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THE ROLE OF ESTROGEN IN HEPATIC LIPID METABOLISM: CLINICAL IMPLICATIONS FOR POSTMENOPAUSAL WOMEN

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Abstract

Estrogen is a major endocrine regulator that contributes to multiple physiological processes, including the control of lipid metabolism within the liver. During menopause, circulating estrogen levels decline markedly, leading to significant metabolic alterations. These changes include increased hepatic fat accumulation, dyslipidemia, and a higher risk of metabolic dysfunction-associated steatotic liver disease. Clinical and epidemiological studies indicate that postmenopausal women experience a greater incidence of hepatic metabolic disorders compared with women of reproductive age. This article examines the biological mechanisms through which estrogen regulates hepatic lipid metabolism and evaluates clinical data regarding the metabolic consequences of estrogen deficiency. In addition, the potential benefits and limitations of hormone replacement therapy are analyzed. Understanding the role of estrogen in hepatic metabolism may support the development of gender-specific strategies aimed at preventing metabolic disorders in aging female populations.

Keywords

Estrogen deficiency, hepatic lipid metabolism, postmenopausal women, hormone replacement therapy, dyslipidemia, non-alcoholic fatty liver disease, estrogen receptors, metabolic syndrome.

Introduction. The liver plays a fundamental role in maintaining systemic metabolic balance. It participates in lipid synthesis, fatty acid oxidation, cholesterol transport, and lipoprotein metabolism. These processes are tightly regulated by hormonal signals originating from different endocrine organs. Among these regulatory hormones, estrogen has received increasing attention because of its influence on lipid metabolism and energy regulation.Menopause is a natural biological stage characterized by the cessation of ovarian function and a sharp

decrease in estrogen production. As estrogen concentrations decline, several metabolic disturbances begin to emerge. These include increased abdominal fat deposition, changes in lipid profiles, insulin resistance, and impaired glucose metabolism. Such metabolic alterations contribute significantly to the increased incidence of cardiovascular disease and liver disorders observed in postmenopausal women.Recent epidemiological evidence suggests that metabolic dysfunction-associated steatotic liver disease has become one of the most common chronic liver conditions worldwide. The prevalence of this disorder appears to increase after menopause, which suggests that estrogen may have protective effects on liver metabolism.The present study aims to examine the regulatory role of estrogen in hepatic lipid metabolism and to analyze the clinical consequences associated with estrogen deficiency in postmenopausal women. Furthermore, the article discusses the potential therapeutic implications of hormone replacement therapy in maintaining metabolic balance.

Scientific Relevance and Research Importance. The metabolic role of estrogen has gained considerable attention in modern biomedical research. Understanding this relationship is essential for several reasons.First, hormonal changes during menopause significantly affect metabolic processes. Estrogen deficiency is associated with redistribution of body fat, particularly increased visceral adiposity. Excess visceral fat promotes the delivery of free fatty acids to the liver, which contributes to hepatic fat accumulation. Second, several clinical studies have demonstrated that the frequency of fatty liver disease is considerably higher in postmenopausal women compared with women who have not yet reached menopause. In a population-based clinical investigation involving more than nine hundred participants, approximately 31–32% of postmenopausal women were diagnosed with hepatic steatosis, whereas the prevalence among premenopausal women remained below 20%. These findings highlight the potential protective role of estrogen in hepatic lipid regulation.Third, experimental studies have shown that estrogen influences the activity of multiple genes involved in lipid metabolism. Therefore, reduced estrogen signaling may disrupt lipid homeostasis and contribute to the development of metabolic disorders affecting the liver.Because metabolic liver diseases are increasing globally, investigating the hormonal mechanisms responsible for these changes is crucial for improving prevention and treatment strategies.

Estrogen Receptor-Mediated Regulation. The biological effects of estrogen are mediated mainly through intracellular estrogen receptors, particularly estrogen receptor alpha (ERα). These receptors are expressed in several metabolic tissues, including the liver. When estrogen binds to these receptors, it initiates signaling

pathways that regulate gene transcription.In hepatocytes, estrogen receptor activation influences genes responsible for lipid synthesis and fatty acid metabolism. Specifically, estrogen suppresses the expression of lipogenic transcription factors such as sterol regulatory element-binding protein-1c. This transcription factor normally promotes the synthesis of fatty acids within liver cells. By inhibiting this pathway, estrogen reduces excessive lipid production.At the same time, estrogen stimulates metabolic pathways involved in fatty acid oxidation. Enhanced oxidation allows hepatocytes to utilize fatty acids as an energy source, preventing their accumulation in the liver. These combined mechanisms contribute to maintaining healthy hepatic lipid balance.Experimental animal studies support this regulatory function. In ovariectomized models, which mimic estrogen deficiency, researchers have observed significant increases in hepatic triglyceride accumulation. When estrogen supplementation was administered, lipid levels in the liver were significantly reduced, indicating that estrogen plays a direct role in metabolic regulation.

