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Project Summary: Evaluation of Intrarenal Gel for Stone Fragment
Containment and Extraction during Endoscopic Procedures

Introduction

The primary objective for the treatment of nephrolithiasis is to render the patient stone-free, defined as elimination of all stone fragments based on a post-operative CT scan as residual fragments, even those ≤ 2 mm in size, are associated with stone recurrence. Flexible ureteroscopy serves as a viable first line therapy for the treatment of ≤ 15 mm stones; however, after laser lithotripsy, approximately 40-45% of patients have stone remnants as stone retrieval baskets are not designed to remove these small fragments. In this study, we intended to capture small stone fragments by infusing the renal collecting system with RTGel™ (UroGen Pharma, New York, NY), a clear, thermosensitive bioadhesive that is liquid at room temperature and transforms into a viscous, semisolid gel at body temperature and has demonstrated safety as MitoGel™/Jelmyto™. In prior studies from our laboratory, we identified the optimal formulation and evaluated efficacy in ex-vivo porcine kidney models. Based on these findings, we proceeded with the in-vivo porcine study presented here.

Methods

Canine calcium oxalate stones were acquired and their volume, dimensions, mass, and density in Hounsfield units were measured. Two pigs (4 renal units) were studied; the right kidney was randomized to either the experimental kidney (with RTGel™) or the control kidney (without RTGel™). The contralateral kidney was assigned the remaining option.

Experimental Kidney

A midline laparotomy incision was made and the previously randomized experimental kidney was exposed. The renal pelvis was identified, exposed, incised with scissors, and the previously prepared canine stone was implanted. A temperature probe was also placed alongside the stone. The pyelotomy was then closed with a 3-0 vicryl suture creating a water-tight seal. The laparotomy was closed with skin staples. Retrograde ureteroscopy was then performed. A 35cm, 16F ureteral access sheath was passed retrograde over an 0.035 Amplatz superstiff guidewire until it resided in the ureteropelvic junction. Proper placement was confirmed with fluoroscopy. A 5Fr angled Kumpe catheter was passed through the sheath under direct visualization to the location of the stone in the renal pelvis. 5cc of RTGel™ was then injected into the area through the Kumpe catheter using supplied high pressure injector. The Kumpe catheter was then removed. A 200 micron sTFL laser fiber was passed via the ureteroscope and using preset dusting settings (0.2J and 80Hz) the stone within the clear RTGel™ was ablated with the goal of creating fragments ≤ 100 microns (i.e. dust). Once the stone was sufficiently treated, the laser fiber was removed and larger fragments were basketed, extracted, and their weights recorded. Then the ureteroscope brush was passed and any remaining pieces of stone embedded within the gel were swept and removed. Finally, cold saline irrigation was instilled to liquify the gel and wash it out of the system.

Control Kidney

A midline laparotomy incision was made and the previously randomized control kidney was exposed. The renal pelvis was identified, exposed, incised with scissors, and the previously prepared canine stone was implanted. A temperature probe was also placed alongside the stone. The pyelotomy was then closed with a 3-0 vicryl suture creating a water-tight seal. The laparotomy was closed with skin staples. Retrograde ureteroscopy was then performed. A 35cm, 16F ureteral access sheath was passed retrograde over an 0.035 Amplatz superstiff guidewire until it resided in the ureteropelvic junction. Proper placement was confirmed with fluoroscopy. The stone was then dusted with the sTFL laser using preset dusting settings (0.2J and

80Hz) with the goal of creating fragments ≤ 100 microns. These fragments were then basketed, extracted, and their weights recorded.

At the conclusion of the experiment, the animal was euthanized, both kidneys were harvested, and the renal pelvis was carefully opened on the benchtop. All remaining fragments were drained and sequentially sieved to measure the size of the fragments. This collection of stones was dried and weighed for further analysis.

Results

The four canine calcium oxalate stones were of similar size and composition, with an average dry mass of 737.5mg, volume of 0.5mL, diameter of 11.8mm, and density of 1331.0 Hounsfield units. A mean of 755.5mg of fragments were retrieved in the experimental RTGel™ group, compared to a mean of 657.4mg in the control group. Further, a mean of 5.45mg of fragments remained in the kidney after extraction in the experimental group compared to 56.95 in the control group. Thus, in the experimental kidneys treated with RTGel™, 99.3% of stone fragments by mass were cleared compared to 92.2% in control kidneys. Finally, the average time for completion of the procedure with RTGel™ was 73 minutes compared to 81 minutes without the RTGel™.

Preliminary Discussion

There is a pressing need for an effective method for the extraction of small stone fragments which contemporary flexible stone baskets fail to extract. Potential techniques presented in the literature to eliminate these residual fragments include aspiration, the use of autologous blood to bind fragments together into a clot large enough to be evacuated using a stone basket, or the use of experimental adhesive agents. This study is a preliminary step in assessing another use for RTGel™, a novel FDA approved bioadhesive with previously proven clinical safety in treating upper tract transitional cell cancer. Given our limited data from only 4 total renal units in 2 pigs, no significant conclusions can be drawn; however, there are several findings worthy of note and further study. First, there was an increase in fragment clearance. In both trials, use of the RTGel™ did not prolong the length of surgery. Also, the RTGel™ could be completely washed out of both kidneys. Further, this study employed the thulium fiber laser, which more effectively dusts stones into fragments smaller than 100 microns than the currently used holmium laser and thus may have also contributed to the high clearance rate even without the RTGel™. Finally, when instilled around the stone, the gel effectively trapped any fragments that would normally escape into adjacent calyces behind the stone during fragmentation. Thus, when exploring the kidney to identify any residual fragments, the calyces behind the stone were clear of any fragments.

Table 1: Preliminary Data

	<i>Experimental</i>	<i>Control</i>
<i>Starting Stone Mass (mg)</i>	761	714
<i>Mass Retrieved (mg)</i>	755.5	657.4
<i>Mass Remaining in Kidney (mg)</i>	5.5	56.6
<i>Percent Mass Cleared (%)</i>	99.3	92.2
<i>Procedure Time (minutes)</i>	73	80.5