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Contents

Weekly Volume 28 Number 35 September 21, 2022

REVIEW

5093 Robotic, self-propelled, self-steerable, and disposable colonoscopes: Reality or pipe dream? A state of the art review

Winters C, Subramanian V, Valdastri P

5111 Noncoding RNAs as additional mediators of epigenetic regulation in nonalcoholic fatty liver disease

Zaiou M

MINIREVIEWS

5129 Combination strategies for pharmacologic treatment of non-alcoholic steatohepatitis

Suri J, Borja S, Lim JK

ORIGINAL ARTICLE

Basic Study

5141 Long noncoding RNA negative regulator of antiviral response contributes to pancreatic ductal adenocarcinoma progression *via* targeting miR-299-3p

Wang HQ, Qian CH, Guo ZY, Li PM, Qiu ZJ

5154 Alcohol promotes epithelial mesenchymal transformation-mediated premetastatic niche formation of colorectal cancer by activating interaction between laminin-γ2 and integrin-β1

Nong FF, Liang YQ, Xing SP, Xiao YF, Chen HH, Wen B

Retrospective Cohort Study

5175 Natural history and outcomes of patients with liver cirrhosis complicated by hepatic hydrothorax

Romero S, Lim AK, Singh G, Kodikara C, Shingaki-Wells R, Chen L, Hui S, Robertson M

Observational Study

5188 Gut microbiota of hepatitis B virus-infected patients in the immune-tolerant and immune-active phases and their implications in metabolite changes

Li YN, Kang NL, Jiang JJ, Zhu YY, Liu YR, Zeng DW, Wang F

5203 Dynamic blood presepsin levels are associated with severity and outcome of acute pancreatitis: A prospective cohort study

Xiao HL, Wang GX, Wang Y, Tan ZM, Zhou J, Yu H, Xie MR, Li CS

Prospective Study

5217 High prevalence of chronic viral hepatitis B and C in Minnesota Somalis contributes to rising hepatocellular carcinoma incidence

Mohamed EA, Giama NH, Abdalla AO, Shaleh HM, Oseini AM, Ali HA, Ahmed F, Taha W, Ahmed Mohammed H, Cvinar J, Waaeys IA, Ali H, Allotey LK, Ali AO, Mohamed SA, Harmsen WS, Ahmmad EM, Bajwa NA, Afgarshe MD, Shire AM, Balls-Berry JE, Roberts LR

LETTER TO THE EDITOR

5230 Urotensin II level is elevated in inflammatory bowel disease patients

Zhang Y, Chen GX

5233 Hepatitis B viral infection and role of alcohol

Muro M, Collados-Ros A, Legaz I

CORRECTION

5237 Correction to "Inhibiting heme oxygenase-1 attenuates rat liver fibrosis by removing iron accumulation"

Wang QM, Du JL, Duan ZJ, Guo SB, Sun XY, Liu Z

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LETTER TO THE EDITOR

Hepatitis B viral infection and role of alcohol

Manuel Muro, Aurelia Collados-Ros, Isabel Legaz

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Abstract

End-stage liver disease is frequently caused by hepatitis B virus (HBV) and alcohol consumption. Notably, the mechanism by which alcohol affects the course of HBV-associated liver disease is unknown, and additional research is needed in this area. A reduced immunological response, oxidative stress, endoplasmic reticulum stress, Golgi apparatus stress, and enhanced HBV replication are a few potential causes.

Key Words: Hepatitis B virus; Alcohol; Hepatocarcinoma; Immunity; Liver disease

Core Tip: In this letter to the editor, we comment on and discuss the combined effects of alcohol consumption and hepatitis B virus (HBV) infection in the progression of liver diseases. In the worst evolution of end-stage liver pathologies, a concordant clinical relationship between alcohol consumption and HBV infection starts to be revealed. There are many potential causes, but some might include increased viral replication, oxidative stress on cellular organelles, and weakened immune responses. Understanding these precepts will open new avenues in managing and treating these patients.

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TO THE EDITOR

We have read with great attention and special interest the review by Ganesan and collaborators entitled "Role of alcohol in the pathogenesis of hepatitis B virus (HBV) infection"[1]. The authors examine the potential mechanisms by which alcohol results in an increased risk of HBV-associated liver disease. HBV infection combined with alcohol usage accelerates the progression of liver damage[2,3], primarily hepatocellular carcinoma, the fifth most common type of cancer. The mechanisms behind these adverse effects of alcohol in HBV-positive patients are unknown. Chronic alcohol consumption changes the architecture of the liver and reduces its functional capability.

