240

Xiao N[1], Huang Y[2], Daneshgari F[2], Liu G[2]
1. *Lanzhou University, Lanzhou, PRC; Case Western Reserve University, Cleveland, OH, USA,* ***2.*** *Case Western Reserve University, Cleveland, OH, USA*

ROLES OF POLYURIA AND HYPERGLYCEMIA IN BLADDER DYSFUNCTION IN LONG-TERM DIABETIC RAT

Hypothesis / aims of study

Diabetic bladder dysfunction (DBD), a collective description of clinical symptoms including decreased sensation, increased capacity, poor emptying, and also detrusor overactivity, is among the most common and costly complications of diabetes mellitus (DM). It is estimated that DBD occurs in approximately 87% of individuals diagnosed with DM, and substantially affects quality of life. Yet, little is known about the pathogenic mechanisms of DBD. Unlike other organs, the bladder experiences not only hyperglycemia, but also an increased volume of urine in DM (1). To aid in our knowledge of the pathophysiology of DBD and to aid development of specific treatments, identification of individual contributions of polyuria and hyperglycemia in the DBD is essential.

Study design, materials and methods

Seventy two female Sprague-Dawley rats were divided into 6 groups: age-matched controls (control), sham urinary diversion (sham), urinary diversion (UD), streptozotocin-induced diabetics after sham urinary diversion (DM), streptozotocin-induced diabetics after urinary diversion (UD+DM), and 5% sucrose-induced diuretics after sham urinary diversion (DIU). UD was performed 10 days before diabetes induction by surgical disconnection of the ureters from the bladder and implantation to uterine cervix. Each group was subsequently evaluated 20 weeks after diabetes or diuresis induction. Twenty-four hour drinking and voided volumes were measured. Conscious cystometry (CMG) was examined. The bladders were harvested for histological examination and quantification of smooth muscle, urothelium, and collagen. The expressions of oxidative stress-related proteins, nitrotyrosine and manganese superoxide dismutase (MnSOD), in bladder were examined.

Results

Diabetes and diuresis caused increases in drinking volume, voided volume and bladder weight. The bladder weight decreased in the UD and UD+DM group. CMG showed increased intercontractile intervals, voided volume and compliance in DIU and DM group, whereas decreased in the UD, and further in UD+DM group. The total tissue area, the tissue area of smooth muscle and urethelium increased in DIU and DM group, whereas decreased in UD and UD+DM group. As a percentage of the total cross sectional tissue area, collagen decreased in DIU and DM group, but increased in UD and UD+DM groups; smooth muscle and urothelium decreased in UD and UD+DM groups. The expression of nitrotyrosine and MnSOD increased in the DM and the UD+DM groups compared with other 4 groups.

Interpretation of results

The bladder weight increased in the DIU and DM groups, but not in UD+DM group compared with UD group, suggest hyperglycemia-induced polyuria is the only reason of bladder hypertrophy in diabetes. Significantly decreased intercontraction interval, functional bladder capacity, voided volume, and compliance were found in the UD+DM group compared with the UD group. Obviously, the differences between UD and UD+DM animals resulted only from hyperglycemia. The relatively reduced detrusor muscle and increased collagen percentage contribute to the reduced compliance in UD and UD+DM animals, whereas the reduced collagen percentage contributes to the increased compliance in DIU and DM group. There were no significant differences in nitrotyrosine and MnSOD proteins among control, sham, DIU, and UD groups. However, we found nitrotyrosine and MnSOD increased in the DM and UD+DM groups. These data suggest that oxidative stress in DBD is induced by hyperglycemia itself but is not related to hyperglycemia-induced polyuria, which may play an important role in the later stage of DBD.

Concluding message

Polyuria and hyperglycemia contribute differently in DBD. Polyuria induced significant bladder hypertrophy, whereas chronic hyperglycemia induces oxidative stress in bladder, which may play an important role in the later stage of DBD.

References

1. Daneshgari F, Liu G, Birder L, Hanna-Mitcell AT, Chacko S. Diabetic bladder dysfunction: Current translational knowledge. J Urol 2009; 182:S18-S26.

Disclosures

Funding: The study was supported by American Diabetes Association (ADA) grant 1-10-JF-29 **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Rat **Ethics Committee:** Case Western Reserve University Institutional Animal Care and Use Committee