

Db/Db 마우스에서 당뇨병성 신증에 대한 항 VEGF 펩타이드 dRK6의 효과

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Different Effects of Arginine-rich Anti-VEGF Hexapeptide, dRK6 on the Diabetic Nephropathy in db/db Mice according to the Stage of Diabetic Nephropathy

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VEGF has been implicated in the pathogenesis of diabetic nephropathy (DN). The several models of diabetes have shown that VEGF and VEGF receptors are increased in the early DN. Recently, however, VEGF blockade may have beneficial effects on DN under dispute. It was recently identified that arginine-rich hexapeptide, dRK6 could bind to the VEGF and thereby block the interaction between VEGF and VEGFR. We examined the renal effects of dRK6 in the diabetic db/db mouse, a model of obese type 2 diabetes, according to the progression of DN.

As control groups, nondiabetic db/m and diabetic db/db mice (n=6, respectively) were used. As treatment groups, db/db mice were divided into whole, early, and late treatment group (n=8, respectively). Whole treatment group were treated with dRK6 for 12 wks of whole study period from 7 wks of age, Early treatment group were treated for the first 4 weeks and late treatment group were treated for the last 4 weeks. All treatment groups received SC injection of dRK6 three times per week. Fasting blood glucose and hemoglobin A1c levels in whole treatment group were higher than those of any other groups from 8 weeks of the study ($p<0.05$). The level of 24-hour urine albumin excretion in whole treatment group was higher than those of any other groups at 8 weeks of the study ($p<0.05$) and Interestingly, the level in late treatment group was lower than those of any other db/db groups at 12 weeks ($p<0.05$). Renal histology studies further demonstrated that glomerular hypertrophy, mesangial matrix expansion, type IV collagen accumulation, F4/80 positive macrophage infiltration, and the expression of 8-OHdG were more prominent in whole treatment group than those of any other groups and less prominent in late treatment group than those of any other db/db groups. Whole treatment group showed weaker nephrin expression and late treatment groups showed more nephrin expression than that of any other db/db groups

Taken together, VEGF seems to be strongly associated with the progression of diabetic nephropathy. Therefore, earlier blockade of VEGF has no beneficial effect on DN. An earlier and prolong VEGF blockade in DN seems to be even more harmful. The VEGF blockade after established DN seems like having a beneficial effect. Our results suggest that the blockade of VEGF using dRK6 could provide different therapeutic effects according to the stage of DN resulting from type 2 diabetes.