Nephroprotective Effect of Erythropoietin in Diabetic Rats : Evaluation of possible underlying mechanisms.

Thesis
Submitted in partial fulfillment for Doctorate degree in
Basic medical science Physiology

By:

Wael Botros Abu-Alyamin Ghaly

.

Supervised by:

Prof.Dr.Nagat younan Mina
Professor of Physiology
Faculty of medicine-Cairo University

Prof. Dr. Samah El-Attar
Professor of Physiology
Faculty of medicine-Cairo University

Prof. Dr. Mira Farouk
Professor of Histology
Faculty of medicine-Cairo University

Dr.Hanan Seddiq
Lecturer of Physiology
Faculty of medicine-Cairo University

Faculty of medicine
Cairo University
٢٠١٥

ABSTRACT

Key words : Type I diabetes mellitus , diabetic nephropathy, Erythropoietin.

The effect of erythropoietin hormone in STZ-induced diabetic nephropathy was evaluated in this study with comparing this effect with insulin treatment. ١١٠ albino rats were randomized into ١١ groups. Type I DM was induced by STZ injection at day ٠ followed by serial measurements of serum glucose , insulin, urea , creatinine, urinary albumin and creatinine clearance levels in all groups. Type I DM was confirmed at week ١ by elevated serum glucose and reduced serum insulin. The diabetic nephropathy was indentified at week ٣ by the elevation in serum urea and creatinine levels with reduced creatinine clearance and the presence of albuminuria. Erythropoietin was given by the dose of I٠٠ IU/kg intraperitoneally starting at day ٠ , week ١ and ٣. Insulin was injected subcutaneously (S .C.) at a dose of ٢U/day starting at day ٠ , week ١ and ٣. Epo treated animals showed improved renal functions in the form of reduced serum urea , creatinine and urinary albumin levels as well as increased creatinine clearance values. Kindey tissues from Epo groups showed a reduction in MDA level and an increase in GTH indicating the anti-oxidant effect. BAX levels also showed a significant reduction with elevation in BCL-٢ levels in these animals confirming the anti-apoptotic effect of Epo in diabetic nephropathy. Similarly, IL-٦ reduction and IL-١٠ elevation suggested the anti-inflammatory effect of Epo. Both VEGF and TGF-β levels were significantly reduced with Epo treatment indicating the anti-angiogenic and the anti-fibrogenic effects of Epo respectively. Animals treated with insulin showed also improved renal functions, while

when both treatments were given together the preservation of renal functions was more evident than in the case of using each one of them separately. Histological examination revealed preservation of renal architecture in combined Epo and insulin treatment more than Epo or insulin separately. In addition to the protective effect on the kidney, Epo showed also a protective effect against type I DM suggested by the improvement in glycemic control in Epo treated animals.