HIV and Hepatitis C Co-infection: Trends and Changing Treatment

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Two of the greatest challenges in health care are the chronic infections with hepatitis C virus (HCV) and human immunodeficiency virus (HIV). They are currently the most prevalent blood-borne chronic viral infections in the United States and worldwide, and both carry high mortality and morbidity rates if left untreated. In recent years there have been tremendous advances in the treatment and management of both viruses individually. However, co-infection with HIV/HCV generally leads to a more complicated disease course: it reduces the effectiveness of treatment because HIV tends to accelerate the progression of HCV and decreases the patient’s susceptibility to the current HCV standard therapy of interferon and ribavirin. Currently, little data exists describing the population co-infected with HIV/HCV. But with the recent approval of two new oral drugs by the FDA for the treatment of hepatitis C and the promise of more to follow, understanding the population dynamics of HIC/HCV co-infected individuals has become much more important for future treatment. Using the patient information collected by Mr. Charles Hansen, Dr. Timothy Lane and their partners at the Regional Center for Infectious Disease in Greensboro, North Carolina, where over a thousand HIV-infected patients receive care yearly, we were able to analyze the cohort of HIV infected patients who are co-infected with HCV. This co-infected cohort is approximately 10% of the total who are HIV-infected. It is our hope that these data will better the understanding of HIV/HCV co-infection and improve the standard of therapy.

Introduction

HIV is the retrovirus responsible for causing Acquired Immuno-deficiency Syndrome (AIDS), a progressive failure of the human immune system resulting from HIV virus infection and destruction of vital immune system cells. HIV alone is one of the most destructive pandemics in human history, with the World Health Organization (WHO) estimating that over 25 million people have succumbed to AIDS between 1981, the year of its first recognition, through 2011 (7). At the end of 2010, it was estimated that 34 million people worldwide are living with the disease, with a disproportionate number living in sub-Saharan Africa (7). That number continues to rise as the disease continues to spread at a rate estimated to be around 2.6 million new infections a year (5). Fortunately, treatments are available; for instance, the effectiveness of highly active antiretroviral therapy (HAART) improves the life expectancy of persons already infected.

HCV infection is even more widespread with an estimated 130-170 million people infected worldwide and an estimated 3 million new infections per year (6). With 4.1 million infected in the United States alone, HCV has become the leading cause for liver transplantation in the U.S. and is on track to surpass alcoholic liver disease as the leading cause of liver-related death (1). There are six known genotypes of HCV, distinguished from each other based on the composition of virus RNA. Genotype 1 is the most common in North America and also the most difficult to treat with the current interferon therapy (1). In addition to infection by genotype 1 HCV, other diagnostic factors that negatively affect responsiveness to interferon-based therapy include old age, African American ethnicity, an IL28B TT haplotype of the human interferon gene, alcohol consumption, advanced liver fibrosis, and HIV co-infection due to the resulting low CD4 lymphocyte counts. Fortunately, unlike the hepatitis B virus and HIV, which can build up reservoirs of their genetic code within the host’s genome, HCV does not integrate its genetic material into the host’s. Without these dormant stores of genetic code, which are difficult, if not impossible, to eradicate, it is possible to attain permanent sustained virologic response (SVR) for most HCV infected patients if successful combinative therapies could be developed. SVR is defined as long term suppression of viral RNA below detectable levels. It is anticipated that a SVR of a year or longer will portend a probable cure, but it is relatively early in the era of antiviral treatment of HCV.

Co-infection with HCV and HIV presents a greater challenge to treat than either of the two infections individually. It is estimated that 4 to 5 million people worldwide are suffering from a chronic infection of the two viruses. Co-infection is characterized by increased rates of disease progression and decreased responsiveness to standard therapy. In a recent review published in the Journal of the American Medical Association, only about 30% of patients with HIV/HCV co-infection receiving pegylated interferon (peginterferon) and ribavirin treatment developed an SVR.
In comparison, approximately 55% of patients with only HCV infection developed SVR after receiving the same treatment (1). Besides being more resistant to treatment, HIV/HCV co-infection is associated with accelerated development of fibrosis, cirrhosis, end-stage liver disease, and hepatocellular carcinoma. This acceleration could be due to the problematic reactive oxygen species or oxidants that are produced by the very active infections of HIV and HCV, resulting from the lower CD4 counts and other immunosuppressing effects associated with the course of HIV infection. Additionally, co-infection treatment is further hampered by complications from ribavirin and HIV anti-retroviral agents. Fortunately, HCV infection does not seem to alter the course of HIV infection and progression to AIDS. A 2002 study showed HCV infection does not significantly alter the risk of death, development of AIDS, or a positive response to HIV antiviral treatment (4).

The current standard of treatment for chronic HCV infection is a 48-week regimen of peginterferon with ribavirin. The treatment subjects the patient to an unpleasant experience due to the side effects of interferon, including flu-like symptoms and depression, and suffers from only a 40-50% chance of success in achieving an SVR (2).

Two new drugs, telaprevir (Incivek) and boceprevir (Victrelis), have shown tremendous improvement in the percentage of patients who achieved an SVR compared to those who only received standard therapy with peginterferon and ribavirin. Both drugs are nonstructural 3/4A serine protease inhibitors that target multiple steps of the HCV life cycle. In a recent double-blind randomized trial, telaprevir plus standard therapy showed an 83% SVR (2). A similar trial of boceprevir showed an SVR of 68% (3). With both drugs showing significant improvement over the current standard of therapy, it is likely that they will become part of a new standard regimen. It will thus be important to identify and understand the populations that are co-infected and to anticipate challenges in delivering such improved therapies.

