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CYSTOMETRY IN CHRONIC, CONSCIOUS SHEEP FOR STUDY OF BLADDER FUNCTION

Hypothesis / aims of study

Cystometry in small animals has been commonly used to study bladder functions. We have recently begun cystometric studies to allow repeated testing of neuromodulation therapies using standard urethral catheterization (U_{cath}) in conscious, standing, sling-restricted sheep (1). While the U_{cath} method allows us to better isolate impacts of therapies on the bladder (vs urethra, for example), it also presents challenges. U_{cath} methods can irritate the urethra, restrict bladder outlet flow, impact therapy measures involving urethral sphincters and may alter normal voiding. In this study, we report a chronic sheep model of direct-to-bladder catheterization (B_{cath}) in which the catheter is chronically implanted through the bladder dome with percutaneous externalization to allow long-term quantitative assessment of bladder physiology.

Study design, materials and methods

In three conscious, standing, sling-restricted female sheep, the bladder capacity (BC) or infused volume (IV) was initially measured by U_{cath}. The urethral-bladder catheter was secured by a saline-filled Foley balloon to block the urethra. Saline infusion (30 ml/min) triggered a large amplitude of bladder contraction (>30 mmHg) that is volume dependent with typical voiding behaviours (arched back, crouched legs and release of urine). Each cystometry session contained at least 3 consecutive fillings to obtain the mean BC. The sheep were then chronically implanted with a bladder catheter through a small incision in the apex of the dome (B_{cath}) under propofol anaesthesia (i.v., 6 mg/kg) in combination with 1-3% isoflurane. The catheter was externalized to the animal's back. After a 2 week recovery period, the cystometry was repeated using B_{cath} with the same fill rate, saline temperature and recording methods with the U_{cath} test. Cystometry parameters were assessed from the mean value of the first 3 voids including basal bladder pressure (BP, mmHg), maximum pressure of the 1st voiding component (MP1, mmHg), maximum pressure of the 2nd voiding component (MP2, mmHg), void volume (VV, ml) and IV.

Results

The B_{cath} remained patent and useful for periods of up to several months. In 2 of 3 sheep an occlusion of the catheter occurred, apparently due to crystalline deposits, after 127 days and 19 cystometry tests and 142 days and 23 tests, respectively. In one sheep the catheter still remained useful after 218 days and 41 tests.

The abdominal pressure was measured in 2 sheep, but it did not appear to contaminate the detrusor pressure, so was disregarded from analysis. An example is shown in Figure 1.

While micturition phases were not consistently observed using U_{cath}, the B_{cath} data consistently revealed two distinguishable pressure components during voiding. MP2 was consistently larger than MP1 in conscious sheep (table 1).

