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TADALAFIL CAN IMPROVE BLADDER BLOOD SUPPLY AND LOWER URINARY TRACT FUNCTION IN DIABETIC RATS

Hypothesis / aims of study

Studies since the late 1990's, have demonstrated that bladder ischemia causes lower urinary tract dysfunction. Chronic bladder ischemia is caused by diabetes, arteriosclerosis, or bladder outlet obstruction caused by conditions such as benign prostatic hyperplasia (BPH). Recent basic studies have provided increasing evidence that chronic bladder ischemia induces bladder overactivity at an early stage and bladder underactivity at an advanced stage. Diabetes impairs vascular endothelia by causing hyposecretion of nitric oxide (NO) and also causes atherosclerosis, which results in lower blood flow. Tadalafil, a phosphodiesterase type 5 (PDE5) inhibitor approved for BPH and erectile dysfunction, may improve pelvic organ blood flow and perfusion. We investigated whether tadalafil improves bladder ischemia and lower urinary tract dysfunction in diabetic rats.

Study design, materials and methods

Female Sprague-Dawley rats weighing 250-300 g were studied. Diabetes was induced using a single intraperitoneal injection of 65 mg streptozotocin per kg. We divided rats into a non-diabetes (ND) group, a diabetes (D) group, and a diabetes with tadalafil (DT) group. We performed cystometry and resected the bladders for immunohistochemistry (staining with HIF-1α and 8-OHdG) to evaluate ischemia 6 weeks after diabetes induction. Tadalafil was orally administered at 2 mg/kg/day for 7 days before cystometry. On cystometry we measured basal pressure (BP), the lowest pressure between contractions; opening pressure (OP), at which urethra opens and urinary flow starts; inter contraction interval (ICI); voided volume (VV); and post-void residual (PVR).

