Higher urinary vasoinhibin excretion in patients with proliferative diabetic retinopathy

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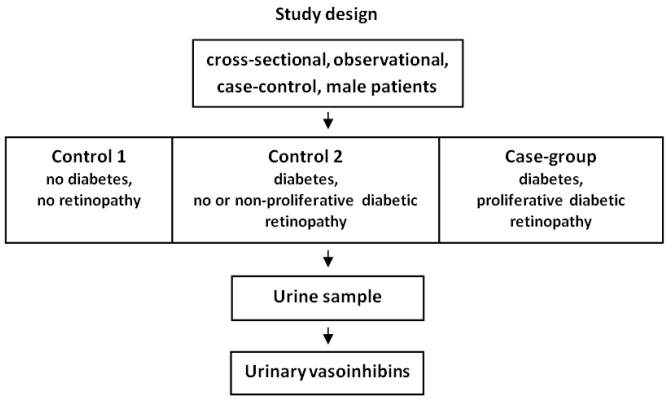
1

Vasoinhibins are a family of PRL-derived peptides with antiangiogenic properties (1). Experimental studies demonstrate protective effects of vasoinhibins against diabetic retinopathy (2), however their clinical relevance is unknown. In patients with diabetic retinopathy, the circulating levels of vasoinhibins are lower (3) and there is an increase in the excretion of albumin in the urine (4). Here, we investigate whether a higher urinary excretion of vasoinhibins also occurs in patients with diabetic retinopathy, which may contribute to their lower circulating levels.



2 Demographic and clinical characteristics of the study population

	Control 1 n=25	Control 2 n=13	Case-group n=22	
age, y	49.9 ± 18.76	58.5 ± 13.19	56.40 ± 11.18	
BMI	26.4 ± 5.17	25.36 ± 7.32	24.99 ± 3.0	
time since DM diagnosis, y	-	12.4 ± 10.43	15.72 ± 8.97	
HbA_{1c}, %	4.93 ± 1.03	7.75 ± 1.98	7.77 ± 2.38	C vs C1, p <0.001 C1 vs C2, p <0.001
DM medication, % patients				
none	-	16.6	0	
oral	-	67	72	
insulin	-	16.6	28	

mean ± SD, BMI = body-mass-index, DM = diabetes mellitus

Serum creatinine and eGFR

	Control 1 n=25	Control 2 n=13	Case-group n=22	
creatinine, mg/dl	1.05 ± 0.39	0.94 ± 0.26	1.39 ± 0.69	NS
eGFR, % patients				
>60 (normal)	84	77	55	
15-60 (impaired)	16	23	45	
<15 (renal failure)	0	0	0	

mean ± SD, eGFR = estimated glomerular filtration rate

Literature

1 Triebel et al. IUBMB Life 2011;63(10):906-810.
2 Ramirez et al. IOVS 2011;52(12):8944-50.
3 Triebel et al. EJE 2009;161:345-353.
4 Cruickshanks et al. Ophthalmology 1993;100(6):862-7.

Acknowledgements

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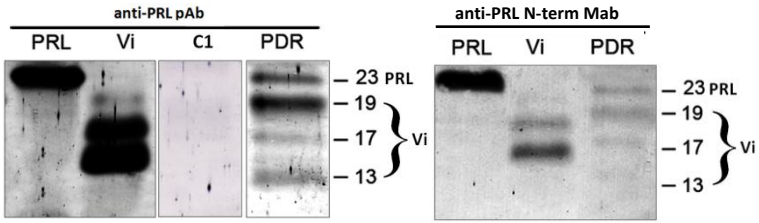
3

Analysis of urine samples by Western blotting demonstrates the presence of vasoinhibins of different molecular weights. Reactivity to anti-PRL N-terminal monoclonal antibody (N-term Mab) confirms their N-terminal structure. Representative images are shown: **PRL** = Prolactin, **Vi** = Vasoinhibins, **C1** = urine sample from a patient in the control 1 group, **PDR** = urine sample from a patient with proliferative diabetic retinopathy (Case).



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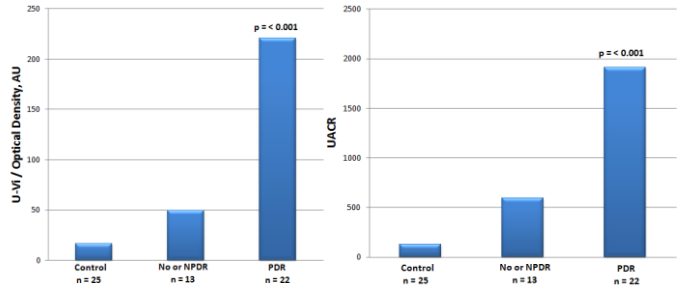
Densitometric analysis of Western blots demonstrates a significantly higher urinary vasoinhibin excretion in patients with proliferative diabetic retinopathy compared to control subjects without diabetes. Across all groups, urinary vasoinhibin excretion positively correlates with the urinary albumin-to-creatinine ratio (Spearman r = 0.62, p = <0.0001).

Urinary vasoinhibins, albumin, and total protein excretion

	Control 1 n=25	Control 2 n=13	Case-group n=22	
UVi, AU	16.72 ± 57.89	49.61 ± 92.81	220.65 ± 268.31	C vs C1, p <0.001 C vs C2, NS
UACR	130.99 ± 178.75	592.48 ± 1035.60	1910.30 ± 2832	C vs C1, p <0.001 C vs C2, NS
Albuminuria, % patients				
normoalbuminuria	16	0	0	
microalbuminuria	76	61	34	
macroalbuminuria	8	39	66	
albumin, mg/dl	10.64 ± 7.27	33.92 ± 48.62	103.82 ± 100.16	C vs C1, p <0.001 C vs C2, NS
total protein, mg/dl	18.4 ± 12.97	53.84 ± 80.67	155.86 ± 137.03	C vs C1, p <0.001 C vs C2, NS
u-creatinine, mg/dl	124.26 ± 72.39	98.02 ± 65.11	79.85 ± 49.04	

mean ± SD, UVi = urinary vasoinhibins, AU = arbitrary units, UACR = urinary albumin-to-creatinine ratio



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Conclusion: Urinary vasoinhibin excretion is higher in patients with proliferative retinopathy and could result in lower serum levels, leading to compromised protective effects of vasoinhibins against the development and progression of proliferative diabetic retinopathy.