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Metformin Decreases High-fat Diet-induced Renal Injury Through a Regulation of the Expression of Adipokine and Renal AMP-activated Kinase in Mice

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Background: Obesity is one of major health problems, which is related to the metabolic syndrome. The metabolic syndrome is characterized by insulin resistance, dyslipidemia and hypertension. These metabolic changes contribute to the development of obesity-induced kidney injury. AMP-activated kinase (AMPK) is a ubiquitous enzyme that is involved in the cellular metabolic response to metabolic stress. Metformin, as an AMPK activator, had been reported to have protective effect on non-alcoholic steatohepatitis. But, little is known about its role in the pathogenesis of obesity-induced renal injury. The purpose of this study is to investigate the effect of AMPK activator, metformin, on the high-fat diet (HFD) induced kidney injury.

Methods: Obesity was induced by HFD (60% of total calories from fat, 20% protein, 20% carbohydrate) in the six-week-old C57BL/6 mice. Mice were treated with 0.5% metformin-containing HFD. The effect of metformin on HFD-induced renal injury was evaluated by metabolic parameters, histologic examination, serum adipokine levels, renal AMPK and TGF-β1 expression.

Results: HFD induced dyslipidemia, systemic insulin resistance, and increased the expression of proinflammatory adipokines, urinary albumin excretion as well as mesangial matrix expansion. Following the treatment with metformin, there was an improvement in not only insulin resistance, inflammation and metabolic derangement but also HFD-induced mesangial expansion and microalbuminuria. Moreover, there was a recovery in the HFD-induced decrease in the activity of renal AMPK and increase of TGF-β1 level following the treatment with metformin.

Conclusion: These results indicate that HFD induces obesity-related kidney injury and treatment of pharmacologic AMPK activator, metformin, reduces not only obesity-induced metabolic changes such as insulin resistance, lipid abnormalities but also obesity-induced kidney injury.

Key Words: 비만, 신장손상, 인슐린저항성, Adipokine, AMP
Obesity, Renal Injury, Insulin resistance, Adipokine, AMPK