One- day Seminar for Update on Hepatitis B & C- 26 October 2016

Tehran Oil Industry Health Education and Research

With Collaboration of

Baqiyatallah Research Center for Gastroenterology and Liver Disease

Iran Hepatitis Network

Digestive Disease Research Institute

Time Table

One- day Seminar for Update on Hepatitis B & C

Wednesday- 26 October 2016

OIL COMPANY HOSPITAL

Time	Topic	Speaker
08:00 – 08:10	Opening	
08:10 – 08:35	Epidemiology and transmission of viral hepatitis in Iran	Dr. Mehdi Saberi Firoozi
08:35 – 09:00	Laboratory diagnosis of viral hepatitis	Dr. Heidar Sharafi
09:00 – 09:25	Prevention of hepatitis B	Dr. Siavash Mansouri
09:25 – 10:00	Break	
10:00 – 10:30	Treatment of Hepatitis C	Dr. Shahin Merat
10:30 – 11:00	The importance of point of care diagnosis in the successful management of individuals infected with hepatitis C virus	Dr. Hosein Poustchi
11:00 – 11:30	Panel	
11:30 – 12:00	Treatment of Hepatitis B	Dr. Bita Behnava
12:00 – 12:30	Treatment of Hepatitis D	Dr. Seyed Moayad Alavian
12:30 – 13:00	Panel	

Target Groups

گروه مادر	گروه هدف	مقطع رشته	نام رشته	کد رشته	رتبه	امتیاز کمیته	هزینه روزانه	هزینه مجموع	فقط هیئت علمی
بهداشت	بهداشت عمومي	کاردانی	بهداشت عمومي	1022	چهارم	1.25	230000	230000	
		کارشناسی	بهداشت عمومي	1139	چهارم	1.25	230000	230000	
	بهداشت محيط و حرفه اي	کارشناسی	مهندسی بهداشت محيط	11275	چهارم	1.25	230000	230000	
		کارشناسی	مهندسی بهداشت حرفه اي	11345	چهارم	1.25	230000	230000	
		کارشناسی ارشد	مهندسی بهداشت حرفه اي	14175	سوم	1.75	230000	230000	
		کارشناسی ارشد	مهندسی بهداشت محيط	1437	سوم	1.75	230000	230000	
پرستاری	پرستاري	کاردانی	پرستاري	1010	چهارم	1.25	230000	230000	
		کارشناسی ارشد	بيهوشي	1486	سوم	1.75	230000	230000	
		کارشناسی ارشد	پرستاری*	1410	سوم	1.75	230000	230000	
پزشک عمومی	پزشکان عمومي	دکترای حرفه ای	پزشکان عمومی*	1510	اول	3.5	230000	230000	
جراحی عمومی- جراحی	جراحي عمومي	تخصص	جراحی عمومی*	1733	دوم	2.5	340000	340000	
علوم آزمایشگاهی	آسيب شناسي	تخصص	آسیب شناسی	1723	دوم	2.5	340000	340000	
	علوم آزمايشگاهي	تخصص	تخصص علوم آزمایشگاهی	1749	دوم	2.5	340000	340000	
		کارشناسی ارشد	علوم آزمایشگاهی	14131	دوم	2.5	230000	230000	
	ويروس شناسي	کارشناسی ارشد	ویروس شناسی	1444	دوم	2.5	230000	230000	
گروه هاي داخلي	بيماري هاي داخلي	تخصص	بیماریهای داخلی*	1710	اول	3.5	340000	340000	
	بيماري هاي عفوني و گرمسيري	تخصص	بیماریهای عفونی و گرمسیری*	1712	اول	3.5	340000	340000	
	خون و سرطان بالغين	فوق تخصص	خون و سرطان بالغین*	2017	اول	3.5	340000	340000	
	گوارش و کبد بالغين	فوق تخصص	گوارش بالغین (داخلی)*	2024	اول	3.5	340000	340000	
مامایی	مامايي	کارشناسی ارشد	مامایی*	1419	سوم	1.75	230000	230000	

وبینار

شبکه هپاتیت ایران به منظور سهولت دسترسی و بهره مندی از سمینارهای استانی خود با تائید سازمان بازآموزی کشور وبینار اختصاصی همراه با دریافت امتیاز بازآموزی را راه اندازی نمود.

