THE RENOPROTECTIVE EFFECTS OF HELIX B SURFACE PEPTIDE IN PUROMYCIN AMINONUCLEOSIDE INDIUCED NEPHROPATHY OF RAT

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Introduction and aims

Glial cell line-derived neurotrophic factor (GDNF), a member of transforming growth factor-β (TGF-β) superfamily, was believed to participate in podocytes remodeling and repairment, but its role has not been totally elucidated in acute puromycin aminonucleoside nephropathy(PAN) of rats. The aims of this study were to explore whether the renoprotection of helix B surface peptide (HBSP) was mediated via GDNF and to find out the intrinsic association between the expression of GNDF and podocytes survival in kidney.

Methods

Wistar Albino rats were randomly divided into three groups, control group (n=6), PAN+vehicle group (n=10) and PAN+HBSP group (n=10), which administered HBSP (8nmol/kg), 4 hour before the injection of puromycin aminonucleoside (60mg/kg) and every 24 hour after. Biochemical parameters, gene expression and histology were assessed at the 7th day. Statistics were analyzed using one-way ANOVA followed by Tukey's multiple comparisons test. Values were considered significant if $P<0.05$.

Results

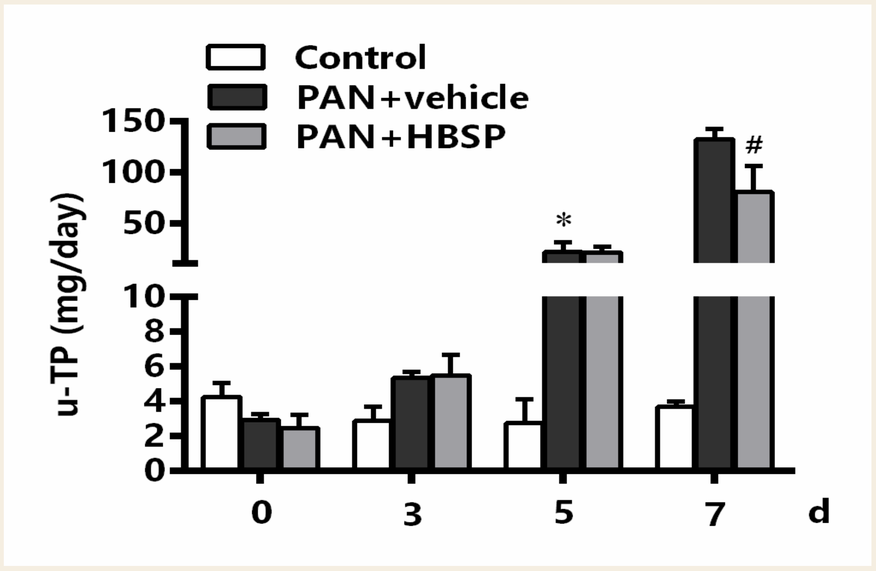

Figure 1. 24h proteinuria After injection of PA, the excretion of total protein in urine was significantly increased in PAN+vehicle group compared with that in control group, on 7th day. Treatment of HBSP reduced the PAN-induced induced in proteinuria.

Table 1. Biochemical Index

Parameter	Control group	PAN+vehicle	PAN+HBSP
Hb (g/dl)	13.50 ± 0.20	13.92 ± 0.19	14.42 ± 1.08
Hct (%)	41.50 ± 0.74	45.40 ± 0.01	46.40 ± 0.04
Urea(mg/dl)	35.64 ± 4.55	37.47 ± 3.47	32.73 ± 9.75
SCr(mg/dl)	0.41 ± 0.02	0.39 ± 0.05	0.48 ± 0.10

Haemoglobin, Haematocrit, Blood urea nitrogen and Serum creatinine have no significant difference among each groups. ($P>0.05$)

