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PROLIFERATIVE EFFECT OF NEUROTRANSMITTERS ON HUMAN BLADDER SMOOTH MUSCLE CELLS

Aims of Study

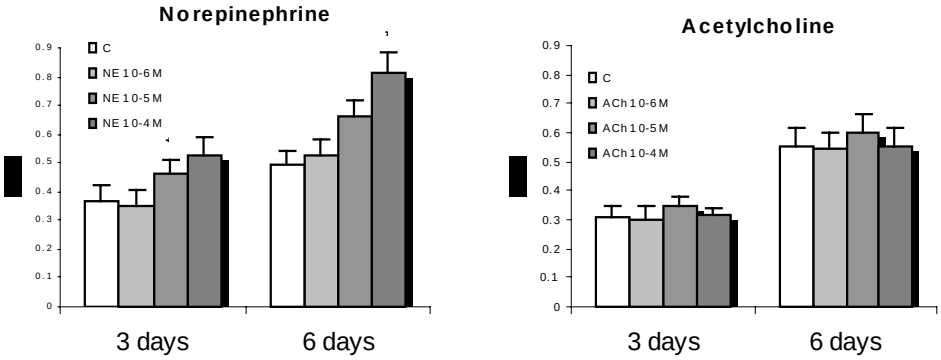
Bladder pathology resulting from neuropathic abnormalities or bladder outlet obstruction, may lead to bladder wall thickening accompanied by an altered innervation pattern. Changes in cholinergic and adrenergic bladder innervation cause pathologic organ dysfunction. Whether neurotransmitters themselves also stimulate structural changes of the bladder wall is not known.
We investigated the effect of increasing concentrations of two important neurotrans-mitters, norepinephrine (NE) and acetylcholine (Ach), on human bladder smooth muscle cell (HBSMC) proliferation.

Methods

HBSMC were cultured in 96 well plates in SmGm medium (containing 5% fetal calf serum) under standard culture conditions. Cells were continuously exposed to various concentrations (10^{-6} M, 10^{-5} M, 10^{-4} M) of norepinephrine (NE) and acetylcholine (ACh) for up to 6 days. Cell proliferation was determined at 3 and 6 day time points using an MTT based assay and a TUNEL assay was used to evaluate for direct cellular toxicity (apoptotic cell death).

Results

Continuous exposure to NE resulted in a dose dependent proliferative effect on HBSMC growth. Concentrations of 10-5 M and 10-4 M NE stimulated proliferation significantly ($p<0.05$) after 3 and 6 days. In contrast, continuous administration of ACh did not affect HBSMC growth. Neither neurotransmitter induced apoptosis.



Conclusions

Exposure of HBSMC to the adrenergic neurotransmitter norepinephrine results in a dose dependent increase in cellular proliferation. Future efforts to alter this response may prove beneficial in the prevention and/or treatment of bladder dysfunction secondary to spinal cord.