ISSN: 2474-3658

Scott et al. J Infect Dis Epidemiol 2023, 9:294
DOI: 10.23937/2474-3658/1510294
Volume 9 | Issue 2
Open Access

Journal of
Infectious Diseases and Epidemiology

PERSPECTIVE

Increasing Cases of Chronic Hepatitis B Virus Infection in West Africa: Is Combination Therapy and Immunomodulators the Best Cure?

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Abstract

West Africa has a high endemicity of chronic hepatitis B, which causes liver cancer, cirrhosis, liver failure, and chronic liver disease, all of which put a severe strain on the region's already crippled healthcare system.

This disease kills nearly 200,000 people in West Africa each year. As a result, finding a cure is critical. Several scientists have developed potential treatments for this disease over the years. However, the majority of them have failed.

In this paper, we shed more light on immunomodulators and combination therapy, two treatments that have shown promise in putting an end to this disease. We compared them to other modes of treatment currently available and explained why they are the best cure for chronic hepatitis B. We also encouraged the scientific community to conduct more research in this area so that better results can be realized as soon as possible.

Keywords

Hepatitis B, Immunomodulators, West Africa, Combination therapy, Cure

Introduction

Chronic hepatitis B (CHB) virus infection is a public health issue in West Africa, causing significant morbidity and mortality [1]. According to the World Health Organization, there are more than 350 million people suffering from the disease worldwide [2]. Other complications, such as liver cirrhosis, hepatocellular carcinoma, and chronic liver disease, are common [3]. The progression of liver disease to more severe forms, as well as the development and complications of hepatocellular carcinoma (HCC), impose a significant burden on low-income countries. Furthermore, political and socioeconomic issues make dealing with the prevention, management, and treatment of CHB infection and associated diseases difficult, if not impossible [4].

Chronic carriers of the hepatitis B virus (HBV) are said to be prevalent in Sub-Saharan Africa. Hepatitis B affects approximately 60 million people in the region. In West Africa, the figures are even higher. In Nigeria, a West African country, chronic carriers account for roughly 40% of the population [5]. Because less than one in ten Africans has access to testing and treatment, the disease frequently progresses to advanced liver disease, with its associated catastrophic financial burden as well as emotional distress and stigmatization, which are involved in nearly half of cases of chronic liver illness [6].

This disease's hyperendemicity in this region and its burden must be reduced as soon as possible. Although the vaccine is available, researchers have been working for years to find a cure. Several drugs have been developed, but no significant success has been recorded. However, immunomodulators and combined therapy have recently shown a glimmer of hope to putting an

Citation: Scott GY, Chinelo NP, Dauda Z, Immanuel A (2023) Increasing Cases of Chronic Hepatitis B Virus Infection in West Africa: Is Combination Therapy and Immunomodulators the Best Cure?. J Infect Dis Epidemiol 9:294. doi.org/10.23937/2474-3658/1510294

Accepted: February 20, 2023: **Published:** February 22, 2023

end to CHB. In this paper, we studied this method of treatment and provided reasons why it is the best cure for CHB.

Epidemiology of Hepatitis B in West Africa

West Africa, a region in Africa with an estimated 400 million people, has the highest prevalence of hepatitis B virus (HBV) in Africa, with an anti-HBc prevalence of more than 85% [7]. According to the World Health Organization, approximately 325 million people worldwide suffer from viral hepatitis, with 70 million from Africa and 60 million infected with the viral virus' hepatitis B variant. Even with these staggering figures, it is unfortunate that the disease is neglected in West Africa and Africa as a whole, resulting in approximately 200,000 deaths each year, the majority of which are youth.

The hepatitis B virus has eight genotypes, A through H, with the E variant being the most common in West Africa. Some countries have two genotypes in circulation. Nigeria and Cameroon, two West African countries with genotypes A and E, are examples of many such countries [8]. Despite HBV hyperendemicity, the results show that hepatitis B is more prevalent in rural than urban areas. It is also said to be more prevalent in the elderly than in the young, peaking in those aged 40 to 67 [9].

In West Africa, chronic hepatitis B is the leading cause of cirrhosis, hepatocellular carcinoma (HCC), and death. Most West Africans are unaware of the disease, which explains the region's low surveillance and high prevalence. The disease is usually transmitted horizontally or perinatally before the age of ten [10]. Horizontal transmission is usually facilitated by a combination of cultural beliefs as well as environmental and behavioral factors among those in the region.

