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Hepatitis C Infection among Intravenous Drug Users. "A Silent Disease in an Invisible Population"

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ABSTRACT: ***Objective:*** *Hepatitis is defined as an inflammation of the liver. Our objective is to highlight the devastating effects Hepatitis C, a subtype of viral hepatitis, has on a subpopulation of patients struggling with Alcohol use disorder (AUD) and SUDs (Substance Use Disorders) and specially IDUs, (Intravenous Drug Users) also known as the invisible population. We also aim to describe the clinical picture, viral genotypes and available treatments.* ***Methods:*** *A literature review was conducted, specifically looking at published materials about the objectives above.* ***Conclusion:*** *Hepatitis C is considered a global health problem. Described as a "silent disease" its complications include liver cirrhosis, end-stage liver disease and hepatocellular carcinoma, co-infection with HIV and super infections with different strains of HCV. Recent advances in understanding HCV virology have led to the development of new drugs targeting replication process and proving to be very successful in clearing the infection it is important to note that there is no vaccine yet for HCV infection.*

Keywords: *Hepatitis C, Silent disease, Alcohol use Disorder, Intravenous drug users, Global health*

Abbreviations: *AUDs: Alcohol Use Disorders; CLIAs: Chemo Luminescence Immunoassays; DDAs: Directly Acting Antiviral Agents; ECLs: Electro Chemo Luminescence Immunoassays; EIAs: Enzyme Immunoassays; IDUs: Intravenous Drug Users; HCV: Hepatitis C Virus; NAT & NAAT: Nucleic Acid Test and Nucleic Acid Amplification Test; RDTs: Rapid Diagnostic Tests; SUDs: Substance Use Disorders*

INTRODUCTION

Hepatitis C is considered to be a major health issue globally. 5 Viral families are known to cause hepatitis and are labelled as: A, B, C, D and E. Hepatitis B (HBV) and hepatitis C (HCV) are the most common viral hepatitis infections transmitted through the risky behaviors that drug users often engage in. (NIH, 2016).

The global prevalence of anti-HCV was estimated at 2.0% (1.7–2.3%) among adults and 1.6% (1.3–2.1%) for all ages corresponding to 104 (87–124) million and 115 (92–149) million infections, respectively. Some parts of the world like Southern and Eastern Europe, Japan, and Africa have very high prevalence rates above 1.5%. The viraemic prevalence was 1.4% (1.2–1.7%) among adults and 1.1% (0.9–1.4%) in all ages corresponding to 75 (62–89) million and 80 (64–103), respectively. (Gower et al 2014). It continues to grow with an estimate of 170 million people infected in 2015. (Webster, 2015). According to the WHO between 350000 and 500000 people die every year from hepatitis C and related liver disease. (WHO, 2014).

The World health Organization (WHO) efforts are to be applauded, where they have declared the 28th of July of each year as hepatitis awareness day, raising awareness, promoting partnerships and mobilizing resources; formulating evidence-based policy and data for action; preventing transmission; and executing screening, care and treatment. (WHO, 2014).

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Hepatitis C infection occurs when blood or other body fluids from an infected person enter the body of an uninfected person. Hence, as a blood borne infection, the virus is spread through one of these ways:

- Injection drug use and unsafe behaviors like sharing infected needles or injection paraphernalia and inadequate sterilization of medical equipment.
- Organ transplants and Blood transfusions. (Screening of the blood supply for HCV began in 1992).
- Outbreaks. (Uncommon but known as a recognized risk).
- Another recognized risk is having a sexually transmitted disease (STD) or HIV. Sex with multiple partners, or rough sex also increases the risk. Tattoos and body piercings in informal settings or the use of non-sterile instruments can spread the infection. Some people just can't be sure of how or when they got infected. (CDC, 2013).
- In pregnancy though mother to baby transmission.

The IDUs face other comorbid disorders like mental illness, and downward social drift and require coordinated response from multiple agencies. This highlights the importance of closing the addiction treatment gap and offer treatment and rehabilitation from drug misuse/abuse especially opioid addiction, since there is good evidence that treating those patients with opioid assisted therapy (Methadone/Suboxone) improves the outcome of treatment of their HCV infection. (Bruce. et al, 2013). It is estimated that each IDU patient infected with HCV is likely to infect about 20 others. This rapid transmission of the disease occurs within the first three years of initial infection (Magiorkinis, et al. 2013).

TIME LINE

1970: NIH, USA researchers described post transfusion hepatitis as non- A non- B hepatitis (NANBH) as they were not due to the known Hepatitis A or B viruses.

