#675 PATHOPHYSIOLOGY OF UNSTABLE URETHRA: DYSFUNCTION OF SMOOTH URETHRAL MUSCULATURE

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Hypothesis / aims of study

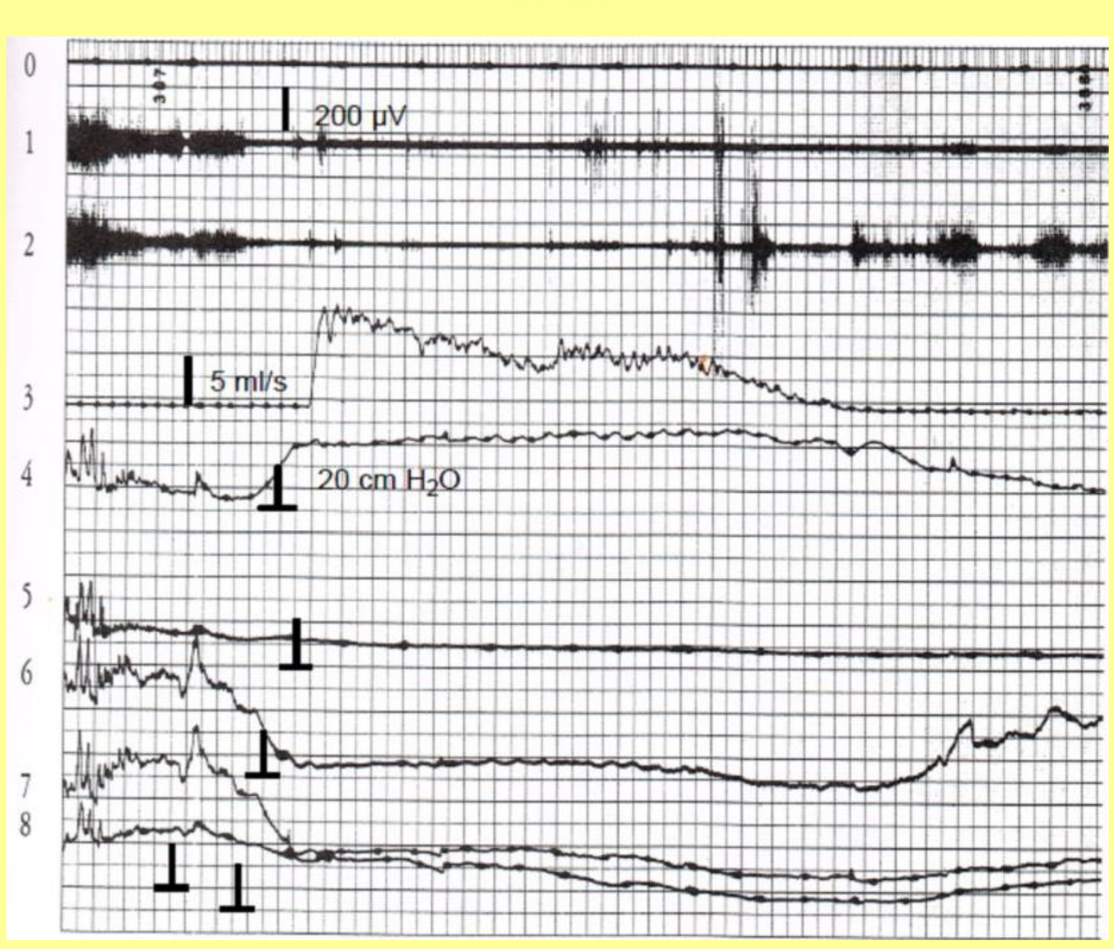
Elucidate the pathophysiological mechanisms of urethral instability. Instead joining the ongoing search in literature to determine which urethral pressure variations should be considered normal and which should not, we decided to analyze the pattern and identify the potential underlying cause of the pressure variations

