抄録

Challenges to Implementation of WHO Hepatitis Guidelines

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Abstract

Hepatitis B virus (HBV) and hepatitis C virus (HCV) are major etiological agents of liver-related diseases, such as liver cirrhosis and hepatoma. Therefore, the prevention of transmission and effective antiviral therapies could greatly reduce mortality due to liver-related diseases,

WHO issued guidelines for the prevention, care, and treatment of persons with chronic hepatitis B infection in March 2015 and for the screening, care, and treatment of persons with chronic hepatitis C infection in April 2014. Both sets of guidelines are targeting not all the countries, but are especially relevant to low- and middle-income countries (LMICs). To implement these guidelines, each LMIC might have different challenges.

The following are possible challenges:

1. Effective Identification of HBV/HCV Infected People
   Each country has different methods for targeting and screening HBV- or HCV-infected individuals
2. Effective Checkup System
   Once HBV- or HCV-infected people are identified, they often don't see doctors and miss a crucial opportunity to receive correct diagnosis and antiviral therapy. Even people are diagnosed as needing no immediate requirement for treatment, they still need regular checkups.
3. Availability of Medical Resources

WHO guidelines are requesting many medical resources for the implementation of:

- Laboratory tests;
  Screening-HBsAg, HCV Ab
  Staging-AST, Platelets for APRI
  AST, ALT, and Platelets for FIB-4
  γGTP, haptoglobin, bilirubin, ApoA1, and α2-macrogrobulin for Fibro test
  Virology-HBV DNA, HBeAg, HCV RNA, and HCV genotype
  Cancer monitoring-AFP
  Others-HIVAb, HDVAb, renal/liver function, complete blood count etc.
- Medical equipment; Ultrasonography with/without FibroScan
- Antiviral medicine
  HBV-Entecavir and Tenofovir
  HCV-PEG-IFN, Ribavirin, and DAAs (Telaprevir, Simeprevir, Sofosbuvir etc.)
- Vaccines; HBV

4. Increasing HBV/HCV Specialized Workers and Facilities

I hope that participants in this symposium will share their knowledge and experiences about hepatitis. Cooperation among national/local governments and healthcare workers is crucial toward controlling this debilitating diseases.

Epidemiology of HBV, HCV, and HDV Infections in Mongolia

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Abstract

Introduction

Mongolia has one of the highest prevalences of hepatitis B, C and D virus infection and consequently, leading mortality rates of liver cirrhosis and hepatocellular carcinoma (HCC) in the world. No random sampled population studies have been carried out in Mongolia in recent years. In order to formulate policies and strategies in combating viral hepatitis, it is imperative to assess the current situation. Therefore, the present study was conducted to survey seroprevalence of HCV in apparently healthy Mongolian adults aged above 20 years.

Methods

The study was approved by the Ethics Committee at the Health Sciences University of Mongolia
and the Health Ethics Committee of the Ministry of Health of Mongolia. Study subjects were chosen based on the three-stage cluster sampling method. A total of 1,158 subjects were enrolled in the study. All participants were on-site tested for anti-HCV and HBsAg using rapid tests (CTK Biotech, San-Diego, US). Also, 5-10ml of blood was drawn from the antecubital vein and sera were separated following a standard protocol. Serum specimens were tested for anti-HCV, HBsAg and anti-HDV by enzyme-linked immunosorbent assays (ELISA) and real-time PCR. All subjects answered a detailed historical survey for risk factor analysis using a specifically designed questionnaire.

Results

In this study, total of 1,158 subjects were enrolled including 599 (43.1%) men and 659 (56.9%)
female. The overall prevalence of anti-HCV and HBsAg among study subjects were 11.1% (128/1158) and 10.6% (123/1158) respectively. Higher percentages of male subjects (11.8% of
male) tested positive for HBsAg while more female subjects (12.6% of female) were tested positive for anti-HCV. Further 67.5% (83/123) of all HBsAg positive subjects were tested positive for anti-HDV. Results of multivariate regression analysis for potential risk factors show that history of blood transfusion 1.8 times (OR=1.563 95%C.I 1.060-2.305 p=0.024), accupuncture 1.3 times (OR=1.303 95%C.l 1.110-1.531 p=0.001), letting blood treatment 1.8 times (OR=1.878 95%C.l 1.427-2.471 p=0.0001) and surgical procedure (OR=1.945 95% CI 1.278-2.451 p=0.0001) were associated with significant risk for transmission of HCV infection. Hepatitis B infection risks were increased with dental treatment 4.2 times (OR=4.293 95%C.l 1.158-15.912 p=0.029) and with hemodialysis 5.1 times (OR=5.078 95%C.I 1.199-21.511 p=0.027).

