

Review Article

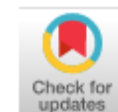
ROLE OF MODERN TECHNOLOGY FOR TREATMENT OF HCV

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Abstract: *HCV is the main reason of the liver disease and worldwide it is one of the major issues of health due to its development into cirrhosis, failure and cancer of liver. The transference of HCV is mainly through the parental but people who use drug like intravenous are also at greatest threat. The life cycle of HCV is now understood in a more precise way due to extensive studies. Due to more understanding of this virus there is establishment of more effectual antiviral medications and also diagnostic devices. Test of nucleic acids are suggested for the validation of active HCV. Serology tests are suggested for the groups that are at the greatest risk. Earlier for the standard medications of HCV interferon (IFN- α) and ribavirin are used. Later FDA approved a number of drugs such as harvoni, simeprevir and boceprevir etc. for the proper treatment of HCV. Antiviral medications will be utilized to treat the infections of HCV. In the management of certain severe viral infection, therapeutic option has improved in a better way. There is need of follow-up and careful consideration as well as there are many new technologies that have developed for the quantitative measurement of viral genome concentration in the body fluid of patients. Initially this measurement led to important insight in the viral infection pathogenesis as well as these test also revolutionized natural history of HCV. In addition viral load test are pure tool for research, these are used in routine viral diagnosis. Viral load test are used in clinical virology for diagnosis and prognosis of patient's.*

Keywords: HCV, liver, ribavirin, cirrhosis, drug, cancer, interferon

Introduction

HCV belongs to flaviviridae family and enveloped in a membrane and its genus is hepacivirus. The RNA of HCV is single stranded and its polarity is positive. HCV result in a disease that is known as hepatitis C that is a disease of liver (Bacon, 2002; Davis, 2002). There are two types of hepatitis C that are caused by HCV. One is acute and second one is chronic. Time span of acute hepatitis C is shorter and it causes very less or almost no sign and symptoms. In majority of the cases infection of acute one get better without any need of treatment. There are main five kinds of viruses of hepatitis that result in acute one. It can also leads towards chronic hepatitis that is a lifelong sickness or disease (Conry-Cantilena et al., 1996; Di Bisceglie and Hoofnagle, 2002). People that are infected with HCV, their disease can progress into cirrhosis in which liver could not work accurately and can also develop into cancer of liver (Association, 1995; Berger and Preiser, 2002). The number of patients that are recognized every year with the infection of hepatitis C virus are approximately four million. Approximately 170 million people of the world are affected with HCV.

At present time there is no vaccine exist that is effective for the treatment of HCV. HCV is the related to Hepatitis C virus. It is a major cause of liver cancer, hepatocellular carcinoma and liver failure (Alberti et al., 2002; Alter et al., 1999; Berger et al., 2001). This infection spread through blood by drug used injection, drug transfusion of blood product and by sexual practices which cause blood exposure. Chronically infected people will be affected by liver cancer or cirrhosis. It is not spread through food, water and breast milk (Briggs et al., 2001; Conry-Cantilena et al., 1996).

There are two stages of HCV one is acute and other is chronic. On the basis of stage of the infection there is variation in signs and symptoms. The symptoms of HCV are vomiting, fever, fatigue, dark urine, poor appetite, jaundice, itchininess on skin, loss in weight and severe pain in joints. The spreading of hepatitis C occurs when blood that is infected with the virus of hepatitis c enter into the bloodstream. It enters either through blood that is contaminated or body fluids of a person that has the disease (Control and Prevention, 2001; Di Bisceglie, 2000; Eddy, 1996). Virus of hepatitis is not spread through bites of mosquito, coughing, sneezing and using eating utensils of an infected person. Due to variation in the genotypes of

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the patients, there is differentiation in the response towards interferon because genotype is very important aspect. The clinical trials show the significance of the genotypes of HCV due to difference in the response of alpha interferon. More reaction is shown from the patients who have genotype 2 & 3 as contrast to the patients who have genotype 1. SVR response that is shown by genotype 2 & 3 is more as compare to the response that is shown by the genotype 1 (El-Zayadi et al., 2005; Fried et al., 2002; Preiser et al., 2000).

