ACADEMIA ONE
PEER REVIEWED JOURNALS

Progress Annals: Journal of Progressive Research
Volume 2, Issue 8, August 2024
ISSN (E): 2810-6466
Website: https://academiaone.org/index.php/8

Studying The Role of Zinc for The Body In Liver Pathology

MM. Madumarova
Senior Lecturer
Andijan State Medical Institute
N.I. Alimov
5th year student
Andijan State Medical Institute

Annotation. The studies conducted provided detailed information on the biological role of zinc for the body. We separately studied the decrease in zinc in liver pathology and the effectiveness of its supplementation.

Key words: zinc, liver, alcoholic steatohepatitis, chronic hepatitis C and B.

RELEVANCE OF THE TOPIC

The main essential element for the body is zinc. It is necessary for cell growth, development and differentiation, for the biosynthesis of more than 300 enzymes. The main organ involved in the metabolism of zinc in the body is the liver. Endogenous zinc deficiency develops in chronic liver diseases: alcoholic steatohepatitis and chronic viral hepatitis B or C, especially in the case of liver cirrhosis.

PURPOSE OF THE STUDY

To study the role of zinc in the body and its significance in liver pathology.

MATERIALS AND METHODS OF RESEARCH

The study was carried out in the hepatology departments of the Andijan Regional Clinical Hospital, the central city hospital, and a multidisciplinary children's hospital. 200 people were examined, patients with alcoholic cirrhosis - 96 people (48%, of which men - 54 (56.25%), women - 32 (33.3%)), whose age ranged from 35 to 55 years, viral hepatitis C – 104 people (52%), of which 37 people are children, aged from 10 to 16 years (35.6%), and the remaining 67 people are adults, aged from 27 to 40 years (64.4%), of which husband. – 37 (55.2%), women. – 30 (44.8%). The study was carried out on the basis of anamnestic and laboratory data of patients.

The functional state of the liver was studied within the framework of 4 biochemical syndromes (cytolytic, cholestatic, mesenchymal-inflammatory and hepatodepressive), as well as using ultrasound of the abdominal organs and dynamic gamma scintigraphy of the liver with Tc-99m-HiDA. The activity of the multicomponent monooxygenase system of the liver was assessed based on the results of the antipyrine test. As control indicators when studying the functional state of the liver, we used data obtained from 25 healthy volunteers (men - 14, women - 11), average age 37.1 ± 1.01 years, whose anamnestic, physical methods and laboratory tests Research methods did not reveal liver diseases.

RESULTS OBTAINED

Zinc is an essential trace element for normal cell growth, development and differentiation. It is involved in DNA synthesis, RNA transcription, cell division and cell activation. Zinc is an

ACADEMIA ONE
PEER REVIEWED JOURNALS
Progress Annals: Journal of Progressive Research
Volume 2, Issue 8, August 2024
ISSN (E): 2810-6466
Website: https://academiaone.org/index.php/8

important structural component of many proteins/enzymes, including transcription factors. The recommended intake of zinc is 8 mg/day for women and 11 mg/day for men over 19 years of age. The absorption of zinc depends on its concentration in the small intestine, mainly in the jejunum. In liver cirrhosis, absorption is impaired and at the same time excretion of zinc is increased. Of the total zinc pool in the body, approximately 10% is metabolically active. The liver is the main organ involved in zinc metabolism. Among the main hormones that regulate zinc metabolism are insulin, glucagon and glucocorticoids. Depending on the characteristics of the physiological situation, hormones regulate zinc metabolism in liver cells, in some cases leading to the development of subsequent deficiency in the blood plasma.

The intracellular level of zinc is one of the homeostatic constants of the body and is maintained within relatively narrow limits. Physiologically significant changes in free zinc Zn^{2+} pools or modulation of the amount of zinc bound to specific ligands can occur without significant fluctuations in cellular concentrations. Zinc cations are hydrophilic and cannot cross the membrane by passive diffusion. The kinetics of their transport has a saturable and unsaturated component depending on the Zn^{2+} concentration. In isolated hepatocytes, complete zinc turnover occurs within 30 hours. Human liver samples contain an average of 2.36 μg/mg N zinc in normal conditions and 1.27 μg/mg N in cirrhosis.

