IP13-07: Electromotive Drug Administration (EMDA) in the Porcine Ureter: First Report of In Vivo Ureteral Dilation Following Alfuzosin Infusion

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INTRODUCTION

Therapeutic ureteral dilation is of increasing interest for improving access during retrograde intrarenal surgery. Local administration of relaxing agents is a challenge due to the relative impermeability of the urothelium. We investigated whether electromotive drug administration (EMDA) of alfuzosin, a non-selective α-blocker, could penetrate the urothelium and induce acute ureteral dilation in a porcine model.

METHODS

- 12 female juvenile Yorkshire pigs underwent bilateral ureteral sizing with sequential *Cook*® urethral dilator insertions in 2 Fr increments up to 3.5 Newtons (N) pre-EMDA, immediately post-EMDA, and 20 minutes post-EMDA.
- Alfuzosin or saline (n = 6/group) was infused at 5 mL/min for 20 minutes bilaterally using UCI-proprietary EMDA catheters; one ureter was treated with a 10-mA pulsed direct current while the contralateral served as passive diffusion (**Figure 1**).

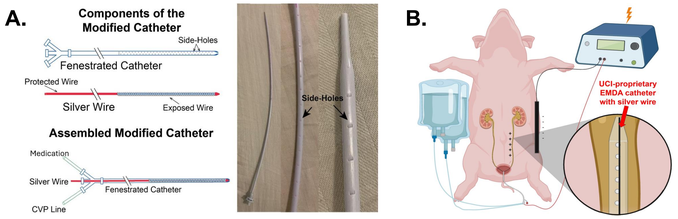

Figure 1. A) Schematics of UCI-proprietary EMDA catheters. **B)** Diagram of EMDA drug instillation in a porcine model.

- Analysis used generalized estimating equations and ANOVA.
- Matrix-assisted laser desorption/ionization mass spectrometry imaging (MALDI-MSI) was used to detect alfuzosin within porcine ureteral tissues.

RESULTS

- EMDA-mediated alfuzosin instillation resulted in an increase of ureteral size by nearly **1 Fr** (dilation score = 2.67 units), **Figure 2**.

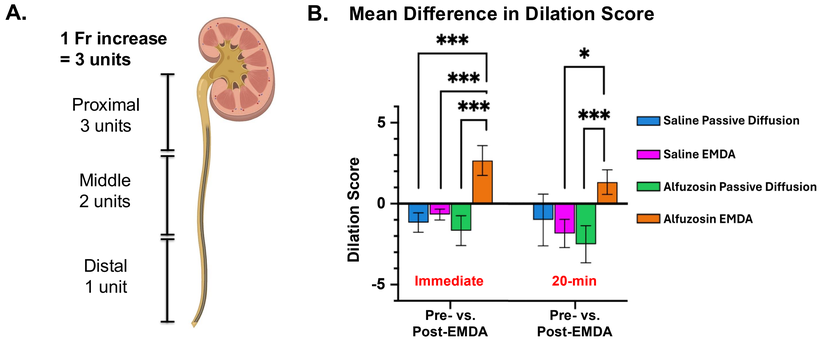

Figure 2. A) Ureteral dilation scoring scale: ureteral size was measured by assigning 1 unit for each dilator progression from one ureteral region to the next. **B)** Mean difference in dilation score between pre- and post-EMDA; pre- and 20-min post-EMDA (*p < 0.05 and ***p ≤ 0.001).

- MALDI-MSI revealed a **12-fold** increase in alfuzosin delivery to tissues with EMDA compared to passive diffusion, **Figure 3**.

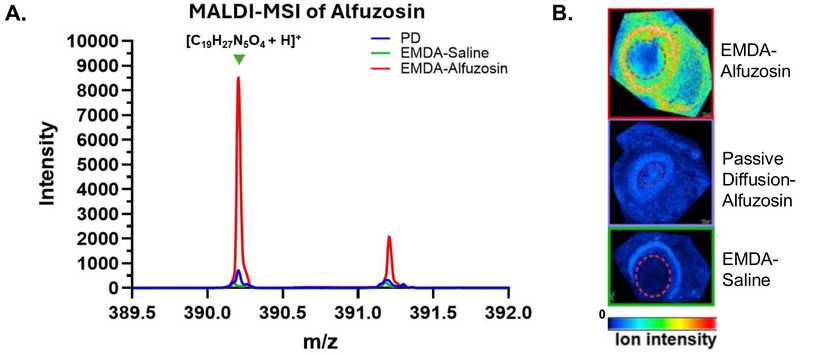

Figure 3. A) Mass spectra of alfuzosin and its ion intensity in different tissue conditions. **B)** Reconstructed mass topography of the ureteral cross-sections highlighting alfuzosin distribution. Red dotted circles denote the ureteral lumen.

RESULTS

- EMDA-mediated delivery of alfuzosin resulted in a significant increase in ureteral size compared to passive diffusion of alfuzosin, EMDA with saline, and passive diffusion with saline (+2.67 vs. -1.67, -0.67, and -1.17, respectively; p ≤ **0.001**), see **Figure 2B**.
- After 20 minutes, EMDA-mediated delivery of alfuzosin continued to show a moderate increase in ureteral size compared to passive diffusion with alfuzosin and EMDA with saline (+1.33 vs. -2.50 and -1.83; p = **0.001** and **0.016,** respectively), see **Figure 2B**.
- MALDI-Imaging mass spectra demonstrated high ion intensity of alfuzosin at 390.2 ± 0.2 m/z (m + H^+) in tissue following EMDA delivery (8501 cps) compared to passive diffusion (712 cps), see **Figure 3A**.
- Reconstructed mass topography of ureteral tissues reveals dense alfuzosin deposition within the urothelium, with moderate distribution throughout the surrounding tissue after EMDA, see **Figure 3B**.

CONCLUSIONS

- Our study represents the first definitive evidence of physiological change following EMDA-mediated drug delivery into the ureter, evident by measurable ureteral dilation.
- MALDI-MSI confirms that EMDA was effective in delivering a drug beyond the surface of the urothelium.
- EMDA-mediated ureteral infusion of alfuzosin achieved greater tissue penetration and significantly increased porcine ureteral distensibility compared to passive diffusion.

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