The effects of alcohol metabolism on protein function, DNA, immune system changes, and oxidative stress impact both hepatocytes and other liver cells. Because the liver is the central location for the replication of hepatotropic viruses (HCV and HBV), ethanol metabolism is linked to viral hepatitis[4,5].

Regarding the immune system, the early stages of viral infections result in the generation of interferon (IFN) type 1 and the activation of natural killer (NK) cells. IFN type 1 and other antiviral cytokines, which HBV induces, are not particularly efficient. According to various investigations of persistent HBV infection, NK cells exhibit varying alterations in quantity, phenotype, and/or function. HBV-infected hepatocytes are cleared more quickly when activated NK cells are present. However, when chronic infection progresses, the tolerogenic actions of liver ligands and cytokines can inhibit both NK and T cells, limiting their antiviral activity[6,7]. According to reports, alcohol has an impact on NK cell antiviral activity during acute HBV infection[8].

The large, medium, and small forms of HBsAg, as well as the hepatitis B virus core antigen (HBcAg) and hepatitis B e antigen (HBeAg), can all be targeted by polyclonal antibodies produced by B cells in chronic HBV-infected patients[9]. During acute HBV infection, distinct antibodies are produced against the HBV surface antigen and the HBV core antigen. Anti-HBc is a marker for current or past infection, whereas anti-HBs signifies sickness remission[10]. Alcohol may reduce the number of B cells, decreasing HBV antibodies by weakening B cell immunological responses[11].

The B cell response to acute HBV infection is less well understood, but HBV-specific CD4+ and CD8+ T cell-mediated responses usually become detectable as HBV replication increases exponentially[12,13]. Numerous studies have demonstrated a substantial correlation and link between acute hepatitis, CD4+ T cell response, and viral shedding[14-16].

Cytotoxic T lymphocytes (CTLs) that express particular T cell receptors are in charge of eliminating HBV-infected hepatocytes in HBV infection. CTL activation may be diminished, which thus prevents clearance of HBV-infected hepatocytes when the viral peptide/MHC class I complex display in HBV-infected hepatocytes is compromised[17]. The body's capacity to eliminate HBV may be diminished due to ethanol consumption, allowing the virus to persist and eventually produce end-stage liver disorders such as cirrhosis and hepatocellular carcinoma.

The immune response in the liver is meticulously regulated by signals from the commensal microbiota in the gut. Additionally, drinking alcohol causes the close connections between intestinal epithelial cells to weaken, allowing germs to enter the bloodstream and cause an infection[18-20].

However, hepatic metabolism of ethanol may increase the production of reactive oxygen species (ROS), principally hydrogen peroxide and superoxide anion[21].

Recent studies have shown that the ethanol metabolite acetaldehyde can suppress proteasome activity, which is essential for producing antigenic peptides for MHC class I-restricted antigen presentation and can also cause lipid peroxidation, the formation of protein adducts with 4-hydroxynonenal and malonaldehydes (oxidative stress markers). This reduces the HBV-MHC peptide class I complex exposure to CTL identification and restricts the removal of infected cells[1], which causes HBV persistence and ensuing end-stage liver disease. HBV and alcohol addiction stresses the endoplasmic reticulum (ER), and these two stresses may have additive or synergistic effects. Alcohol has been shown to synergistically cause ER stress when other substances, the environment, or a viral illness are present [22]. The increase in HBV DNA, HbsAg, and HBx protein caused by alcohol may be the mechanism by which alcohol induces ER stress in HBV infection. A strained Golgi apparatus frequently matches a stressed ER.

Further study in this area is required since the interaction of alcohol misuse and HBV infection can be harmful. Future research should examine how alcohol metabolism affects innate IFN responses and IFN-stimulated gene activation throughout the pathogenesis of HBV infection, as well as if IFN therapy might be an effective treatment option for alcoholics with HBV infection.

Additionally, there is a significant gap between the role of alcohol in controlling B cell function and its contribution to the pathogenesis of HBV, necessitating further research in this area. To fully comprehend the processes of alcohol-induced impairment and investigate the effects of ethanol on MHC class II presentation, which is mainly catalyzed by effector cells, additional studies examining the relationship between alcohol and HBV adaptive immune response are required.

FOOTNOTES

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