Conclusion

It is estimated that currently in Mongolia live over 300 thousand people (over 20yrs age) infected with HBV, HCV and HBV/HDV. The risk factor analysis shows that the nosocomial infection risk is still high.

STRATEGY FOR TREATMENT OF THE PATIENTS WITH CHRONIC HEPATITIS C IN MONGOLIA

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Abstract

7018.8 cases for 1000 population by statistic information data of Mongolia in 2013 such as digestive system disease (1056.79) was second place, and 29 cases increased to compare in 2012.

23.4 percent tumor was caused of death in 2013; especially cancer of liver is the first place which is not depended on ages and gender. However 4.7 percent of digestive systems diseases caused by death which is 4th place that was recorded.

World population mortality deaths is to be included in cardiac ischemia, cerebrovascular disease, chronic obstructive pulmonary disease in 2030, when the first cause of mortality in our country as a percentage of ischemic heart disease, cerebrovascular disease and mortality caused by cirrhosis of the liver disease tops.

HCV prevalence was 10.7% (D.Davaalkham 2004), 15.6% (O.Baatarkhuu 2003), 19.7% (Division 1999) and 1b genotypes were determined to have accounted 98%(Ts.Oyunsuren)in our country.

322 cases admissions inKHBEST of SHUGTE (2009) 30.12% was caused by the virus, 14.6% was caused by alcohol, 55.28% of viruses and alcohol causes cirrhosis of the liver associated with a viral infection than 14.6% of non-viruses compared with virus infections. 39.7% of "B" virus infection, 41.6% of "C" virus infection, and 4.0% of "B" and "C" viruses associated infections accounted, and "C" was dominated by the virus by the study.

WhenInterferon therapywas used alone, its result is 38.9%, long-term treatment results is 49.4%, 11.7% were ineffectiveprovide short-term results, PEG interferon and ribavirin combination therapy was 36-70% effect.

Strategy for the management for chronic hepatitis B patients in China

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Abstract

Chronic hepatitis B infection is a significant global health problem throughout the world, particularly in China. According to a nationwide seroepidemiological survey(1992-1995), the infection rate and HBsAg carrier rate was 59.17% and 9.75%, respectively. It is estimated that more than half a million of HBV-infected persons die annually from end-stage hepatitis B complications. Obviously, the socioeconomic burden of HBV-related disease in China is very heavy. The Chinese Ministry of Health recommended HBV vaccination and integrated it into its Expended Progamme on Immunization in 1992, enforced it since 2002, and offered it as a completely free vaccination service for newborns since 2005. Now, the implementation of HBV vaccination programme has come into effect. According to a seroepidemiological survey on HBV infection conducted in 2006, the HBsAg carrier rate in chinese general people 1-59 years of age decreased to 7.18%, especially in children 1- 4 years of age, the HBsAg carrier rate decreased from 9.67% in 1992 to 0.96% in 2006. These data showed that there has been a one-third decrease of the HBV carrier population since 1992. This great achievement changes China from a highly endemic area for HBV infection to an intermediate one.

Although HBV infection can be prevented by vaccination, for those CHB patients, it is important to assess the severity of the patients and treat those who meet antiviral treantment criterion. To standardize the prevention and management of HBV patients in China, the Chinese Society of Hepatology and the Chinese Society of Infectious Disease jointly published an evidence-based guideline in 2005 and subsequently renewed it in 2010. This guideline will be updated in this year. In this latest guideline, it provides recommendations about assessing disease, treatment indication, drug choice, drug withdrawal index and monitoring during follow-up. At present, there are three conventional interferons (alpha1b, 2α and 2b), two pegylated interferons (alpha2α and 2b) and five nucleos(t)ide analogues (lamivudine, adefovir, telbuvidine, enticavir and tenofovir) licenced and applied to clinical practice in China. In consideration of the main advantages of IFN over NAs which are the absence of resistance, high HBeAg seroconversion rate and limited course of treatment, IFNs are still recommended to treat some CHB patients in China, who can get much better outcome accoring to factors predicting therapeutic outcome of IFNs. Due to high potency against HBV and low resistanc, enticavir and tenofovir are strongly recommended to suppress HBV replication in spite of their costs. Fortunately, these antiviral drugs are included in medical insurance and partially reimbursed in some areas, mainly in the developed region. Because of economic imbalance, lamivudine and adefovir are widely used in some low income areas, such as western and remote rural areas. With the reform and improvement of Chinese Natioanl Medical Insurance Programme, more and more CHB patients can afford antiviral drugs and receive treatment.