Regulation of Lipoprotein Metabolism. Another important function of estrogen involves the regulation of lipoprotein metabolism. Estrogen enhances the expression of low-density lipoprotein receptors in the liver. These receptors are responsible for removing LDL cholesterol from the bloodstream.Increased receptor activity leads to more efficient clearance of circulating LDL particles, which reduces overall cholesterol levels. In addition, estrogen promotes the production of high-density lipoprotein particles, commonly known as protective cholesterol.As a result, women of reproductive age typically exhibit more favorable lipid profiles compared with men. However, after menopause, when estrogen levels decline, LDL cholesterol levels tend to increase while HDL levels may decrease. This shift in lipid balance contributes to higher risks of metabolic and cardiovascular complications.

Interaction with Insulin Signaling. Estrogen also interacts with insulin signaling pathways that regulate glucose and lipid metabolism. Research suggests that estrogen improves insulin sensitivity in both hepatic and peripheral tissues. Enhanced insulin sensitivity allows cells to respond more effectively to circulating insulin, thereby reducing excessive glucose production in the liver. When estrogen levels decline, insulin resistance becomes more common. Insulin resistance stimulates lipogenesis in hepatocytes, increasing triglyceride accumulation and contributing to the development of fatty liver disease.

Increased Risk of Fatty Liver After Menopause. A growing number of clinical investigations have confirmed that menopause is associated with a higher risk of hepatic steatosis. Population-based cohort studies indicate that hormonal changes

contribute significantly to metabolic alterations affecting the liver.In several cross-sectional studies evaluating liver imaging results, researchers found that approximately one third of postmenopausal women exhibited signs of hepatic fat accumulation. In contrast, the prevalence among younger women was significantly lower.These findings suggest that estrogen deficiency may play a direct role in the development of metabolic liver disease.

Alterations in Lipid Profiles. Clinical data also demonstrate significant changes in serum lipid levels following menopause. Longitudinal studies monitoring women before and after menopause show increases in total cholesterol, triglycerides, and LDL cholesterol levels. These changes are often accompanied by modest decreases in HDL cholesterol.Such alterations reflect impaired lipid metabolism and contribute to both cardiovascular disease and hepatic fat deposition.

Effects of Hormone Replacement Therapy. Hormone replacement therapy has been extensively investigated as a potential method for alleviating menopausal symptoms and improving metabolic health. Randomized clinical trials indicate that estrogen therapy can positively influence lipid metabolism. Women receiving estrogen-based therapy frequently show reductions in LDL cholesterol and improvements in HDL cholesterol levels.In some clinical trials, LDL cholesterol levels decreased by approximately 10–15%, while HDL cholesterol increased by 5–10% after several months of hormone therapy.However, the metabolic effects of hormone replacement therapy depend on several factors, including dosage, route of administration, and patient characteristics. Oral estrogen therapy may increase triglyceride levels in certain individuals, highlighting the need for careful patient selection.

Conclusion. Estrogen plays an essential role in regulating hepatic lipid metabolism through multiple biological pathways. By influencing gene expression, lipoprotein metabolism, and insulin signaling, estrogen contributes to maintaining metabolic balance within the liver.The decline in estrogen levels during menopause leads to metabolic disturbances that increase the risk of hepatic steatosis, dyslipidemia, and cardiovascular disease. Clinical evidence demonstrates that postmenopausal women exhibit higher rates of metabolic liver disorders compared with women of reproductive age.Hormone replacement therapy may partially restore metabolic balance by improving lipid profiles and insulin sensitivity. However, therapeutic approaches should be individualized to ensure safety and optimal outcomes.A deeper understanding of estrogen-mediated metabolic

regulation will support the development of targeted interventions aimed at improving metabolic health in postmenopausal women.

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