Labortary Testing

There are three classes of assays that are serologic assay, molecular assay and genotype assay.

Serologic Assays

Table 1: Tools for the diagnosis of hepatitis C virus infection and hepatic fibrosis stage

Assay/Manufacturer	Methods	Reaction sample volume (µL)	Lower limit for detection (IU/mL)	Instruments	IVD registration	References
APTIMA HCV RNA Qualitative Assay, Hologic-Gen-Probe	TMA	500	5.3	Not automated, PANTHER System's functionality currently in development	FDA	(Panneer et al., 2014)
COBAS AmpliPrep/COBAS, TaqMan HCV Qualitative Test v2.0, Roche Molecular System	Real-time RT-PCR	650	15	Fully automated: cobas p 630 Instrument (Primary Tube Handling), COBAS AmpliPrep (Extraction and MM setup), COBAS TaqMan Analyzer or the COBAS TaqMan 48 Analyzer (Amplification and detection)	CE, FDA	(Butcher et al., 2014; Deeks, 2015; Mazzuti et al., 2016)
VERSANT HCV RNA Qualitative Assay, Siemens	TMA	50	5.3	TMA modules (TCS, Luminometer HC+, etc.)	CE, FDA	(De Keukeleire et al., 2015; Grüner et al., 2015)
COBAS AmpliPrep/COBAS AMPLICOR HCV Test v2.0, Roce Molecular Systems	Real-time RT-PCR	250	50 (Plasma) 60 (seum)	COBAS AmpliPrep (Extraction), COBAS AmpliPrep/COBAS AMPLICOR Analyzer (Amplification and detection)	CE, FDA, Canada	(Deeks, 2015; Pyne and Hillyard, 2013)
COBAS AmpliPrep/COBAS AMPLICOR HCV Test v2.0, Roche Molecular Systems	Real-time RT-PCR	500	50 (Plasma) 60 (seum)	COBAS AmpliPrep/COBAS AMPLICOR Analyzer (Amplification and detection)	CE, FDA, Japan	(Deeks, 2015; Pas et al., 2013)

Molecular assay

It detects nucleic acid of virus. This is a qualitative assay and more sensitive than quantitative assay. The availability of transcription mediated amplification assay and polymerase chain reaction based assay, has reduce the need of qualitative assay (Fried, 2002; Gross et al., 1994; Hodinka, 1998).

Genotype Assay

It detect particular antibody to anti HCV. By using immunoassay, anti HCV detect in the plasma or serum. By the US food and drug administration, two enzyme immune assays are Abbott HCV EIA 2.0 and ORTHO HCV version 3.0 ELISA, as well as one enhanced CHEMILUMINESCENCE immune assay (CIA). The particularity of present EIAs is greater than 99%. When we perform test among those people having low prevalence of hepatic C, false positive result occurred (Table 1). False negative result occurs in severe immuno separation *i.e.*, solid organ transplant recipient, infection with HIV or in patients having hemodialysis (Hodinka, 1998; Hoofnagle, 2002; Hu and Tong, 1999; Preiser et al., 2000).

It is usually done in clinic study and epidemiological studies determining the therapy. There are six major genotype of HCV. Genotype 1 is followed by genotype 2 and 3. Genotype 1 is the most common in US. Genotype 4 and 6 are among less common genotype due to its growing culture in United States (Berger and Preiser, 2002; El-Zayadi et al., 2005; Fattovich et al., 2004).

Treatment of HCV

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The standard treatment for hepatitis C is direct acting antiviral (DAAs).

DAAs

DAAs acts on various targets in HCV virus. Some drugs has not function alone, but they perform their activity by combining them with other drugs. DAAs drug combination is prescribed for 12-24 weeks, once or twice a day by oral pathway. DAAs drug combination is not injected in patients. Sometimes they are in single tablet as they are very effective. In some instance DAAs drug combination is prescribed for only 8 week to those patients that are not suffering from liver disease (Berger et al., 2001; Fattovich et al., 1997; Feld and Hoofnagle, 2005; Hadziyannis et al., 2004). Except old treatment (DAAs) directly effect on hepatitis C virus.

