10-WEEK, BUT NOT 7-WEEK, DAPAGLIFLOZIN TREATMENT IMPROVES SEVERE RENAL IMPAIRMENT IN UNI-NEPHRECTOMIZED SDT FATTY RAT, A 10-WEEK MODEL OF ADVANCED RENAL COMPLICATIONS AND GLOMERULAR FILTRATION RATE DECLINE.

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BACKGROUND

Sodium glucose cotransporter 2 inhibition (SGLT2i) represents a promising new class of glucose lowering drugs but may not be recommended in type 2 diabetic patients with severe renal impairment. Here we evaluated the effects of dapagliflozin (DAPA) treatment in uni-nephrectomized Spontaneously Diabetic Tori (SDT) fatty rat. This novel hypertensive, obese, type 2 diabetic model, develops advanced renal complications and >50% glomerular filtration rate (GFR) decline within 10 weeks.

METHODS

Male, 6-week old SDT fatty rats underwent unilateral nephrectomy (Unx). After a 1-week recovery, rats were put on a salt-supplemented diet (Purina 5008 chow diet and drinking water supplemented with 0.3% salt) for 10 weeks. Rats were treated without or with DAPA 1mg/kg/day in the chow diet either upon diet start (10-week treatment) or after 3 weeks of diet to enhance kidney complications (7-week treatment). A group of control/sham operated rats was included to evaluate kidney complications induced by nephrectomy and salt supplementation.

Data are presented as mean±SEM. Statistical analysis was performed using either an unpaired, 2 tailed Student t-test, Mann-Whitney test or a 2-way ANOVA + Bonferroni post-test. A p<0.05 was considered significant.

RESULTS

1. Dapagliflozin treatment for 7 weeks improves glycemic control but not kidney dysfunction in Unx SDT fatty rat under 0.3% salt.

2. Dapagliflozin treatment for 7 weeks does not alter kidney complications in Unx SDT fatty rat under 0.3% salt.

3. Dapagliflozin treatment for 7 weeks does not change kidney histopathology scoring in Unx SDT fatty rat under 0.3% salt.

4. Dapagliflozin treatment for 10 weeks improves glycemic control but not GFR in Unx SDT fatty rat under 0.3% salt.

5. Dapagliflozin treatment for 10 weeks improves kidney complications in Unx SDT fatty rat under 0.3% salt.

6. Dapagliflozin treatment for 10 weeks improves kidney histopathology scoring in Unx SDT fatty rat under 0.3% salt.

CONCLUSION

•Dapagliflozin for 10 weeks, but not 7 weeks, significantly prevents advanced renal complications in Unx SDT fatty rats.

•Long-term SGLT2i may be beneficial against kidney complications in the context of type 2 diabetes.