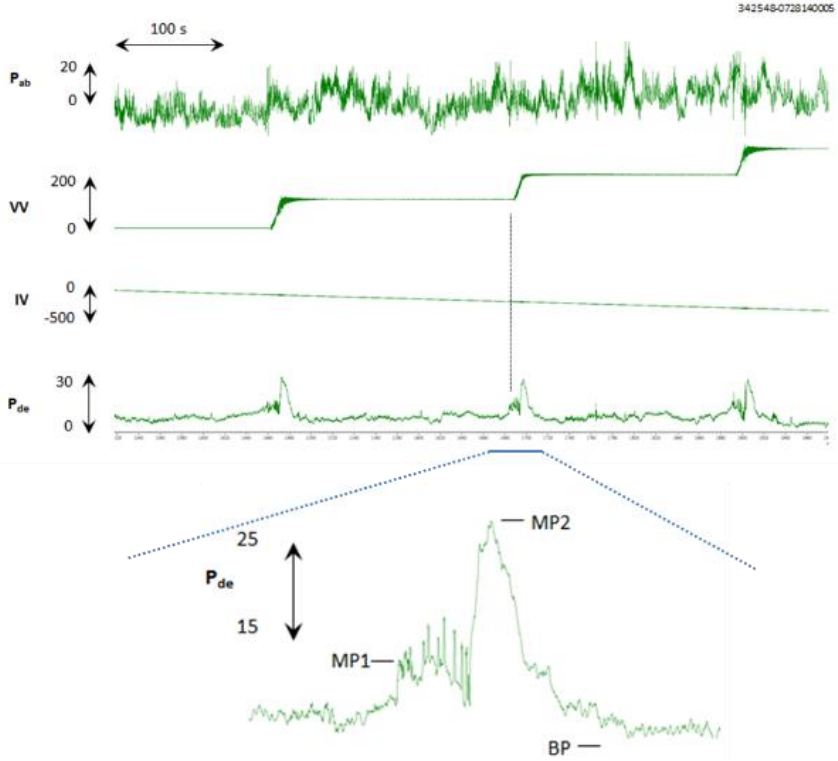

Figure 1. Cystometric tracing showing the abdominal pressure (P_{ab}, mmHg), voiding volume (VV, ml), infused volume (IV, ml) and detrusor pressure (P_{de}, mmHg)

Cystometry parameters are different among 3 sheep. For each sheep, with the same speed of saline infusion, the mean BCs (IV) using B_{cath} were similar to that using U_{cath} (table 1). The BCs vary over time, but there is no overall trend toward decreasing

(hyperreactive) or increasing BC. The IV was consistently similar to the VV in each test. The residual volume (RV) was also assessed after the 2nd void by ultrasound for 4 tests (sheep 2 and 3). The average estimated RV was 24 ± 18 ml.

Table 1. Cystometric parameters of three sheep

	IV-U_{cath} (ml)	IV-B_{cath} (ml)	VV-B_{cath} (ml)	BP-B_{cath} (mmHg)	MP1-B_{cath} (mmHg)	MP2-B_{cath} (mmHg)
Sheep 1	107 ± 47 (n=10)	106 ± 44 (n=19)	118 ± 51	25 ± 3.58	42 ± 7.45	66 ± 21.1*
Sheep 2	133 ± 72 (n=5)	140 ± 70 (n=23)	136 ± 83	21 ± 5.43	32 ± 5.19	47 ± 13.5*
Sheep 3	129 ± 48 (n=8)	143 ± 49 (n=41)	143 ± 50	3 ± 3.11	16 ± 3.51	30 ± 13.7*

mean ± standard deviation; n: measurements from each animal over 217-218 days;
* P<0.05, paired student's t test, MP2 vs. MP1

Interpretation of results

Over duration of 218 days there are obvious variations in cystometry parameters among the 3 animals. The variables among and within the sheep probably reflect several uncontrolled factors such as different measurement times of day, different animal experiences prior to and during testing, and other environmental changes. The bladder capacities (IV) measured using urethral and direct-to-bladder methods are comparable.

Both the U_{cath} and B_{cath} methods have distinct sets of advantages and disadvantages. For the urethral catheter method the BC is calculated using infused volume based on multiple visual cues (increase in P_{de}, voiding position, etc.). Void volume along with cystometry parameters are not measured. Also Foley balloon used to block the urethra limits sheep from completely natural voiding. The B_{cath} method avoids these limitations. Interestingly, the two components of voiding contractions obtained from P_{de} traces were observed in 3 sheep and the 2nd component seemed predominant in all of them. This is different from that measured for in the rat (2), where the 1st component of purinergic contraction is similar in magnitude to the 2nd component of cholinergic contraction (29 mmHg vs 28 mmHg). In future work it will be useful to understand the neurotransmitters that participate in two contraction components in sheep and their physiological significance to voiding contractions.

Concluding message

Cystometry using a direct-to-bladder catheter represents one opportunity for precise and objective assessment of urodynamic functions over extended durations. Although catheter occlusions or similar challenges may impact long term testing, we were able to maintain the direct-to-bladder catheter for at least 4 months without the use of antibiotics.

References

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Disclosures

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