Zinc absorption, transport and excretion are carried out by two large classes of transporters that have opposite effects (ZnT and Zip, respectively). The Zip family of transporters transports zinc from the extracellular space into the cell cytoplasm. Thus, Zip4 plays an important role in the intestinal absorption of zinc, and the absence of this transporter causes acrodermatitis enteropathica. Under physiological conditions, the development of zinc deficiency, including increased absorption and decreased excretion through changes in the number and activity of zinc transporters, is counteracted by multiple mechanisms. Inflammatory/stress hormones can reduce serum zinc levels with internal (interorgan) redistribution of zinc. Such stress reactions are often accompanied by hypoalbuminemia. Albumin is the major zinc-binding protein, but serum zinc concentrations may be decreased by inflammation even in the absence of hypoalbuminemia. This occurs, in part, due to changes in the activity and quantity of zinc transporters, especially the induction of the synthesis of Zip14 and hepatic metallothionein. Metallothionein is a metal-binding protein that, in addition to transporting zinc, is an antioxidant and modulator of zinc absorption. A close relationship has been shown between zinc supply and IL-6 secretion. Zinc affects the synthesis of acute phase proteins in the liver, gluconeogenesis, and the formation of oxygen radicals and nitric oxide. In addition, it regulates the activity of the zinc transporter Zip14 in the liver, contributing to the development of hypozincemia during the acute phase response.

Metabolic changes caused by zinc deficiency occur in many types of liver damage, including alcoholic liver disease and viral liver disease. Among the reasons for the development of zinc deficiency are a decrease in its intake from food, increased excretion in urine, activation of some zinc transporters, and induction of metallothionein synthesis in the liver. Zinc deficiency may manifest itself in liver disease as skin lesions, impaired wound healing and liver regeneration rate, changes in mental status, or immune disorders.

Violations of zinc homeostasis are particularly severe in liver cirrhosis. Liver cirrhosis is changes in the liver parenchyma, characterized by two main signs: necrosis and regeneration. The initial cause of the lesion is the loss of hepatocytes due to apoptosis and necrosis. The immune system can promote the death of hepatocytes by inducing apoptotic mechanisms or directly carrying out the destruction of liver cells. During hepatocyte regeneration, the extracellular matrix undergoes remodeling due to the ongoing action of inflammatory factors, which leads to abnormal collagen deposition, parenchymal fibrosis and structural abnormalities of the liver lobules.

ACADEMIA ONE
PEER REVIEWED JOURNALS
Progress Annals: Journal of Progressive Research
Volume 2, Issue 8, August 2024
ISSN (E): 2810-6466
Website: https://academiaone.org/index.php/8

Hepatocytes are in a non-proliferating state, but they acquire a high ability to regenerate within a few hours after injury. In turn, regenerating liver cells require large amounts of zinc over a short period of time. This need is realized at the very initial stage of regeneration through the induction of a protein that binds zinc and copper, metallothionein. This protein transports zinc to various metalloenzymes and transcription factors. Liver regeneration is impaired in metallothionein knockout mice. Although metallothionein is considered a cytoplasmic protein, it can also be localized in the nuclei of hepatocytes. High levels of metallothionein in cell nuclei may reflect an increased requirement of zinc for metalloenzymes, transcription factors, during rapid cell growth. The function of nuclear metallothioneins may be to protect cells from DNA damage and apoptosis, as well as to regulate gene expression during relevant stages of the cell cycle.

Alcoholic liver damage is the result of a complex interaction between the resulting dysfunction of the intestines, the immune system and the liver. In particular, chronic alcohol consumption leads to increased permeability of the intestinal barrier. Alcohol consumption leads to a decrease in zinc concentrations in the jejunum, which is associated with the accumulation of free radicals. Even a slight zinc deficiency enhances the destructive effect of ethanol on the epithelial barrier. Zinc deficiency has been repeatedly shown in patients with alcoholic cirrhosis and in experimental chronic alcohol intoxication of animals. Thus, the level of zinc in the blood serum in patients with chronic alcoholism was 7.52 μmol/l, which was significantly lower than in the control group - 12.69 μmol/l. Moreover, a decrease in blood zinc levels correlated with the progression of liver damage. Patients with alcoholic cirrhosis had lower serum zinc levels (80 μg%) than patients without cirrhosis (97 μg%), decreasing by -37 and -24%, respectively, compared with healthy controls (127 μg%). Zinc supplements reduce alcohol-induced liver damage. Zinc prevents the destruction of the intestinal barrier, preventing endotoxemia, reducing the production of proinflammatory cytokines and oxidative stress.

Zinc levels are often reduced in patients with viral hepatitis C, which correlates with a negative prognosis for the disease. An impaired antiviral immune response leads to constant activation of the secretion of proinflammatory cytokines and prolongation of the action of nonspecific effector mechanisms. This leads to hepatocyte damage, fibrogenesis and malignant transformation. The imbalance between cellular and humoral immunity in viral hepatitis C is a consequence of the imbalance between cytokines secreted by Th1 and Th2 lymphocytes. It has been shown that zinc salts in keratinocytes inhibit the expression of toll receptors. Stimulation of toll receptors by LPS agonists limits the expression of zinc transporters in dendritic cells, thus leading to a decrease in free intracellular zinc.

