New Concepts in Relation to Urge and Detrusor Activity

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Investigations of micromotion characteristics of bladder wall strips and pressure wave phenomena in total bladders in vitro and in vivo indicate that micromotion phenomena occur in the bladder wall. Local contractions can occur without an increase in tension or pressure, because other parts are in antiphase. Local contractions stretch surrounding tissues, which can stimulate fast stretch receptors. Synchronisation of these micromotion phenomena appears to be possible. Hence, above threshold levels urge can theoretically occur, even in the absence of a pressure increase. This hypothesis could explain the weak relation between urge and pressure. The distinction between motor and sensory urge could be artifactual based on a misunderstanding of fundamental bladder wall processes.

Key words: instability, bladder wall, spontaneous activity

INTRODUCTION

Urge is the sensation of the inability to voluntarily postpone micturition. It usually causes frequency, sometimes nocturia, and interferes with the quality of life, especially when it causes incontinence. Its incidence and clinical significance increase with age [Abrams, 1985]. Changes at the proximal urethra have been repeatedly reported to be associated with these complaints. Stress incontinence [McGuire and Savastano, 1985], as well as affections of the prostate, either obstructive or unobstructive, are frequently related to urge symptoms [Coolsaet and Blok, 1986]. Bladder properties during filling have been reported [Coolsaet, 1985].

The causal relation between these symptoms and detrusor overactivity has been clinically evaluated in several studies. Knowledge about the clinical “urge” problem has made little progress during recent years. This is due to the fact that detrusor pressure has been accepted as the key factor. Pressure increases during the bladder filling phase which exceed 15 cm H₂O have been arbitrarily labeled as detrusor instability or motor urge. Patients who did not fulfill this criterion were labelled as having sensory urge. Most authors still use these criteria, although the clinical rele-

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Advancement of subthreshold pressure increases has been demonstrated [Coolsaet et al., 1985]. The International Continence Society adapted the definition accordingly. The main interest of urodynamic research has been to find techniques to confirm the patient’s complaint of urge in terms of pressure: ambulatory urodynamics and provocative tests such as changes of diuresis, position, catheter position, and many others.

The relation between detrusor pressure and urge was recently questioned. Notwithstanding the use of "instability indices," there appears to be a poor correlation between pressures and symptoms [Murray et al., 1982; Jorgenson et al., 1987]. Abrams [1985] reported that in a group of benign prostatic hypertrophy (BPH) patients, only 47% with preoperative unstable bladders complained of urgency and only 16% of them complained of instability after the operation. It is a common experience that pressure increases occur without urge and that pharmacotherapy can cure the symptom without changing the pressure and vice versa.

In this contribution we will try to go back from the bladder lumen to the bladder wall, an essential part of the musculoneuronal urge problem.

**OBJECTIVES OF THE STUDY**

The aim of the study was to further investigate the spontaneous micromotion activity of bladder wall strips and total bladders. The observation of the presence of contracting and relaxing areas provides fundamental information on local wall mechanisms which produce afferent input to the central nervous system. This input does not necessarily need to be coupled with significant pressure increases.

**IN VITRO OBSERVATIONS ON BLADDER WALL STRIPS**

**Methods**

The technique to study patterns of spontaneous microdisplacements (<0.1 mm) have been described earlier [Van Duyl, 1985a]. Strips of pig bladder wall are connected to an isometric force transducer, while microdisplacements are measured by means of thin fibers, which are stuck through the tissue and follow the local motions. The fibertips are lighted, and the motions of the light spots are analysed (Fig. 1).
Results

As the results of this study have been published earlier [Van Der Hoeven et al., 1990; Van Duyl et al., 1990], here we will only summarize the conclusions. Spontaneous activity is distributed in the bladder wall and is composed of two frequency components, the lower frequency component in the range of 0.02–0.05 per second and the higher at about twice this frequency. Areas of synchronized motion of the two frequency components coexist independently of each other and are independently distributed in the tissue. Figure 2 is a snapshot showing the regions of spontaneous activity of both frequency components. The study on a large series of such snapshots reveals several fundamental aspects of spontaneous detrusor activity:

(a) the two frequency components occur in different areas
(b) the areas of the two frequencies may overlap
(c) these micromotion areas migrate over the course of time
(d) for each frequency component, different areas are in antiphase, which means that some regions are in the contracting phase while others are relaxing
(e) the two different frequency components are generated separately
(f) the two frequency components have different characteristics: the lower frequency component is inhibited by oxyphenomiumbromide [Hak et al., 1988]
(g) local contractions may occur without a rise in force across the strip

IN VITRO OBSERVATIONS ON TOTAL PIG BLADDERS

Methods

A fast stretch generates a contraction of smooth muscle by depolarising the cell membrane. Based on this property, Van Duyl et al. [1992] postulated that rhythmic straining of the bladder wall in the frequency of one of the components of micromo-
tion activity might interfere with this activity in such a way that synchronization occurs. In order to investigate this phenomenon, fresh total pig bladders with partly intact urethra were suspended in a metabolic solution (Krebs solution at 37°C, bubbled with 95% O₂/5% CO₂. A catheter was introduced in the bladder lumen via the urethra, which was subsequently sutured around the catheter.

