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Overactive and underactive bladder dysfunction is reflected by alterations in urothelial ATP and NO release

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ATP and NO are released from the urothelium in the bladder. Detrusor overactivity (DO) following spinal cord injury results in higher ATP and lower NO release from the bladder urothelium. Our aim was to study the relationship between ATP and NO release in (1) early diabetic bladders, an overactive bladder model; and (2) "diuretic" bladders, an underactive bladder model. To induce diabetes mellitus female rats received 65mg/kg streptozocin (i.v.). To induce chronic diuresis rats were fed with 5% sucrose. At 28 days, in vivo open cystometry was performed. Bladder wash was collected to analyze the amount of ATP and NO released into the bladder lumen. For in vitro analysis of ATP and NO release, a Ussing chamber was utilized and hypoosmotic Krebs was perfused on the urothelial side of the chamber. ATP was analyzed with luminometry or HPLC-fluorometry while NO was measured with a Sievers NO-analyzer. In vivo ATP release was increased in diabetic bladders and unchanged in diuretic bladders. In vitro release from the urothelium followed the same pattern. NO release was unchanged both in vitro and in vivo in overactive bladders whereas it was enhanced in underactive bladders. We found that the ratio of ATP/NO, representing sensory transmission in the bladder, was high in overactive and low in underactive bladder dysfunction. In summary, ATP release has a positive correlation while NO release has a negative correlation with the bladder contraction frequency. The urinary ATP/NO ratio may be a clinically relevant biomarker to characterize the extent of bladder dysfunction.

Editorial Comment

Munoz et al. report on the importance of urinary ATP/NO ratio as a biomarker of bladder dysfunction. Nitric oxide has gained importance over recent years as it has been shown to play an important role on the relaxant activity of different non striated muscle tissues including bladder, corpus cavernous and vessels wall. The end product of the nitrergic pathway is the activation of calcium channels, but a step before that, cyclic GMP is the trigger element.

Understanding the mechanisms involved in bladder contraction and relaxation at a molecular level opens new horizons for therapeutic targets and pharmacological treatments. Not only NO donors may be promising tools to promote bladder relaxation, but also NO-independent guanilate cyclase stimulators may become part of this armamentarium.

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