تمام افرادی که امکان حضور در محل برگزاری سمینار را ندارند، می توانند با ثبت نام در فرم زیر و دریافت نام کاربری و گذرواژه خود تا ۱ روز قبل سمینار به صورت مجازی از این سامانه استفاده نمایند و اقدام به دریافت امتیاز نمایند. همچنین می توانند در روز کنگره به عنوان میهمان از سامانه استفاده نموده و از برنامه های اجرایی در کنگره مطلع شوند.

به منظور استفاده از این سامانه، می توان از طریق تلفن همراه و کامپیوتر شخصی اقدام نمود.

نحوه اتصال به سامانه

به منظور دستیابی و همچنین استفاده از این سامانه لطفا به یکی از دو روش زیر به شکل زیر اقدام نمایید.

- کامپیوتر شخصی
  ۱- مرورگر Firefox را بر روی کامپیوتر شخصی نصب نمایید.
  ۲- آخرین نسخه فلش پلیر را بر روی سیستم خود نصب نمایید.
  ۳- Addon مربوطه را نصب نمایید.
- تلفن همراه اندروید و IOS

همچنین به منظور دریافت نرم افزار وبینار لطفا در app store و یا play store عبارت adobe connect رو جستجو نمایید و نرم افزار را نصب نمایید .

بعد از باز کردن نرم افزار آدرس http://92.50.2.122/hepatit را وارد نمایید.

در صورتی که ثبت نام کرده اید با نام کاربری و گذرواژه خود وارد شوید و در غیر اینصورت از طریق میهمان وارد شوید.

Viral Hepatitis and Related Disorders in Iran; Epidemiology and Prevention

Mehdi Saberifiroozi, MD
Professor of Internal Medicine and Gastroenterology, Digestive Disease Research Institute, Tehran University of Medical Sciences, Tehran, I. R. Iran
Email: mehdisaberifiroozi1390@gmial.com

Viral hepatitis is the 7th of the first 10 Leading Causes of Death Worldwide. The common Viral Hepatitis which have an important impact on the health economics and burden could be divided to enterically and parenterally transmitted viral hepatitis. Hepatitis A virus and hepatitis E virus are the main enterically transmitted ones. Other important viruses which cause significant liver disease are hepatitis B (may be associated with Hepatitis D virus), and hepatitis C virus. There are other viruses with liver involvement named as non-A–E viruses, such as GBV-C, TTV, EBV, CMV, HSV, SARS, and Yellow fever. Diagnosis of non A-E viruses needs careful exclusion of major hepatitis viruses and of hepatotoxins, the liver damage is usually mild with no jaundice, rarely, may result in acute liver failure and death, and don't develop to chronic hepatitis.
For evaluation of epidemiology of viral hepatitis, in addition to the prevalence, incidence, mortality, morbidity, fatality, we can also use the measures of the burden of disease such as Disability-adjusted Life-years (DALYs) which is equal to Years of Life Lost (YLLs) + Years Lived with Disability (YLDs), which can compare the burden of different disease in a community for better program design.

In the study of Global Burden of Disease, between 1990 and 2013, the numbers of deaths and DALYs attributed to viral hepatitis increased by 62% and 34% respectively. This contrasts with other major infectious diseases (including diarrhoeal disease, tuberculosis and malaria) whose fall in relative rankings reflects the global transition towards non-communicable diseases. Among Top 15 causes of mortality for 1990 and 2013 viral hepatitis is the main infectious disease with Increased burden. Also among the Top 20 causes of DALYs for 1990 and 2013, viral hepatitis is the main infectious disease with increasing burden.

