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Synergistic Effects of Alirocumab and Atorvastatin in Adenine Induced Non-Dialysis CKD: Modulating PCSK9 and Statin Activity for Renal and Cardiovascular Protection

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Objectives : Non-dialysis chronic kidney disease (ND-CKD) is a progressive condition marked by declining kidney function before reaching end-stage renal disease (ESRD) that requires dialysis. It is primarily associated with diabetes, hypertension, polycystic kidney disease, cardiovascular disorders, obesity, nephrotoxic drugs, and obstructive uropathy. Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors and statins play critical roles in managing diabetes-related cardiovascular complications. This study investigates the synergistic effects of alirocumab and atorvastatin in mitigating adenine induced ND-CKD by modulating PCSK9 expression and statin activity, with the goal of improving renal and cardiovascular health
Methods : An ND-CKD rat model was established using adenine (60 mg/kg) and a high-fat diet. Co-administration of PCSK9 (10 mg/kg/day) and statin (20 mg/kg/day) demonstrated significant therapeutic potential. Key parameters assessed included PCSK9 inhibition, statin activity, lipid metabolism, insulin resistance (HOMA-IR, HOMA-S), oxidative stress markers (AMPK, PPARα, SOD, CAT, GSH), and proinflammatory cytokines (IL-6, TNF-α, adiponectin). Kidney function was evaluated using serum creatinine, albumin-to-creatinine ratio, serum cystatin C, blood urea nitrogen (BUN), and γ-GT levels, while histological analysis confirmed renal tissue integrity.
Results : The treatment significantly suppressed PCSK9 and HMG-CoA reductase activity, reducing PCSK9 levels by 43.4±3.2% and significantly ($P < 0.05$) lowering HMG-CoA reductase levels. Lipid metabolism improved, with triglycerides (TG) decreasing by 36%, VLDL dropping by 22%, and HDL levels increasing. Additionally, inflammatory markers (IL-6, TNF-α) were reduced, antioxidant capacity improved, and kidney function was preserved, as evidenced by lower serum creatinine, albumin-to-creatinine ratio, serum cystatin C, and BUN levels
Conclusions : PCSK9 inhibition and statin therapy improved renal and cardiovascular health in ND-CKD by reducing inflammation, enhancing lipid metabolism, antioxidant activity, and insulin sensitivity, suggesting a promising therapeutic strategy for further clinical investigation.