ASSOCIATIONS BETWEEN LOWER URINARY TRACT SYMPTOMS AND METABOLIC SYNDROME IN OLETF RATS

Hypothesis / aims of study
The metabolic syndrome (MetS) is a clustering of several metabolic abnormalities or risk factors, including central obesity, dyslipidemia, hypertension, insulin resistance with compensatory hyperinsulinemia and glucose intolerance. Recent epidemiological surveys demonstrated a significant association between MetS and lower urinary tract symptoms (LUTS). This association has also been suggested in dietary fat rat model with MetS induced by long-term fructose feeding (1). Recent research indicates that an individual's genetic background can interact with their dietary fat exposure to affect risk of the MetS(2). So far as we known, the genetic animal model resemble human MetS is scare. The OLETF (Otsuka Long-Evans Tokushima Fatty) rat is reported to be a new animal of human MetS that has been established from an outbred Long-Evans strain by selective breeding and subsequently maintained at the Otsuka Pharmaceuticals (Tokushima, Japan) (3). In this study, we tried to investigate the association between MetS and LUTS using this model.

Study design, materials and methods
Forty male OLETF rats and forty control male LETO (Long-Evans Tokushima Otsuka) rats were fed a normal diet from age 4 weeks to 72 weeks in University of Fukui Animal Center. Body weight, systolic blood pressure (tail-cuff method) and urine output were monitored every 8 weeks. Characterization of plasma glucose, triglyceride, cholesterol, and insulin levels were examined at the age of 24 and 56 weeks. Cystometry under waking conditions was also performed at these two ages. The amounts of ATP, PGE2 and NGF released from the stretched bladder epithelium were measured with luciferin-luciferase and ELISA assays at the age of 56 weeks. 8-OHdG amounts were measured to evaluate the oxidizative stress in bladder tissue with ELISA assay at the age of 56 weeks. The mRNA expression of alpha 1A, alpha 1D, P2X1 and P2Y4 receptors, respectively, increased 2.18 ± 0.84, 5.25 ± 1.09, 6.87 ± 1.70, 21.42 ± 5.13, 1.95 ± 0.64, 2.42 ± 0.28 times as much as those of LETO rats. The amount of 8-OHdG in the bladder of OLETF rats was 4.71 ± 0.68 times higher than that of LETO rats. Compared with those of LETO rats, the mRNA expression of M2, M3, P2X3, iNOS, EP1 and EP2 receptors, respectively, increased 2.18 ± 0.84, 5.25 ± 1.09, 6.87 ± 1.70, 21.42 ± 5.13, 1.95 ± 0.64, 2.42 ± 0.28 times in urinary bladder of OLETF rats, while the mRNA expression of alpha 1A, alpha 1D, P2X1 and P2Y4 receptors showed no obvious change.

Interpretation of results
In this study, MetS-associated bladder dysfunction was remarkable in OLETF rat model. It is hypothesized that the increased oxidative stress in MetS stimulates the neurotransmitters, such as ATP, PGE2 and NGF, releasing from the bladder epithelium. Those neurotransmitters were mediated by over-expressed receptors of EP2X3, EP1, EP2, M2 and M3 to activate the afferent C-fiber pathway, resulting in the induction of detrusor overactivity and frequency of urination.

Concluding message
The results of our study have shown that there is a significant association between MetS and LUTS in genetic background model OLETF rats.

References

Disclosures
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