The global premature death due to viral hepatitis related diseases is one million per year, and 10,000 of them are from Iran. Hepatitis B and C cause the majority these deaths.

Hepatitis B and C infections are asymptomatic until the later stages. About two-thirds and half of people infected with hepatitis B and C respectively do not know of their condition. Both infections are common in socially marginalized groups such as drugs abusers or prisoners.

HBV is the cause of most deaths and DALYs related to viral hepatitis, after that HCV infection has the second mortality and DALYs. In acute viral hepatitis, the hepatitis A virus is the cause of most YLLs. Due to high HAV infection in our country, decision about routine HAV vaccination is not recommended, however we suggest availability of vaccine for selected populations and susceptible persons.

HBV vaccination with high efficacy and safety is the main strategy for control of HBV infection, but it's elimination needs long time, and adequate resources, so we suggest focus on control of infection which is more feasible at this time.

We suggest continuing screening all pregnant women for HBV and prevention of infection in new born, vvaccinating all adult <35 who have not received HBV vaccine up to now, and to screen all subject with risk factor for HBV and treat all with HBV DNA >100,000 infected people.

With the availability of newer anti HCV drugs with high rate of sustained virological response control of this infection could be feasible. Screening all subject with risk factor for HCV and treating all people with high HCV RNA, is suggested for this goal.

Due to high prevalence of HAV in our community routine vaccination of general population is not recommended at present time, but the HAV vaccine should be available for prevention in special conditions. For HAV and HEV control we suggest more improvement of sanitary conditions, waste disposal, and early detection for special precautions.

Laboratory Diagnosis of Viral Hepatitis

Heidar Sharafi, PhDc
Department of Molecular Hepatology, Middle East Liver Disease (MELD) Center, Tehran, IR Iran
Email: h.sharafi@meldcenter.com

Laboratory diagnosis of viral hepatitis relies on serological and molecular methods. Nowadays everyone believes in the impact of molecular methods in diagnosis of viral hepatitis. The following molecular tests are used for diagnosis, prognosis and monitoring of viral hepatitis: detection of HCV-RNA and HBV-DNA in plasma and peripheral blood mononuclear cells (PBMC), quantification of HCV-RNA and HBV-DNA levels in plasma, HCV genotyping, detection of HCV variants with resistance to direct-acting antiviral agents and detection of HBV variants with nucleos(t)ide analogues resistance. Various methods with different sensitivity, specificity, and cost-effectiveness can be applied for each of these tests. These methods are quantitative Real-time PCR, RT-PCR, Reverse hybridization, PCR-RFLP, DNA Sequencing, Next-generation Sequencing and etc. Clinicians should interpret the results considering the methods used for the requested test.

پیشگیری از هپاتیت B

سیاوش منصوری- متخصص بیماریهای گوارش و کبد، **سازمان بهداشت و درمان صنعت نفت**

ایمیل: siavashmansouri@gmail.com

در حقیقت بیماری های ویروسی کبد پرجالش ترین بیماری گوارشی هستند که بخش عظیمی از سرمایه های جهانی را صرف خود میکنند شاید بعد از کانسرهای گوارشی بیشترین سهم GNP درمانی متعلق به بیماری کبدی را ازان خود کرده اند.

پیشگیری از هپاتیت B در چند بخش صورت میگیرد:

۱- رعایت امور بهداشتی در همه سطوح بهداشتی درمانی و حفاظت مستمر از اقدامات تهاجمی در کشور اعم از دندانپزشکی، اندوسکوپی و انتقال خون و جراحی ها

۲- اموزش سراسری در همه مراکز اموزشی و ورزشی و مراکز امکان پذیر برای اشنایی با نحوه انتقال بیماری

۳- بیماریابی و درمان بیماران و نشانگر نمودن بیمارانی کاریر هستند و اموزش به خانواده های مربوط و سرانجام واکسیناسیون که میتواند مهمترین بخش پیشگیری باشد.