The catheter was connected to a pressure transducer via a Y-connector. The other limb of the Y-connector was connected to a homemade controlled infusion pump. The bladder was filled with the same metabolic solution of 37°C, to a baseline volume of 100 ml. Then the bladder was allowed to equilibrate for 30 minutes. Subsequently volume changes of 20 ml were applied blockwise by means of the controlled infusion pump at a frequency in the range of 0.01–0.10/sec. Intravesical pressure was registrated during the period of equilibration, during application of volume changes, and after stopping of the volume changes.

Similar series of measurements have been performed on four pig bladders.

Results

During the period of equilibration, the detrusor pressure shows some irregular spontaneous variations (Fig. 3a). Figure 3b shows the pressure during and after blockwise volume changes. As appears from Figure 3b, the detrusor activity indeed has become more rhythmic, with larger amplitudes during and after blockwise volume changes. After stopping the volume changes, while the intravesical volume is kept at the baseline volume of 100 ml, large phasic pressure variations are observed at a remarkably stable frequency (Fig. 3c). The experiments have shown that spontaneous phasic rhythmic pressure waves can be evoked and increased by blockwise variation of bladder volume on total pig bladders in vitro.

IN VIVO OBSERVATIONS ON HUMAN BLADDERS

Methods

The observation in total pig bladders in vitro that spontaneous phasic variations in detrusor pressure can be induced by rhythmic variation of bladder volume motivated us to perform similar studies on human bladders in vivo. For this investigation we selected patients whose bladders showed obvious detrusor overactivity in a previous urodynamic investigation.

In principle, we used the same setup and followed the same procedure as for measurements on total pig bladders in vitro. A catheter (8 Fr) was introduced in the bladder via the urethra. The catheter was connected to a pressure transducer via a Y-connector (Fig. 4). The other limb of the Y-connector was connected to a controlled infusion pump. A baseline volume of 200 ml was introduced into the bladder. Blockwise volume variations of 30 ml were applied at a frequency of 0.025/sec during periods of 5–10 minutes. Detrusor pressure was recorded before, during, and after the applied volume changes.

Results

Figure 5 shows the pressure recording obtained in a female patient. The bladder was filled via the urethra, until a baseline volume of approximately 200 ml was reached. Figure 5a shows some spontaneous activity previous to stimulation by rhythmic volume changes. Figure 5b shows that rhythmic contractions are increased by
Fig. 3. Recording of intravesical pressure of pig bladder in vitro: —indicates periods of increased bladder volume. (a) Recording showing spontaneous activity previous to stimulation. (b) Recording of pressure variation during rhythmic blockwise volume changes. (c) Recording after stopping rhythmic volume changes showing manifest spontaneous rhythmic activity.

rhythmic straining; however, the contractions are not synchronized to the frequency of the applied straining.

In Figure 5c it is shown that after stopping the applied rhythmic straining, phasic rhythmic contractions continue for some time, and this spontaneous activity is considerably larger than in the period previous to stimulation. After a period of approximately 10 minutes, rhythmicity seems to be lost, indicating that the spontaneous activity becomes less synchronized. In Figure 5d the situation is restored after re-applying a period of rhythmic straining.

DISCUSSION

Bladder wall properties have been evaluated extensively. The passive and active properties have been taken as characteristics of two bladder conditions: the fully passive state [Van Mastriegt et al., 1978] and the fully activated state [Griffiths et al.,
In situ, both extreme bladder conditions are very rare. Van Duyl [1985a] introduced the concept of spontaneous micromotion. It was postulated that in a normal bladder wall, a certain degree of spontaneous micromotion continuously exists. Depending on the degree of micromotion, the actual condition of the bladder is situated along a bladder performance scale (BPS) between the extreme conditions of fully passive and fully activated [Van Duyl, 1985b]. According to this concept, detrusor activity, either spontaneous or stimulated, is a gradual phenomenon and will change during filling and micturition phase. This phenomenon is probably under the control of substances outlined by De Groat and Kawatani [1985]. Detrusor pressure is only a partial reflection of detrusor wall phenomena [Coolsaet and Elhilali, 1988].

Recent studies on bladder wall strips revealed that micromotion in areas of the wall is the origin of spontaneous activity, which can be observed as variations of force across a strip or as pressure waves in detrusor pressure [Van Der Hoeven et al., 1990; Van Duyl et al., 1990]. The amplitude of the contraction in a certain area of the bladder wall depends on the degree of synchronization of micromotions within that area.

