Calcitriol attenuates renal tubular cells apoptosis via inhibiting p38 MAPK signaling in STZ - induced DN rats

Yinfeng Guo, Ying Yang, Yu Zhao, Bicheng Liu, Xiaoliang Zhang

Institute of Nephrology, Zhong Da Hospital, School of Medicine, Southeast University

This study was supported by China National Natural Scientific Fund (No.81370826 and No.81570612)

Background

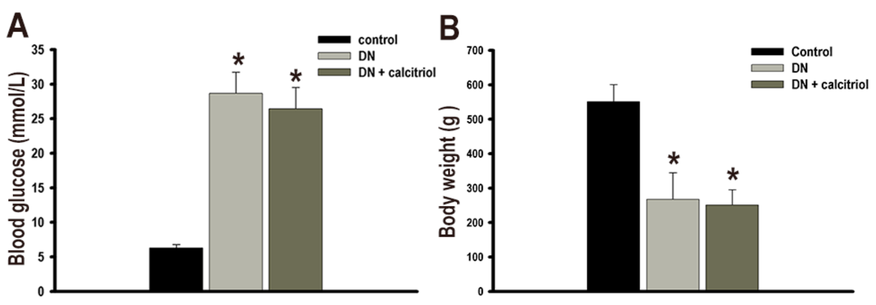
Renal tubular apoptosis is a key event in initiating kidney damage in diabetic nephropathy (DN). Although calcitriol is renoprotective, its role in renal tubular apoptosis in DN and its potential mechanisms are not completely elucidated. p38 mitogen-activated protein kinase (p38 MAPK) activated under the conditions of oxidative stress, plays an important role in cell apoptosis. In the present study, we examined the effect of calcitriol on tubular apoptosis in DN and whether p38 MAPK signaling is involved in such renoprotection of calcitriol.

Materials and Methods

DN model rats were established by intraperitoneal injection with streptozocin (STZ). The rats were subsequently receiving either calcitriol (0.1μg/kg/d) or vehicle by gavage. The rats were euthanized at 18 weeks for histological and molecular analysis. TUNEL assay was used to analyze apoptotic rate of tubular cells. Proteins expression of Bax, Bcl-2, cleaved caspase-3, p-p38MAPK and p38MAPK were detected by Western Blot.

Results

3.1. Diabetic model induced by STZ



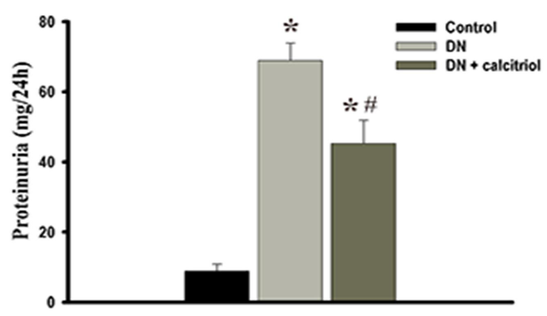
3.2. Calcitriol improves biochemical parameters in DN rats

Table 1. Effects of calcitriol on the general parameters in experimental animals

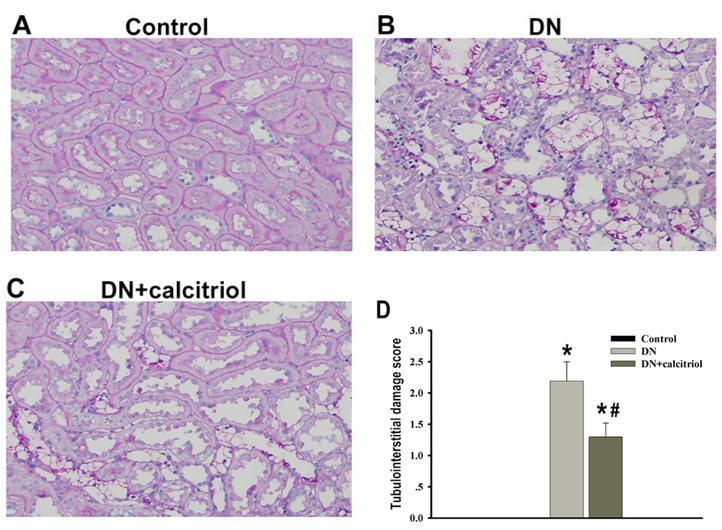
	Control	DN	DN+calcitriol
Scr (μmol/L)	46.66±2.08	126.5±12.26*	75.67±8.51*#
BUN (mmol/L)	5.33±0.4	14.80±1.65*	9.33±1.84*#
Ca (mmol/L)	2.56±0.04	2.37±0.23*	2.69±0.16#
P (mmol/L)	2.52±0.10	2.99±0.34*	1.98±0.10#

Scr: serum creatinine; BUN: blood urea nitrogen; Ca: serum calcium; P: serum phosphate. Data are presented as mean±SD (n=8). *p<0.05 vs control; #p<0.05 vs DN group.