واکسیناسیون بخش مهمی از پیشگیری از هپاتیت B است و شامل:

۱- در جوامعی که کاریرهای B بیش از ۲ در صد است پیشنهاد میشود واکسیناسیون جزء واکسیناسیون سراسری در نوزادان است که میتواند به همراه واکسیناسیون عمومی انها به همراه سه گانه متداول تزریق شود.

۲- کلیه افراد با ریسک بالا همچون کارکنان مراکز بهداشتی درمانی، دیالیزی ها، افراد با رفتار جنسی پرخطر، بیماران مزمن کبدی و HCV وHIV مثبت ها و انها که با بیماران HBs Ag مثبت در تماس هستند یا کارکنان در مراکز کودکان عقب افتاده باید تحت واکسینایون کامل قرار گیرند. انجام واکسیناسیون با تزریق سه تزریق در ماههای ۰ و ۱ و ٦ انجام گیرد و برای افراد خاصی همچون کارکنان مراکز بهداشتی درمانی پیگیری سطح کافی انتی بادی (۱۰ واحد پر میلی) باید صورت گیرد. واکسنهای ضد هپاتیت B سه نوع مهم دارند: ۱- واکسن های مهندسی سازهای با استفاده از قارچ ۲- واکسن مهندسی ساز از سلول های پستانداران ۳- واکسنهای استفاده از عناصر انتی ژن HBs Ag که قابلیت تولید انتی بادی را داراست. واکسیناسیون بلافاصله پس از تزریق های ناخواسته سوزن در بدن افرادی که با بیماران مشکوک تماس دارند باید شروع شود و در مواردی که فرد مجروح سابقه واکسیناسیون ندارند تزریق HBIG هم ضروری است نوزادانی که از مادران HBs Ag مثبت هستند بلافاصله پس از تولد باید واکسینه شوند و در مدت ٢٤ ساعت پس از تولد باید HBIG هم دریافت کنند.

Treatment of Hepatitis C

Shahin Merat, MD
Professor of Medicine,
Deputy of Research, Digestive Disease Research Institute
Tehran University of Medical Sciences,
Email: shahin.merat@gmail.com

The treatment of hepatitis C has been revolutionized by the introduction of new direct acting antivirals (DAA). Due to the short treatment duration, lack of significant side effects, and high efficiency these medicines have rapidly become the standard treatment for all patients with hepatitis C.

There are various combinations available which have been approved for treating hepatitis C. Most combinations have been designed for genotype 1 as this is the most common genotype in western countries and most resistant to the old interferon-based treatments. Later on, combinations effective against all genotypes of hepatitis C have been developed.

Genotype specific combinations effective only against genotype 1 (and 4) include the combinations of sofosbuvir/ledipasvir (Harvoni), grazoprevir/elbasvir (Zepatier), and Ombitasvir/ paritaprevir/ ritonavir/ dasabuvir (Viekira pack). With the availability of pangenotypic treatments, which are frequently cheaper it is expected that the production of genotype specific combinations will soon be discontinued.

Pangenotypic treatments are named as such because they are effective against all genotypes of hepatitis C. There are currently two

such treatment combinations available: sofosbuvir/daclatasvir (Sovodak) and sofosbuvir/velpatasvir (Epclusa). Using pangenotypic combinations eliminates the need for genotype testing and more importantly provides confidence against genotyping errors or cases of mixed infection which might be as frequent as 40% among IV drug users.

The usual duration of treatment with any of these combinations is 12 weeks. The efficacy can be boosted by either adding ribavirin, or extending treatment period to 24 weeks, or both. Such boosting might be required in patients known to be resistant to treatment such as cirrhotics or previous DAA failures.

The importance of point of care diagnosis in the successful management of individuals infected with hepatitis C virus.

