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ROLE OF AQUAPORIN-2 AND CLAUDINS IN WATER METABOLISM IN THE RAT BLADDER

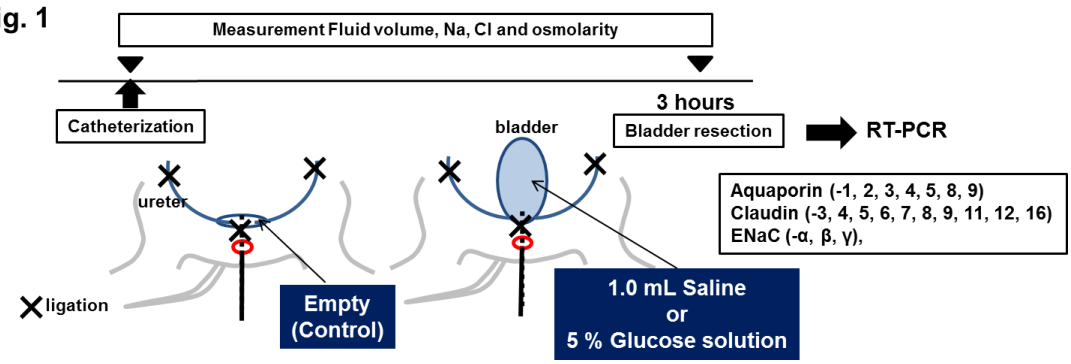
Hypothesis / aims of study

The bladder is often perceived as a simple reservoir of urine that does not itself affect water metabolism. However, previous clinical reports have suggested that the human bladder influences the secretion of arginine vasopressin and absorbs urine. Studies have suggested that the bladder absorbs water and solutions. For example, the bladder of rats has been found to absorb saline. Moreover, urea, sodium, potassium, and chloride move across rat urothelial cells [1], but the mechanism has not been elucidated. We previously demonstrated that the urinary bladder has an AVP-independent absorptive function, associated with smaller solutes such as electrolytes. Water effectively permeates the urothelium in the presence of small molecules. Claudins are a family of proteins that are important components of tight junctions, where they establish the paracellular barrier that controls the flow of molecules in the intercellular space between epithelial cells. Some claudins function within ion-flow pathways, which are selective for specific ions and are associated with water flow [1]. Aquaporins play a role in bulk water movement across the urothelium [2], and Na transport across the apical membrane of the urinary bladder epithelium is mediated primarily by the epithelial Na channel (ENaC) [3]. We investigated the molecular mechanism of water movement in the urinary bladder, focusing on aquaporins, claudins, and ENaC, factors expressed on the urothelium that have been implicated in the transport of water and solutions.

Study design, materials and methods (Fig. 1)

Female Sprague-Dawley rats weighing 300 g were used in the study to investigate the molecular mechanism of water metabolism in the bladder. In all rats, ureters were ligated bilaterally at the level of bifurcation of the abdominal aorta. The proximal urethra into, which the transurethral bladder catheter was inserted, was ligated to prevent leakage of intravesical fluid, and blood flow to the bladder was maintained. In the saline group, the bladder was filled with 1.0 mL of saline. In the glucose group, the bladder was filled with 1.0 mL of a 5% glucose solution. In the control group, the bladder was empty. The bladder was filled with 1.0 mL of saline or a 5% glucose solution for 3 hours. Bladders were resected to measure gene expression levels of aquaporins (-1, 2, 3, 4, 5, 8, 9) and claudins (-3, 4, 5, 6, 7, 8, 9, 11, 12, 16), and ENaC (-α, β, γ) using quantitative reverse-transcription–polymerase chain reaction (RT-PCR).

Fig. 1



Results

Gene expression levels of aquaporin-2, claudin-3, claudin-6 and claudin-11 were higher in the saline group compared with those in the control and glucose groups (Fig. 2A-D). Expression of ENaC (-α, β, γ) was lower in the saline group compared with that in the control group (Fig. 2E-G). Expression of α-ENaC in the saline group was lower than that in the glucose group (Fig. 2E).

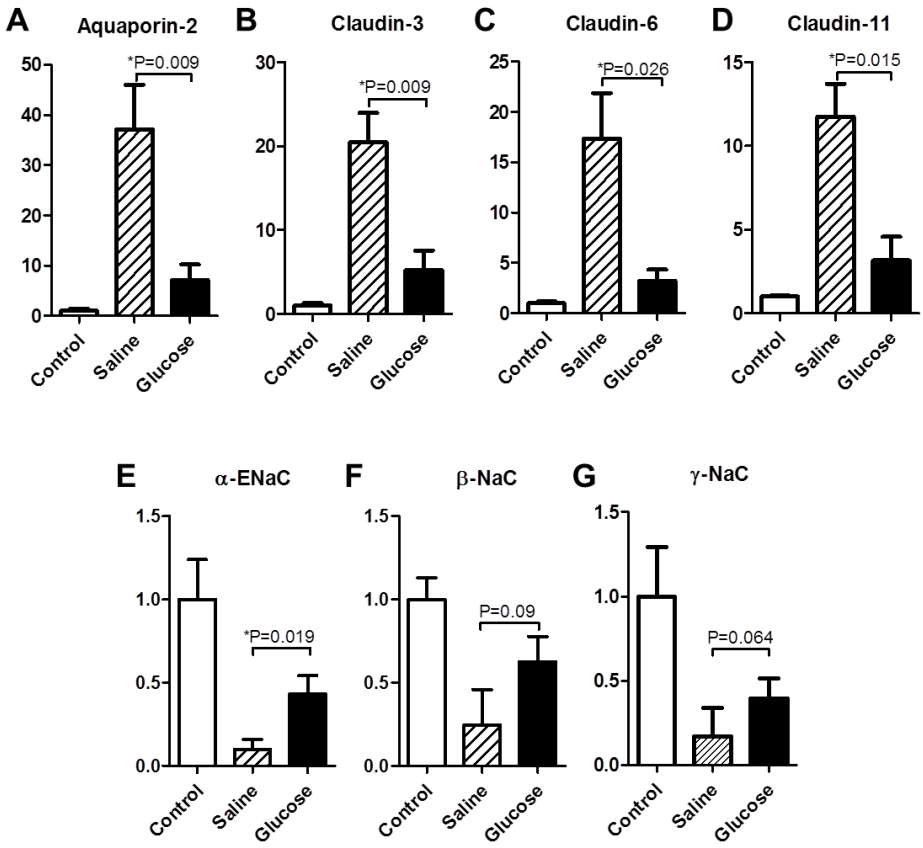
Interpretation of results

Aquaporin-2, claudin-3, claudin-6 and claudin-11 were associated with sodium-linked water absorption through the bladder urothelium in the full-filled bladder condition, while ENaC was not.

Concluding message

Aquaporin-2, claudin-3, claudin-6 and claudin-11 are implicated in urinary bladder absorptive function.

Fig. 2



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Disclosures

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