Results

Extensive data on patients co-infected with HCV and HIV has been collected from the medical records of patients receiving treatment at the Regional Center for Infectious Disease (RCID) in Greensboro, North Carolina. Over a thousand patients receive HIV treatment currently at the RCID, and approximately 10% of the patients are co-infected with HCV. The age, years since HIV diagnosis, HCV/ HIV viral loads, and CD4 count are analyzed and subdivided according to gender and ethnicity to provide a better description of the co-infected population.

The co-infected sample comprises of 49 African American males (44%), 15 white males (14%), 37 African American females (34%) and 9 white females (8%). The data indicates a higher co-infection rate in African Americans regardless of gender, which is consistent with studies in other locales and is supported by large population surveys, such as the U.S. National Health and Nutrition Assessment.

The average age of the entire group was 51.7 years with a standard deviation of +2.42 years. Both African American males and females tend to be a few years older than their white counterparts, though this slight difference is not significant.

Also remarkable is the consistency in the years since diagnosis. In the co-infected sample, an average of 14.21 years has passed since the original HCV diagnosis. The standard deviation here is +2.71 years, slightly larger than the average age standard deviation. Again there is slight difference between African Americans and whites, with white males being diagnosed about 3 years before African American males and white females about 3 years after African American females. This difference, however, is not significant.
Blood transfusion histories were not available in the co-infected cohort and would be another possible source of HCV infection since HCV testing of donated blood did not begin until approximately 1990. With the development of HCV screening, the majority was diagnosed in the mid to late 1990s and only very few (10 patients of the 117 in this sample group) have received any treatment for HCV, mainly because of cost and fear of side-effects. These HCV infections have clearly been present for some time but now there is cause for some optimism for those with HCV. If one patient were to have a positive response to the new therapies and achieve an HCV SVR, then the remaining and relatively homogeneous population would also be good candidates for treatment.

A few notable differences do arise when comparing the latest average HCV/HIV viral loads and average CD4 counts between ethnicities and genders. White males and females have the lowest (1.9 million IU/mL) hepatitis C viral loads based on testing done an average of 4.4 years ago. They are followed by those of African American females (5 million IU/mL), while African American males have the highest average viral load (6.3 million IU/mL). This further suggests that African American ethnicity is a negative prognostic factor for hepatitis C virus and may partially explain the 10%-15% lower SVR rates to the new HCV antivirals compared to the response in white populations.

Figure 3: Average hepatitis C viral load in IU/mL

HIV viral loads and CD4 counts taken an average of 0.4 years ago show that white males have an average viral load of 803 copies of HIV RNA/mL, with 67% having undetectable (<48 copies of RNA/mL) levels of the virus in their blood, and an average CD4 count of 558/ml. 68% of African American females in the co-infected sample have undetectable HIV RNA levels and an average CD4 count of 504/ml. 49% of African American males in the co-infected sample have undetectable viral loads and an average CD4 count of 443/ml. Finally, only 33% of white females in the co-infected sample display undetectable HIV viral loads and an average CD4 count of 466/ml.

Overall, it appears that white males tend to have overall better control of their HIV infection in terms of lower HIV viral loads and higher CD4 counts. Breaking the trend seen in HCV viral loads, African American females appear to be the second healthiest subgroup followed by African American males. White females seem to have the least control of their HIV infections. These differences among the subgroups could be attributed to a wide variety of factors, including difference in treatment history, social issues, economic status, accessibility of care, and differences in ethnicity. Though these are interesting trends, their usefulness in determining who will benefit from the new HCV treatment is limited as the telaprevir and boceprevir studies were not conducted with HIV co-infected person. Until studies are done analyzing HCV treatment response with regard to HIV progression, this data can only offer a unique demographic breakdown of the co-infected population.

Figure 4: Average HIV viral load in copies/mL

Figure 5: Average CD4 count in cells/mL

Conclusion

Analyzing patient statistics can offer a wealth of information by illuminating trends in disease progression. Physicians can use these patterns to tailor individual treatment based on group factors that prove to be beneficial or detrimental to treatment success. In the cohort of co-infected HIV and HCV patients studied...
here, it was determined that the group was remarkably similar in age and the number of years since HCV diagnosis. This suggests that if one patient were to have a positive response to the new treatment, the remaining patients are likely to as well. If the homogeneity of HIV/HCV co-infection were to extend beyond the sample studied here, patients around the globe might have equally high chances of success.

In the next few years, telaprevir and boceprevir will likely become part of the standard of treatment for chronic HCV. Both are expensive drugs: $55,500 for 12 weeks and $28,500 for 24 weeks, respectively. With one in four patients in this population without any type of health insurance, it is crucial that populations who will potentially benefit from these treatments be identified and access to treatment be provided. Through improvements in medicine and further research in HCV and its co-infection with HIV, it may be possible to obtain sustained virologic responses in a much larger proportion of patients. Additionally, because humans are the only known natural hosts for HCV, it is theoretically possible with improving treatments for HCV to be eradicated from the global population.

**References**


