

## Study the effects of metformin on renal function and structure after unilateral ischemia-reperfusion in rat

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**Background and Aims:** Metformin is the first-line drug of choice for the treatment of type 2 diabetes. There is evidence that metformin with activation of adenosine monophosphate-activated protein kinase (AMPK) and endothelial nitric oxide synthase have tissue protective effects. Renal ischemia and reperfusion (I/R) injury is the major cause of acute renal failure and may also be involved in the development of some forms of chronic kidney disease. Thus, we investigated whether metformin administration prevents the functional and structural damage induced by I/R.

**Methods:** Five groups of Spargu-Dawley male rats were studied: sham-operated animals, rats that underwent 45 min of ischemia and 3 hrs of reperfusion, and three groups that received metformin as 25, 50 or 100 mg/kg oral prescription (O.P) 7 days before I/R, respectively. Following anesthesia a mid-line abdominal incision was performed and left renal pedicle clamped for 45 min (ischemic phase), after which the clip was removed to start the reperfusion phase which lasted for 3 hrs then kidney was removed.

**Results:** Histopathological findings showed normal appearance in sham group. In kidneys from I/R group animals, histological examination revealed severe renal damage including infiltration of neutrophils, formation of protein casts, dilatation of Bowman's capsule and necrosis of podocytes. In this study Metformin provided some renal protection against I/R induced injury. Despite the histopathologically protective effect of metformin, biochemical results (elevation of BUN, serum creatinine and reduction in the level of blood proteins) showed no difference as compared to I/R group. It can be explained by hypoxia and decrease in renal blood flow through the reduction of cardiac output induced by lactic acidosis side effect of metformin.

**Conclusions:** In summary and according to other studies we conclude that the protective effects of metformin could be due to inhibition of mitochondrial respiratory chain complex I cause decrease of ATP production that activated AMPK prevent from hypoxia.

**Keywords:** Metformin; Kidney; Ischemia- reperfusion