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THE ROLE OF PCSK9 INHIBITORS IN HYPERLIPIDEMIA AND CARDIOVASCULAR DISEASES

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Abstract

Atherosclerotic cardiovascular diseases remain the leading cause of mortality worldwide and represent a major global health burden. Low-density lipoprotein cholesterol plays a central role in the pathogenesis of atherosclerosis. Although statins have long been the cornerstone of lipid-lowering therapy, a considerable number of patients either do not achieve target lipid levels or develop intolerance. These limitations have stimulated the development of novel pharmacological approaches, among which PCSK9 inhibitors have emerged as one of the most promising strategies. This article analyzes the clinical efficacy, pharmacological mechanisms, and practical significance of PCSK9 inhibitors in the management of hyperlipidemia and prevention of cardiovascular diseases, with special attention to patients with hepatic dysfunction.

Keywords

PCSK9 inhibitors, hyperlipidemia, cardiovascular diseases, LDL cholesterol, atherosclerosis, statins, liver dysfunction, lipid-lowering therapy.

Introduction

Atherosclerotic cardiovascular diseases continue to be among the most significant causes of morbidity and mortality worldwide. Elevated levels of low-density lipoprotein cholesterol are directly associated with the progression of atherosclerosis and subsequent cardiovascular complications. Statins have historically been the main therapeutic option for reducing LDL cholesterol levels; however, some patients experience inadequate lipid control or intolerance to statin therapy. Consequently, the development of alternative lipid-lowering therapies has become an important area of modern cardiology and pharmacology.

PCSK9 inhibitors have recently gained attention as innovative biological agents capable of significantly lowering circulating LDL cholesterol levels. Their mechanism of action differs fundamentally from that of statins and offers additional therapeutic opportunities, especially in patients with hepatic disorders or familial hypercholesterolemia.

Materials and Methods

This article is based on an extensive review of international clinical studies, evidence-based medical literature, and meta-analyses related to PCSK9 inhibitors. Comparative evaluation of statins and PCSK9 inhibitors was performed with emphasis on pharmacodynamics, pharmacokinetics, mechanisms of action, clinical efficacy, and safety profiles. Relevant European and American guidelines and clinical trial results were systematically analyzed.

Results and Discussion

PCSK9 inhibitors are monoclonal antibodies directed against the proprotein convertase subtilisin/kexin type 9 enzyme, which regulates LDL receptor degradation in hepatocytes. Under physiological conditions, PCSK9 binds to LDL receptors and promotes their lysosomal destruction, thereby reducing receptor availability on hepatocyte surfaces and increasing plasma LDL cholesterol levels.

By inhibiting this interaction, PCSK9 inhibitors increase LDL receptor recycling and enhance hepatic uptake of circulating LDL cholesterol. Clinical studies have demonstrated that these agents can reduce LDL cholesterol concentrations by approximately 60–70%, significantly decreasing cardiovascular risk and slowing atherosclerotic progression. In certain cases, regression of established atherosclerotic plaques has also been observed.

Unlike statins, which undergo metabolism through cytochrome P450 pathways in the liver, PCSK9 inhibitors are degraded primarily through proteolytic pathways and exhibit minimal hepatic metabolism. Their prolonged half-life of approximately 11–17 days allows administration once every two to four weeks, improving treatment adherence.

Patients with hepatic disorders, including hepatic steatosis and early-stage cirrhosis, may particularly benefit from PCSK9 inhibitors because these drugs demonstrate minimal hepatotoxicity and limited drug-drug interactions. Nevertheless, several limitations remain, including high treatment cost and local injection-site reactions.

Conclusion

PCSK9 inhibitors represent an important advancement in contemporary lipid-lowering therapy and provide an effective therapeutic option for patients who are intolerant to statins or fail to achieve adequate lipid control with conventional treatment. Their unique pharmacokinetic properties make them especially valuable in patients with liver dysfunction. Wider integration of PCSK9 inhibitors into clinical practice may contribute substantially to reducing cardiovascular morbidity and mortality worldwide. Future studies and strategies aimed at reducing treatment costs are necessary to improve accessibility and expand their routine clinical application.

References

1. Sabatine M.S., Giugliano R.P., Keech A.C., et al. Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease. New England Journal of Medicine. 2017;376(18):1713–1722.
2. Schwartz G.G., Steg P.G., Szarek M., et al. Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome. New England Journal of Medicine. 2018;379(22):2097–2107.
3. Ference B.A., Ginsberg H.N., Graham I., et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease. European Heart Journal. 2017;38(32):2459–2472.
4. Mach F., Baigent C., Catapano A.L., et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias. European Heart Journal. 2020;41(1):111–188.
5. Grundy S.M., Stone N.J., Bailey A.L., et al. 2018 AHA/ACC Guideline on the Management of Blood Cholesterol. Circulation. 2019;139:e1082–e1143.
6. Rosenson R.S., Hegele R.A., Fazio S. The Evolving Future of PCSK9 Inhibitors. Journal of the American College of Cardiology. 2018;72(3):314–329.
7. Stoekenbroek R.M., Kastelein J.J.P., Huijgen R. PCSK9 inhibition: the way forward in the treatment of dyslipidemia. BMC Medicine. 2015;13:258.
8. Seidah N.G., Awan Z., Chretien M., Mbikay M. PCSK9: A key modulator of cardiovascular health. Circulation Research. 2014;114(6):1022–1036.
9. Giugliano R.P., Pedersen T.R., Park J.G., et al. Clinical efficacy and safety of achieving very low LDL-cholesterol concentrations with evolocumab. Lancet. 2017;390(10106):1962–1971.
10. Goldberg A.C., Leiter L.A., Stroes E.S., et al. Effect of Alirocumab on Lipids and Cardiovascular Events. The Lancet. 2015;385(9965):331–340.