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Bilirubin Ameliorate Kidney Fibrosis Through Regulation of Hypoxia-inducible Factor Pathway

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Purpose: Bilirubin is a protective factor with antioxidant and anti-inflammatory properties to inhibit the scavenge oxygen radicals, and counteract oxidative stress. Here, we evaluated that direct administration of bilirubin could attenuate kidney fibrosis.

Methods: Bilirubin was daily pretreated by intraperitoneal administration for a week (30 mg/kg/day). Unilateral ureteral obstruction (UUO) was used as a model of kidney fibrosis in C57BL/6 mice. Bilirubin was persistently treated with same dose for a week more. We analyzed the histological findings and mRNA expression in a 7-day UUO mouse.

Results: Serum bilirubin level significantly increased in bilirubin-treated group compared with vehicle-treated group (0.62±0.08 vs. 0.11±0.01 mg/dl, $p<0.01$). Bilirubin-treatment significantly improved tubulointerstital fibrosis and infiltration of inflammatory cells. Fibroblast specific protein 1 and transforming growth factor β expressions were also significantly decreased by bilirubin treatment ($p<0.001$). In addition, expressions of hypoxia-inducible factor 1α and vascular endothelial growth factor were up-regulated significantly ($p<0.01$).

Conclusion: Bilirubin treatment could improve kidney fibrosis by regulation of hypoxia-inducible factor 1α pathway.

Key Words: 빌리루빈, 신섬유화, HIF1α
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