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The effect of bladder diverticula on bladder function: An experimental study in rabbits

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ABSTRACT

Objective: This study aims to evaluate the effect of bladder diverticula (BD) on bladder function using a rabbit model, based on urodynamic findings.
Methods: A total of 32 New Zealand white rabbits were randomly assigned to four groups: (1) sham surgery; (2) a single, 1-cm-diameter BD; (3) a single, large, 3-cm-diameter BD; and (4) four (multi) 1-cm-diameter BD. Urodynamic evaluations were performed preoperatively, and 1 week and 1 month postoperatively, to measure the postmicturition residual (PMR), maximum bladder capacity (MBC), filling and voiding detrusor pressure (Pdet), compliance, and unstable detrusor contractions. At the end of the study, the animals were sacrificed and assessed for pathologic evaluation and stone formation.
Results: In groups 3 and 4, the rabbits all had PMR. At 30 days postsurgery, the MBC was found to be 28% and 31% lower than the reference range in groups 3 and 4 and compliance was decreased ($p < 0.05$). Further, the filling Pdet was significantly higher for large and multiple BD than in the 1-cm diverticula or sham groups (6.33 ± 1.73, 4 ± 1.26, $p = 0.0001$). Groups 3 (62%) and 4 (50%) had unstable detrusor contractions. There was also a muscular/collagen ratio increase in the large and multiple BD groups. Four rabbits in the large group and one rabbit in the multiple BD group exhibited stone formation.
Conclusions: Large or multiple BD can alter bladder storage and emptying, and can decrease the capacity of the bladder and reduce its elasticity. Large or multiple bladder diverticula can lead to involuntary contractions, causing dysfunctional voiding.

Bladder diverticula most often occur because of high pressure secondary to an infravesical obstruction or a neurogenic bladder [1], while primary (nonobstructive) diverticula can occur without any infravesical obstruction [2]. High pressure voiding over time results in the herniation of the bladder mucosa through the smooth muscle layer. Such herniations are often thin walled and lack the ability to contract, thus causing the dysfunctional voiding stasis of urine, and also serving as a nidus for stone formation and infection [3,4].

To date, bladder diverticula (BD) have garnered only a small amount of interest in the urological literature. Most reports concern small, retrospective studies [5,6] or case reports [7] with little or no long-term follow-up, while prospective, randomized trials and experimental studies do not yet exist. There is, therefore, considerable debate as to how symptomatic diverticula should be managed when encountered [8].

Most BD are thought to be occult, and there have been reports of cases that have resolved spontaneously [1]. Small bladder diverticula may be present within this group and are mostly asymptomatic. However, the behavior of large or multiple small diverticula is unknown, and these types exhibit somewhat different behavior, e.g., causing lower urinary tract disorders in terms of micturition function, detrusor coordination, and contraction, or an involuntary activity of the bladder [7]. This is the first preliminary experimental study to focus on this important subject.

It is possible to use rabbit bladders for research into the partial obstruction-induced activity of the detrusor [9,10]. This is the first experimental study to define the pathologic and physiologic aspects of the effects of diverticula on bladder functions within a urodynamic study, and our preliminary report outlines the results of diverticula in male rabbits.

1. Methods

Approval of this study was gained from the Animal Welfare Committee (experimental protocol number HADYEK/2014-34). The study comprised 32 New Zealand adult male rabbits, each weighing 3 ± 0.2 kg.

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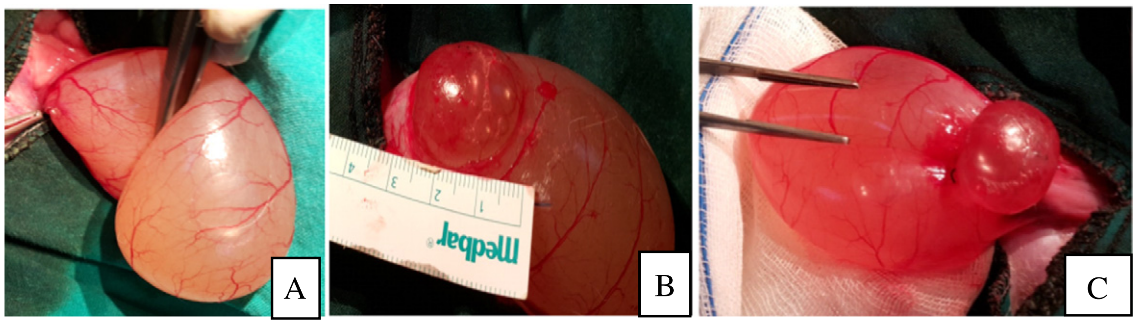

Fig. 1. Experimentally created diverticulum model. (A) The bladder was explored through a lower midline laparotomy. (B) A space was created and the detrusor excised to provide a mucosal prolapsus. (C) Creation of a small neck. To narrow the entrance hole of the diverticulum, a 5/0 absorbable suture was applied around the hole of the diverticulum from the surrounding detrusor layer.