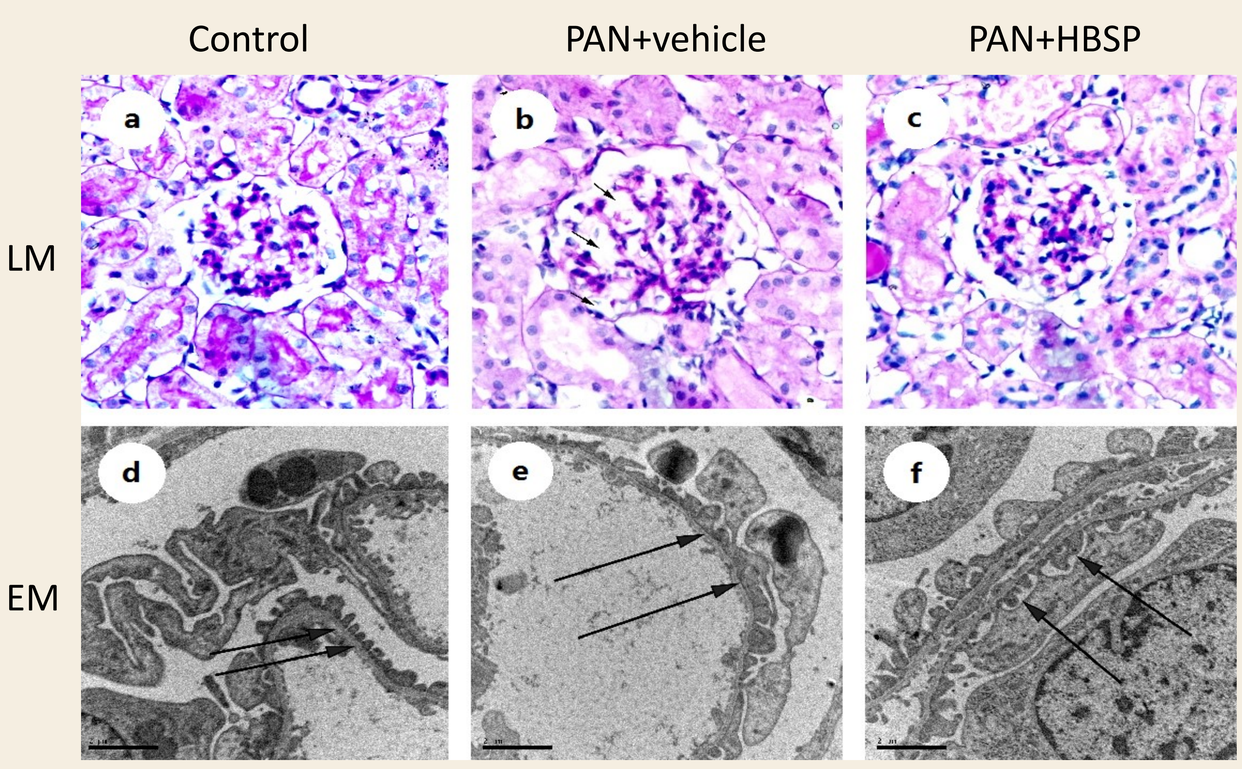

Figure 2. Histopathology Compared with the glomerulus in control rats (a), PAS-stained kidney of PAN-treated rats showed hypertrophy of the glomerulus, especially podocyte vaculation(b). HBSP administration prevent these changes. Transmission electron microscope demonstrated effacement and detachment of podocytes(e), however, these changes were attenuated by HBSP.

