**Case Report**

**MEDICAL RESEARCH WORK ON VIRAL DISEASE [HEPATITIS B AND C]**

**MARIA BATOOL1\***

***1****\*Student of Pharmacy, University of Sargodha, Punjab, Pakistan*

*\*Corresponding author’s email: mariabatool12198@gmail.com*

**ABSTRACT**

Dual hepatitis C virus (HCV)/hepatitis B virus (HBV) infection is not uncommon in HCV or HBV endemic areas and among subjects at risk of parenteral transmission. In patients dually infected with hepatitis C and B, the disease manifestations are usually more severe than those with either virus infection. In the past decade, the following issues have been resolved. In dually infected patients with active hepatitis C, combined pegylated interferon alfa plus ribavirin was effective, the treatment outcomes being similar to patients with HCV monoinfection. During long-term follow-up, the HCV response was sustained in around 97% of patients; and the long-term outcomes including the development of hepatocellular carcinoma and liver-related mortality were improved. However, several clinical issues remain to be resolved. First, host and viral factors influencing the long-term outcomes and treatment options in patients with dual HCV/HBV infection await further studies. Second, about 60% of dually infected patients with baseline undetectable serum HBV DNA levels develop HBV reactivation after the start of treatment. How to prevent and treat HBV reactivation should be clarified. Third, about 30% of dually infected patients lose hepatitis B surface antigen at 5 years after the end of combination therapy; the mechanisms need further investigations. Fourth, the optimal treatment strategies for dually infected patients with active hepatitis B or established cirrhosis should be explored in future clinical trials. Finally, the role of new direct-acting antiviral-based therapy for the treatment of patients with dual HCV/HBV infection also remains to be evaluated.

***Keywords:*** Dual infection, HBsAg clearance, Hepatitis B virus, Hepatitis C virus, ISGs, cccDNA, Cell culture model, Interferon, Primary human hepatocytes.

**1.0 INTRODUCTION**

Worldwide majority of hepatitis patients have chronic hepatitis C virus [HCV] monoinfestion. In area or countries where hepatitis B virus [HBV] infection is endemic it is not uncommon to encounter patient infected with both hepatitis viruses[1,2,3].In patients with dual chronic hepatitis C and B, the disease manifestations are usually more severe than those with either virus infection[4,5].A large follow-up study demonstrated the combined effect of HCV and HBV infection on the progression of chronic liver disease[6].Therefore, patients dually infected with hepatitis C and B should be followed more closely and require effective treatment .Hepatitis B and C virus pose a serious health problem around the globe. Worldwide, about 350 million have chronic HBV infection and 170 million people chronic HCV and 3-4 million people are newly infected each year [7]**.** Pakistan has huge burden of these viral disease l For HCV the prevalence within the provinces is 5% in Sindh, 6.7% in Punjab, 1.1% in NWFP and 1.5% in Balochistan. For HBV the figures are 2.5% in Sindh, 2.4% in Punjab, 1.3% in NWFP and 4.3% in Baluchistan [8]. Seven hepatitis agents have been identified with the likelihood that there are still others that await full characterization [9]. Hepatitis viruses have been classified into enterically transmitted hepatitis; A and E and parenterally transmitted Hepatitis; B, C and D.

**1.1** **SIGNS AND SYMPTOMS**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Symptoms and Sign of Chronic Viral Hepatitis by Stage of Disease** | | | | |
|  | **Chronic Hepatitis B** | | **Chronic Hepatitis C** | |
| **Symptoms** | **Signs** | **Symptoms** | **Signs** |
| Early and/or slowly progressive liver disease | Generally none | Often none  Hepatomegaly | Often none  Lethargy  Anirexia  Nausea  Abdominal discomfort  Intolerance to alcohol and fatty foods | Often none  Hepatomegaly |
| Progressives liver disease | Often episodic  Hepatic flares | Hepatomegaly  Mild jaundice  Peripheral stigmata of CLD | Often none  Lethargy  Anorexia  Nausea  Abdominal discomfort  Intolerance to alcohol and fatty foods | Sometime none  Hepatomegaly  Peripheral stigmata of CLD |
| Advanced liver disease | Increasing lethargy  Fluid retention  Brusining  Prolonged  Bleeding | Peripheral stigmata of CLD  Gynaecomastia  Ascites /oedema  Splenomegaly  Distented abdominal  Veins  Bruising  Hepatic  Encephalopathy  Jaundice[Poor prognostic sign] | Increasing lethargy  Fluid retention  Bruising  Prolonged bleeding | Peripheral stigmata of CLD  Gynaecomastia  Ascites/oedema  Splenomegaly  Distented abdominal  Veins  Bruising  Hepatic  Encephalopathy  Jaundice[poor prognostic sign] |