Chinese government also pays a special attention to promote the research on control of hepatitis B. During the Chinese National Eleventh Five-Year Plan and Twelveth Five-Year Plan, many projects have been launched to support HBV basic and clinical researches. Chinese patients and physicians have been actively involved in the global and domestic clinical trials on new antiviral agents or new regiments. In the future, more important data, focussing on optimization of the efficacy of antiviral drugs, will be released from China. Due to lack of HBV knowledge in chinese general public, the HBV discrimination is still severe in China. To eliminate discrimination, chinese government, professional society and fundations have done a lot of work in recent years. There are many projects launched to make chinese

people understand more about HBV, such as “land of hope”, a health education project for CHB patients and their family, and the training programmes are also involved to improve different level’s medical staff’s treatment and diagnosis skills.

Althrough HBV infection is a significant health problem in China, both economic development and healthcare system reform will make antiviral agents more accessible to chinese patients. We can predict that the mortality and morbidity caused by HBV in China will be largely decreased in the future.

Strategy for the management for chronic hepatitis C patients in China

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Abstract

The prevalence of hepatitis C virus (HCV) infection in China was 3.2% in 1992. It was 0.43% among 1 to 59 years old people in 2006, but it was about 2% among the high-risk groups. There is no exact information about the prevalence of HCV infection recently, but it is estimated as about 1% in China. Genotype 1b is the major genotype in China, followed by genotype 2a.

The majority of chronic hepatitis C patients were the recipients of infected blood products in 1980-1990s. With the careful anti-HCV screening of blood donors, the newly infection of HCV because of blood transfusion rapidly declined. In addition, intravenous drug-use and high-risk sexual behavior are also the main transmission routes of HCV infection.

The first guideline for hepatitis C prevention and treatment in China was announced in 2004 and will be renewed this year. The guideline for HCV of hospital-acquired infection in China was announced in 2012. A standard for screening and management of viral hepatitis C in China was published by Ministry of Health of the People's Republic of China in 2014.

The screening and management of HCV infection in China were requested for the following groups: First, the high-risk groups including intravenous drug abuser, high risk sexual behaviors, recipients of infected blood products or invasive procedures in health-care facilities with inadequate infection control practices, etc; Second, people who prepare for a special or invasive medical operation including blood transfusions, invasive procedure, endoscopy, hemodialysis, etc; Third, people with unexplained abnormal liver function.

The standard antiviral treatment of hepatitis C in China is IFN-α plus ribavirin. Both PegIFN-α and recombinant IFN-α are permitted to treat hepatitis C and some of the costs can be reimbursed from medical insurance. DAA has not yet to be approved in mainland China, but there were a few patients brought DAA from Hongkong or other countries.

In this report I would like to present two parts: The latest guidelines on diagnosis and treatment of chronic hepatitis B (CHB) of Vietnam Ministry of Health, and some preliminary results in the treatment of CHB patients at the Haiphong Medical University Hospital. The study results showed that 97.7% (166/170) of the CHB patients responded well to antiviral drugs. After 12 months of treatment, the rates of undetectable plasma HBV DNA, HBe antigen seroclearance, and ALT normalization were 82.2%, 31.4%, and 74.7%, respectively. The remaining 2.3% of the patients who failed therapy, showed virologic breakthrough during treatment with appearance of HBV strains harboring drug resistance-associated mutations: L80I, L180M, A181T/V, and/or M204I/V of *pol*-RT gene. Tenofovir (TDF)-including regimens; TDF/lamivudine and TDF/entecavir, were the best for the treatment of CHB in Haiphong, Vietnam as well.

Checkup Strategy for Hepatitis Patients in Ishikawa, Japan

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Abstract

In Japan, approximately 2% of the population is estimated to be infected with hepatitis C virus (HCV) or B virus (HBV). It is believed that, within this 2%, many people do not know they are infected. It is vital to find, diagnose and correctly treat HBV/ HCV infected people because, if left untreated, these viruses can cause death from liver disease. Fortunately, effective anti-viral therapies have become available, therefore, the Japanese Government is strongly suggesting that all citizens get hepatitis tests for HBV and HCV at least once in their life.