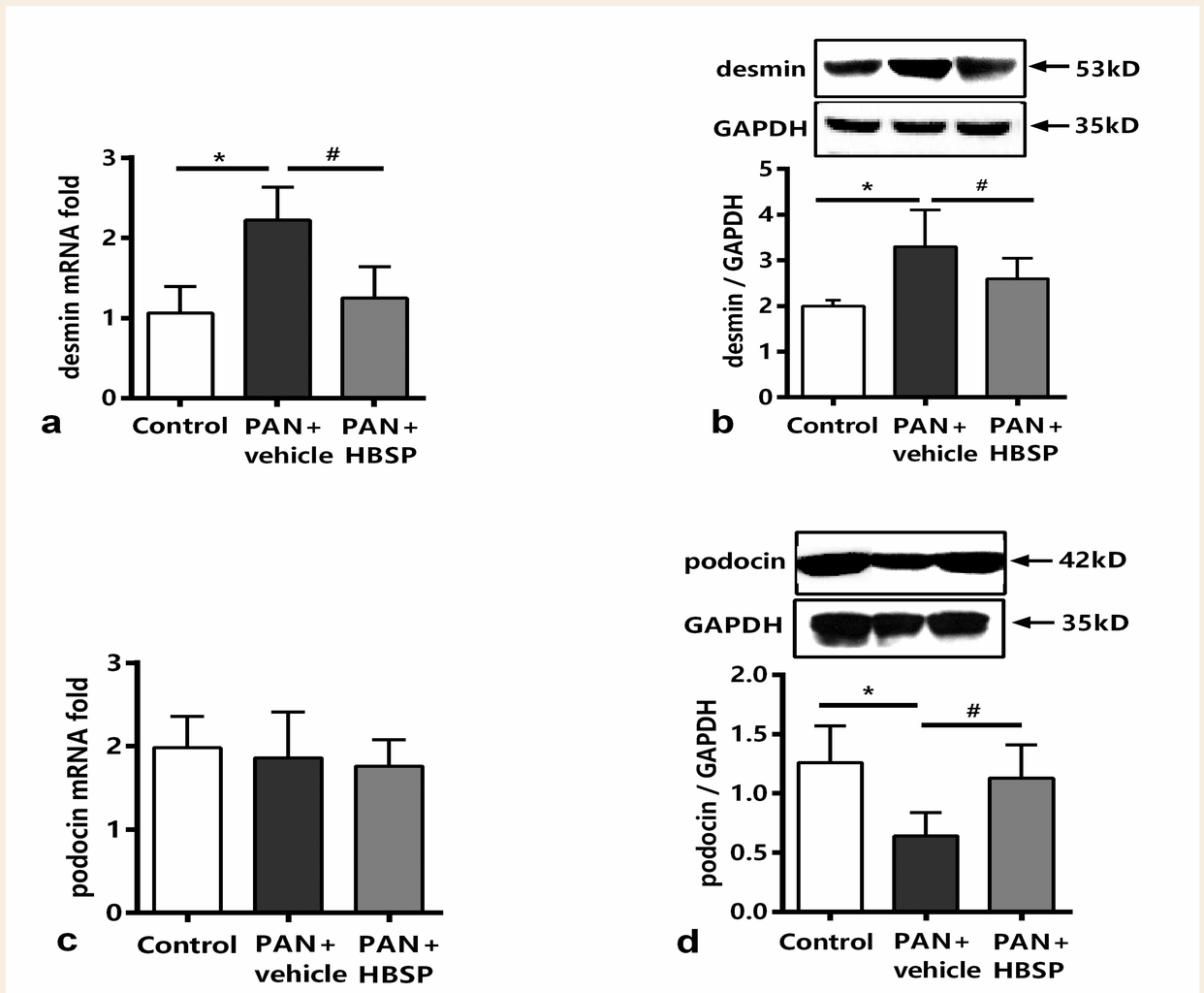

Figure 3. Real-time PCR and Western Blot PAN+vehicle significantly increased expression of desmin in mRNA and protein levels compared with control group. PAN+HBSP significantly descreased expression of desmin.(a,b) There is no difference of podocin mRNA among all groups. Podocin protein reduced in PAN+vehicle and PAN+HBSP group. HBSP could increase podocin protein levesl compared with PAN+vehicle. (c,d).

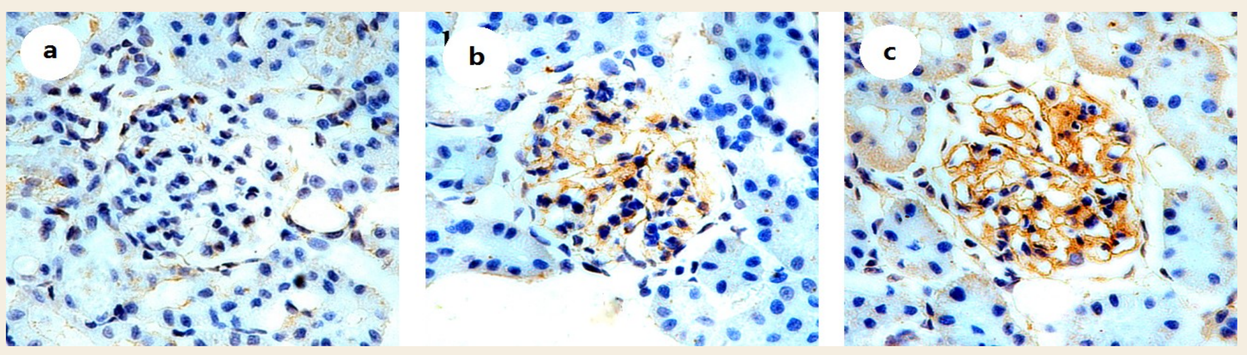

Figure 4. Immunohistochemistry Compared with control group(a), GDNF was markedly upregulated in the glomeruli of PA administration rats.(b,c) HBSP further elevates the expression of GDNF, when compared with PAN+vehicle.(c)

Conclusion

HBSP could upregulate the expression of GDNF in vivo. Persistent activation of the RAS/ERK signaling pathway might be involved in the renoprotection of GDNF, which might take effect in an autocrine mode. HBSP could also alleviate proteinuria by inhibiting increase of desimin and deletion of podocin.

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