CLD=Chronic liver disease [10]

The signs and symptoms of Hepatitis **C** are the following.

Fatigue, Joint pain, Belly pain, Itchy skin, Sore muscles, Dark urine and Jaundice, a condition in which the skin and the whites of the eyes look yellow. Hepatitis C infection can cause damage to your liver (cirrhosis). If you develop cirrhosis, you may have: Redness on the palms of your hands caused by expanded small blood vessels. Clusters of blood vessels just below the skin that look like tiny red spiders and usually appear on your chest, shoulders, and face. Swelling of your belly, legs and feet. Shrinking of the muscles. Bleeding from enlarged veins in your digestive tract, which is called variceal bleeding. Damage to your brain and nervous system, which is called encephalopathy. This damage can cause symptoms such as confusion and memory and concentration problems [11].

Signs and symptoms of Hepatitis **B** usually appear about three months after you've been infected and can range from mild to severe. Signs and symptoms of hepatitis B may include:

Abdominal pain, Dark urine, Fever, Joint pain, Loss of appetite, Nausea and vomiting, Weakness and fatigue Most infants and children with hepatitis B never develop signs and symptoms. The same is true for some adults [12].

**1.2 CAUSES**

HBV and HCV are blood borne viruses and are primarily transmitted by percutaneous and mucosal exposures.Percutaneous and permucosal exposure to infectious blood and body fluids is the main mode of transmission; however, transfusion-related hepatitis has virtually disappeared in countries applying routine blood screening [13]. Due to the sharp rise in intravenous drug use, currently, injection-drug use is the most common risk factor for contracting the HBV, HCV and HDV infection worldwide.

In developing countries, nosocomial exposure is a leading cause of infection due to lapses in recommended disinfection techniques [14]. High prevalence of anti-HCV in hemodialysis centers, ranging from 2% to 64%, was reported [15]. Studies suggest that outbreaks of HCV transmission occurs between hemodialysis patients when multiuse medication vials and improper decontamination of shared dialysis equipment were practiced [16]. Nosocomial transmission of HBV from inadequate sterilization of medical and dental instruments, and unsafe injection practices continues to be a problem and may account for a majority of infections [17].In developing countries, percutaneous exposures in other settings such as tattooing, body piercing, scarification, commercial barbering and other practices done as a part of cultural and ritual practiceshave been reported to be responsible for HBV and HCV infection [18]. Although, perinatal (vertical) and sexual transmission of HCV is less common and even difficult to document, the perinatal transmission of HBV is of significant importance especially in high prevalence areas [19]. Beasley in 1983has shown that in South-east Asia the predominant route of HBV transmission is mother to child transmission [20]. Women with an active HBV infection (acute or chronic) can transmit infection to their newborn either in utero or after delivery from mucous membrane exposure to blood and during the early years of life. As well as, it can be transmitted horizontally during childhood through close contact [21]. Unfortunately, the rate of progression from acute to chronic HBV is more than 90% for perinatal infection, but less than 5% for adult infection. Thus more than 90% of infants born to HBeAg positive mothers will become infected [22].

**2.0 CASE STUDY**

A lady of age 35 was suffering in a disease of hepatitis B and C. At start she felt pain in bones, in muscles, in shoulders and in joint even it is very difficult for her to walk. Her sleep reduced. Gradually these symptoms increased more severely. And then it was difficult for her to walk. She also felt restlessness. She also wanted to eat sand. She also felt pain in stomach. She feels vomiting. When this condition occurs for about 5 to 6 month. And condition gradually becomes more severe then she consulted to doctor. He gave her some blood test. From these test it has been proved that she was suffering with Hepatitis B and C.