To encourage hepatitis testing, the Japanese national and local governments provide free hepatitis testing, at five year intervals, for citizens aged 40 – 70 from years 2002-2006. To support identification, proper diagnosis and treatment for hepatitis virus infected people, the Ishikawa Prefectural Government started its own checkup program in 2002.

The 2002 program's main goals were:

1. Allow local governments to get personal information consent from hepatitis applicants which would allow direct contact by local government health care workers (LGHCWs).
2. Support LGHCW's yearly checkups for hepatitis-positive people.
3. Establish standard protocols for liver imaging at detailed examinations.

Even after 2006, local governments have continuously provided people several chances to get free hepatitis tests, and unique subsidies for hepatitis treatment costs started from 2009.

In 2009, Kanazawa University Hospital (KU), became a regional core institution and took over annual checkups of hepatitis patients from local governments and created a program: the Ishikawa Hepatitis Network.

The 2009 program's main goals are:

1. Organize local government and KU checkup testing for hepatitis-positive people.
2. Administer private information between citizens, local governments and the KU Ishikawa Hepatitis Network. (Previously, only local governments were allowed to possess individuals' private information. Now, based on signed consent from citizens, local governments can share certain hepatitis-related information with Ishikawa Hepatitis Network.)

So far, 1221 out of 2922 hepatitis virus-infected patients have agreed to participate in this program. KU directly contacts consenting patients and checks to confirm they annually see specialized doctors in addition to primary doctors. Local governments continue to contact people who do not respond or accept direct contact with KU.

In conclusion, the condition of all hepatitis-infected patients found by local governments can be checked annually by the local government or KU. This kind of checkup system for hepatitis patients in Ishikawa has been distributed throughout Japan as a promising model.

Strategy for the Treatment for Chronic Hepatitis B Patients in Japan

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Abstract

Hepatitis B virus (HBV) is one of the most distributed viruses which infect humankind. More than 3 billion people, one half of the world's population, have been exposed to HBV during their life. More than 400 million people worldwide are chronically infected with HBV and are at risk of developing life-threatening complications including liver cirrhosis and hepatocellular carcinoma. HBV is a major public health problem worldwide especially in East Asia and Africa. In Japan, approximately 1.5 million people are infected with HBV and it is one of the major causes of HCC and chronic hepatic failure. Japanese government introduced the low for prevention of mother to infant infection in 1986. This treatment would prevent about 95% of the vertical transmission. However, horizontal transmission became important problem from 2000. Japanese government will introduce universal vaccination from 2016 to prevent horizontal transmission of HBV.

The consensus meeting for diagnosis, management and treatment for hepatitis B was held during the 45th annual meeting of the Japan Society of Hepatology (JSH) in June 2009. Once the liver is persistently infected with HBV, it is difficult to eradicate the virus. It is reported that the natural clearance rate of HBsAg in asymptomatic HBsAg carriers is approximately 1-2% per year. Therefore, the first goal in treating chronic hepatitis B is to prevent patients from progression to cirrhosis and occurrence of HCC. Introduction of antiviral therapy should be considered on the biochemical and virological findings. In treatment by nucleoside analogues for chronic hepatitis B in Japan, LDV, ADV, ETV and TDF are mainly used at present. When patients with chronic hepatitis B are treated with nucleoside analogues, ETV or TDF should be given at the first-line drug because of its high efficacy and low emergence of viral resistant mutant. The control of viral load using nucleoside analogues reduces the risk of complicating HCC in patients with chronic hepatitis B. Interferon was the first antiviral treatment approved for chronic HBV infection. Younger age, high ALT levels, low HBV load, genotype A or B and high inflammatory activity in liver biopsy are predictive of good response to IFN. IFN therapy should be considered in patients fulfilling these predictors. Interferon shoud be avoided for patients with decompensated cirrhosis. IFN therapy prevents progression to cirrhosis or the development of HCC. Moreover, IFN therapy is associated with improved survival. IFN therapy and nucleoside analogue therapy are effective treatment of chronic hepatitis B. It is imperative to fully understand the characteristics of each therapy and select the appropriate treatment method for each case.