Internal Medicine

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THE ROLE OF HISTONE DEACETYLASE INHIBITORS IN THE TREATMENT OF METABOLIC DYSFUNCTION ASSOCIATED STEATOTIC LIVER DISEASE

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Introduction. In recent years, increasing attention has been directed toward the role of epigenetic modifications in the management of metabolic dysfunction associated steatotic liver disease (MASLD). Given the critical involvement of epigenetic enzymes in regulating inflammatory processes that drive MASLD progression, pharmacological modulation of these pathways represents a promising avenue for the development of novel therapeutic strategies. Unlike conventional treatments, epigenetic-based therapies are designed to influence gene expression through the targeting of chromatinmodifying enzymes. Among these, histone deacetylase (HDAC) inhibitors have attracted particular interest in hepatology due to their antiproliferative effects and their capacity to trigger cell death through modulation of multiple HDAC-dependent substrates. Aim. Elucidating the role of HDAC inhibitors in the treatment of MASLD.

Materials and methods. PubMed, Scopus, and the Cochrane Library databases were searched to identify all reports related to HDAC inhibitors in the treatment of MASLD. The following search terms were included: “histone deacetylases inhibitors”, “histone deacetylases”, “epigenetic-modifying enzymes”, “epigenetic inhibitors”. Key outcomes reported in individual studies included the role of HDAC inhibitors in the treatment of MASLD. Results. Accumulating evidence indicates that HDAC1 and HDAC2, key members of the HDAC family, are implicated in the regulation of hepatocyte apoptosis, highlighting their potential contribution to liver disease pathogenesis. Lei W.W. et al. (2010) demonstrated that HDAC inhibitors such as trichostatin A, sodium butyrate, and MS-275 modulate apoptosis in mouse hepatocytes, leading to reduced cell death and enhanced cell viability. Additionally, sodium valproate, a broad-spectrum class I and II HDAC inhibitor, has been shown to inhibit myofibroblast activation and attenuate fibrogenesis in experimental models of liver fibrosis. Furthermore,

HDAC11 has been reported to be significantly upregulated in both in vitro and in vivo models of MASLD. Targeting this enzyme with a novel hydrazide-based HDAC11 inhibitor was found to suppress de novo lipogenesis while enhancing fatty acid oxidation, thereby reducing hepatic lipid accumulation and improving histopathological features in MASLD models.

Conclusion. Despite the growing interest in HDAC inhibitors as potential therapeutic agents for liver diseases, including MASLD, further research is necessary to evaluate their safety profiles, improve target specificity, and confirm their clinical efficacy in human populations.