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ALTERATION IN THE PROFILE OF PROTEIN KINASE C ISOZYMES IN THE UROTHELIUM AND DETRUSOR OF DIABETIC RAT

Aims of Study

Protein Kinase C (PKC) modulates the effects of cholinergic and adrenergic neurotransmission in many tissues/cells. Upregulation of muscarinic receptors in diabetic rat bladder has been reported. In addition, alterations of the PKC isozymes has been linked to impairment of smooth muscle function in vascular and gasterointestinal system. The objective of our study was to investigate the profile of PKC isozymes in the tissues of the bladder.

Methods

After sacrifice, the urothelium and bladder muscle were isolated from the wild type (WT-Sprawl-Dawling) and transgenic rat model of diabetes mellitus (DM). Animals were age matched for early (5 weeks of age) and late stages of diabetes (25-30 weeks old). Total RNA and protein were isolated for the analysis of specific PKC isozymes (PKC alpha, βI, β II, epsilon, zeta, delta and lambda) using RT/PCR and western blot methods. The bands were quantified and relative levels of expression were analyzed. Chi-Square and t-test were used for analysis of dichotomous and continuous variables; with 95% confidence intervals reported for all estimates; and 80% power at the 0.05 significance.

Results

Twenty animals were used for the experiments, 6 animals per each group of early DM with age matched WT; and late stage DM with age-matched WT. In the urothelium, PKC-bI, b II and delta isozymes were reduced at the early DM (p=0.05), where as PKC epsilon, zeta and lambda isozymes showed no changes under diabetic conditions, except for PKC epsilon which showed a marked decrease in the urothelium in the late stage of the disease. In the Detrusor muscle, the PKC b1 was markedly inactive in early and late stages of the DM (p=0.05). In contrast to urothelium, the PKC bII showed slight increase in the protein levels in the muscle followed by a slight reduction in the late stages of the diabetes.

Conclusions

The study shows a significant change in the protein and RNA expression of PKC bI, bII and delta isozymes in the urothelium and bI, bII isozymes in the Detrusor muscle of rat bladder under diabetic condition. Correlations of these findings with in-vitro contractility studies are needed to find out whether these changes corresponds to impaired contractility seen in diabetic cystopathy.