Side effects of DAAs are headache, vomiting and fatigue.

There are various mechanisms to fight HCV. These include,

Protease Inhibitors

The protease inhibitors for hepatitis C are Simeprevir and Voxilaprevir. These DAAs block the enzyme protease and stop the replication (Feld and Hoofnagle, 2005; Hadziyannis et al., 2004).

Polymerase Inhibitors

It stops the replication ability of virus. Doctors use sofosbuvir by combining it with other medicines for the treatment of hepatitis C (Gerlach et al., 2003; McQuillan et al., 1999; Pawlowsky, 2002).

NS5A Inhibitor

There is a protein that has important role in replication of hepatitis C , NS5A protein that is directly target by NS5A inhibitors are Daclatasvir, Elbasvir, Velpatasvir, Ombitasvir and Pibrantasvir (Pawlowsky et al., 1998; Schreiber, 1996; Shah and Wong, 2006).

Ribavirin

When ribavirin combine with peginterferon alpha. It can cause common side effects that are tiredness, headache, shivering, mood changing, trouble sleeping, heart attack, liver problem, depression and pneumonia. When we stop this treatment, it leads to weight gain. For the treatment of hepatitis C, Doctor use ribavirin, interferon. Ribavirin also stops the replication of hepatitis C in the body. It has no function alone, people use it with combination of other medications e.g. interferon. Drug has serious black box varining from the food and drug administration (Hadziyannis et al., 2004; Hu and Tong, 1998; McQuillan et al., 1999).

Interferon

Interferon is natural proteins that increase immune activity in body. When we use interferon for the treatment of hepatitis C, it lead to flu like symptoms and other side effects are chills, headache, muscle

aches, loss of appetite, changes in mood, anemia, changes in vision, decreased thyroid function, depression and anxiety. When we combine interferon with ribavirin then it cause lowering in red blood cells (Hoofnagle, 2002; Kamal et al., 2004; Woolf and Sox, 1991).

Management

People who are suffering from HCV can manage their symptoms by following guidelines are to maintain body weight, avoid smoking, avoid alcohol and liver damaging substances. There is no vaccine exists for HCV (Hoofnagle and Seeff, 2006; Pawlowsky et al., 1998).

Rate

During 2017, HCV affected 71 million persons and estimated 19 people were diagnosed with chronic infection of HCV. At the end of 2017, 5 million were treated by DAAs. There should be more research and work on HCV to achieve 80% HCV by 2030 (Hoofnagle, 2002; Shah and Wong, 2006).

Future Perspective

In last five years there are many advancements have been done in the treatment of hepatitis C disease. For the treatment of chronic type of hepatitis C there are many new strategies that are under clinical phase. Much advancement has been done in the dose and time span of the current treatments. Higher rates of SVR are obtained when ribavirin is provided at higher levels. It is observed when a small trial is conducted (Hofer et al., 2003; Hu and Tong, 1999). Latest types of interferon are under clinical trials and being tested. There is development of inhibitors (small molecules) that target the enzymes and these enzymes are virally encoded like proteases (Kim, 2002; Pawlowsky, 2002).

Conclusion

The medications that are currently available for the treatment of chronic form of HCV infection are interferon and ribavirin. Various side effects are related to these types of treatments. Latest therapeutic strategies are under development and inhibitors of HCV are focused in latest clinical trials. The rates of mortality & morbidity are decreased due to advancements in the treatments of HCV. The positive outcome is obtained from inhibitors of protease that are under initial trials. There are six main types of genotypes (1-6) of this virus and the divisions of these genotypes vary globally. Response rates of these six genotypes have been improved due to the advancement in the treatment.

Conflict of interest

The authors declared the absence of any conflict of interest.

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