1987: collaboration between Chiron and CDC in USA led to the identification of the organism and development of a diagnostic test.

1988: presence of the virus in NANBH panel specimens confirmed at the NIH. (Boyer, 2001)

1989: Hepatitis C virus (HCV) was described as a cause of post transfusion hepatitis.

1991: Complete HCV genomic sequence identified and conception of hybridization probes and primers to amplify viral genome by polymerase chain reaction (PCR). (Choo et al., 1991).

GENOTYPES

Hepatitis C virus (HCV) is a single-stranded RNA (Ribonucleic acid) virus. That means the genetic code of each virus particle is contained within one continuous piece of the nucleic acid RNA.

Hepatitis C is divided into six distinct genotypes with multiple subtypes in each genotype class. A genotype is a classification of a viruses based on the genetic material in the RNA strands of the virus.

The following is a list of the different genotypes of chronic Hepatitis C:

Genotype 1a, 1b, Genotype 2a, 2b, 2c and 2d, Genotype 3a, 3b, 3c, 3d, 3e and 3f.

Genotype 4a, 4b, 4c, 4d, 4e, 4f, 4g, 4h, 4i and 4j,Genotype 5a, Genotype 6a.

Genotype 1 is the most common type and the most difficult to treat.

IDUs are at a particular risk of Super infection (where a cell previously infected by one virus becomes co-infected with a different strain of the virus which is highly mutable) (Table 1).

CLINICAL PICTURE

Hepatitis C virus causes the liver disease that can be acute or chronic with an incubation of 2 weeks to 6 months. 80% of those infected with the virus do not show any symptoms. The commonest symptoms of HCV infection include: fever, loss of appetite, fatigue, nausea, vomiting, abdominal pain, dark urine, gray colored stool and jaundice. The infection itself may be acute or chronic. The acute form is usually asymptomatic. In most people it leads to a chronic infection 75% to 85%. (CDC, 2017). The chronic form lasts a lifetime leading to chronic liver disease including cirrhosis (15% to 30% of patients) and cancer. Besides the liver other organs may be affected as the result of the body's immune system response. In some cases of Hepatitis C, the most significant organs involved are the kidneys, which can be damaged due cryoglobulinemia (precipitation of a specific type of protein called cryoglobulin), which precipitate at a temperature degree below 37°C (normal body temp) resulting in an inflammation and blockage of blood vessels.

DIAGNOSIS

The following blood tests are available to diagnose HCV:

» ELISA (Enzyme-Linked Immunosorbent Assay).

» RIBA (Recombinant Immunoblot Assay).

» PCR (Polymerase Chain Reaction).

The following facts should be kept in mind:

1. A positive result for anti-HCV detection or a suspected case of HCV exposure should be followed by HCV RNA – PCR testing. (CDC, 2013).
2. When people with early infections have not developed antibody levels high enough that the test can measure, a false negative occurs.
3. Also, some people may lack the immune response necessary for the test to work well. For that reason, the most sensitive research based tests, such as the RT-PCR, commonly called PCR (polymerase chain reaction) may be considered.
4. ***Liver biopsy*** can aid in determining decisions with regard to if and when treatment should be started, based on the findings.
5. Serological assays detect the host immune response

Table 1.
List of drugs approved for HCV treatment and the year they were approved and relevant information

Year	Drug	Comments	Genotype	SVR & comments
2016	Zepatier	Elbasvir and Grazoprevir combined	1-4	Up to 97% SVR for genotype 1.
				Up to 100 % for genotype 4.
	Epclusa	Sofosbuvir/Velpatasvir	1-6	98% SVR for Genotype 2 and 3.
2015	Daklinza	Daclatasvir	3	Reduced SVR in genotype 3 patients with cirrhosis. For use with sofosbuvir.
	Technivie	Ombitasvir, Paritaprevir and Ritonavir)	4	In combination with ribavirin
2014	Harvoni	Ledipasvir/Sofosbuvir	1	The first pill to be given once-daily. no requirement for interferon or ribavirin
	Viekira Pak	Ombitasvir/Paritaprevir/ Ritonavir and Dasabuvir	1	--
2013	Olysio	Simeprevir	--	In combination with peginterferon alfa and ribavirin or in combination with Sofosbuvir
	Sovaldi	Sofosbuvir	1, 2, 3, 4	used in combination with ribavirin or with pegylated interferon and ribavirin
2011	Victrelis	Boceprevir	1	In combination with peginterferon alfa and ribavirin
	Incivek	Telaprevir	1	With peginterferon alfa and ribavirin
	Pegasys	Peginterferon alfa-2a	--	--
	Pegintron	Peginterferon alfa-2b	--	--
	Rebetol	Ribavirin	--	Interferon alfa-2b.
1997	Infergen	Interferon alfacon-1	--	Injection.
1991	Intron	--	--	Credited with the status of being the first Hepatitis C treatment.

