Decreasing Arterial Flow in the Ex Vivo Functional Pig Bladder Model Demonstrates Preservation of Tissue Oxygenation and Non-linear Decrease in Perfusion Pressure: Potential Mechanisms for Underactive Bladder and Vascular Autoregulation

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INTRODUCTION

Chronic ischemia is a recognized factor in the pathophysiology of underactive bladder (UAB). Although relative ischemia is known to occur during filling, little is known regarding the pathophysiology that leads to UAB. Therefore, we developed an ex vivo functional porcine model to investigate the role of transient ischemia and whether autoregulation, a mechanism that maintains tissue oxygenation in certain vital organs, also exists in the bladder.

METHODS

Using bladders from slaughtered pigs, we prepared an isolated perfused model where we studied the effects of bladder perfusion flow rate on perfusion pressure and tissue oxygenation during the filling phase. Bladders were perfused at an initial flow rate of 20 ml/min and then clamped in a sequentially decreasing stepwise manner down to no flow and back to the initial flow rate.

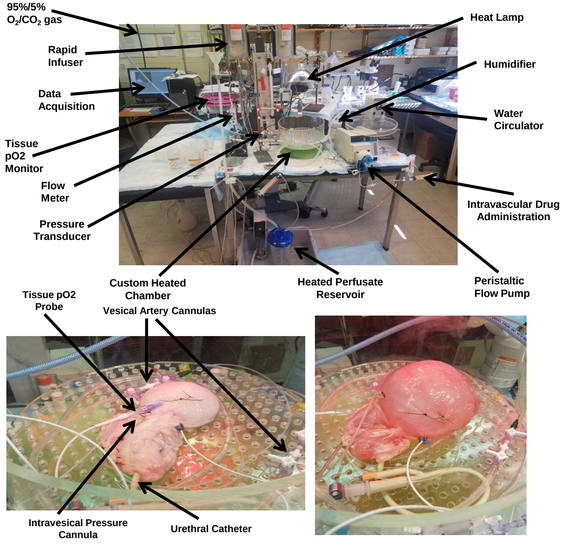

Figure 1. Experimental setup with bladder preparation.

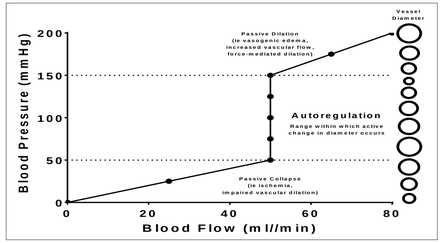

Figure 2. Example of autoregulation of blood flow. There is a blood pressure range in which blood flow is maintained through active changes in blood vessel diameter.

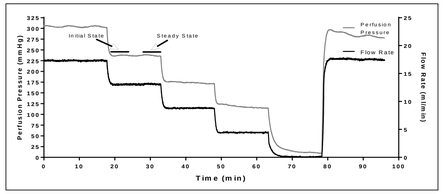

Figure 3. Representative tracing of flow rate modulation and corresponding perfusion pressure. As flow rate was decreased, a corresponding decrease in perfusion pressure was observed. Perfusion pressure during first 5 min was designated "Initial State" and last 5 min prior to flow rate change was "Steady State."

RESULTS

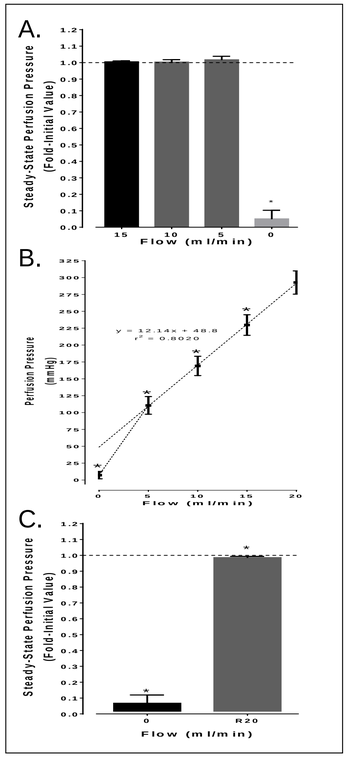

Figure 4. Observations in bladders (n=6) with baseline flow set to 20 ml/min. A) Fold change in initial perfusion pressure to steady-state. When flow was decreased below 5 ml/min, there was a significant decrease in the ratio of steady to initial state perfusion pressure compared to baseline. B) Relationship between average perfusion pressure and flow rate. There was a linear relationship as flow rate was decreased to 5 ml/min; however, this relationship (ie resistance) changed below 5 ml/min. C) The ratio of steady to initial state returned to baseline when flow is returned to 20 ml/min.

