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TREATMENT OF HEPATITIS C VIRUS IN HIV/HCV CO-INFECTION

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Abstract:

Introduction: *Hepatitis C is an RNA flavivirus that infects 4 million people in the United States making up approximately 1.8% of the population, and 150-200 million worldwide. In persons with HIV, its prevalence is estimated to be approximately 50%.* ***Objectives:*** *The basic aim of the study is to find the treatment of Hepatitis C Virus in HIV/HCV co-infection in Pakistan.* ***Material and methods:*** *This cross sectional study was conducted at Jinnah hospital, Lahore during June 2019 to December 2019. This study was done to find the treatment of hepatitis C virus in HCF co-infection in Pakistan. The treatment of hepatitis C virus (HCV) infection is rapidly evolving. Patients with HCV/HIV coinfection treated with all-oral, direct-acting antiviral (DAA) HCV regimens can achieve sustained virologic response (HCV cure) at rates comparable to those of patients with HCV mono-infection.* ***Results:*** *Initiation of ART for persons with HCV/HIV coinfection should follow the recommendations for all persons with HIV infection, taking into account the need for concurrent HCV treatment with oral DAA regimens, drug-drug interaction potentials, and the individual's HBV status. The same regimens that are recommended for initial treatment of HIV in most ART-naive persons are also recommended for persons with HCV/HIV coinfection.* ***Conclusion:*** *It is concluded that In order to maximize therapeutic efficacy, we will need to determine the immunological defect that is responsible for the diminished cellular immune response to HCV in HIV/HCV co-infected patients.*

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INTRODUCTION:

Hepatitis C is an RNA flavivirus that infects 4 million people in the United States making up approximately 1.8% of the population, and 150-200 million worldwide. In persons with HIV, its prevalence is estimated to be approximately 50% [1]. Main sources for transmission include IV drug use, transfusion of blood products prior to screening, and to a lesser extent sexual intercourse and needle sticks. It is almost universal among hemophiliacs who received transfusions prior to July 1992 [2]. HCV is the leading indication for liver transplantation in the U.S. today, and is responsible for approximately 10000 deaths per year. It is estimated that by 2015, HCV will be responsible for 40000 deaths per year.

Seventy to eighty percent of acute HCV infections become chronic. Approximately 25% of these patients develop end stage cirrhosis after 20 to 25 years, and 1% to 4% of patients with cirrhosis develop hepatoma each year. The median time to cirrhosis is about 19 years. Once cirrhosis is present, the risk of hepatoma increases dramatically. The median time to develop hepatoma is about 29 years. Factors that promote progression of HCV include: alcohol intake, age over 45 at the time of infection, HIV co-infection, male gender, and co-infection with hepatitis B or other viruses. HIV infection and alcohol consumption are independently associated with accelerated progression of fibrosis [3].

Co-infection with hepatitis C virus (HCV) and human immunodeficiency virus (HIV) is common as both viruses share similar modes of transmission. The management of HCV infection in the HIV infected population poses a serious challenge for physicians. Approximately two thirds of co-infected patients do not receive anti-HCV treatment for reasons such as poor compliance with highly active anti-retroviral therapy (HAART), decompensated liver disease, co-morbidities, active substance use, ongoing alcohol use, and advanced HIV disease [4]. Thus, only a minority of such patients receive anti-HCV treatment [5]. In order to improve the outcome in co-infected patients, it is important to have a good understanding and knowledge of HAART and its interaction with drugs used for HCV treatment.

Aims and objectives

The basic aim of the study is to find the treatment of Hepatitis C Virus in HIV/HCV co-infection in Pakistan.

Material and methods

This cross sectional study was conducted at Jinnah hospital, Lahore during June 2019 to December 2019. The treatment of hepatitis C virus (HCV) infection is rapidly evolving. Patients with HCV/HIV coinfection treated with all-oral, direct-acting antiviral (DAA) HCV regimens can achieve sustained virologic response (HCV cure) at rates comparable to those of patients with HCV mono-infection. This section of the guidelines focuses on hepatic safety and drug-drug interaction issues related to HCV/HIV co infection and the concomitant use of antiretroviral (ARV) agents and HCV drugs.

Among patients with chronic HCV infection, approximately one-third progress to cirrhosis, at a median time of <20 years. The rate of progression increases with older age, alcoholism, male sex, and HIV infection. A meta-analysis found that patients with HCV/HIV coinfection had a three-fold greater risk of progression to cirrhosis or decompensated liver disease than patients with HCV mono infection. The risk of progression is even greater in patients with HCV/HIV coinfection who have low CD4 T lymphocyte cell counts. All patients with HIV should be screened for HCV infection using sensitive immunoassays licensed for the detection of antibodies to HCV in blood. At-risk HCV-seronegative patients should undergo repeat testing annually or as clinically indicated. HCV-seropositive patients should be tested for HCV RNA using a sensitive quantitative assay to confirm the presence of active infection.

