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Can Hepatitis B Virus Inhibit Covid-19 Virus

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1. Abstract

1.1. Introduction: Covid-19 is a global pandemic around the world and entered India in March,2020 and has led to substantial morbidity and mortality till date. There had been many drug trials all over world for it but, many time treatment strategies have been revised in different parts of world, including India but still no treatment has been proven to be totally successful in curing it.

1.2. Aims and objectives: To determine the prevalence of COVID 19 infection in inactive carriers of chronic hepatitis B or acute hepatitis B, not on any antiviral treatment, thus determining preventive role of Hepatitis B virus in COVID-19 infection.

1.3. Materials & Methods: It was prospective study conducted at Department of Medical Gastroenterology, PGIMS, Rohtak, over a period of two and half years. All the registered patients who were inactive carrier and were coming on regular follow up for Fibroscan, viral load and other lab testing and acute hepatitis B patients, not on any antiviral treatment, since 1st March 2020 were followed for thirty months and it was determined that what percentage of patients developed COVID-19 infection.

1.4. Results: Out of three thousand inactive carrier patients of Chronic hepatitis B, only two patients developed mild Covid-19 infection which required only home isolation and became COVID-19 negative within one week. Two hundred and ten patients of acute hepatitis B were diagnosed and followed over these two and half year period and none of them developed COVID-19 infection.

1.5. Conclusion: We already know that HBV and HCV inhibit each other existence in human body, thus co-infection of HBV and HCV are not common, despite being having common route of infection. Whether HBV can also inhibit presence of COVID -19 virus in human body is point to ponder and above research ignites this aspect for further researches.

2. Introduction

COVID-19 is an ongoing global pandemic in which majority of infected cases appear mild, in some cases individuals present respiratory complications with possible serious lung damage. The treatment policy for it has seen paradigm shift in last two and half years but till date no uniform consensus has been reached. Many kind of vaccines have been developed which have proven to be able to substantially decrease morbidity and mortality but due to repeated mutations, they are not able to prevent entry of COVID-19 virus in human body. Now, intranasal vaccine have become available which challenge the entry of it through nasal cavity. Human pathogenic coronaviruses (SARS-CoV and SARS-CoV-2) bind to their target cells through angiotensin-converting enzyme 2 (ACE2), which is expressed by epithelial cells of the lung, intestine, kidney, and blood vessels [1,2,3]. The ability of SARS-CoV2 to enter and infect the human nervous system, based on the strong expression of the ACE2 target throughout the brain [4], should be also considered. Researchers from Johannes Gutenberg University Mainz (JGU) in Germany simulated the way that about 42,000 different substances listed in open databases bind to certain proteins of SARS-CoV-2, and thereby inhibit the penetration of the virus into the human body or its multiplication. They found that compounds from the four hepatitis C drugs simeprevir, paritaprevir, grazoprevir, and Velpatasvir have a high affinity to bind SARS-CoV-2 very strongly and may therefore be able to prevent infection. Sofosbuvir and daclatasvir, two antiviral drugs used to treat hepatitis C, were associated with faster recovery, shorter hospitalization and improve survival among people with moderate or severe COVID-19, researchers reported at the COVID-19 Confer-

ence that concluded the 23rd International AIDS Conference (AIDS 2020: Virtual).

3. Aims and Objectives

To determine the prevalence of COVID 19 infection in inactive carriers of chronic hepatitis B or acute hepatitis B, both of groups were not on any antiviral treatment, thus determining preventive role of Hepatitis B virus in COVID-19 infection.

4. Material and Methods

It was prospective study conducted at Department of Medical Gastroenterology, PGIMS, Rohtak, over a period of two and half years. All the registered patients who were inactive carrier and were coming on regular follow up for Fibroscan, viral load and other lab testing and acute hepatitis B patients, not on any antiviral treatment, since 1st March 2020 were followed for thirty months and it was determined that what percentage of patients developed COVID-19 infection. The permission for conducting of above study was given by Director General Health Services, Haryana and PGIMS, Rohtak.

5. Stastical Analysis

All the data was entered in Microsoft Excel and was analysed using SPSS 15.0 version.

Table 1: Showing Development of Covid-19 Infection in Patients.

Total Patients Enrolled	**Chronic HBV Inactive carrier (3000 patients)**		**Acute Hepatitis B (210 patients)**	
	COVID-19 Positive	**COVID-19 Negative**	**COVID-19 Positive**	**COVID-19 Negative**
3210	2 0.06%	2998 99.94%	0 0%	210 100%

Table 2: Showing Sex and Geographical Distribution of Patients.

Total Patients (3210)	**Males**	**Females**	**Rural**	**Urban**
Chronic HBV (3000 Patients)	70 % (2100)	30% (900)	65% (1950)	35% (1050)
Acute HBV (210 Patients)	71.90% (151)	28.10% (59)	66.66% (140)	33.33% (70)

Table 3: Indicating the total number of patients of Chronic HBV and Acute HBV.

