Transient Receptor Potential V3 (TRPV3) channels as a potential target for treatment of overactive bladder

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TRP channels have been shown to act as mechanosensory and pain receptors in a wide variety of organ systems, including the bladder. Their pharmacologic modulation has not been shown to be effective in treatment of overactive bladder. This study utilizes wild-type (WT) and TRPV3-knock out (KO) mice, coupled with novel drug compounds to clarify TRPV3's role in regulation of bladder function and sensory signaling. Immunohistochemistry was performed on bladder wall and dorsal root ganglia (DRG). Myograph studies were used to evaluate the response to TRPV3, TRPV1, TRPA1, and neurokinin (NK)-specific agonist and antagonists. TRPV3 expression was documented in bladder and neurons. Expression was increased in animals after partial bladder outlet obstruction. TRPV3 agonists increased the amplitude of baseline phasic contractions in bladder muscle wall strips ($n=7$, $p < 0.01$). This was potentiated with concurrent TRPV1 activation using capsaicin. TRPV3 suppression with TRPV3 antagonists had no effect, however combination of TRPV3 and TRPA1 antagonists decreased detrusor muscle tone ($n=5$, $p < 0.01$). NK receptor antagonists suppressed bladder phasic contractions during application of TRPV3 agonists ($n=6$, $p < 0.05$). Pre-treatment of muscle strips from global TRPV3 KO mice with the TRPV3 agonist did not result in significant changes to the bladder tone or phasic activity ($n=4$). Adding TRPA1 antagonists to TRPV3 KO mice suppressed the amplitude of bladder phasic contractions, and demonstrated no difference as compared to both TRPV3 and A1 antagonists in WT mice ($n=4$).These data suggest TRPV3 plays a critical role in mediating bladder function and sensation through their effects on bladder phasic contractions. TRPV3-specific compounds appear to act through the release of neurokinins. Understanding and targeting TRP channel pathways may provide possible future avenues for treatment of overactive bladder.