1.1. Technique and study groups

Prophylactic antibiotics were administered preoperatively, and oral feeding was stopped 6 h before the start of the operation. The rabbits were anesthetized intramuscularly (i.m.) (first, ketamine 25 mg/kg i.m. + xylazine 0.4 mg/kg i.m., along with an analgesic, butorphanol 0.3 mg/kg i.m., in a single injection at the start of surgery, and then an anesthetic, propofol 15 mg/kg intravenously, administered continuously throughout the operation), and the bladder was entered through a lower midline laparotomy with the rabbits placed in a supine position. The bladder was then exposed. The posterolateral wall of the bladder was opened longitudinally until the mucosa was accessed and the detrusor was excised. A herniation of the bladder mucosa via the smooth muscle layer was then created, with care taken to preserve the integrity of the mucosa. Following this, 5/0 Vicryl with purse string suturing was applied to the junction of the detrusor and mucosa to cause the diverticula (neck) to be narrowed, allowing an 8 Fr urethral catheter to pass (Fig. 1). Animals were excluded from this study if there was a disruption of mucosal integrity when creating the diverticula.

The rabbits were divided into four groups based on the type of diverticulum created: (1) sham surgery — in the sham surgery group only the bladder was exposed using a midline incision; (2) a single, 1-cm-diameter (small) diverticulum; (3) a single, 3-cm-diameter (large) diverticulum; and (4) four 1-cm-diameter diverticula (multidiverticula) (Fig. 2). Postoperatively, all rabbits received free access to water on the first day and food the following day.

1.2. Urodynamic evaluation

Urodynamic studies were performed on rabbits that did not receive any anesthesia before or during the procedures. The rabbits' comfort was maintained by administering a little relief to them on the operating table [11]. With the animal in the supine position, urethral and rectal catheters were used to obtain the intravesical and intraabdominal pressure. Measurements were recorded using a double-lumen urodynamic catheter (6 Fr) inserted into the bladder through the urethra and connected to an Aymed Locum (Aymed Medical Technologies, Istanbul, Turkey) pressure transducer via a three-way stopcock. Saline at room temperature was injected into the bladder at a speed of 10% of the bladder capacity (2–3 ml/min). Pressure-flow measurements and recording were performed with the Aymed Locum videourodynamics system. Averaged urodynamic findings were recorded, and the detrusor pressure was calculated by continuously subtracting the intraabdominal pressure from the intravesical pressure. This procedure was repeated three times, and typical volume-pressure profiles were obtained. The bladder capacity was defined to be that at the start of the rapid increase in intravesical pressure, or the deflection point on the curve. The rate of change of volume per unit pressure during the initial phase of the cystometrogram was used as a relative measurement of compliance [7]. The filling detrusor pressure (FPdet), maximum voiding pressure (VPdet), the postvoid residual urine volume (PMR), and the compliance were additionally measured. Low compliance was accepted as a fall in the intravesical pressure. Involuntary contractions of the detrusor plus a low vesical volume or nonsimultaneous urinary leakage were considered as uninhibited contractions, and were thought to be pathological if they occurred during filling.

At the end of the study the animals were sacrificed and their bladders were exposed and assessed. Bladders were retrieved, trimmed of fat, and cut into small pieces. Formalin-fixed specimens were then embedded in paraffin and sectioned at 6 μm. Standard hematoxylin and eosin stains and Masson-trichrome stains were used for the histological evaluation of the specimens and morphometric analysis. Each slide was evaluated in a random order under standard light microscopy by two pathologists blind to the rabbit grouping. Detrusor thickness and the semiquantitative increase in connective tissue between the muscle fibers in the muscularis propria were evaluated between 0 and 3.3 for obvious connective tissue growth, and slight increases of +1 and +2 intervening were reviewed. The muscular and collagen ratio was also calculated. If stone formation had occurred in the bladder, the stones underwent analysis by Fourier transform infrared spectroscopy

Fig. 2. Creation of the bladder diverticula. (A) Single, small (1 cm) diverticulum posterolaterally located in the bladder. (B) Single large (3 cm) diverticulum posterolaterally located in the bladder. (C) Creation of multiple small (four pieces, 1 cm) bladder diverticula posterolaterally located in the bladder.