Factors behind Increasing Cases of Hepatitis B in West Africa

The widespread prevalence of hepatitis B varies by region. Unfortunately, it is not just prevalent but is on the increase in West Africa. Noemi Tousignant, a University College London historian of science and health who has been researching West Africa since 2005, claims that Hepatitis B has killed members of the majority of Senegalese households. Almost every family has an uncle or a cousin who is affected [11].

The disease's low surveillance in Africa contributes a great deal to the problem. In terms of prevalence, the AIDS, malaria, and tuberculosis epidemics, as well as COVID-19, have long surpassed the hepatitis B virus. It is therefore shocking that it is rarely discussed, particularly in elementary schools, prenatal appointments, and other health educational events. When the virus was discovered in Sub-Saharan Africa, public ignorance of transmission gave the illness a bad rap, similar to HIV. There is a significant knowledge gap because hepatitis B is often neglected. Even HIV patients are given high priority for antiretroviral medications, despite the fact that having both infections increases the risk of premature death [12].

The Hepatitis B vaccine is one tool that is very underutilized. In Nigeria, it was discovered that less than 1% of mothers with a high viral load received antiviral medication to reduce mother-to-child transmission [13]. West Africa is made up of developing countries with predominantly rural populations. Hepatitis B vaccine coverage was found to be 41% in low-resource settings. Despite its availability, coverage for the Hepatitis B vaccine remains woefully inadequate. As a result, children are more likely to be exposed to the infection and infected, increasing the likelihood that the infection will spread more quickly. In addition, only about 5% of adult cases of hepatitis B result in chronic hepatitis, compared to 95% of infant and young child infections [14].

Because its carriers do not at first exhibit symptoms, hepatitis is sometimes known as a silent epidemic. After contracting the virus, symptoms may take anywhere between one and six months to manifest. One-third of those who have this disease are unaware of it. Hence, the barrier to getting tested for the infection, care, and treatment is a reasonable basis for its prevalence. This barrier may be connected to culture or the health system; West Africa is a region renowned for its deeply ingrained and varied societal and religious traditions. In a study in Ghana, 18 people with Hepatitis B (PWHB) and 15 healthcare professionals (HCP: physicians, nurses, and midwives) had in-person interviews. The main cultural prejudices that prevent people from understanding the causes of chronic Hepatitis B are - (1) The idea that people with chronic Hepatitis B are being punished by the gods for touching corpses (2) Bewitchment or some form of spiritual poison as a cause of chronic Hepatitis B [15]. Another interviewee mentioned specifically that "… You don't discuss such kinds of health problems; it's almost like a secret. Considering that it is believed that "you did something to receive this condition" [16]. In addition to delaying or preventing diagnosis and treatment, these hurdles allow potentially infected people to continue living regular lives while engaging in unprotected sex, sharing needles, etc. without being aware of the necessary safety measures.

Overview of Progress Made to Find Cure for Hepatitis B

Infection with the chronic hepatitis B virus (HBV), which affects 292 million people globally, continues to be a significant global health burden [17,18]. The adoption of quick diagnostic tests can considerably reduce logistical elements, and it is theoretically simple to diagnose chronic HBV infection. However, for the extension of HBV screening to be effective, strong educational outreach to the most impacted

communities is required, as well as an effective connection to treatment facilities [19].

The existing screening and diagnosis of HBV have helped in the development of treatments for HBV. Although they have been around for about 20 years, interferons (IFNs) and nucleotide analogs (NAs) are effective treatments for reducing HBV replication [20]. As chain terminators, while the pleotropic molecular and immunological effects of PEG IFN on viruses are currently unknown, PEG IFN reduces cccDNA transcription in experimental systems via epigenetic modification [21]. These antivirals can reverse some lesions, but they are not a cure; rather, they are part of the existing arsenal for secondary prevention [22].

The two primary possible methods for curing HBV are (i) Intensifying the inhibition of HBV replication or (ii) Reducing HBsAg presentation for ultimate HBsAg seroclearance. The good news is that the fight against hepatitis B infection has seen significant advancements. In phase 2 studies, chain terminators and inhibitors of DNA synthesis initiation did not achieve significantly improved on-treatment reductions or seroclearance of HBsAg. Patients who are participating in phase 2 clinical studies include those who are HBeAg-positive and negative, naive, and nucleoside analog-suppressed [23].