There are important prerequisites for prescribing zinc preparations for viral hepatitis C: 1) antioxidant function, 2) regulation of imbalance in the secretion of cytokines by Th1 and Th2 cells, 3) increasing the antiviral effect of interferon, 4) inhibitory effect on hepatitis C virus replication, 5) hepatoprotective effect zinc-containing protein metallothionein. Zinc improves the effect of standard antiviral therapy. It helps inhibit the development of fibrosis. When polyprezinc (N-(3-aminopropionyl)-L-histidinatozinc) was prescribed to patients with viral hepatitis C for 3 years at a dose of 150 mg per day, biochemical parameters in the blood were more quickly normalized, and the risk of developing hepatocarcinoma was reduced.

Zinc supplements for patients with chronic hepatitis C reduce the incidence of gastrointestinal complications, prevent weight loss, hair loss, and restore general status. Administration of zinc in combination with interferon is more effective for chronic viral hepatitis C than treatment with interferon alone.

A decrease in the concentration of zinc in the blood serum is often observed in viral hepatitis B, which accelerates the development of cirrhosis. It is important to note that the presence of

ACADEMIA ONE
PEER REVIEWED JOURNALS
Progress Annals: Journal of Progressive Research
Volume 2, Issue 8, August 2024
ISSN (E): 2810-6466
Website: https://academiaone.org/index.php/8

an initial zinc deficiency in the body reduces the effectiveness of vaccination against hepatitis B.

Patients with hepatocellular carcinoma have reduced serum zinc levels. At the same time, patients with cirrhosis and hepatocellular carcinoma have lower levels of metallothionein than patients with chronic hepatitis or healthy people. In tumor tissue, the level of zinc and metallothionein is significantly lower than in healthy tissue surrounding the tumor.

CONCLUSION

Thus, endogenous zinc deficiency is observed in the most common types of liver damage - alcoholic and viral, especially when they are severe. The effectiveness of zinc supplementation has been best studied in the experimental setting of alcoholic liver injury, where it blocks mechanisms of liver injury, including increased intestinal permeability, endotoxemia, oxidative stress, excess production of proinflammatory cytokines, and hepatocyte apoptosis. Zinc deficiency may, to a certain extent, inhibit the full antiviral effect of hepatitis C viral therapy.

REFERENCES USED

1. Zinc metabolism in alcoholic liver disease. / CJ McClain, [et al.] // Alcohol. Clin. Exp. Res. - 1986. - Vol. 10. - P. 582–589.
2. Boyett, JD Zinc and collagen content of cirrhotic liver / JD Boyett, JF Sullivan // Dig. Dis. - 1970. - Vol. 15, No. 9. - P. 797–803.
3. Zinc homeostasis and signaling in health and disease / T. Fukada [et al.] // J Biol. Inorg. Chem. - 2011. - Vol. 16. - P. 1123–1134.
4. Wang, X. Dietary zinc absorption: a play of Zips and ZnTs in the gut / X. Wang, B. Zhou // Life. - 2010. - Vol. 62, No. 3. - P. 176–182.
5. King, JC Zinc: an essential but elusive nutrient / JC King // Am. J. Clin. Nutr. - 2011. - Vol. 94. - P. 679–684.
6. Effects of endotoxin on zinc metabolism in human volunteers / L. Gaetke [et al.] // Am. J Physiol. - 1997. - Vol. 272. - P. 952–956.
7. Molecular dissection of the structural machinery underlying the tissue-invasive activity of MT1-MMP / XY Li [et al.] // Mol. Biol. Cell. - 2008. - Vol. 19. - P. 3221–3233.
8. Expression of matrix metalloproteinases and their inhibitors during hepatic tissue repair in the rat / T. Knittel [et al.] // Histochem. Cell. Biol. - 2000. - Vol. 113. - P. 443–453.
9. Sheybak, L.N. Biological role of zinc and prospects for the medical use of zinc-containing drugs: monograph / L.N. Sheybak, V.M. Shebak. - Grodno, 2003. - P. 82.
10. Jacobson, BPM Immunopathogenesis of hepatitis C viral infection: Th1/Th2 responses and the role of cytokines / BPM Jacobson, MG Neuman // Clin. Biochem. - 2001. - Vol. 34. - P. 167–171.