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## Glucagon-like peptide-1 receptor agonist improves kidney structure and function in chronic kidney disease

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**Objectives :** Glucagon-like peptide-1 (GLP-1) is one of the incretin hormones involved in blood sugar control by promoting insulin secretion and suppressing glucagon secretion in response to food intake. GLP-1 receptor agonist (GLP-1 RA) is a drug designed to have a sustained effect on the body and has recently been in the spotlight as a treatment for diabetes. However, the renal effects and mechanisms of GLP-1 receptor agonists (GLP-1 RAs) in chronic kidney disease (CKD) are unclear. Therefore, we sought to determine the renoprotective effects and mechanisms of GLP-1 RA in CKD.

**Methods :** We used immunofluorescence staining to determine GLP-1 receptor (GLP-1R) expression in kidney tissue of humans, rats, and mice. A non-diabetic CKD rat model was induced with a 0.2% adenine diet, and exendin-4 (10 µg/kg) or saline was intraperitoneally administered daily for 6 weeks to confirm the renoprotective effect of GLP-1 RA exendin-4 in CKD. In vitro studies were performed in HK-2 cells treated with TGF-β1 (10 ng/ml) with or without exendin-4 (1 µM).

**Results :** We found that GLP-1Rs are expressed in the proximal tubules and blood vessel walls of humans, rats, and mice kidneys. In CKD, GLP-1Rs are significantly reduced. In animal studies, exendin-4 improved BUN and cystatin C levels and reduced kidney damage and extracellular matrix accumulation (ECM). In vitro, exendin-4 reduced ECM accumulation and increased GLP-1R expression in HK-2 cells stimulated with TGF-β1. Additionally, exendin-4 restored LAMP1, lysosome-associated membrane protein 1, and reduced the autophagosome marker LC3 in a CKD rat model. In vitro, exendin-4 improved lysosomal function. Additionally, exendin-4 reduced lipid droplet accumulation and aldosterone levels in kidney tissue.

**Conclusions :** Our result showed that exendin-4 improved kidney function and structure in CKD. In addition, exendin-4 restored lysosome function, lipid droplet accumulation, and aldosterone levels. Therefore, it suggests that exendin-4 could be used as an effective therapeutic drug for CKD.