

제2형 당뇨병 모델인 db/db mice에서 Fibroblast Growth Factor 21의 투여가 당뇨병성 신증의 진행에 미치는 영향

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The Effects of Fibroblast Growth Factor 21 on db/db Mouse Model of Type 2 Diabetic Nephropathy

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Aims: Fibroblast growth factor 21 (FGF21) is an emerging metabolic hormone assumed to have an important role in regulating energy balance. FGF21 is predominantly produced by the liver and, to some extent, white adipose tissue and exerts adaptive starvation response by inducing gluconeogenesis, fatty acid oxidation, and ketogenesis. In addition, transgenic overexpression of FGF21 improves insulin sensitivity, glucose tolerance, and lipid profiles in obese animal model. However, there has been no study exploring its effects on renal changes in diabetic milieu. Therefore, we tested the effects of exogenous FGF21 administration on db/db mouse model of type 2 diabetic nephropathy.

Methods: db/db mice or lean normal mice were injected with FGF21 intraperitoneally once daily for 12 weeks from the age of 8 weeks and compared to control db/db mice or control lean normal mice with vehicle treatment, respectively.

Results: At 20 weeks of age, FGF21-treated db/db mice, compared to control db/db mice, showed significantly improved lipid profiles and insulin tolerance test results. In addition, serum adiponectin level was significantly higher, whereas serum insulin level, serum and urine isoprostane levels, and the homeostatic model assessment (HOMA) index were significantly lower in the FGF-treated db/db mice than control db/db mice. Furthermore, FGF21 administration significantly reduced both mesangial expansion and expression of fibrotic markers, such as TGF- β , collagen-IV, and plasminogen activator inhibitor-1 in renal pathology as well as urinary albumin excretion, whereas such differences were not observed in lean normal mice irrespective of FGF21 treatment.

Conclusion: These results suggest that FGF21 is a potential candidate for therapeutic strategy for obesity-related diabetic nephropathy.

Key Words: FGF21, 당뇨병성 신증, 제2형 당뇨병
 FGF21, Diabetic nephropathy, Type 2 diabetes mellitus