

Pentoxifylline for Diabetic Nephropathy-Current Status

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Diabetic nephropathy, or diabetic kidney disease (DKD), is the most serious complication of diabetes mellitus (DM). Despite recent advances in therapy, DKD still often progresses to end-stage renal disease (ESRD). The current standard therapy of diabetic nephropathy involves intensive treatment of hyperglycemia and strict blood pressure control, mainly via blockade of the renin-angiotensin system (RAS). However, potential risk of hyperkalemia and on other hand antiproteinuric effects of RAS combination therapy do not seem to enhance the prevention of renal disease progression to complete extent. (1)

Recent studies have suggested that pentoxifylline (PTX) may be efficacious in the treatment of DKD. PTX is a rheologic modifier approved for use in the USA for the symptomatic relief of claudication. It competitively inhibits phosphodiesterase (PDE), resulting in increased intracellular cyclic AMP (cAMP), activation of protein kinase A (PKA), inhibition of interleukin (IL) and tumor necrosis factor (TNF) synthesis, and reduced inflammation. PTX improves red blood cell deformability, reduces blood viscosity, and decreases platelet aggregation.(2)

Han SJ, *et al* (3) reported that Pentoxifylline therapy reduced proteinuria and improved glucose control and insulin resistance without significant change of serum TNF-alpha in patients with type 2 diabetic nephropathy.

Navarro JF, *et al* (4) in their study reported that administration of PTF to patients who have type 2 diabetes and are under long-term treatment with an ARB produces a significant additive antiproteinuric effect associated with a reduction of urinary TNF-alpha excretion.

Tian ML, *et al* (5) in their met analysis of randomised clinical trials suggested similarly that Pentoxifylline can significantly provide additive antiproteinuric effect independent from the decrease in BP or improvement in glycemic control in DN patients under blockade of angiotensin system.

Shan D, *et al* (6) in their Cochrane Database reviewed that pentoxifylline seems to offer some beneficial effects in renal function improvement and reduction in albuminuria

and proteinuria, with no obvious serious adverse effects for patients with DKD.

Diskin CJ1, *et al* (7) however reported contrary results that no statistical benefit in proteinuria reduction or preservation of renal function by the addition of pentoxifylline to maximal doses of ACEIs and ARBs.

Although, evidence to support the use of pentoxifylline for DKD are existing but are insufficient at present to develop recommendations for its use in this patient population. Thus, rigorously designed, randomised, multicentre, large scale studies of pentoxifylline for DKD are needed to further establish its therapeutic effects so that it can be recommended to prevent progression of diabetic nephropathy.

References

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