Total Patients (3210)	**10-20 yrs**	**21-30 yrs**	**31-40 yrs**	**41-50 yrs**	**51-60 yrs**	**61-70 yrs**
Chronic HBV (3000 Patients)	10 % (300)	28% (840)	24% (720)	18% (540)	14% (420)	6% (180)
Acute HBV (210 Patients)	3.33 % (7)	26.19% (55)	35.71% (75)	26.19% (55)	6.66% (14)	1.90% (4)

6. Observations & Results

Out of total pool of 3210 patients, 3000 patients were having Chronic hepatitis B inactive carrier stage and 210 were diagnosed to be of acute hepatitis B. Out of 3000 patients of chronic hepatitis B, only two patients developed COVID-19 infection during follow up of thirty months. Whereas in pool of 210 patients of acute hepatitis B, all of whom were not on antiviral treatment, none developed COVID-19 infection during this period. In both groups, there was predominance of males in young age group and majority of patients belonged to rural background with poor socio-economic status.

7. Discussion

According to [5,6], SARS, MERS and SARS-CoV-2 coronaviruses, like Hepatitis C virus (HCV) and the Flaviviridae [7], are positive-sense single-strand RNA viruses and these viruses share a similar replication mechanism requiring a RNA-dependent RNA polymerase (RdRp). So, there is a strong possibility that Sofosbuvir, Ribavirin, AZT (and other HCV/HIV nucleoside/nucleotide analogues such as Remdesivir) can tightly bind to SARS-CoV-2 RdRp. In a recent in silico (preliminary) study, sequence analyses as well as homology modeling were used to build a new SARS-nCoV RdRp model which then targeted by anti-polymerase drugs, including the approved drugs Sofosbuvir and Ribavirin [8]. The docking scores suggested possible eligibilities of Sofosbuvir, Ribavirin, (and Remdesivir) as potent drugs against the new coronavirus. These theoretical data needed to be confirmed by the experimental observations. Using polymerase extension experiments, in vitro, Chien M, et al. also demonstrated that the biologically activate triphosphate forms of four well-known nucleotide/nucleoside analogue anti-viral (anti-HCV/HBV, anti-HIV/AIDS) drugs; Sofosbuvir, Tenofovir alafenamide, Alovudine were incorporated by RNA-dependent RNA polymerase (RdRp) enzymes of SARS-CoV as well as SARS-CoV-2,

and permanently blocked further incorporation (further polymerase extension was terminated). They considered all these compounds as permanent/strong terminators for the SARS-CoV-2 RdRp [7,8]. Due to widely availability of these FDA approved drugs (Sofosbuvir, Tenofovir), they expressed hope that the drugs would be more evaluated quickly in laboratory and clinical trials for COVID-19 treatment. The motivation from above mentioned trials led to conducting of present study at Department of Medical Gastroenterology which is also Model Treatment Centre (MTC) under National Viral Hepatitis Control Program (NVHCP) where free diagnostic and treatment facility is provided to patients of hepatitis C & B. As there were number of patients of hepatitis B who were coming regularly for follow up which was provided uninterrupted even during Covid-19 Pandemic. The data of all these patients was regularly updated when they came on follow up and also repeated telephonic contact was also maintained with all these patients by staff of Gastroenterology Department. In our previous study, we have already suggested, the preventive role of antiviral drugs for hepatitis B and C like Tenofovir, Sofosbuvir, Daclastavir and Velpatasvir [9]. It prompted us to closely follow chronic hepatitis B inactive carrier and acute hepatitis B patients, to see whether at any point of time, they develop COVID-19 infection. In our backdrop of mind, we were thinking on lines of mutual inhibition of HBV and HCV in human body which has been already proven by many studies. In clinical settings, one virus is typically dominant over the other. Dominance occurs when there is reciprocal inhibition of one viral genome by the other virus when both HBV and HCV are present in the same cell [10]. Thus, we wanted to see that whether HBV has any potential to inhibit presence of COVID-19 virus in human body. The initial results are encouraging, as only two patients i.e. 0.06% in chronic hepatitis B inactive carrier and zero patient in acute hepatitis B developed COVID-19 infection, over a prolonged period of two and half years. The two patients also had mild disease which recovered in one week that too with home isolation without requiring any hospitalization, oxygen or antiviral therapy. It is too early to draw comparison between our two groups of chronic hepatitis B and acute hepatitis B, as there was significant difference in number of patients in both the groups i.e. 30000 vs 210. But Surprisingly nobody in acute hepatitis B developed COVID-19 infection which may be due to high HBV DNA viral load in this stage which may have more potential to inhibit COVID-19 virus infection but this has to be confirmed by future researches. It is pertinent to note that all the patients in our study group, belonged to same strata of society who was being devastated by COVID-19 pandemic, despite that they were saved from the same.

8. Conclusion

Many smaller drug trials done in different countries highlight role of oral antiviral drugs used in treatment of hepatitis C and B in Covid-19 infection have shown optimistic results. Our study can be taken as indirect evidence of effectivity of above antiviral drugs in treatment of Covid-19 infection but this requires large scale studies directly evaluating the role of these antiviral drugs in treatment of Covid-19 infection.

9. Limitation of Study

The present study is an indirect evidence for inhibitory potential of HBV for COVID 19 virus in human body role but large scale studies are required for establishing it.

10. Conflict of Interest

The authors disclose that there was no conflict of interest in the study.

11. Financial Disclosure

The authors disclose that no finances were involved in the research.

12. Author Contribution

Parveen Malhotra - Conceived, Designed and Formulated this retrospective analysis

Usha Gupta- Data Analysis

Yogesh Sanwariya, Mahima Vohra- Reviewed draft of paper

Shobhit Singh, Sugam - Data collection

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