**2.1 INVESTIGATION/DIAGNOSIS   
[All Clinical, Biochemical, Radiological and Microbiological Test]**

At start doctor gave her blood tests and its results are following from which it has been proved that she suffered with Hepatitis B and C.

|  |  |  |
| --- | --- | --- |
| **Haemotology Report** | | |
| **Blood Complete Picture** | **Results** | **Normal Values** |
| Hemoglobin | 12.0 | 12-17gm/dl |
| ESR | **70** | 2-17mm/Fh |
| WBC’S | 5300 | 4000-11000/cmm |
| **Differential Count** | | |
| Neutrophils | 66% | 40% -70 % |
| lymphocytes | 26% | 20% - 45% |
| Monocytes | 04% | 01% -10% |
| Eosinophils | 04% | 01% -06% |
| Blood group | O + ive |  |

|  |  |  |
| --- | --- | --- |
| **Blood Chemistry** | | |
| **Test Name** | **Result** | **Normal Value** |
| **Renal Profile** | | |
| Urea | 35 | 10-45mg/dl |
| Creatinine | 0.8 | 0.6-1.3mg/dl |
| Uric acid | **8.2** | M=3-7mg/dl |
| **LFT Profile** | | |
| Bilirubin Total | 1.0 | upto 1.2mg/dl |
| Un-conjugated | 0.4 | upto 0.9 mg/dl |
| SGPT[ALT] | **75** | F=up to 36u/l  M=9 to 42u/l |
| Total lipid | 832 | 400-1000mg/dl |
| Cholesterol | 184 | 120-200mg/dl |
| Triglycerides | 115 | 50-150mg/dl |
| HDL | 56 | 35-60mg/dl |
| LDL | 148 | upto 190mg/dl |

|  |  |
| --- | --- |
| **Serology and Immunology** | |
| HBs Ag Rapid Screening | Positive |
| Anti HCVAb Rapid Screening | Positive |

From these tests it has been confirmed that patient was suffering with Hepatitis B and C. Then Doctor gave her Lanzol 30mg [before breakfast], Scitin 16mg [1+1], Carlov [1+1], Vit-k [1+1]. From these medicines the patient feels much better. When she again consulted to the doctor he gave Esomaga 40mg [before breakfast], Carlov 12.5mg[1+1], Vit-k [1+1], Lysovit [two spoon at noon], Unix 100mg [1+1] for fever, Scitin 16mg. From these medicines the hepatitis B is removed within one year and patient feel much better and satisfied with treatment. When hepatitis B is recovered the patient condition is much better. Pain in muscles, joints and bones reduced. Restlessness and fever also much recovered. Then time to time doctor gave her blood tests to check the condition. Every time there occur variations in

|  |  |  |
| --- | --- | --- |
| **Hemoglobin level** | **ESR** | **Platelets** |
| 10.9g/dl | 115mm/hour | 118000/cmm |
| 11.8g/dl | 81mm/hour | 145000/cmm |
| 11.6g/dl | 65mm/hour | 168000/cmm |
| 11.6g/dl | 80mm/hour | 132000/cmm |

Sometime uric acid level also increases 6.4mg/dl  
But gradually **Serology**

|  |  |  |
| --- | --- | --- |
| HBs Ag ELISA | 0.2675 | Non Reactive |
| Anti-HCV ELISA | 2.792 | Reactive |

So hepatitis B is removed but Hepatitis C is under treatment

**2.2 PHARMACOTHERAP**

|  |  |
| --- | --- |
| **Current treatment** | |
| **Drug** | **Dose** |
| Risek 20mg | 1+1 Before breakfast |
| Carlov 12.5mg | 1+1 |
| Pregesic | 1+1+1 |
| Lilac 30cc | Two tea spoons (When required) |
| Evion 400mg | 1+1 |
| Etoxib 60mg | 1 |

From these medicine patient is feeling much better.