Fig. 1

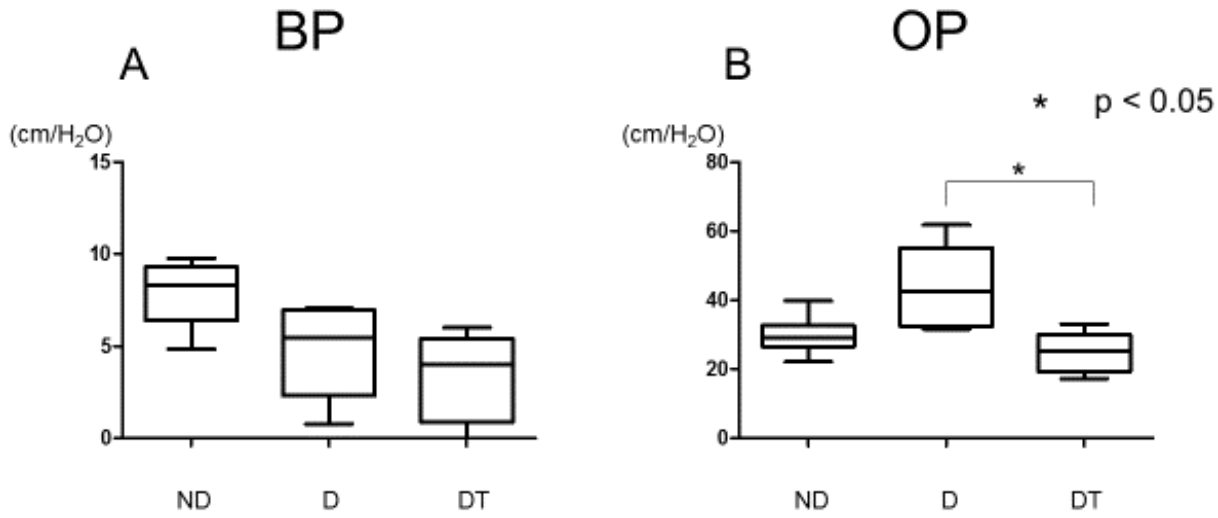


Fig. 2

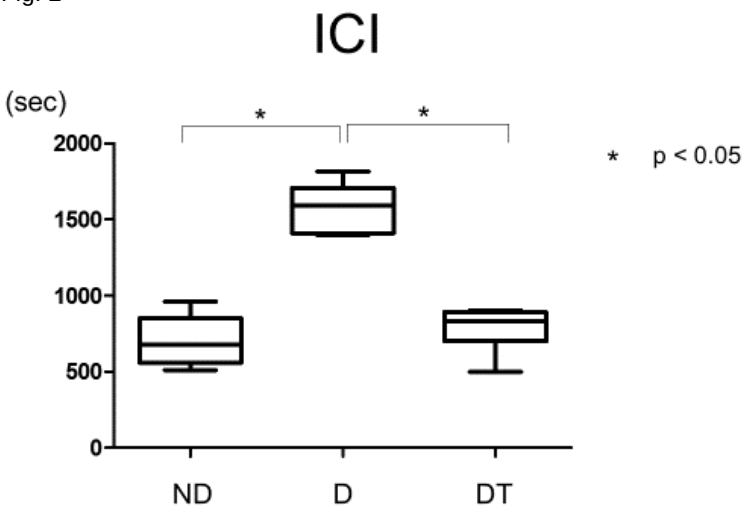
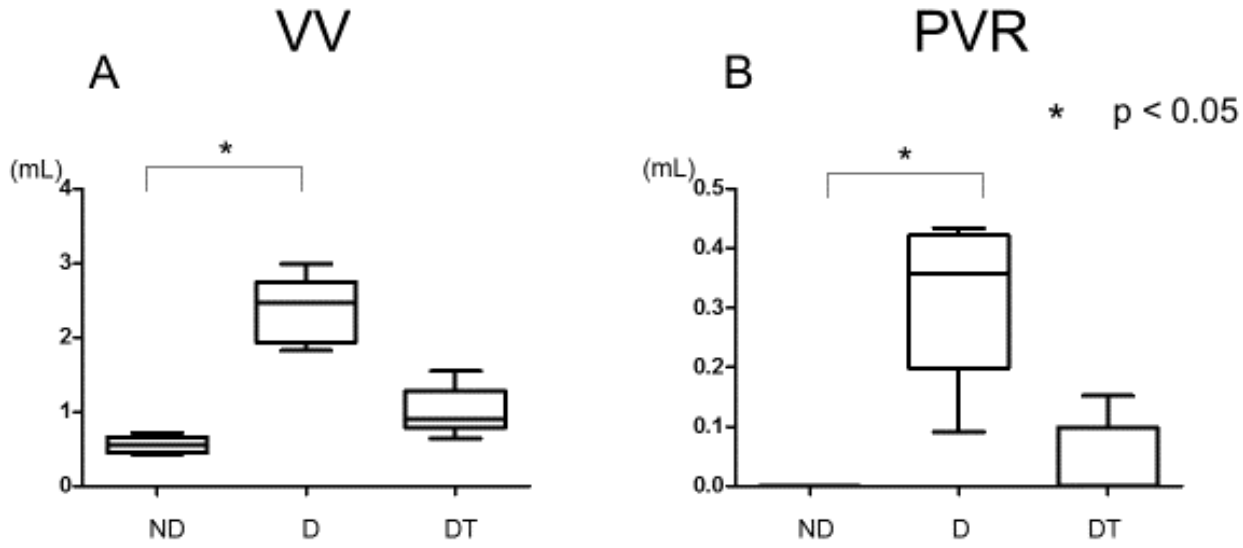


Fig. 3



Results

All 3 groups showed no significant difference in mean BP (Fig. 1A). Mean OP was significantly lower in the DT group than in the D group (Fig. 1B). Mean ICI was significantly longer in the D group than in the ND and DT groups (Fig. 2). Mean VV and PVR were significantly higher in the D group than in the ND and DT groups (Fig. 3A, B). Mean OP, ICI, VV and PVR were not significantly different between the ND and DT groups. Immunohistochemistry showed that both HIF-1α and 8-OHdG were positive in urothelial layers in the D group while both of them were negative in the ND and DT groups.

Interpretation of results

This study is the first report the effect of tadalafil on bladder ischemia due to diabetes.

The reduction in OP, ICI, and VV in the DT group probably indicates improvement in afferent nerve function. The reduction in OP and PVR probably indicates improvement of efferent nerve function. Immunohistochemistry revealed that tadalafil improved blood supply in the diabetic bladder. Collectively, tadalafil likely improved lower urinary tract function and afferent and efferent nerve functions, which were impaired by diabetic ischemia.

Concluding message

Tadalafil can improve bladder blood supply and lower urinary tract function in diabetic rats.

Disclosures

Funding: None **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Rat **Ethics Committee:** Nara Medical University Animal Experiment Committee