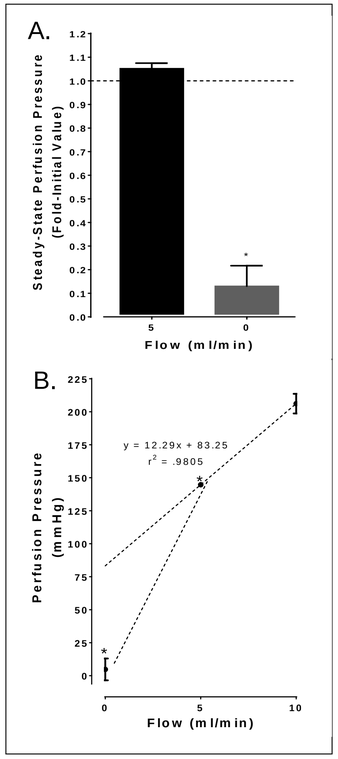

Figure 5. Observations in additional bladders (n=3) with baseline flow rate set to 10 ml/min. A) Fold change in initial perfusion pressure to steady-state during low flow rate study. The ratio of steady to initial perfusion pressure significantly decreased when flow rate was decreased below 5 ml/min. B) Relationship between average perfusion pressure and flow rate. There was a linear relationship between flow rate and perfusion pressure until flow rate decreased below 5 ml/min.

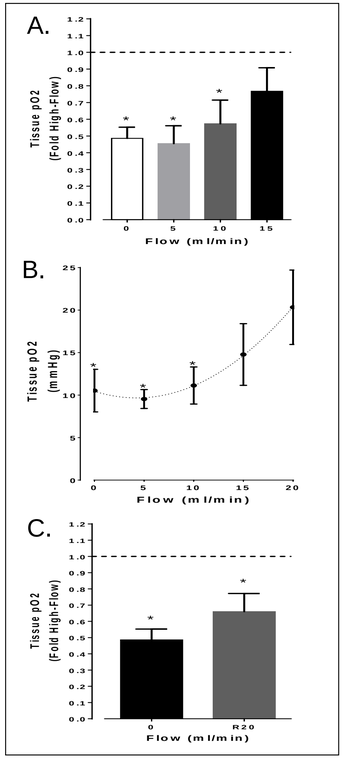

Figure 6. Measurement of tissue pO2 (n=5). A) Fold change in initial tissue pO_2 during high flow study. B) Average tissue pO_2 measured during high flow study. Tissue pO2 initially decreased with decreasing flow rate but stabilized below 10 ml/min. C) Return to baseline flow rate. With return to baseline flow rate, the average tissue pO2 increased but did not return to the baseline value.

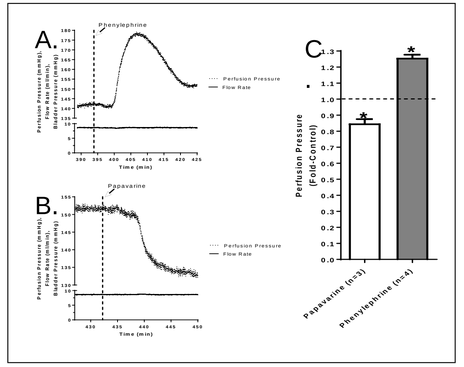

Figure 7. To assess the viability and vasoreactivity of the vesical arteries during perfusion, vasoactive agents were administered at the conclusion of experiments. Representative tracing demonstrating effect of A) phenylephrine and B) paparavine on perfusion pressure. C) Fold change in baseline perfusion pressure following administration of vasoactive agents. Papavarine caused a decrease in perfusion pressure (vasodilation) and phenylephrine caused an increase in perfusion pressure (vasoconstriction).

CONCLUSIONS

The bladder undergoes periods of relative ischemia during normal filling and these findings suggest that there is a compensatory mechanism (ie autoregulation) whereby, at low flow rates, tissue oxygenation is maintained. Factors that overcome this mechanism such as complete or chronic ischemia may be critical in the progression to detrusor underactivity and thereby highlight the importance of intervention during the early phases of this disease process.