EFFICACY OF LIPID-LOWERING THERAPY IN COMBINATION WITH EZETIMIBE IN PATIENTS WITH CORONARY HEART DISEASE AND RENAL DYSFUNCTION

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Abstract: Coronary heart disease (CHD) remains a leading cause of morbidity and mortality worldwide, especially in patients with comorbid renal dysfunction. Dyslipidemia is a major modifiable risk factor in both conditions, and effective lipid-lowering therapy is essential to reduce cardiovascular events. This article reviews the clinical efficacy and safety of combination therapy using statins and ezetimibe in patients with CHD and impaired renal function. The article discusses the pharmacological rationale, current evidence from clinical trials, renal-specific lipid targets, and the potential of ezetimibe to optimize lipid control without exacerbating renal impairment. Special attention is given to the impact of combination therapy on LDL-C reduction, inflammation, and long-term cardiovascular outcomes in this high-risk population.

Keywords: ezetimibe, statin, dyslipidemia, coronary heart disease, renal dysfunction, LDL-C, cardiovascular risk.

INTRODUCTION

Patients with coronary heart disease (CHD) and renal dysfunction represent a particularly vulnerable population characterized by accelerated atherosclerosis, systemic inflammation, and high cardiovascular mortality. Chronic kidney disease (CKD), even in its early stages, is associated with lipid abnormalities such as elevated triglycerides, reduced high-density lipoprotein cholesterol (HDL-C), and the presence of small dense low-density lipoprotein cholesterol (LDL-C) particles, all of which contribute to vascular damage.

Statins are the mainstay of lipid-lowering therapy in CHD, proven to reduce LDL-C and cardiovascular events. However, their efficacy may be limited in patients with renal impairment due to altered drug metabolism and increased risk of adverse effects, including myopathy and hepatotoxicity. In this context, ezetimibe—a cholesterol absorption inhibitor—has emerged as a valuable adjunctive agent that enhances LDL-C reduction when combined with statins without significantly increasing side effects or systemic drug load [1].

MATERIALS AND METHODS

In patients with CKD, lipid metabolism is significantly altered. The reduction in lipoprotein lipase activity, increased levels of apoC-III, and impaired HDL maturation contribute to an atherogenic profile. Furthermore, oxidative stress and endothelial dysfunction, common in CKD, potentiate the deleterious effects of dyslipidemia. Therefore, standard lipid targets in the general population may not suffice for patients with renal impairment. Guidelines now advocate more aggressive LDL-C reduction in these patients [2].

Statins inhibit HMG-CoA reductase, the rate-limiting enzyme in cholesterol synthesis, thereby reducing intrahepatic cholesterol levels and upregulating LDL receptors. However, high doses of statins may not be well tolerated in CKD patients. Ezetimibe complements statins by blocking the Niemann-Pick C1-Like 1 (NPC1L1) transporter in the small intestine, inhibiting dietary and biliary cholesterol absorption. The dual mechanism—reduction of endogenous synthesis and exogenous absorption—results in enhanced LDL-C reduction with lower statin doses.

RESULTS AND DISCUSSION

Patients with renal dysfunction often present with altered pharmacokinetics, which affects drug clearance and tolerability. Statins such as atorvastatin and fluvastatin are preferred in CKD due to their hepatic clearance. Ezetimibe, largely metabolized in the intestinal wall and liver, does not require dose adjustment in CKD and has minimal systemic exposure, making it well-suited for combination therapy [3].

Moreover, statin monotherapy may be insufficient in CKD due to a diminished LDL receptor response and altered cholesterol handling. The addition of ezetimibe bypasses these limitations, enabling LDL-C targets to be achieved without escalating statin dosage.

The safety profile of ezetimibe is favorable. It does not significantly elevate liver enzymes or creatine kinase levels, and adverse effects such as gastrointestinal discomfort or fatigue are generally mild and transient. Importantly, the combination therapy has not been associated with worsening renal function or increased proteinuria in clinical trials, even with long-term use.

In contrast, high-dose statin therapy alone can increase the risk of myopathy and rhabdomyolysis, especially in patients with reduced glomerular filtration rate (GFR). Using ezetimibe allows for lower statin dosages, thus improving safety without compromising efficacy.

Recent evidence suggests that ezetimibe may exert modest anti-inflammatory effects, as indicated by reductions in C-reactive protein (CRP) levels when used in combination therapy. Given the inflammatory milieu of CKD and CHD, this property adds to the therapeutic value of ezetimibe.

Additionally, by improving lipid parameters, combination therapy may have indirect benefits on endothelial function, plaque stabilization, and slowing of atherosclerosis progression—all of which are critical in renally impaired CHD patients [4].

CONCLUSION

The combination of statins with ezetimibe represents an effective and well-tolerated strategy for lipid management in patients with coronary heart disease and renal dysfunction. It allows for enhanced LDL-C lowering, improved cardiovascular outcomes, and reduced statin-related toxicity. Clinical guidelines increasingly recommend this approach, especially in high-risk populations where monotherapy may fall short of lipid targets.

As the burden of comorbid CHD and CKD continues to rise globally, individualized lipid-lowering strategies that include ezetimibe will be essential in optimizing care. Future research should continue to explore the long-term renal and cardiovascular outcomes of such combination therapy, particularly in advanced CKD and dialysis populations.

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