The absence of waves in the overall force across a strip, or of waves in the detrusor pressure, does not mean that there is no spontaneous activity in the bladder wall. Spontaneous wall activity patterns probably are the key phenomenon in the origin of symptoms. Urge is not necessarily coupled to pressure variations in the bladder lumen. Local contractions can occur in the absence of an increase in pressure. The contraction per se is not necessarily the origin of urge. Local contractions can stretch the surrounding tissues, which can stimulate fast receptors [Kuru, 1965; Talaat, 1937]. The distinction between motor and sensory urge has probably been based on a misunderstanding of the fundamental process. Pressure in the bladder lumen ought to be dealt with primarily as a consequence of bladder wall phenomena.
Fig. 5. —indicates periods of increased bladder volume. Recording of intravesical pressure in a patient. (a) Recording showing spontaneous activity previous to stimulation. (b) Recording during rhythmic blockwise volume changes. (c) Recording after stopping stimulation, which demonstrates enhancement of spontaneous activity after stimulation and subsequent loss of synchronisation. (d) Recording during and after restimulation, which demonstrates recovery and subsequent loss of synchronisation.
This conclusion confirms the statements made earlier that, strictly speaking, no
detrusor is stable [Coolsaet and Blaivas, 1985]. The consequences are important. The
apparently fundamental pathophysiologic difference between sensory and motor urge
appears to be rather misleading. It is possible, indeed, that the origin of urge symp-
toms is in local stretch, detected by fast stretch receptors and transported to the
cortical areas via fibers, with the C-fibers possibly playing an important role. It is not
necessarily the contraction per se, as a source of tension and pressure, which causes
the symptom, although the symptom can be correlated with these contractions. In
relation to our concept, we can furthermore assume that a well-coordinated contrac-
tion with total bladder wall involvement does not necessarily cause urge. Indeed,
although pressure is increased, no parts of the wall are stretched. On the contrary, a
localized contraction can stretch parts of the wall which are in a relaxed state,
generating afferent pulses and subsequently urge.

Our concept explains why the correlation between detrusor pressure and symp-
toms is weak, notwithstanding bladder wall activity. The results on total bladders
explain the clinical observation that fast stretch can evoke urge. The conditions under
which local stretch and symptoms can be evoked are posture change, stepwise bladder
filling [Susset, 1983], and hyperdiuresis cystometry [Coolsaet and Elhilali, 1988; Van
Venrooy et al., 1987]. In harmony with the concept of synchronizable spontaneous
micromotion, rhythmic spontaneous contractions can be induced and enhanced by
rhythmic straining of the pig bladder wall in vitro. The results obtained from similar
experiments on human unstable bladders are consistent with this observation in vitro.
Our results show that spontaneous activity observed in vitro is more than an artifact,
as was concluded by Levin et al. [1986]. Phasic spontaneous pressure waves may be
induced by blockwise straining of the bladder wall. A neurogenic mechanism is
probably responsible for the loss of synchronization observed after a period of in-
duced rhythmic contraction activity.

Regional stretching phenomena can generate different input to the central ner-
vous system via C-fibers, which appear to be enhanced in urge conditions [De Groat
and Kawatani, 1985].

Steers [1990] observed morphological and electrophysiological alterations in
neural pathways in hypertrophic bladders, which are supposed to be related to sensory
symptoms. Similarly, Elbadawi [1991] suggests that more attention be paid to the
macrostructural basis of detrusor contractility.

The above considerations suggest that detrusor pressure has been overestimated
as a key criterion in the urge symptom complex. Indeed, contraction phenomena in
the wall can cause detrusor pressure increases, but they do not necessarily do so.
The classical definition of motor urge (detrusor instability) has to be interpreted within a
range of the BPS. The threshold of 15 cm H₂O is just an arbitrarily chosen mark on
the BPS but it has no pathophysiologic basis.

**CONCLUSIONS**

A new theory on the relation between bladder wall phenomena and urge symp-
toms has been presented. According to this theory the key factor might be local
stretch, caused by locally synchronized contracting areas, as demonstrated in vitro by
micromotion dynamics. Detrusor pressure variations are not only incomplete reflec-
tions of bladder wall phenomena, they mislead the clinician away from the basic
problem, which concerns local stretch. Contractions per se do not necessarily cause symptoms. Synchronization of local micromotions is possible by stretch stimulation, as demonstrated in these investigations and as clinically observed. The pathophysiologic localisation of the patient’s complaint “urge” can be in the bladder wall, neurotransport and neurocontrol [de Groat and Kawatani, 1985], and perception. Further research has to be shifted from complicated pressure-monitoring systems (ambulatory cystometry) towards the investigation of bladder wall phenomena and their neural control.

REFERENCES