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The Mechanism of Alcoholic Liver Damage

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Annotation: Liver diseases, especially acute toxic, ischemic and alcoholic liver damage, remain one of the main causes of liver failure. These diseases can lead to severe consequences, such as cirrhosis of the liver, liver failure, and require urgent medical intervention. Allogeneic hepatocytes, as a treatment method, open up new perspectives in restoring liver function, while it is poorly understood how this correction affects metabolic and immunological parameters in patients with acute liver damage.

Keywords: ADH, ALDH, ROS, Allogeneic hepatocytes.

The aim of the study was to study the relationship between metabolic and immunological parameters in patients after correction with allogeneic hepatocytes.

Literature review: Alcoholic liver damage is one of the leading causes of liver disease in the world and represents a wide range of pathological changes, including fatty degeneration, alcoholic hepatitis, fibrosis and cirrhosis of the liver. It occurs as a result of prolonged and excessive alcohol consumption, which causes various metabolic, immunological and cellular changes. It is important to understand exactly how alcohol affects liver tissue in order to develop effective methods of treatment and prevention of this disease.

Mechanisms underlying alcohol damage печени

Alcohol metabolism in the liver: Alcohol (ethanol) is metabolized in the liver through several key enzymatic systems:

Alcohol Dehydrogenase (ADH): This enzyme first metabolizes ethanol to acetaldehyde, which is a toxic substance.

Acetaldehyde Dehydrogenase (ALDH): Acetaldehyde, in turn, is converted to acetic acid, which is then used in metabolism.

With chronic alcohol abuse, acetaldehyde accumulates in liver cells, which leads to various damages, such as:

Oxidative stress: Acetaldehyde stimulates the formation of reactive oxygen radicals (ROS), which causes oxidative stress and damage to cell membranes, mitochondria, and DNA.

Violation of the antioxidant system: Chronic alcohol consumption reduces the activity of antioxidant enzymes, which exacerbates the damage caused by ROS.

Impaired fat metabolism: One of the early manifestations of alcohol damage is fatty liver disease, or steatosis. This process is caused by a violation of fat metabolism.:

Activation of fat synthesis: Ethanol stimulates the synthesis of fatty acids in the liver, which leads to the accumulation of fat in hepatocytes.

Impaired fatty acid oxidation: Chronic alcohol consumption disrupts the process of fatty acid oxidation in the mitochondria, which also contributes to the accumulation of fat in the liver.

At first, the accumulation of fat in the liver may be reversible (steatosis), but if alcohol abuse continues, it can lead to more serious damage.

Inflammation and cytokine activation: Cytokine production: Chronic alcohol consumption increases inflammation through the activation of macrophages and micronutrient cells, which leads to the release of inflammatory mediators (e.g. TNF-α, IL-6, IL-1b).

Activation of NF-kB: One of the key mechanisms of inflammation is the activation of the transcription factor NF-kB, which regulates the expression of cytokines that stimulate inflammation.

Inflammation in the liver can cause damage to hepatocytes and activate fibrosis, as well as contribute to the progression of the disease to cirrhosis of the liver.

Fibrosis and cirrhosis of the liver: Prolonged inflammation in response to alcohol damage leads to activation of Kupffer cells and liver stellate cells, which causes the production of collagen and other components of the extracellular matrix. This process leads to liver fibrosis, the replacement of normal liver tissue with scar tissue. Over time, fibrosis can progress to cirrhosis, which significantly impairs liver function and leads to liver failure.

Mechanisms of mitochondrial damage: Alcohol causes damage to mitochondria, cellular "energy stations", which leads to disruption of their function. This is due to an increase in the production of reactive oxygen species and a decrease in the activity of antioxidant systems, which also contributes to cellular apoptosis (programmed cell death) and disruption of normal cellular function.

Impaired vascular blood supply to the liver: Alcohol consumption can also affect the vascular system of the liver. Alcohol increases vascular permeability and also stimulates the formation of intrahepatic vascular changes such as port fibrosis and port hypertension. These changes can contribute to the replacement of normal vascular structures in the liver, which leads to a decrease in blood supply and deterioration of organ function.

Pathogenesis of alcoholic hepatitis: Alcoholic hepatitis is an inflammatory liver disease that occurs due to prolonged alcohol consumption. It is characterized by:

Accumulation of fat in the liver (steatosis).

Inflammation, which involves the activation of immune cells and the release of cytokines.

Hepatocellular death caused by exposure to toxic metabolites of ethanol (in particular, acetaldehyde).

Stages of alcoholic hepatitis development include: Mild forms: In the early stages of alcoholic liver damage, fat accumulates in liver cells (steatosis), which can be reversible upon cessation of alcohol consumption. Severe form: If the disease progresses, inflammation (alcoholic hepatitis), cell necrosis and fibrosis develop against the background of prolonged alcohol abuse, which can lead to cirrhosis of the liver.

Conclusion: Alcoholic liver damage is a complex and multifactorial process that includes metabolic disorders, inflammation, cell death, and fibrosis. Prolonged alcohol consumption leads to the accumulation of fat in the liver, damage to mitochondria, activation of inflammation and fibrosis of liver tissue, which can progress to cirrhosis and liver failure. Understanding these mechanisms is important for developing effective methods for the diagnosis and treatment of alcoholic liver damage, as well as for preventing its progression.

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