The Best Cure for Hepatitis B Disease: Immunomodulators and Combination Therapy

Combination and immunomodulatory therapies are seen as the future of Chronic Hepatitis B treatment (CHB). The reasons for this aren't entirely implausible. With the barrier of finding a cure for hepatitis B being selective immune dysfunction and covalently closed circular (cccDNA) resistance, combination therapy, and immunomodulators will break that barrier through multiple targeting, thereby finding a solution to the HBV mechanism of evading host response, such as evolving all of its transcripts to resemble cellular mRNAs, and other mechanisms, thereby showing the potential to be able to put an end to an age-old issue [24].

Several combinations of antiviral therapy and immunomodulatory agents have been tested as potential cures for CHB over the years. Prednisone and interferon; alpha and gamma interferon; alpha interferon and acyclovir; lamivudine and alpha interferon, and so on, have all been tried in the past and have shown promising results in putting an end to CHB. Although the difference in response rate between this combination therapy and other monotherapies such as interferon and lamivudine alone was not statistically significant (10% and 11% difference, respectively), it is expected that a larger study will show the combination to be more effective [24].

A.M, et al. reported in 2002 that several nucleoside analog agents, including dipivoxil, entecavir, DAPD, L-FMAU, adefovir, and L-dT, were under development and would have very strong antiviral activity against HBV. They hypothesized that these drugs would not only be effective in preventing HBV infection but would also reduce the development of drug-resistant viral mutants, similar to the combination therapy used to treat Human Immunodeficiency Virus (HIV) infection [25].

With great progress in the success of immunotherapy in cancer as well as a better understanding of the HBV-host interaction, more immunomodulators that were said to be in clinical development were discovered in 2016, raising the hope of everyone in the scientific world about a possible total therapeutic approach towards finding a functional cure for the disease [26]. Toll-like receptor antagonists, immune checkpoint inhibitors, therapeutic vaccines, and engineered T cells are among the immunomodulators proposed. These approaches, as well as the use of newer strategies at the time, such as CRISPR/Cas9 and RNAi, have the potential to lower HBsAg levels, thereby increasing the efficacy of these immunomodulators not only at the time but also in the future, not just curing CHB but in a shorter time unlike monotherapy and with other forms of treatment.

Recently, studies have been conducted to assess the role of IL-35, a novel cytokine belonging to the IL-12 family, in the treatment of CHB. For the time being, little is known about the role of IL-35 in HBV replication. However, studies have shown that IL-35 stimulation inhibits the differentiation of HBV core-specific (CD4+CD25+Foxp3+) Tregs into IL-17-secreting CD4+ T cells (Th17), and both Th subsets have been linked to disease progression or liver damage in CHB patients [27]. Upstream and downstream pathways can be used to assess its immunoregulatory function. Generally, IL-35 stimulation is seen to possess a very strong immunosuppressive feature and a form of immunomodulatory therapy with so much potential to act as a functional cure for CHB.

Combination and immunomodulatory therapy offer the prospect of a long-term cure for chronic hepatitis. This method has provided a glimmer of hope in addressing HBV's immune evasion and cccDNA persistence. Combination and immunomodulatory therapy have no doubt answered many questions about the cure of CHB and are without a doubt the best cure. The challenge will be defining the appropriate combination and duration of therapy in each population, as well as ways to measure progress.

Recommendations and Conclusions

In endemic areas and low-income nations of sub-Saharan Africa, hepatitis B continues to be a serious public health issue. Significant efforts are being made to increase the cure rates for hepatitis B, and the hunt for a solution has advanced. Despite the promise of new medications, the most effective combinations and orderly courses of action will require a thorough empirical examination.

It must be understood that educational outreach to the majority of the affected populations will increase HBV screening, improve the connection to treatment providers, and increase the likelihood of finding a cure sooner.

Additionally, increasing the likelihood of discovering a long-term treatment for Hepatitis B by addressing the key issues related to the development of new medications for the disease (safety, convenience of administration, and cost). Shortly, point-of-care viral load and other assays should make routine therapy monitoring simpler and more cost-effective. These will make it possible to test and monitor HBV properly.

Immunomodulators and complex combination therapies are promising treatments that could end the threat of viral hepatitis to public health and contribute to long-term objectives, including achieving sustainable development goals. We recommend that more research is carried out in this area and it should be adopted as the cure for CHB when adequate data has been collected as to its effectiveness.

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