

당뇨병성 신증에서 Nox 억제 효과에 관한 연구

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The Effect of Nox Inhibitor on Diabetic Kidney Disease

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Introduction: Excess reactive oxygen species generated by NADPH oxidases (Nox) have been implicated in the inflammatory and fibrotic processes in chronic kidney disease. Recent studies have suggested the importance of renal Nox in the progression of diabetic nephropathy. Therefore, we investigated the effect of a novel NOX-inhibitor APX-15 on diabetic nephropathy in experimental model of type 2 diabetic mice.

Methods: 8 to 10 week old db/m and db/db mice were treated with APX-15 for 12 weeks. APX-15 was administered by oral gavage at a dose of 60 mg/kg/day. To compare the effects of APX-15 with other Nox inhibitor, db/db mice were treated with GKT136901 according to same protocol.

Results: Interestingly, APX-15 significantly improved insulin resistance (insulin tolerance test, HOMA-IR) and oxidative stress (plasma 8-isoprostane level) in diabetic mice similar to GKT136901. All lipid profiles, both in plasma and in adipose tissue improved with Nox inhibition. Total cholesterol and triglyceride levels were significantly lower in APX-15 group than in GKT136901 group. Nox mRNA expressions were significantly downregulated in adipose tissue (Nox1, Nox2) and in kidney tissue (Nox4) by APX-15 compared to normal diabetic control. In the kidney, nox1 and 4 protein expressions were also decreased when treated with APX-15, similar to GKT136901. At 12 week of treatment, APX-15 treated group showed significant decrease in urinary albumin excretion compared to diabetic control, whereas GKT136901 group only showed trend toward decrement. Structural changes in the kidney such as mesangial expansion and fibrosis were significantly improved in APX-15 group compared to diabetic control and GSK136901 group. PAI-1 and TGF- β , nephrin expressions in the kidney were all improved in both APX-15 and GKT136901 groups. F4/80 infiltration in the adipose tissue was significantly attenuated with APX-15, not with GKT136901

Conclusion: Our finding suggests that Nox inhibition by APX-15 demonstrated greater renoprotective effects compared to GKT136901 in experimental animal model of diabetic nephropathy.

Key Words: 당뇨병성 신증, Nox 억제제, APX-15
 Diabetic nephropathy, Nox inhibitor, APX-15