LETTER TO THE EDITOR

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The renoprotective effects of pentoxifylline: beyond its role in diabetic nephropathy

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To the Editor,

I read with great interest the article by Sun et al. [1]. Pentoxifylline may exert a number of renoprotective effects, besides its role in attenuating diabetic nephropathy. Pentoxifylline attenuates kidney damage secondary to hepatic ischemia/reperfusion injury. It mediates this action by decreasing malondialdehyde levels [2]. Simultaneously, it restores intracellular glutathione. As a result, oxidative injury to the kidneys is mitigated. Obviously, conditions such as hepato-renal syndrome can be avoided with pentoxifylline pretreatment. The coming years may very well see increased use of pentoxifylline as a prophylactic agent to prevent hepatorenal syndrome in patients with concurrent cirrhosis and ascites.

Pentoxifylline is also beneficial in chronic renal disease. It benefits the kidneys by stabilizing renal function and the glomerular filtration rate. Concurrent decreases in inflammatory markers such as tissue necrosis factor-α and high-sensitivity C-reactive protein reflect the attenuation of inflammatory damage in the kidneys. The interleukin-6 level also decreases at the same time [3]. In addition, pentoxifylline helps reduce proteinuria in chronic kidney disease (CKD) patients. Renke et al. [3] recently reported a 26% decline in proteinuria following pentoxifylline therapy in comparison with placebo therapy. Pentoxifylline also decreases proteinuria in CKD patients following renal transplantation. Moreover, pentoxifylline modulates hepcidin function and augments iron release, thereby improving hemoglobin levels in CKD patients.

By virtue of its antioxidant properties, pentoxifylline also mitigates and reduces renal damage secondary to exposure to cigarette smoke. Similarly, pentoxifylline is of benefit in cardiac surgery because it prevents and attenuates acute renal injury [4]. When used in conjunction with albumin, pentoxifylline protects the kidneys from injury following endotoxemic shock, by decreasing inducible nitric oxide synthase expression in the kidneys [5]. Similarly, the postlaparoscopy administration of pentoxifylline attenuates renal ischemia associated with laparoscopy.

These examples clearly illustrate the renoprotective effects of pentoxifylline.

Keywords: Pentoxifylline; Renal insufficiency, chronic; Renal

Conflict of interest

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REFERENCES

1. Sun HK, Lee YM, Han KH, Kim HS, Ahn SH, Han SY. Phosphodiesterase inhibitor improves renal tubulointerstitial hypoxia of the diabetic rat kidney. Korean J Intern Med 2012;27:163-170.
2. Seifi B, Kadkhodaee M, Delavari F, Mikaeili S, Shams S, Ostad SN. Pretreatment with pentoxifylline and N-acetylcysteine in liver ischemia reperfusion-induced renal injury. Ren Fail 2012;34:610-615.
3. Renke M, Tylicki L, Rutkowski P, et al. Effect of pentoxifylline on proteinuria, markers of tubular injury and oxidative stress in non-diabetic patients with chronic kidney disease: placebo controlled, randomized, crossover study. Acta Biochim Pol 2010;57:119-123.
4. Barkhordari K, Karimi A, Shafiee A, et al. Effect of pentoxifylline on preventing acute kidney injury after cardiac surgery by measuring urinary neutrophil gelatinase-associated lipocalin. J Cardiothorac Surg 2011;6:8.
5. Bansal S, Wang W, Falk S, Schrier R. Combination therapy with albumin and pentoxifylline protects against acute kidney injury during endotoxemic shock in mice. Ren Fail 2009;31:848-854.

In reply

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We thank Dr. Kapoor for the precise comments on the effect of pentoxifylline (PTX) in diabetic nephropathy [1] and other diseases.

Currently, PTX is used to treat peripheral vascular and bronchoconstrictive diseases [2,3]. Recently, the effects of PTX have been determined under various conditions, including antiphospholipid syndrome, alcoholic hepatitis, and wound healing. Several clinical trials of PTX in nonalcoholic steatohepatiti), contrast-induced nephropathy, radiation injury, and other conditions have been conducted.

Unfortunately, the effects of PTX in patients with diabetic nephropathy are unclear. This might be due to the heterogeneous clinical nature of diabetic nephropathy. Of diabetics with chronic kidney disease, 24% to 51% do not have albuminuria [4,5]. The resistance of the intrarenal arteries was increased in type 2 diabetics with impaired renal function regardless of proteinuria [6]. These findings suggest that vasculopathy is a very important risk factor for the progression of diabetic nephropathy. Therefore, the effect of PTX in diabetic patients could differ according to the vascular changes.

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REFERENCES

1. Sun HK, Lee YM, Han KH, Kim HS, Ahn SH, Han SY. Phosphodieste rase inhibitor improves renal tubulointerstitial hypoxia of the diabetic rat kidney. Korean J Intern Med 2012;27:163-170.
2. Boolell M, Allen MJ, Ballard SA, et al. Sildenafil: an orally active type 5 cyclic GMP-specific phosphodiesterase inhibitor for the treatment of penile

erectile dysfunction. Int J Impot Res 1996;8:47-52.
3. Teixeira MM, Gristwood RW, Cooper N, Hellewell PG. Phosphodiesterase (PDE)4 inhibitors: anti-inflammatory drugs of the future? Trends Pharmacol Sci 1997;18:164-171.
4. Kramer HJ, Nguyen QD, Curhan G, Hsu CY. Renal insufficiency in the absence of albuminuria and retinopathy among adults with type 2 diabetes mellitus. JAMA 2003;289:3273-3277.
5. Retnakaran R, Cull CA, Thorne KI, Adler AI, Holman RR; UKPDS Study Group. Risk factors for renal dysfunction in type 2 diabetes: U.K. Prospective Diabetes Study 74. Diabetes 2006;55:1832-1839.
6. MacIsaac RJ, Panagiotopoulos S, McNeil KJ, et al. Is nonalbuminuric renal insufficiency in type 2 diabetes related to an increase in intrarenal vascular disease? Diabetes Care 2006;29:1560-1566.2009;31:848-854.

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