CURRENT TRENDS IN THE MANAGEMENT OF HEPATITIS C

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Introduction

- Hepatitis C virus is one of the leading causes of chronic liver disease worldwide.
- Variable clinical impact from minimal histologic changes, extensive fibrosis and cirrhosis with or without hepatocellular cancer.
- About 160 million people infected worldwide and most are unaware.
Epidemiology

- Prevalence varies across regions and populations studied.
- World wide prevalence is estimated at 3%.
- In developed countries it accounts for
  - 60% of HCC cases.
  - 40% of end stage cirrhosis
  - 30% of liver transplant cases.
Epidemiology

- Africa has the highest prevalence of 5.2%.
- In Nigeria various grouped studied revealed the following prevalence.
  - Blood donors- 2.4-7%
  - Pregnant women-0.4-12.3%
  - SCD- 5-7%
  - Community studies: Rural-12.1% Urban-2.7%
- Overall prevalence in Nigeria is 2-7%
HCV is a small 55-65nm enveloped single stranded RNA virus of the family flaviviridae.

Consists of core of genetic material surrounded by a protective shell and further encased in a lipid envelope with 2 viral envelope glycoprotein embedded in it.

HCV can remain infectious for 16 days at 25 degrees and 2 days at 37 degrees and only 8 and 4 mins at 60 and 65 degrees respectively.
Replication

- Replication takes place in the liver hepatocytes and peripheral blood mononuclear cells.
- HCV enters the cell through a complex interaction with the cell membrane.
- It takes over portions of the intracellular machinery to replicate.
- The HCV genome is translated into a poly protein which aids in the formation of proteins that recruit the genome into the RNA replication process. The RNA is then replicated and packaged into virions which bud into the secretory pathway and are released at the cell surface.
HCV peculiarities

- Ten times more infectious than HIV.
- High rate of progression to chronicity.
- High risk of hepatocellular cancer (HCC).
- No vaccine available.
- Presence of several genotypes (1-6) due to high rate of mutation. This has an impact on treatment options and duration.
Transmission

- Mainly through infected blood and blood products.
- Sharing of sharp objects.
- Unsafe practices - tattooing, scarification, uvulectomy, injection from quacks.
- Multiple sexual partners and vertical transmission not as prominent as in hepatitis B.
- Up to 60% of infections are seen in IVDU in the developed world.
- Risk factor in Nigeria is unclear as documented by Obienu et al in 2011.
Presentation

- Most patients are asymptomatic and hence unaware of the disease.
- Patient may present with extra hepatic manifestations.
- Symptoms begin to appear when significant hepatic damage may have occurred.
- They include jaundice, abdominal pain and swelling, leg swelling, weight loss.
- Hence the need for screening especially in at risk groups - SCD, patients on hemodialysis, HIV, IVDU, patients who received blood transfusion or organ transplant before 1999.
Screening

- Recommended for at risk groups as earlier stated. Including health care professionals.
- Due to the obscure nature of risk factors in Nigerian population it is advised that everyone be screened at earliest opportunity.
- Screening is done by ELISA to detect antibodies to HCV and if positive an RNA PCR is done for detection, quantification and genotyping.
Treatment Goals

- Primary goal is to eradicate the infection early in the course of the disease.
- Primary endpoint - Sustained Virological Response (SVR). Usually durable in chronic hepatitis C and patient can be considered cured.
- Intermediate endpoints -
  - Normalisation of ALT
  - Loss of serum HCV RNA
  - Improvement in histology
Effects of Achieving endpoints

- Decrease in rate of disease progression. Regression of cirrhosis in 50% of patients.
- Decrease in need for liver transplant by 90%
- Decrease in rate of development of HCC by 75%
- Improvement in survival - 90% reduction in liver related mortality.
- Decrease in spread of infection by erradicating viraemia
WHOM SHOULD WE TREAT
Pre therapeutic assessment

- Establish causal relationship between HCV and liver disease.
- Assess severity of liver disease - ALT levels, Liver biopsy, noninvasive markers,
- Baseline virological markers that will be useful for tailoring therapy. HCV RNA in IU/ml, HCV genotypes including subtypes of genotype 1.
Pre therapeutic assessment

- Search for other causes of liver disease- HBV, autoimmunity, metabolic diseases e.g. DM, obesity, hemochromatosis, drug induced hepatotoxicity, alcohol/herbal consumption, HIV coinfection.
- The above have implication in course and severity of disease.
Indication for treatment

- All HCV positive patients with active disease.
- All treatment naïve and treatment experienced patients with decompensated or compensated CLD
- Prioritize for patients with significant fibrosis or cirrhosis.
- Patient with decompensated cirrhosis should be treated urgently.
Indication for treatment

- Prioritize treatment regardless of fibrosis stage in the following patients:
  - HIV or HBV coinfection
  - Pre and post transplant
  - Significant extra hepatic manifestations.
  - Debilitating fatigue
  - IVDU
  - Haemodialysis patients
  - Women who wish to get pregnant.
  - Incarcerated patients.
- Not recommended in patients with limited life expectancy.
Treatment options

- Treatment options and duration of treatment are individualized. Factors affecting this include presence of compensated or decompensated cirrhosis, treatment naïve or experienced patient (those who failed prior treatment.)
Treatment options

- Former standard of care was pegylated interferon and ribavirin. This combination was fraught with a lot of side effects and SVR was only achieved in 45% in genotype 1. Better responses in genotype 2 and 3 but relapse rate was high.
- Due to the high rate of side effects patients with decompensated CLD could not benefit from treatment.
Treatment options

- Directly Acting Antivirals (DAA) - with the introduction of these group of drugs better SVR rates have been achieved with fewer side effects.

- These drugs include - Sofosbuvir, Ledispavir, simepravir, Daclatasvir, Ombitasvir, Dasabuvir.

- IFN free regimens using a combination of two of these drugs with or without Ribavirin have proven to be very effective.
Treatment options

- **Sofosbuvir+Ribavirin** for 12 weeks - genotype 2,3 (extend to 16-20 weeks if cirrhotic gen 2 but not used if cirrhotic gen 3)
- **Sofosbuvir+Daclatasvir** for 12 weeks - all genotypes (in cirrhotics 24 weeks without RBV or 12 weeks with RBV in gen 1,4,5,6. 24 weeks with RBV in gen 3, 12 weeks without RBV in gen 2.
- **Sofosbuvir+Ledispavir** for 12 weeks - Gen 1,4,5,6 (12 weeks with RBV or 24 weeks without RBV in cirrhotics.
Treatment options

- Sofosbuvir+Simeprevir for 12 weeks in gen 1,4 (12 weeks with RBV or 24 weeks without RBV in cirrhotics).
- PegIFN+RBV+SOF for 12 weeks in all genotypes in compensated cirrhotics and non cirrhotics.
In summary

- HCV is increasingly recognised as a cause of CLD with prevalence of about 2-7% in Nigeria.
- Most patients are asymptomatic until significant hepatic damage occurs.
- Screening is recommended for at risk groups.
- Pre therapeutic assessment is necessary to determine need to treat and options to use.
- Treatment should be prioritized in patients with evidence of advanced liver disease and significant comorbid conditions which worsen liver disease.
- Several treatment options are now available including interferon free regimens.
THANK YOU
References

- American Association for the Study of Liver Disease (AASLD) treatment guidelines 2014
- Okeke E. HCV the Nigerian experience. AMAGE 2012