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Chancellor M[1], Tyagi P[1], Li Z[1], de Groat W [2], Yoshimura N[1], Huang L[1]
1. University of Pittsburgh, 2. Univesity of Pittsburgh

URODYNAMIC AND IMMUNOHISTOCHEMICAL EVALUATION OF INTRAVESICAL CAPSAICIN DELIVERY USING THERMOSENSITIVE HYDROGEL & LIPOSOMES

Aims of Study

Intravesical delivery of capsaicin in the treatment of detrusor hyperreflexia is restricted by aqueous insolubility. Our objective in the present work was to study the safety and efficacy of intravesically administered thermosensitive hydrogel and liposomes as alternative vehicles for capsaicin over the clinically used 30% ethanolic saline.

Methods

Positively charged liposomes composed of phosphatidylcholine and cholesterol in the molar ratio 2:1 were prepared with or without 1mM capsaicin. Aqueous dispersion of thermosensitive polymer PEG-PLGA-PEG in 0.1 M phosphate buffer (30%w/v) was prepared with or without 1mM capsaicin. 1mM capsaicin in 30% ethanol in saline was used as positive control. Capsaicin in various vehicles was instilled using transurethral PE-50 tubing into normal adult female Sprague dawley rats under halothane anaesthesia. Capsaicins in various vehicles were retained in the bladder for 1hr after instillation. Continuous transurethral cystometry (0.04ml/min) was performed on these animals 48hrs after instillation under urethane anaesthesia (1.2g/kg s/c). Bladders were harvested for CGRP immunostaining and H&E staining.

Results

We observed that both liposome and 30% ethanol delivered capsaicin to cause near complete impairment of micturition reflex in urethane anaesthetized rats and the mean bladder contraction frequency (BCF) also did not differ much (0.05025 versus 0.045/min), but hydrogel-capsaicin was significantly higher (0.1154; $p<0.05$). Pressure threshold for micturition (PT), was higher in all the groups compared to saline and the mean amplitude of micturition contractions (MAC) were significantly reduced in vehicles with capsaicin treated groups compared to vehicles alone ($p<0.05$)n=8. CGRP immunoreactivity was completely abolished in the suburothelium by capsaicin delivered by ethanol and liposomes compared to hydrogel with capsaicin and vehicles alone. H&E staining revealed denuding of uroepithelium and vascular congestion in capsaicin in ethanol treated groups, which was absent in liposome and hydrogel treated groups.

Conclusions

Based on urodynamic and immunohistochemical studies, liposomal capsaicin is comparable in efficacy and superior in safety over 30% ethanol. Thermosensitive hydrogel is safer, but comparatively less efficacious vehicle for intravesical delivery of capsaicin.