EFFECT OF PENTOXIFYLLINE ON RENAL OUTCOMES IN CHRONIC KIDNEY DISEASE PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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OBJECTIVES

Chronic kidney disease (CKD) represents an important health problem worldwide and the search for new therapeutic approaches for retarding CKD progression is a timely issue. Recent evidence suggest that the anti-inflammatory and hemorrheologic agent Pentoxifylline (PTX), may produce favorable effects on kidney function. In order to investigate whether PTX derivatives, alone or in combination to other treatments, may be useful in slowing down disease progression in patients with diabetic or non-diabetic CKD, we conducted a systematic review and meta-analysis of randomized controlled trials (RCTs).

METHODS

Cochrane CENTRAL, Ovid-MEDLINE and PubMed databases were searched for English-language articles without time or follow-up restriction. We included any randomized controlled trial (RCT) and quasi-RCT providing information on the effects of PTX on renal endpoints in patients with CKD. Outcomes of interest were change in renal function (GFR and/or serum creatinine), proteinuria and albuminuria and adverse effects to PTX treatment.

Fig.1 – Effects of pentoxifylline vs. control treatment on proteinuria

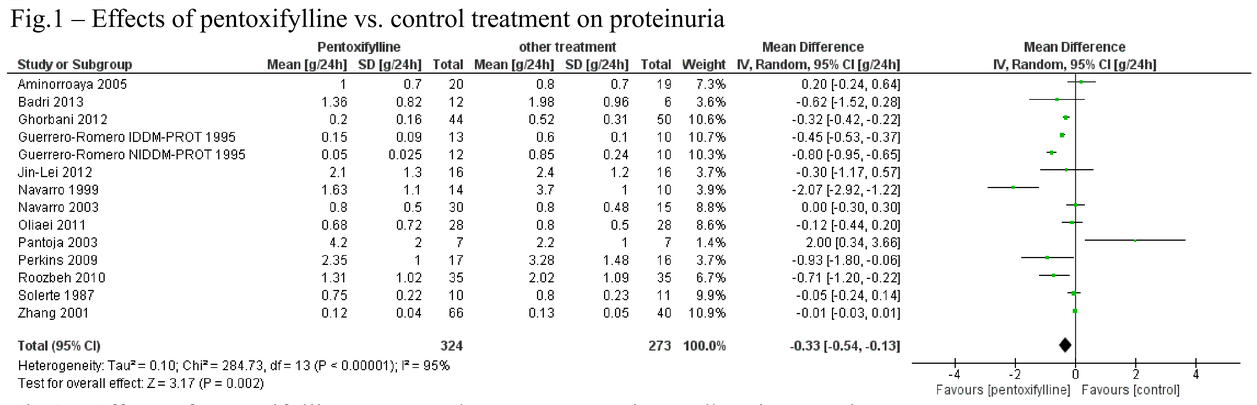


Fig.2 – Effects of pentoxifylline vs. control treatment on urinary albumin excretion