**3.0 DISCUSSION**

Active hepatitis C is found in more than 50% of dually infected patients.[23] Besides, HCV can be successfully eradicated in at least 70% of patients with chronic HCV mono-infection using combination therapy of Peg-IFN and RBV in Asian-Pacific region.[24] Accordingly, HCV seems to be the priority target to be managed in dually infected patients with active hepatitis C.

Early small care series found that interferon (IFN) alone was not effective in the clearance of HCV RNA in dually infected patients.[25] Later on, we demonstrated that combination therapy of conventional IFN plus RBV had better, albeit not satisfactory, HCV SVR rates.[26,27]

Whether Peg-IFN and RBV combination therapy could reduce the risk of HCC or improve survival in HCV/HBV dually infected patients was evaluated in a large population-based cohort from Taiwan.[28] We examined the risk of HCC, mortality, and adverse events in 1096 treated and 17 562 untreated HCV/HBV dually infected patients. After adjustment, combination therapy significantly reduced the risk of HCC ([HR] 0.75, 95% confidence interval [95%CI] 0.58–0.96), liver-related mortality (HR 0.45, 95% CI 0.35–0.57), and all-cause mortality (HR 0.39, 95%CI 0.32–0.48). Nevertheless, the underlying HBV infection was still a risk factor for HCC and mortality after treatment. Our data demonstrated that combination therapy decreased the risk of developing HCC and improved survival in HCV/HBV dually infected patients [ 29].

Risek [Omeprazole] is in a group of drugs called proton pump inhibitors. Risek decreases the amount of acid produced in the stomach. Risek is used to treat symptoms of gastro esophageal reflux disease (GERD) and other conditions caused by excess stomach acid. Risek may also be given together with antibiotics to treat gastric ulcer caused by infection with helicobacter pylori (H. pylori). It may cause diarrhea or watery fluid. It may also cause fever, nausea, vomiting and headache. It is usually taken before eating [30].

Carlov is used to treat the high blood pressure and congestive heart failure. It is used by itself or with diuretic. It is used twice a day. It can be taken with calcium channel blocker. It allow at least for 4 months or used with the doctor advised [31].

Evion reduces the fatty food intake. It can be taken twice a day [32]. Etoxib is the NSAID’S prescribed for osteoarthritis. It is taken once a day. Lilac syrup is a type of sugar that may be used to treat chronic constipation, and is also prescribed to prevent portosystemic encephalopathy, which is a possible complication of advanced liver disease. This product, which is a synthetic sugar, creates a more acidic environment in the patient's intestines. The end result is that the stool is softened and the levels of ammonia in the blood are reduced. Pregesic has analgesic, antipyretic and anti-inflammatory action. Its mechanism of action is closely associated with the inhibition of prostaglandin synthesis. Pregesic is taken once a day. That is, you take one pill either in the morning or in the evening. These medicines which are given by the doctor are good. Patient is much recovered. Doctor also changed the medicine after its time period [33].

**4.0 CONCLUSION**

HCV/HBV dual infection is not uncommon in areas endemic for HCV or HBV infection and among subjects at risk of parenteral transmission. Before the implementation of antiviral therapy, thorough serological and virological examinations are required to determine the viral dominance as well as to determine the optimal antiviral regimen. For dually infected patients with active hepatitis C, the same genotype-dependent treatment recommendations for single chronic hepatitis C still hold true [34,35]. However, for dually infected patients with active hepatitis B or with established cirrhosis [36], more studies are needed to determine the optimal regimen to treat both viruses at the same time. The value of DAA-based triple therapy in this population also remains to be clarified.

**5.0 RECOMMENDATIONS**

Awareness-raising among the general population and among people at increased risk of hepatitis B and C infection. Developing the knowledge and skills of healthcare professionals and others providing services for people at increased risk of hepatitis B or C infection. Testing for hepatitis B and C in primary care, prisons and youth offender institutions, immigration removal centers, drugs services and in genitourinary medicine and sexual health clinics. Contact tracing. Providing and auditing neonatal hepatitis B vaccination. Commissioning hepatitis B and C testing and treatment services. Laboratory services for hepatitis B and C testing.

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