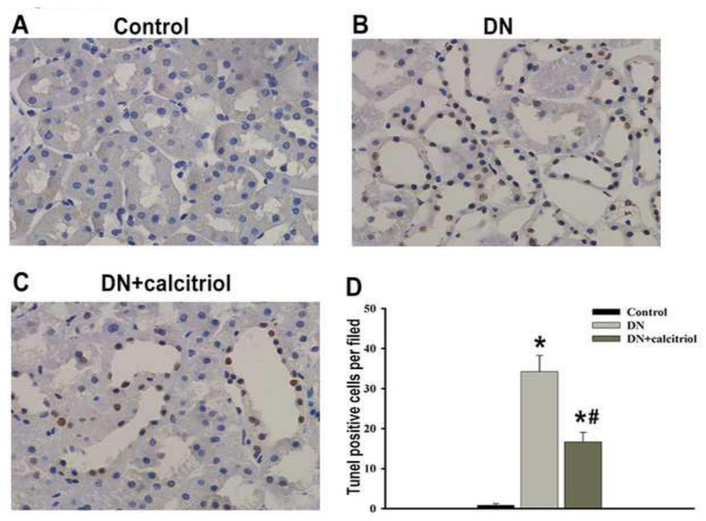
3.3. Calcitriol improves proteinuria in DN rats



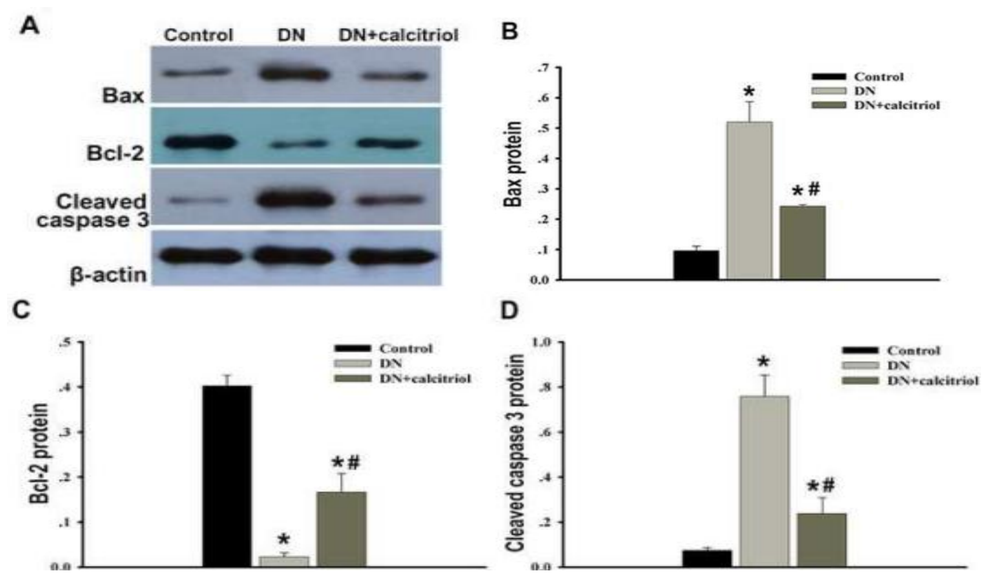
3.4. Calcitriol ameliorates renal tubulointerstitial damage in DN rats



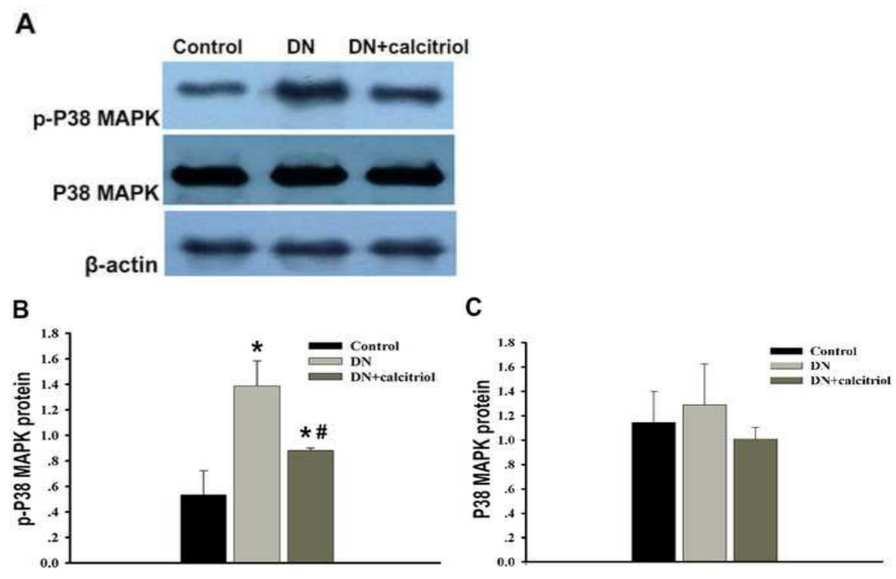
3.5. Calcitriol attenuates tubular cells apoptosis in DN rats



3.6. Calcitriol decreases pro-apoptotic proteins and increases anti-apoptotic proteins in DN rats



3.7. Calcitriol inhibited p38 MAPK signaling activation in DN rats



Data are presented as mean ± SD. *P<0.05 vs control; #P < 0.05 vs DN group.

Conclusion

Calcitriol attenuates renal tubular cells apoptosis by inhibiting p38 MAPK signaling in STZ-induced DN rats

DOI: 10.3252/pso.eu.54ERA.2017