RESULTS:

Antiretroviral Therapy in HCV/HIV Co-infection

Initiation of ART for persons with HCV/HIV co-infection should follow the recommendations for all persons with HIV infection, taking into account the need for concurrent HCV treatment with oral DAA regimens, drug-drug interaction potentials, and the individual's HBV status. The same regimens that are recommended for initial treatment of HIV in most ART-naive persons are also recommended for persons with HCV/HIV co-infection [6]. Special considerations for ARV selection in persons with HCV/HIV co-infection include the following:

- When both HIV and HCV treatments are indicated, the ARV regimen should be selected with careful consideration of potential drug-drug interactions with the HCV treatment regimen.
- In persons with HCV/HBV coinfection, HBV reactivation has been observed during HCV treatment with DAAs. Therefore, persons with HCV/HIV coinfection and active HBV infection (HBsAg positive) should receive ART that includes agents with anti-HBV activity prior to initiating HCV therapy (AIII). Cirrhotic patients should be evaluated for signs of liver

decompensation according to the Child-Turcotte-Pugh classification system. All patients with Child-Pugh class B or C disease should be evaluated by an expert in advanced liver disease and considered for liver transplantation (table 01).

Table 01. Treatment of HCV for Adults and Adolescents with HIV Co-infection

Preferred Therapy, Duration of Therapy, Chronic Maintenance	**Alternative Therapy**	**Other Options/Issues**
Genotype 1, 4, 5, or 6 Peginterferon alfa-2a 180 µg SQ weekly, or Peginterferon alfa-2b 1.5 mg/kg SQ weekly + Ribavirin PO (weight-based dosing) <75 kg: 600 mg QAM and 400 mg QPM; ≥75 kg: 600 mg QAM and 600 mg QPM **Genotype 2 or 3** Peginterferon alfa-2a 180 µg SQ weekly, or Peginterferon alfa-2b 1.5 mg/kg SQ weekly + Ribavirin (fixed dose) PO 400 mg QAM and 400 mg QPM **Duration of therapy:** 48 weeks -- genotypes 1 or 4, 5, or 6 and genotypes 2 and 3 At least 24 weeks -- treatment of acute HCV infection (<6 months from HCV exposure)	**In patients for whom ribavirin is contraindicated (eg, unstable cardiopulmonary disease, preexisting anemia unresponsive to erythropoietin, renal failure, or hemoglobinopathy)** Peginterferon alfa-2a 180 µg SQ weekly, or Peginterferon alfa-2b 1.5 µg/kg SQ weekly **In patients with decompensated liver disease** Liver transplantation if feasible	For patients with CD4 count of <200 cells/µL, initiation of ART may be considered before HCV treatment. Didanosine + ribavirin may lead to increased mitochondrial toxicities; concomitant use is contraindicated. HCV therapy is not recommended for patients with hepatic decompensation. Liver transplantation, if feasible, should be the primary treatment option. (Treatment after liver transplantation may be indicated, if the transplanted liver becomes infected.) Interferon is abortifacient in high doses and ribavirin is teratogenic. HCV treatment is not recommended for pregnant women or women who are not willing to use birth control.

DISCUSSION:

HIV patients have been living longer making the HCV infection a pressing problem [6]. Regarding treatment of HCV in co-infected patients, the main factor in deciding who should be treated is the CD4 count. Patients with CD4 counts greater than 500 have been found to have response rates not significantly different from patients without HIV. Patients with CD4 counts less than 200 have been shown to have no significant response. Hence, therapy in those cases is not recommended. Patients with CD4 counts less than 500, but greater than 200 have intermediate response rates. Accordingly, patients are generally treated with HAART first to optimize the immune system before initiating anti-HCV therapy.

Liver toxicity is a potential problem with all of the HAART medications [7]. There is a higher rate of hepatotoxicity in co-infected patients who are being treated with HAART therapy. Of the protease inhibitors, several sources cite Ritonavir as the most liver toxic. Ritonavir trough levels are often twice as high in patients with HCV infection. Indinavir can

cause severe hyperbilirubinemia in patients with HCV co-infection [8,9].

Ribavirin may interact with selected nucleoside reverse transcriptase inhibitors (AZT, ddi, d4T) and reduce their anti-HIV activity due to interference with intracellular phosphorylation. If AZT is given concomitant with ribavirin, there is an increased incidence of anemia and complete blood counts should be carefully monitored [10].

CONCLUSION:

It is concluded that In order to maximize therapeutic efficacy, we will need to determine the immunological defect that is responsible for the diminished cellular immune response to HCV in HIV/HCV co-infected patients. It will be of value to determine the mechanism causing the defect that leads to an increase in hepatotoxicity in anti-retroviral drugs so that drug therapy can be better managed.

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