Objectives - Overactive bladder, affecting over 17 million people in the United States, is most commonly caused by involuntary detrusor muscle contraction, referred to as detrusor overactivity (DO). Underlying mechanisms of DO are still unknown, but a current theory suspects that calcium homeostasis is disrupted, directly affecting urinary bladder smooth muscle (UBSM) contractility. Calcium levels are controlled by voltage-dependent calcium channels (VDCCs). Selected VDCCs, activated by high voltages (HVAs), have distinctive functional properties vital in mediating urinary bladder function. Ni^{2+} has been widely used as an effective non-selective blocker of VDCCs, and its concentration-dependent ability to affect selective HVA VDCCs has been shown. The aim of this study was to examine Ni^{2+} effects on the nerve-mediated UBSM contractility and urodynamic parameters in healthy animals and animals with partial bladder outlet obstruction (PBOO).
Methods - Nerve-mediated bladder contractions were elicited using electric field stimulation (EFS) with a PHM-152V stimulator (MED Associates). Stimuli of 0.5, 2.0, 3.5, 5.0, 7.5, 10, 12.5, 15, 20, 30, 40, and 50 Hz at 20V of AC were applied every 3 minutes. Two frequency-response curves, one control and one after 10 minutes of preincubation with Ni^{2+} (10μM, 50μM, 100μM or 1mM), were compared. Cystometry was performed by continuous intravesical infusion of NaCl followed by 50μM Ni^{2+}.
Results - EFS in the presence of 10μM and 50μM Ni^{2+} significantly reduced UBSM nerve-mediated contractions at low frequencies ≤10Hz (~18.13% and ~25.4%) and of 100μM at all frequencies (~39.85% for low and ~24.58% for high frequencies) in animals with PBOO when compared to controls. 1mM Ni^{2+} equally inhibited UBSM contractile response to all frequencies in both groups. Continuous intravesical instillation of 50μM Ni^{2+} evoked an enhanced bladder capacity in both control (~137.8%) and PBOO groups (~118.0%). Voided and infused bladder volumes were larger and intermicturition intervals longer. Changes in threshold, peak micturition, and average filling pressures, and number of non-voiding bladder contractions didn't significantly differ between control and PBOO Ni^{2+} treated groups.
Conclusions - The data reported provides new evidence for enhanced sensitivity to Ni^{2+} in overactive bladders and affirms a previously published work that Ni^{2+} affects UBSM contractility in a concentration-dependent manner.