Beside this meta-analysis, several studies have evaluated the role of adding pentoxifylline to Rennin-Angiotensin System (RAS) blockers and the finding were supportive to the previous assumption of pentoxifylline beneficial role in reducing proteinuria. Roozbeh et al. conducted a study that included 74 type 2 DM patients (with overt proteinuria) who were divided into two groups for who either captoprialone or combine captopri and pentoxifylline (400 mg per day) were given; the group received combined treatment reported greater reduction in proteinuria beside reduction in blood pressure by a modest fraction [15]. in another study carried out by Oliaei et al., 50 patients with type 2 DM and overt proteinuria who were also divided into two groups referring to the agents used to reduce proteinuria (RAS inhibition versus pentoxifylline); the results showed greater decline in proteinuria but similar creatinine clearance [16]. Ghorbani et al included 100 patients with type 2 DM (with proteinuria) "randomized to pentoxifylline 400 mg/day or placebo for 6 months". Either groups received enalapril and losartan in combination. Following six months, pentoxifylline therapy was accompanied by less proteinuria and greater creatinine clearance [17]. All these studies are in accordance with the findings of the present study.

Proteinuria is an essential indicator of ESRD in patients with DN. [18]. Decreasing proteinuria is successful in retarding the progression of chronic kidney disorder, in addition to reducing cardiovascular complications [19, 20].

The mechanisms behind the proteinuria reduction by pentoxifylline is still unclear, however some postulation may be considered. The first possible way is adenosine 2 receptors blocking that modify GFR and the kidney function of atrial natriuretic factor [19, 21]. The second possible effect is the the hemorheologic action of pentoxifylline that induces beneficial alterations in flow of blood by enhancing fluidity of blood in the peritubular venous plexus and decreasing "low-molecular-weight proteins overload" into the proximal tubule, effects that decrease the pressure inside glomeruli [20]. The third way, pentoxifylline reduces inflammatory reaction inside kidney through its anti-TNF-α effects [22, 23].

In conclusion, Pentoxifylline is an efficient adjuvant therapy to treat diabetic nephropathy.

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