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# CHRONIC HYPERLIPIDEMIA-INDUCED INCREASES IN URINARY PROSTAGLANDIN E2 (PGE2), NERVE GROWTH FACTOR (NGF) AND BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) CONTRIBUTE TO BLADDER DYSFUNCTION IN RABBITS

Hypothesis / aims of study

Life style diseases and metabolic syndrome have been suggested as one of important etiological factors in lower urinary tract dysfunction. Recently, we demonstrated that chronic hyperlipidemia caused bladder dysfunction including detrusor overactivity in heritable hyperlipidemic rabbits (myocardial infarction-prone Watanabe Heritable Hyperlipidemic rabbits: WHHLMI rabbits) (1). It has been suggested that $PGE_2$, NGF and BDNF are released from urothelial and detrusor smooth muscle cells. The mediator may act by binding to each receptor expressed in bladder urothelial cells and primary afferents, resulting in bladder dysfunction. In the present study, to evaluate the effects of hyperlipidemia on lower urinary tract function, we examined the relationship between hyperlipidemia-induced bladder dysfunction and urinary $PGE_2$, NGF and BDNF levels in WHHLMI rabbits.

Study design, materials and methods

WHHLMI (hyperlipidemic) rabbits and the age and sex-matched Japanese white rabbits (control group) were prepared. All rabbits were housed in metabolic cages, and the frequency-volume chart (FVC) was recorded for three days, and 24-h urine samples of all rabbits were collected. Cystometrograms were performed under anaesthesia using constant infusion of saline into the bladder to elicit voiding. 24-h urinary $PGE_2$, NGF and BDNF levels were assayed by enzyme immunoassay. The relationships between parameters of FVC and cystometrograms, and urinary $PGE_2$, NGF and BDNF levels were evaluated.

Results

The number of micturition per day was higher in hyperlipidemic rabbits than in control rabbits, and the voided volume was lower in hyperlipidemic rabbits than in control rabbits. In cystometrograms, hyperlipidemic rabbits showed detrusor overactivity, higher frequency of micturition and lower voided volume than in control rabbits. Urinary $PGE_2$, NGF, and BDNF in hyperlipidemic rabbits were 5.37±1.37 pg/mgCre, 2904±1527 pg/mgCre, and 8.50±0.96 pg/mgCre, respectively. The values in hyperlipidemic rabbits were significantly higher as compared to each value of the control rabbits. Analysis of relationship between parameters of bladder function of cystometrograms and urinary $PGE_2$, NGF and BDNF levels in hyperlipidemic rabbits indicated a significantly negative correlation between urinary $PGE_2$, NGF or BDNF and voided volume, and a significant positive correlations between urinary $PGE_2$, NGF or BDNF levels and the number of micturition. In addition, there were significant positive correlations among $PGE_2$, NGF and BDNF (Fig).

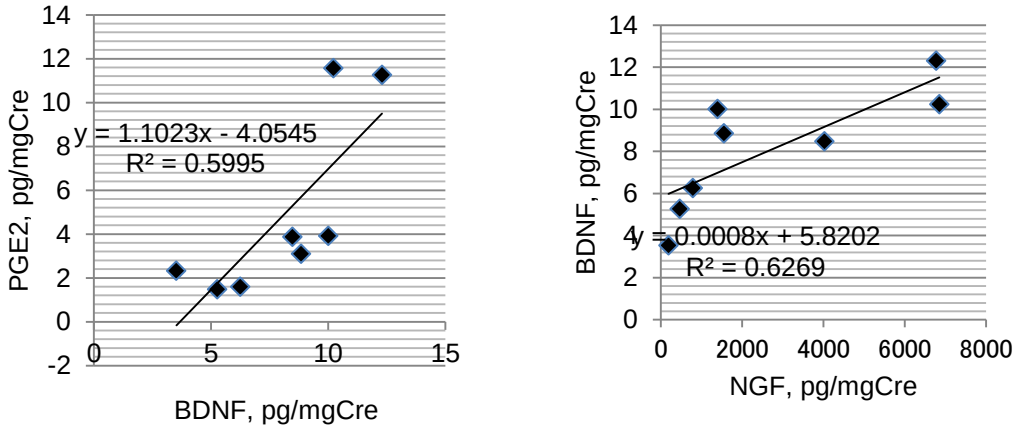
Interpretation of results

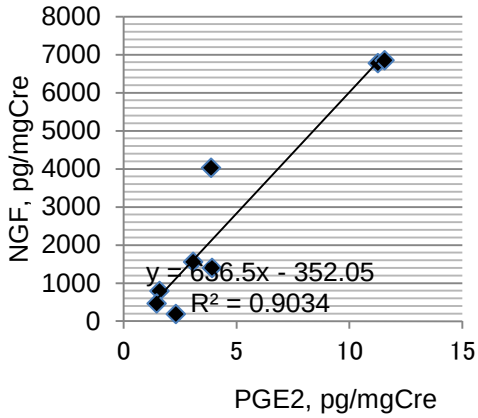
The present data demonstrated that chronic hyperlipidemia caused detrusor overactivity. The increased urinary $PGE_2$, NGF and BDNF in hyperlipidemic rabbits may contribute to bladder dysfunction. Recent report suggested that $PGE_2$ contributed to synthesis of BDNF in primary sensory neuron in ganglion explant cultures and in a neuropathic pain model (2). The present date may imply that NGF also involved in $PGE_2$-induced BDNF synthesis in bladder of the hyperlipidemic rabbits.

Concluding message

The present study suggested that chronic hyperlipidemia caused increase in urinary $PGE_2$, NGF and BDNF. The relationship among the factors may contribute to detrusor overactivity in hyperlipidemic rabbits.

Fig. Relationship among uinary $PGE_2$, NGF and BDNF in hyperlipidemic rabbits



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Disclosures
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