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Glycogen Synthase Kinase-3 이 당뇨 조건 하의 족세포 사멸에 미치는 영향

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The Role of Glycogen Synthase Kinase-3 in Podocyte Apoptosis Under Diabetic Conditions

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Background: Glycogen synthase kinase-3β (GSK-3β) is involved in the pathogenesis of various kidney diseases. This study was undertaken to examine the changes in GSK-3β activity in podocytes under diabetic conditions and to elucidate the functional role of GSK-3β in podocyte apoptosis, a characteristic finding in diabetic nephropathy.

Methods: In vivo, thirty-two rats were injected with either diluent (n=16, C) or with streptozotocin intraperitoneally (n=16, DM), and 8 rats from each group were treated daily with 0.2 mg/kg 6-bromoindirubin-3'-oxime (BIO) by subcutaneous injection for 3 months. In vitro, immortalized mouse podocytes were cultured in media containing 5.6 mM glucose (NG) or 30 mM glucose (HG) with or without 10 μM BIO. Western blot using sieved glomeruli and cultured podocytes, and TUNEL or Hoechst 33342 staining were performed to identify apoptosis.

Results: Urinary albumin excretion was significantly higher in DM rats ($p<0.01$), and this increase was significantly abrogated in DM rats by BIO treatment ($p<0.05$). The protein expression of phospho-GSK-3β was significantly lower in DM glomeruli and in cultured podocytes exposed to HG, indicating that GSK-3β activity was significantly decreased in podocytes under diabetic conditions. Western blot analysis revealed that the protein expression of Bax and active fragments of caspase-3 were significantly increased, whereas Bcl-2 protein expression was significantly decreased in DM glomeruli and HG-stimulated podocytes. Apoptosis determined by TUNEL assay and Hoechst 33342 staining were also significantly increased in podocytes under diabetic conditions. The changes in the expression of apoptosis-related molecules and the increase in the number of apoptotic cells in DM glomeruli as well as in HG-stimulated podocytes were significantly ameliorated by BIO.

Conclusions: These findings suggest that enhanced GSK-3β activity within podocytes under diabetic conditions is associated with podocyte loss in diabetic nephropathy.

Key Words: GSK-3β, 당뇨병성 신증, 족세포
GSK-3β, Diabetic nephropathy, Podocyte