Hossein Poustchi MD, PhD
Deputy of Education, Digestive Diseases Research Institute
Tehran University of Medical Sciences Shariati Hospital
Email: h.poustchi@gmail.com

An estimated 186,500 individuals (0.24 of the general population) are currently infected with hepatitis C virus (HCV) in Iran and require treatment. Despite the recent success in introducing new treatment agents that can achieve cure in almost 98% of cases, and reducing HCV treatment costs, the treatment rates has not exceeded 2.5% of the HCV infected population. This trend in diagnosis and treatment policies can lead to marked and steady increase in number of HCV infections, and HCV related advanced liver disease and mortality in the next decades. HCV as a major public health threat cannot be eliminated unless an active case finding and timely diagnosis and treatment policies be implemented, especially in the priority populations. Recent epidemiologic studies have shown that 75% of HCV infected people have gained infection through injecting drug use (IDU), and that the majority of HCV infected population belong to people who inject drugs (PWID) and people in custodial settings. The problems in these populations are that they are not accessible and that they are not willing to undergo time consuming laboratory testing and treatments, and therefore many of them do not refer for treatment. In order to overcome these problems, the world

health organization (WHO) have encouraged the countries to develop and utilize point of care policy for the management of HCV infection. Point of care policy emphasizes on delivering the healthcare tests, products and services to patients at the time and place of patient care, therefore instead of waiting days for laboratory results and several visits to guide treatment decisions, in a single visit the patient can know his HCV infection status and receive the desired treatment. This point of care policy has been undertaken by a number of developed countries that showed promising results in the management of HCV infected people.

Treatment of Hepatitis B Infection

Bita Behnava, MD
Middle East Liver Disease (MELD) Center, Tehran, Iran
Email: bita_behnava@yahoo.com

Approximately 350–400 million people are chronic HBV surface antigen (HBsAg) carriers worldwide. The spectrum of disease and natural history of chronic HBV infection are diverse and variable, ranging from an inactive carrier state to progressive chronic hepatitis B (CHB), which may evolve to cirrhosis and hepatocellular carcinoma (HCC). The natural history of chronic HBV infection can be schematically divided into five phases, which are not necessarily sequential:
1)The ‘‘immune tolerant’’ phase is characterised by HBeAg positivity, high levels of HBV replication normal levels of aminotransferases, mild or no liver necroinflammation and no or slow progression of fibrosis. 2) The ‘‘immune reactive HBeAg-positive phase’’ is characterized by HBeAg positivity, increased orfluctuating levels of aminotransferases, moderate or severe liver necroinflammation. 3) The ‘‘inactive HBV carrier state’’ may follow seroconversion from HBeAg to anti-HBe antibody. It is characterized by very low or undetectable serum HBV DNA levels and normal serum aminotransferases. 4) ‘‘HBeAg-negative CHB’’ These patients are HBeAgnegative and harbor a predominance of HBV virions with nucleotide substitutions in the precore and/or the basal core promoter regions that are hence unable to express or express low levels of HBeAg and characterized by periodic reactivation with a pattern of fluctuating levels of HBV DNA and aminotransferases and active hepatitis. 5) In the ‘‘HBsAg-negative phase’’ after HBsAg loss,

low-level HBV replication may persist with detectable HBV DNA in the liver. The goal of therapy for CHB is to improve quality of life and survival by preventing progression of the disease to cirrhosis, decompensated cirrhosis, end-stage liver disease, HCC and death. This goal can be achieved if HBV replication can be suppressed in a sustained manner. The indications for treatment are generally based mainly on the combination of three criteria: Serum HBV DNA levels. Serum ALT levels. Severity of liver disease (histologic findings). Patients should be considered for treatment when they have HBV DNA levels above 2000 IU/ml, serum ALT levels above the upper limit of normal (ULN) and severity of liver disease assessed by liver biopsy (or non-invasive markers once validated in HBV infected patients) showing moderate to severe active necroinflammation and/ or at least moderate fibrosis using a standardised scoring system (A1). Immunotolerant patients: HBeAg-positive patients under 30 years of age with persistently normal ALT levels and a high HBV DNA level, without any evidence of liver disease and without a family history of HCC or cirrhosis, do not require immediate liver biopsy or therapy. Follow-up at least every 3–6 months is mandatory (B1). Consider liver biopsy or even therapy in such patients over 30 years of age and/or with a family history of HCC or cirrhosis. HBeAg-negative patients with persistently normal ALT levels and HBV DNA levels above 2000 but below 20,000 IU/ml, without any evidence of liver disease, do not require immediate liver biopsy or therapy (B1). Close followup with ALT determinations every 3 months and HBV DNA every 6–12 months for at least 3 years is mandatory (C1). Patients with obviously active CHB:
HBeAg-positive and HBeAg-negative patients with ALT above 2 times ULN and serum HBV DNA above 20,000 IU/ml may start treatment even without a liver biopsy. Patients with compensated cirrhosis and