(antibodies to HCV) or a viral antigen (HCVcAg). They are based on the immunoassay principle, and are available in the form of rapid diagnostic tests (RDTs) or laboratory-based enzyme immunoassays (EIAs), chemo luminescence immunoassays (CLIAs) and electro chemo luminescence immunoassays (ECLs).

6. In contrast, NAT (nucleic acid test) are typically used to detect the presence of the virus, determine if the infection is active and if the individual would benefit from antiviral treatment. NAT technologies are also used to determine when antiviral treatment should be discontinued (due to non-response or resistance) or to confirm virological cure (HCV).

7. Nucleic acid testing or assays detect the presence of viral nucleic acid –RNA – through targeting a specific segment of the virus, which is then amplified. The amplification step enables the detection of low levels of the virus in the original specimen, which might not otherwise have been detectable.

8. WHO recommends the use of standardized testing strategies to both maximize the accuracy of HCV antibody testing while simplifying the process through streamlining procurement and training? The choice between a one-assay versus two-assay serological testing strategy will depend on the sero prevalence in the population to be tested and diagnostic accuracy (sensitivity and specificity) of the assays used.

9. If the HCV antibody test is non-reactive this means no HCV antibodies are detected and the sample can be reported as nonreactive for HCV. No further action is required and the test should be repeated at 3 and 6 months post exposure.

10. However if the test is reactive, it is presumed that there is an HCV infection either current or a resolved past infection. A false positive result should also be kept in mind.

11. Once HCV-RNA is detected and a current infection is diagnosed then counseling is initiated and a referral secured to the appropriate treatment specialist.

12. We should also keep in mind two situations, an HCV indeterminate serology, and inconclusive HCV serology where in the absence of risk factors, the reactivity is likely to be non-specific (i.e., false positive). If risk factors are present, the results may indicate early sero-conversion. In such situation it is recommended to do HCV PCR. Anti-HCV could be repeated in 4 – 6 weeks in both situations to exclude sero-conversion.

13. There are specific recommendations for reporting following qualitative HCV PCR testing. Guidelines should be followed for a positive and negative results and many departments of health provide algorithms to follow and the authors recommend the Australian, NSW Department of health hepatitis C control guidelines. (NSW.gov.au, 2012).

TREATMENT

Since HCV discovery in 1989, we are indebted to generations of scientists who conducted outstanding research in the field. Together with advances in diagnostic techniques and public health awareness campaigns this has led to a decrease in HCV transmission and the development of new treatments to delivering the desired outcome i.e., curing patients.

Interferon, the first component of treatment regimens has been surpassed by new medications in recent years which deliver higher sustained virologic response (SVR) rates, especially for genotype 1, the most predominant genotype in the world.

Standard treatment regimen included, Interferon and Ribavirin, and they used to be the mainstay against most genotypes i.e., pan-genotypic. Poor tolerance is a well-known nuisance of Interferon and extreme depressed mood was something that generations of patients had to endure. The new antiviral drugs have certainly demonstrated better efficacy, tolerability and safety profiles. They are called DDAs (oral directly acting antiviral agents). Access to DDAs is still limited due to their high prices.

We need to accept that Antiviral treatment is successful in 50 to over 100% of patients treated, depending on the treatment used. Treatment also been shown to reduce the development of liver cancer and cirrhosis, according to the World Health Organization. (WHO, 2014).

CONCLUSION

Persons infected with HCV are currently looking at some promising and clear breakthroughs in the battle to diagnose, control and cure this disease. Systematic and dedicated research has been rewarded with the development of many new antiviral drugs improving the odds of living with hepatitis C just like it had with chronic diseases like HIV and many cancers.

Intravenous drug users "the invisible population", stand to benefit from these developments like the rest of the population. These patients needs to adopt a positive view of the situation, maintain their motivation to get treatment and tap into the available resources of personal strength, family and friends and support groups. More research is needed in areas of early detection and prevention and the availability of new drugs to a wider population, especially in the developing world.

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