Introduction

- The specific mechanisms of pelvic floor injury following childbirth that lead to stress urinary incontinence (SUI) are unclear
- Animal models of simulated birth trauma utilizing vaginal distension have been widely utilized to investigate the mechanisms involved in vaginal delivery induced SUI
- We have previously demonstrated transient over-expression of monocyte chemoattractant protein-3 (MCP-3) in the urethra following vaginal distension.
- MCP-3 has been shown to be a homing factor for mesenchymal stem cells in cardiac ischemia models

Specific Aims:
- Demonstrate feasibility of plasmid injection into the urethra via injection of luciferase gene
- Determine the lowest dose of plasmid injection necessary for maintained expression
- Demonstrate that MCP-3 plasmid injection into the urethra results in sustained urethral expression of MCP-3 that is confined to the urethra

Methods

- A pilot study was conducted in which urethral injection of varying doses of luciferase-tagged plasmid was injected into 5 mice and followed with imaging
- Based on the pilot results, we conducted a study using 30 mice randomly assigned to receive 20 μg of plasmid (control) or MCP-3
- Mice were euthanized after 1, 3, or 5 weeks
- Heart, liver, lung, kidneys, ovaries, uterus, urethra and bladder were harvested and evaluated by ELISA/immunohistochemistry for presence and levels of MCP-3
- Venous sampling for quantification of serum MCP-3 was also performed

Results

- The initial pilot study with luciferase-tagged plasmid revealed our ability to inject the plasmid in the urethra by imaging
- The minimal plasmid dose for sustained expression was 20 μg
- Following MCP-3 plasmid injection, there was a statistically significant difference in the three and five week levels of MCP-3 in the urethra after injection compared to levels measured in all other harvested organs
- Consistently elevated levels during weeks one through five of MCP3 were shown in the harvested urethra and serum of mice after injection

Conclusions & Future Directions

- We were able to inject MCP-3 into the mouse urethra
- MCP-3 levels were persistently elevated levels in the mouse urethra over time
- The persistent expression of MCP-3 was selective to the urethra
- Further research will investigate the impact of MCP-3 plasmid injection on incontinence recovery and stem cell homing in SUI models

References


Acknowledgments

This work has been supported by University Hospitals of Cleveland Family Medicine Fund Award# P0089 (PI:Hijaz, Adonis)