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THE ROLE OF PCSK9 INHIBITORS IN HYPERLIPIDEMIA AND CARDIOVASCULAR DISEASES

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Abstract

This article examines the role of a new generation of drugs—PCSK9 inhibitors (Evolocumab, Alirocumab)—in the treatment of hyperlipidemia. In particular, their advantages over statins in patients with liver diseases are analyzed from pharmacokinetic and pharmacodynamic perspectives. Research findings indicate that PCSK9 inhibitors significantly reduce levels of LDL (low-density lipoproteins) cholesterol without causing damage to liver enzymes.

Keywords: PCSK9 inhibitors, hyperlipidemia, cardiovascular disease, statins, liver, pharmacokinetics, pharmacodynamics

Introduction

Atherosclerotic cardiovascular diseases (ASCVD) remain the leading cause of mortality worldwide. For many years, statins have been the primary drugs used to lower lipid levels. However, in many patients—especially those with impaired liver function or statin resistance—there has been a need for new therapeutic approaches. PCSK9 (Proprotein convertase subtilisin/kexin type 9) inhibitors have become a revolutionary advancement in this field.

Pharmacodynamics: Mechanism of Action

The primary function of PCSK9 inhibitors is to protect LDL receptors from degradation. Under normal conditions, the PCSK9 protein binds to LDL receptors on the surface of liver cells and leads to their breakdown (lysosomal degradation). As a result, the number of receptors responsible for reducing cholesterol levels in the blood decreases.

PCSK9 inhibitors (monoclonal antibodies) block these proteins in the bloodstream. This leads to:

• An increase in the number of LDL receptors on the surface of liver cells;
• A reduction of low-density lipoprotein cholesterol (LDL-C) levels in blood plasma by up to 50–70%;
• A decrease in the formation of atherosclerotic plaques and their regression.

Pharmacokinetics

Parameter	Statins (oral)	PCSK9 Inhibitors (injection)
Metabolism	Liver (via CYP450 system)	Proteolysis (protein degradation)
Half-life	Short (2–20 hours)	Long (11–17 days)
Administration	Daily, oral tablet	Every 2–4 weeks, injection

Advantages for Patients with Liver Diseases

In patients with liver pathologies (such as hepatitis, steatosis, and early-stage cirrhosis), the use of statins often leads to an increase in liver enzymes (ALT/AST). The advantages of PCSK9 inhibitors in this regard include:

1. **Lack of hepatotoxicity:** They are not metabolized through liver enzymes (Cytochrome P450 system), therefore they do not place additional burden on liver cells.
2. **No drug–drug interactions:** Patients with liver disease often take multiple medications (polypharmacy). PCSK9 inhibitors do not interfere with the metabolism of other drugs.
3. **No need for dose adjustment:** In patients with mild to moderate hepatic impairment, dose adjustment is not required.

Disadvantages and Side Effects

Like any medication, PCSK9 inhibitors also have certain drawbacks:

- Local injection site reactions (redness, swelling);
- High cost (significantly more expensive compared to statins);

Conclusion

In conclusion, PCSK9 inhibitors are opening a new era in the treatment of hyperlipidemia. From a pharmacokinetic perspective, since they are independent of liver metabolism, they are considered one of the safest and most effective options for patients with liver diseases. In the future, as the cost of these drugs decreases, they are likely to become as widely used in cardiology practice as statins. Therefore, integrating these medications into the healthcare system of Uzbekistan could significantly improve the effectiveness of cardiovascular disease treatment.

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