detectable HBV DNA must be considered for treatment even if ALT levels are normal (B1).

Patients with decompensated cirrhosis and detectable HBV DNA require urgent antiviral treatment with nucleoside/nucleotide analogues (NA(s)). Currently, there are two different treatment strategies for both HBeAgpositive and HBeAg-negative CHB patients: treatment of finite duration with (PEG-) IFN or a NA and long-term treatment with NA(s). NAs for HBV therapy can be classified into nucleosides (lamivudine, telbivudine, emtricitabine, entecavir) and nucleotides (adefovir and tenofovir). The most potent drugs with the optimal resistance profile, tenofovir or entecavir, should be used as first-line oral therapies. In patients treated with PEG-IFN, A sustained offtreatment virological response (at 6 and 12 months post-treatment) with HBV DNA <2000 IU/ml is generally associated with remission of the liver disease. In HBe Ag positive patients:The objective of finite treatment with a

NA is sustained off-treatment anti-HBe seroconversion with HBV DNA <2000 IU/ml and normal ALT, or even HBsAg clearance. Long-term treatment with NA(s). is necessary for patients who are not expected or fail to achieve a sustained off-treatment virological response and require extended therapy, i.e. for HBeAg-positive patients who do not develop anti-HBe seroconversion and HBeAg-negative patients..HBV DNA reduction to undetectable levels by real-time PCR (i.e below 10–15 IU/ml) should ideally be achieved to avoid resistance. HBV DNA monitoring is thus critical to detect treatment failure.

Therapy of Hepatitis D Infection

Seyed Moayed Alavian, MD
Professor of Gastroenterology and Hepatology,
E mail: Alavian@thc.ir

Hepatitis delta virus infection (HDV) is the least common form of chronic viral hepatitis but is the form most likely to lead to cirrhosis. Delta hepatitis is serologically complex, so effective therapy is difficult. HDV is a defective RNA virus that replicates efficiently only in the presence of HBsAg. Thus, delta hepatitis occurs only in patients who are HBsAg-positive. Infection is acquired parenterally and probably also via close personal contact in endemic areas. HDV infection is strongly associated with injection drug abuse. Chronic HDV infection often results in severe liver disease. The diagnosis is made on the basis of the presence of antibodies against HDV (anti-HDV) and HBsAg in the serum of a patient with chronic liver disease and it is confirmed by the finding of HDV antigen in the liver or HDV RNA in serum (by reverse-transcription–polymerase-chain-reaction assay).

There are currently no specific direct antiviral treatments for HDV. This is mainly due to the fact that the virus does not encode enzymatic activities, and fully relies, even more than other viruses, on host-cell machinery for its replication. Interferon alpha (IFNa) remains the only drug recommended by international guidelines for the treatment of CHD. Both conventional and pegylated interferon (Peg-IFNa) have been shown to suppress HDV viremia in a subset of patients. Sustained virologic response (SVR) rates vary between 14 to 50% for conventional IFNa and 17 to 44% for Peg-IFNa. Several questions relative to interferon treatment remain unanswered.

One- day Seminar for Update on Hepatitis B & C
26 October 2016