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Therapeutic Effects of GLP-1 Agonist in Gentamicin-Induced Kidney Injury in Rats

Joon Seok Choi[1], Chang Seong Kim[1], Jeong Woo Park[1]
Eun Hui Bae[1], Seong Kwon Ma[1], JongUn Lee[2], Soo Wan Kim[1]

Department of Internal Medicine[1] Chonnam National University Medical School
Department of Physiology[2] Chonnam National University Medical School

Background: Glucagon-like peptide-1 (GLP-1) has various extra-pancreatic actions. Although the kidney also has GLP-1 receptors, a role GLP-1 in aminoglycoside-induced nephropathy has not been examined. We investigated effect of exendin-4 in gentamicin (GM)-induced nephropathy in rats.

Methods: Two groups of rats were treated with GM (100 mg/kg/day), one of which was cotreated with exendin-4 (5 μg/kg/day) for 14 days and the other was not. The control group was treated with vehicle only. We evaluated renal function and the expression of inflammatory cytokines and adhesion molecules. In another series of experiment, effects of exendin-4 were determined in human proximal tubular cells (HK-2 cells) cultured in the presence of GM.

Results: Fasting blood glucose levels, blood pressure, creatinine clearance and albuminuria were not affected by exendin-4 in GM-treated rats. There was an upregulation of inflammatory cytokines such as IL-1β, IFN-r and TNF-α, which was prevented by exendin-4. Exendin-4 also effectively reversed the increases of ICAM-1, VCAM-1and MCP-1 mRNA expression in GM-treated rats. The expression of ED-1 and i-NOS was increased by GM, of which magnitude was attenuated by exendin-4. Exendin-4 treatment attenuated the expression of phosphorylated ERK1/2.

Conclusion: Exendin-4 has reno-protective effects through its anti-inflammatory actions.

Key Words: GLP-1 agonist, 염증반응, 겐타마이신
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