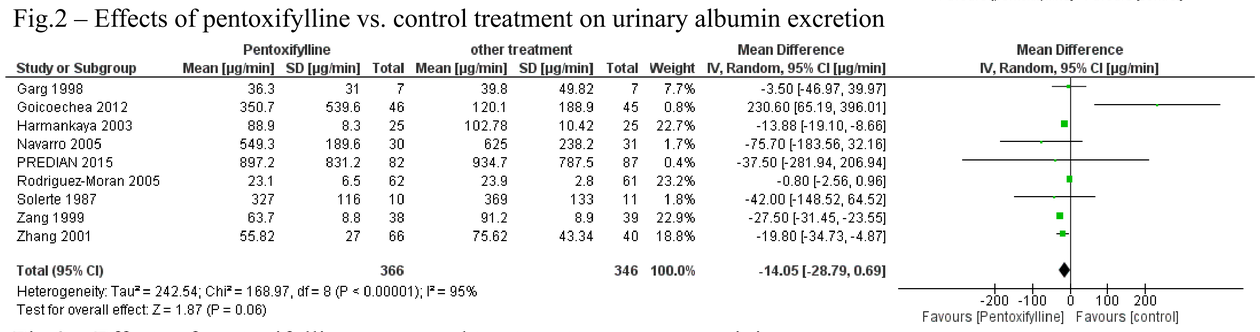


Fig.3 – Effects of pentoxifylline vs. control treatment on serum creatinine

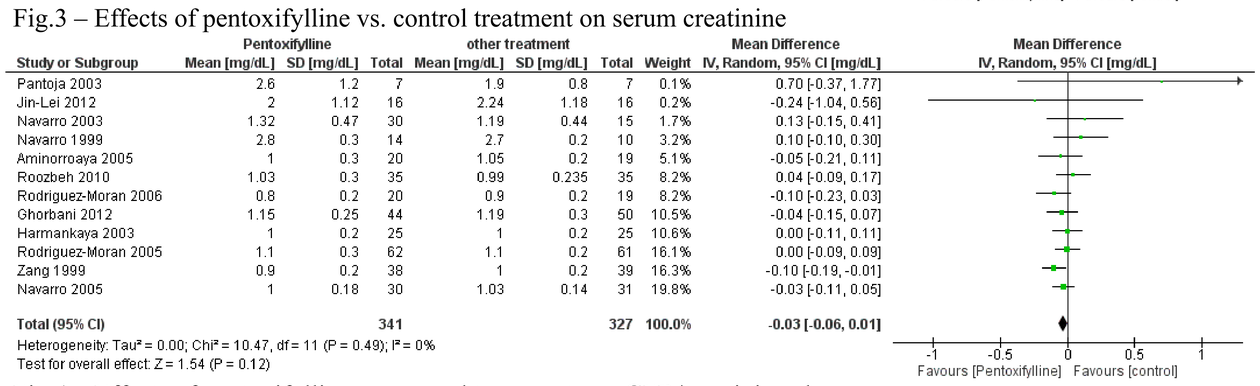


Fig.4 – Effects of pentoxifylline vs. control treatment on eGFR/creatinine clearance

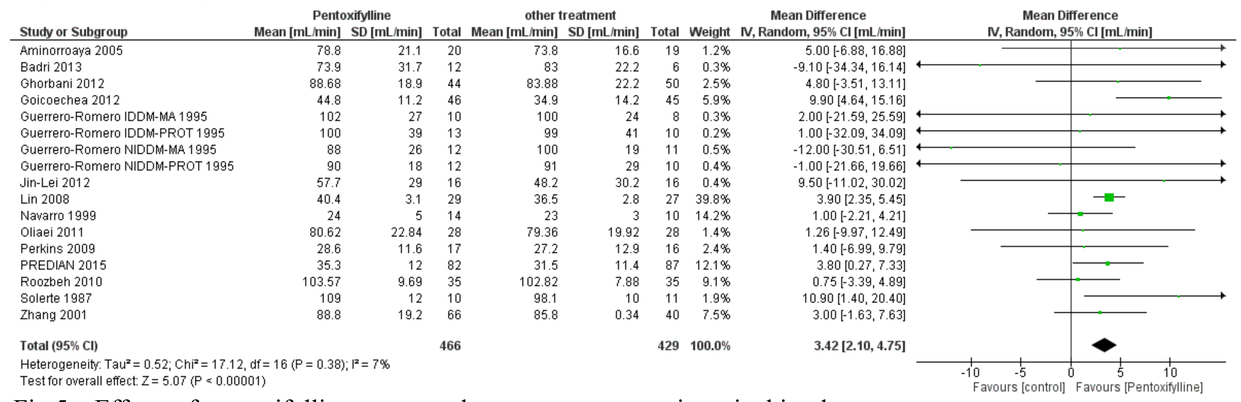
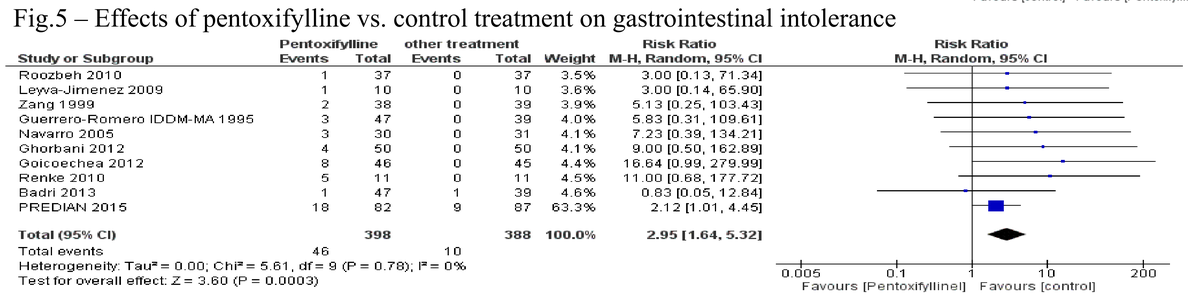


Fig.5 – Effects of pentoxifylline vs. control treatment on gastrointestinal intolerance



RESULTS

From a pool of 289 articles retrieved, we found 26 studies (1518 subjects) matching our search criteria. Among these, 24 studies were focused on diabetic patients while 2 were conducted on non-diabetic CKD population. There was high heterogeneity among studies with respect to sample size, CKD stage, dose of PTX employed, severity of proteinuria, type of comparator (e.g. placebo, standard therapy or RAS blockers). Information on the effects of PTX on hard renal outcomes (doubling of serum creatinine or need for chronic dialysis) were lacking in all the reviewed trials. PTX was effective in reducing proteinuria compared to control (MD -0.33 g/24h; 95% CI -0.54 to -0.13), a benefit that was more evident in patients with type-1 diabetes mellitus, higher proteinuria at baseline and early renal impairment. A slight improvement in renal function (MD 5.10 mL/min; 95% CI 2.53 to 7.67) was observed particularly in patients with more advanced CKD stage and in studies with longer follow-up. Conversely, cumulative analyses did not reveal any evident reduction in urinary albumin excretion, even in diabetic patients. The use of PTX was relatively safe as most trials recorded only minor gastrointestinal adverse effects.

CONCLUSIONS

Although these findings point at some reno-protective effects of PTX, there is no conclusive evidence proving the usefulness of this agent for retarding end-stage kidney disease in subjects with CKD of various etiology. Future trials adequately powered and designed on hard clinical end-points are needed.

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