Letter to the Editor

The Declaration of Rabat: An update

On February 7th, 2015 and in the context of the 5th African Middle East Congress on Digestive Oncology in Rabat, Morocco a group of experts convened to update the Declaration of Rabat “Africa against viral hepatitis and hepatocellular carcinoma”.

The panel included Rhimou Alaoui (Morocco), Najet Bric-Belhadj (Tunisia), Alain Bougouma (Burkina Faso) Thérèse Ndri Yoman (Ivory Cost), Pape. Seliou Nbaye (Senegal), Abdel Meguid Kassem (Egypt), and Naima Amrani (Morocco), President of African Middle East Society of Digestive Oncology with the following thematic contributions:

– From chronic hepatitis to HCC. Cihan Yurdaydin (Turkey)
– Can prevention, screening and management of chronic hepatitis B and C infection prevent HCC? Jérôme Gournay (France)
– Should HVC screening and treatment be promoted in Africa and Middle East to prevent HCC? Mohamed El-Kassas (Egypt), Gamal Esmat (Egypt)

– WHO strategies to reduce the burden of liver cancer in Africa and Middle East. Fatos Hande Harmanci (WHO) and with the support of Fernand Vicari (France) in drafting. Meinhard Classen (Germany) initiated and supervised the process ever since the first version of the Declaration of Rabat has been issued in 2008.

It has been agreed upon the previous versions of the Declaration of Rabat (2008 and 2011) should be updated. The following is a consensus on the new version of the declaration.

Updates Declaration of Rabat: Africa against viral hepatitis and hepatocellular carcinoma, February 7th, 2015

Preamble

Hepatocellular carcinoma (HCC, also known as primary liver cancer) is the second most common cause of death from cancer and the 6th most frequent cancer globally. [1] Unlike many other cancers, the incidence and death rate due to HCC are rising, primarily due to the continued prevalence of hepatitis B and C virus infection.
The distribution of these cases is far from uniform with >80% of HCC cases occurring in Sub-Saharan Africa, Eastern Asia, where China accounts for more than 50% of the world’s cases, and the eastern Mediterranean countries. In these areas rates of chronic hepatitis B infection range from 8% to >20%. Over 60% of their populations will be infected during their lifetimes, and 45% of the world’s population lives in these geographic areas. Infection with hepatitis B virus increases the risk of developing HCC 100-fold and is secondary only to tobacco as a known carcinogen. In contrast, in parts of North Africa, infection with hepatitis C virus is responsible for up to 75–100% of HCC cases. Additional risk factors for HCC include exposure to environmental carcinogen aflatoxin B1 and dietary iron overload, a problem unique to Africa. Co-infection with HIV virus also increases the rate of progression to cirrhosis and HCC. Hepatitis B and C viruses are carried in the blood and body fluids. In countries with high rates of endemicity, e.g. Sub-Saharan Africa, transmission, particularly of hepatitis B virus, occurs primarily during the first five years of life, due to maternal/social contact with cuts, skin sores, scrapes, bites and scratches (horizontal transmission). The virus can also be passed from infected mother to her child at the time of birth, when blood exposure always occurs (perinatal transmission). This infection during early childhood leads to chronic infection in up to 95% of those exposed. Acute hepatitis is uncommon in infants and most infections are asymptomatic, increasing the chances for inadvertent transmission. Those acquiring infection later in life usually are infected through unprotected sex, unsafe injection practices, needle-stick injuries or unsafe practices such as tattooing and scarification.

A safe and effective vaccine to prevent infection with hepatitis B has been available since 1982. New hepatitis B infections could eventually be eliminated with the institution of universal vaccination. As a critical additional benefit, the hepatitis B vaccine would also eliminate the major cause of HCC. Hepatitis B vaccine is the first true anti-cancer vaccine and it has already been around for 25 years. Success of hepatitis B vaccine programs is well-documented in highly endemic areas such as China and Gambia where the prevalence of chronic hepatitis B infection in children was reduced from levels around 10% to less than 1% after the introduction of routine childhood immunization. By the end of 2013, 182 of 194 World Health Organization Member States had adopted routine infant or childhood vaccination against hepatitis B and the world coverage for the hepatitis vaccine third dose has reached 81% in 2013 [2].

Beginning in the year 2000, the Global Alliance for Vaccines and Immunization (GAVI) and the Vaccine Fund provided five years of funding for new and underused vaccines including hepatitis B, to the 72 poorest countries. Building on the success of their Phase I program, the GAVI Alliance extended availability of its resources to the 72 poorest countries in Phase II (2006–2015). Additional funds have become available through the International Financing Facility for Immunization. Following these efforts, as of 2013, 45 out of 47 Member States in the WHO African Region and all 21 Member States in the Eastern Mediterranean Region have hepatitis B vaccine programs.

Essential actions to be taken

The following list of fundamental areas identifies the required elements of a complete action plan. The recommendations are listed with consideration that current resources vary between countries and may be quite limited in many.