Study design, materials and methods

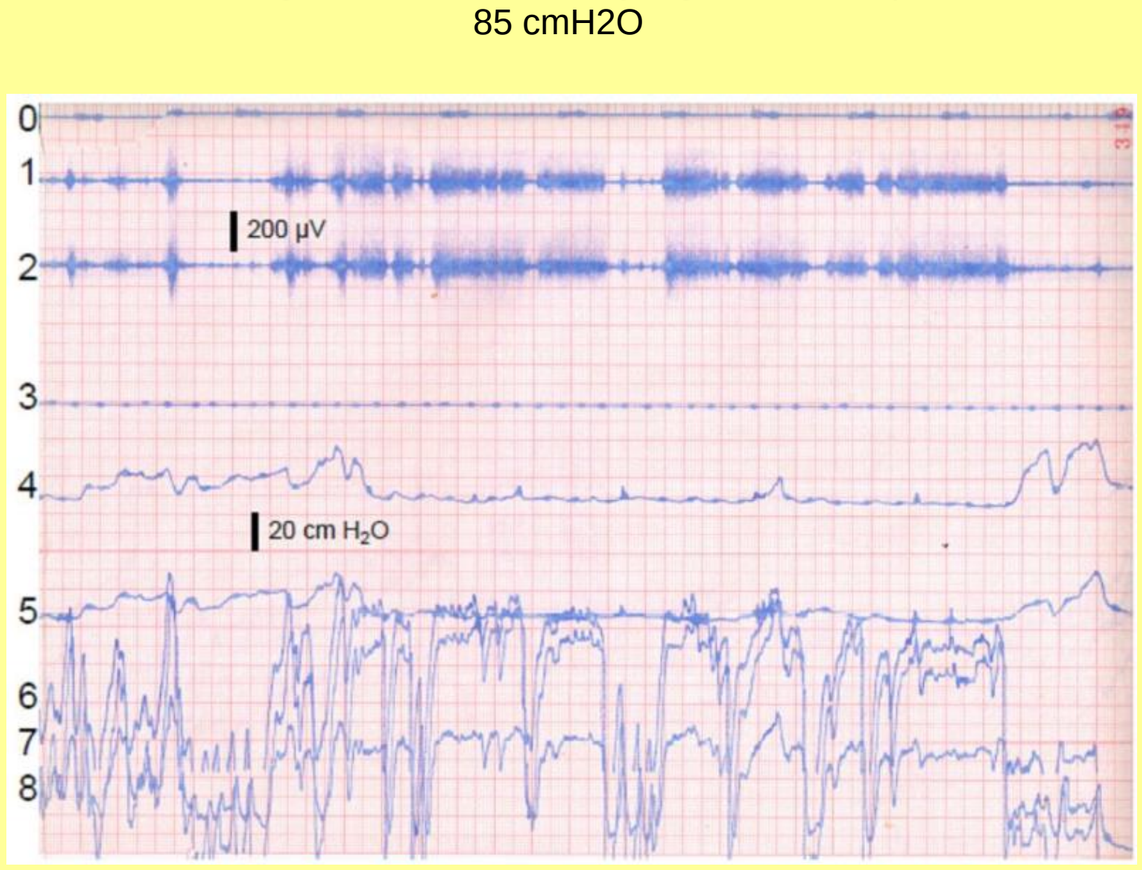
Comparative analysis of urodynamic data from two female subjects:
one with urethral instability (exhibiting rapid urethral pressure variations >30 cmH2O during bladder filling)
one without lower urinary tract dysfunction.
Urethral pressure was measured at three points alongside continuous needle EMG of the external urethral sphincter (EUS). Bladder and abdominal pressures were recorded according to established guidelines.
A literature review on urethral muscle dynamics was also performed

Results

Normal Micturition: Urethral pressure gradually decreases over approximately 9 seconds after cessation of EMG-activity of external sfincter



Urethral Instability: Rapid urethral pressure decline follows EMG silence, with a sudden rise in pressure due to a burst of EUS activity, coinciding with urgency to void. Urethral instability begins at bladder filling onset with arelatively high maximum pressure of 85 cmH2O



0: Time tracking; 1 s markers
1: Urethral EMG; scale 1 cm ≡ 200 µV
2: Anal EMG; scale 1 cm ≡ 200 µV
3: Urinary flow; scale 1 cm ≡ 5 ml/s
4: Intravesical pressure; scale 1 cm ≡ 20 cm H_2O
5: Abdominal pressure; scale 1 cm ≡ 20 cm H_2O
6: Urethral pressure, proximal; scale 1 cm ≡ 20 cm H_2O
7: Urethral pressure, mid; scale 1 cm ≡ 20 cm H_2O
8: Urethral pressure, distal; scale 1 cm ≡ 20 cm H_2O

Interpretation of results

Review of the literature supported both our observations that the
1.onset of urethral instability is already at the start of the bladder filling and
2.the assumption that urethral pressure is determined by the activity of smooth urethral musculature

Urethral instability is possibly triggered by altered smooth muscle behavior at the start of bladder filling, leading to a loss of urethral tone. The subsequent rise in pressure likely reflects a guarding reflex by the EUS in response to fluid entering the urethra, to prevent urine loss.

Literature indicates that the bladder urothelium's neuron-like properties may also play a role in sensory transduction mechanisms. Activation of adrenoceptor B3 (ADRB3) on urothelial cells triggers production and release of nitric oxide (NO). For the urethra, no similar findings have been reported. Presence of ADRB3 was demonstrated, but with lack of contact between ADRB3 and neurons in the submucosal layer. This could suggest the presence of an extra afferent signaling network originating from the urethral epithelial layer resulting in NO release as well when stimulated. Past studies suggested that alterations in NO-levels may play a role in urothelial signaling in the bladder. The female urethra has a rich vascular plexus and vascular smooth muscle cells are recognized as targets for NO.

If we want to focus om potential treatments with currently available medication, cyclic nucleotide phosphodiesterase 5 (PDE5) inhibitors, which are known to promote potent relaxation of animal and human smooth muscle, could have an effect om female urethral function as well – an interesting hypothesis for future research.

Conclusions

Urethral instability results from EUS contractions in guarding reflex response to smooth muscle dysfunction, leading to impaired closure and urgency to void. This may be due to high basal tension in urethral smooth muscles, causing them to relax early in response to low-level vesical afferent firing during the filling phase of the bladder
Therapeutic strategies should focus on reducing basal urethral tension, to maintain urethral closure during bladder filling. Further research could explore the role of pharmacotherapy in managing urethral instability, particularly ifin the urethra similar afferent signaling pathways exist as in the bladder.

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