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THE ROLE OF miRNAs INHIBITORS IN THE TREATMENT OF METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

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Abstract. Metabolic dysfunction-associated steatotic liver disease (MASLD) occupies a leading place in modern hepatology. A growing body of literature identifies MASLD as a global epidemic. Accumulated data from hepatology studies support the view that MASLD represents a hepatic manifestation of a systemic metabolic disease. In recent years, there has been increasing interest among researchers in elucidating the role of epigenetic modifications in the treatment of MASLD. In contrast to traditional therapies, drugs targeting epigenetic-modifying enzymes, such as micro ribonucleic acid (miRNA) inhibitors, have been developed with a focus on gene regulation.

Objective: To explore the role of miRNA inhibitors in the treatment of MASLD.

Materials and methods. PubMed, Scopus, and the Cochrane Library databases were searched to identify all reports related to the use of miRNA inhibitors in the treatment of MASLD. The following search terms were included: “metabolic dysfunction-associated steatotic liver disease”, “metabolic dysfunction-associated

steatohepatitis", "epigenetic", "epigenetic-modifying enzymes", "miRNA inhibitors".

Results. Over recent decades, extensive experimental evidence has indicated that suppression of specific miRNAs can modulate the progression of MASLD. Experimental studies have shown that antagonism of miRNA-34a leads to a marked restoration of mitochondrial membrane potential, enhancement of mitochondrial function, and attenuation of hepatic lipid accumulation in murine models of MASLD [1]. Meta-analytical data further demonstrate that therapeutic intervention with miRNA-34a antagonists results in a significant reduction of hepatic triglycerides (TG), total cholesterol (TC), alanine aminotransferase (ALT), and aspartate aminotransferase (AST). These findings support the concept that endogenous miRNA-34a exerts a pathogenic effect in MASLD and metabolic dysfunction-associated steatohepatitis (MASH). Mechanistically, miRNA-34a inhibition promotes fatty acid oxidation, suppresses hepatocellular steatosis, decreases reactive oxygen species production in hepatocytes, and downregulates the expression of profibrogenic genes [2].

Studies employing complementary animal models of MASH have demonstrated that genetic or pharmacological ablation of miRNA-21 markedly alleviates hepatic steatosis, inflammatory responses, and fibrotic changes [3]. In line with these observations, administration of miRNA-21 antagonists to MASLD mice was associated with reduced serum levels of triglycerides, total cholesterol, low-density lipoproteins, and hepatic transaminases. Concurrently, the expression of genes involved in de novo lipogenesis was significantly suppressed, indicating that inhibition of miRNA-21 can mitigate lipid accumulation and inflammation during the transition from MASLD to MASH [4].

Additional experimental evidence indicates that treatment of MASLD mice with miRNA-103a-3p inhibitors leads to a significant decline in circulating TG, TC, ALT, and AST concentrations [5]. Moreover, blockade of miRNA-103-3p attenuates lipid droplet deposition, inflammatory signaling, dysregulated lipid metabolism, and oxidative stress in hepatic tissue. Collectively, these findings suggest that targeting miRNA-103-3p may represent a promising therapeutic approach for MASLD management.

Conclusions. Despite the promising therapeutic potential of miRNA inhibitors, evidence supporting the efficacy of individual miRNA-based interventions in MASLD and MASH remains limited. Well-designed and rigorously controlled preclinical studies evaluating miRNA inhibitor-based therapies are therefore essential to facilitate the translation of miRNA-targeted strategies into effective treatments for patients with MASLD and MASH.

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ДИНАМІКА ДОСТУПНОСТІ СТОМАТОЛОГІЧНОЇ ДОПОМОГИ В УКРАЇНІ ПРОТЯГОМ 2013-2021 РОКІВ

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Серед усіх хвороб найбільш поширеними в світі вважаються хвороби ротової порожнини. Так у 2021 р. стандартизована за віком поширеність основних захворювань ротової порожнини (нелікований карієс, тяжкий пародонтит, беззубість та ін.) становила 45900 випадків на 100000 населення, при цьому у світі цим захворюванням страждало 3,69 млрд. людей [1, с. 897]. Стоматологічне здоров'я населення значною мірою залежить від доступності стоматологічної допомоги, яку, в свою чергу, характеризує відвідуваність населенням лікарів-стоматологів. Метою дослідження було вивчення відвідуваності населенням лікарів-стоматологів протягом у 2013 та 2021 роках за даними вибіркового соціологічного опитування домогосподарств (суб'єктивна оцінка населення), що регулярно проводиться Державною службою статистики України та поширюється на всі домогосподарства України за допомогою процедури статистичного зважування [2, с. 15-93; 3, с. 12-93, 127].

З огляду на значні рівні поширеності хвороб порожнини рота частота відвідувань до лікарів-стоматологів мала б бути найвищою, однак вона вища до