Therefore, they are grouped by priority, with the most critical and least expensive, and thus quickly achievable, is given first priority.

Prevention

A. Awareness and education

- African leadership: African nations should collaborate to develop a comprehensive strategy to prevent infection with hepatitis B and C and treat if indicated.
- The support of the World Health Organization, the World Gastroenterology Organization, the African Association for the Study of Liver Diseases and the International Association for the Study of Liver Diseases as well as relevant national societies should be used for educating the population, health care providers, government officials and other stakeholders about this major health issue.
- Advocacy groups should work with government officials to raise awareness and understanding of viral hepatitis in order to provide a clear and consistent message wherever individuals access the health care system.
- Community leaders should be engaged to encourage participation in screening and appropriate prevention and treatment programs.

B. Hepatitis B Immunization

- All infants should receive a dose of HBV vaccine as soon as possible after birth, preferably within 24 hours, followed by 2 or 3 doses to complete the primary series.
- HBV vaccine should be included in national childhood immunisation schedules.
- Catch-up vaccination should be considered for cohorts of children with low coverage as a way to increase the number of protected children.
- Catch-up strategies targeted at adolescents can be considered as a supplement to routine infant vaccination, depending on the epidemiological setting.
- HBV vaccine should also be offered to those at increased risk of acquiring or transmitting the virus including people who frequently require blood or blood products, dialysis patients, recipients of solid organ transplantations, prisoners individuals with illicit drug abuse, household and sexual contacts of individuals with chronic HBV infection, subjects with multiple sexual partners, healthcare workers and others who may be exposed to blood and blood products through their work, travellers to endemic areas, and patients with active HCV infection, or other chronic liver disease.

C. Health-care associated transmission including injection safety

- Establish systems to ensure a safe supply of blood, blood products, tissues and organs.
- Strengthen routine infection control practices in all healthcare settings including sharps waste management.
- Plan to switch to safety engineered injection devices including reuse-prevention syringes and sharp injury protection devices for therapeutic injections by 2020.
D. Reduction of exposure to aflatoxin

- Programs should be developed and implemented to reduce exposure to dietary aflatoxin and should include:
  o Agricultural strategies to reduce aflatoxin exposure in food
    - Genetic modifications of crops to enhance fungal resistance
    - Bio control of aspergillus by flooding fields with non-toxic fungi
  o Methods to reduce humidity to limit fungal growth
    - Drying crop in the sun
    - Discarding visibly moldy kernels or nuts before storage
    - Placing these on wooden pallets to keep the crop dry
  o Shifting the staple diet from corn to rice limiting exposure to aflatoxin

E. Iron overload

- Drinks stored or processed in iron containers may lead to serious iron overload of the liver and should be avoided.

Africa-wide surveillance

A priority should be placed on allocating adequate funds to determine the burden of illness posed by hepatitis B and C. A program of surveillance to determine the true incidence and prevalence of hepatitis B and C infections and to determine the occurrence of HCC by means of population based cancer registries should be implemented.

- Screening for hepatitis B and C should be made available in all health and community settings, in particular in high risk groups.
- Screening for HCC.

Early detection of HCC, in particular a combination of alfa fetoprotein blood test and an ultrasound liver examination every six months in patients with cirrhosis is recommended in several guidelines.

Detection and treatment

- Healthcare professionals should be trained in hepatitis B and C, and HCC prevention. Innovative approaches with community health workers may be required in regions with insufficient healthcare services.
- Treatment
  - Effective drugs are currently available to cure hepatitis C, control hepatitis B, and treat patients with HCC effectively if diagnosed early enough or offer palliative care. While universal hepatitis B vaccination will eventually eliminate the vast majority of hepatitis B infections and subsequent development of HCC, it will have no effect on the 350 million chronic carriers worldwide who will remain at risk of death from complications of cirrhosis or HCC unless their disease is treated.

Resources

- Additional resources should be sought to overcome financial barriers to prevention and care and to fund basic and clinical research.

Conclusion

This document has laid out a series of recommendations which should be taken forward in order to ensure that the burden imposed on the African continent by infection with hepatitis B and hepatitis C and the frequent consequence of hepatocellular carcinoma is dramatically reduced in the coming years.

Universal vaccination against hepatitis B of all infants, adolescents, health workers and persons at risk should be implemented. Sustainable funds must be secured to guarantee universal hepatitis B vaccination and appropriate care for those already affected with hepatitis B, hepatitis C and HCC.

It is recognized that major new resources will be required to achieve all the above goals. Funds for universal vaccination are available now and this should be a priority of all government and national healthcare bodies with a goal to achieve universal hepatitis B vaccination. Similarly, simple and inexpensive approaches to reduce aflatoxin exposure and dietary iron overload will may great benefits in decreasing the incidence of HCC and should receive major emphasis in countries where this is a severe problem. The longer term goals of providing appropriate care for those already affected with viral hepatitis and HCC must be approached now if success is ultimately to be obtained.

References


Further reading


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