Comment On: Protective Role of Recombinant Human Erythropoietin in Kidney and Lung Injury Following Renal Bilateral Ischemia-reperfusion in Rat Model

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Letter to Editor

DEAR EDITOR,

We read with great interest the nice published an article by Moeini, *et al*. in the esteemed "International Journal Preventive Medicine" entitled: Protective role of recombinant human erythropoietin (EPO) in kidney and lung injury following renal bilateral ischemia/reperfusion (I/R) in the rat model. Article has some interesting points need more explain. In this study Moeini *et al*. aimed to study the role of EPO on kidney function makers and tissue damage; and lung endothelial permeability and lung water content in bilateral renal I/R injury model in rats.[1] In the study on male Wistar rats, which were divided into three groups of sham, I/R and I/R treated with EPO (I/R + EPO) groups. The I/R and I/R + EPO groups were assigned to bilateral renal I/R injury, while the I/R + EPO group received EPO (500 IU/kg, i.p.) 2 h before ischemia surgery and the same dose was continued once a day for 3 days after ischemia. In the study on male Wistar rats, which were divided into three groups of sham, I/R and I/R treated with EPO (I/R + EPO) groups. The I/R and I/R + EPO groups were assigned to bilateral renal I/R injury, while the I/R + EPO group received EPO (500 IU/kg, i.p.) 2 h before ischemia surgery and the same dose was continued once a day for 3 days after ischemia. They measured serum blood urea nitrogen (BUN) and creatinine (Cr) levels. They also assessed kidney tissue damage score. They found, EPO administration decreased levels of BUN and Cr significantly. Furthermore administration of EPO increased the renal level of nitrite.[1] They concluded that, EPO protected the kidney against I/R injury. In a study of 40 male Wistar rats, conducted to test the protective effect of EPO on tubular cells, we observed that EPO was capable to prevent the increase in serum Cr and BUN levels against gentamicin renal toxicity. Moreover, co-administration of gentamicin and EPO efficiently reduced the kidney tissue injury induced by gentamicin, compared with the control group.[2] Our investigation revealed the kidney protective effect of EPO, when the drug was administered in combination with gentamicin.[3-6] Nevertheless, the protective properties of EPO were evident even when the drug was given after induction of renal tubular injury by gentamicin and it was still effective after tissue damage.[2-6] This indicates that EPO may have a curative impact, along with its preventive properties.[5-9] Hence, EPO is a promising renal protective medication

that can prevent, ameliorate, or attenuate tubular injury induced by gentamicin or other injurious insults such as I/R.[7-10] Previous investigators also showed the efficacy of EPO on kidney allograft survival too.[11] Recently much attentions has been directed toward renoprotective property of EPO beyond stimulating erythropoiesis.[12-16] In a preclinical study on 6 weeks old male rats, which treated with cyclosporine, Abe *et al*. found that carbamylated EPO suppressed macrophage infiltration, phenotypic alteration of interstitial myofibroblasts and interstitial fibrosis in the cyclosporine nephropathy model. They also observed that, carbamylated EPO administration decreased transforming growth factor-β1 messenger ribonucleic acid levels in cyclosporine – Treated kidneys. In the present study, tubular apoptosis was persistently stimulated after central sleep apnea treatment, while carbamylated EPO significantly inhibited tubular apoptosis. They concluded carbamylated EPO administration reduced cyclosporine – Induced tubulointerstitial injury in two ways by protection of tubular epithelial cells from apoptosis and inhibition of interstitial fibrosis.[17] Recently also some investigators envisage to administer the EPO therapy in chronic kidney disease prior to anemia, benefiting its kidney protective efficacy of EPO in chronic kidney disease too.[18] Indeed it may be reasonable that we start EPO prior to erythropoiesis. Hence, to better understand the renoprotective properties of EPO, more experimental or clinical studies are suggested.

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