10]

Protocols

General. After surgical preparation a 30-minute rest period was included before the start of bladder filling. Three protocols were performed. All rats first underwent intermittent cystometry. In a few rats this protocol was followed by continuous and isovolumetric cystometry. To perform isovolumetric cystometry the urethra had to be ligated so that this was the last protocol performed. A 30-minute rest period was included between each protocol.

Intermittent cystometry with bladder filling and open urethra. In the first part of the study we evaluated the effect of 60 mm Hg CRD on MTV, MTP and the amplitude of the ensuing micturition contraction during intermittent filling-voiding cycles. Baseline MTV was defined as the volume at which the micturition contraction was initiated during 3 consecutive measurements with a deflated rectal balloon. After completing the baseline recordings 1 filling cystometry was performed during 60 mm Hg CRD. The protocol was concluded with a followup measurement using a deflated rectal balloon.

After each bladder contraction the catheter was opened for 5 minutes and gentle abdominal pressure was applied to remove possible residual urine from the bladder. To avoid bladder damage the bladder was filled to a maximum of 160% of baseline MTV or until bladder pressure reached 30 cm H_2O.

Continuous cystometry with bladder filling and open urethra. In the second part of the study we examined the effect of 60 mm Hg CRD on micturition contractions during continuous cystometry. ICI, BCF, MTP and