Vaccine 31 (2013) 341–346

Contents lists available at SciVerse ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Control of viral hepatitis infection in Africa: Are we dreaming?

Richard Mihigo[a], Deo Nshimirimana[a], Andrew Hall[b], Michael Kew[c], Steven Wiersma[d], C. John Clements[e,*]

[a] Immunization and Vaccine Development Programme, World Health Organization Regional Office for Africa, Brazzaville, Congo
[b] London School of Tropical Medicine and Hygiene, London, UK
[c] University of Cape Town, South Africa
[d] Expanded Programme on Immunization, World Health Organization, Geneva, Switzerland
[e] The University of Melbourne, Australia

ARTICLE INFO

Article history:
Received 9 July 2012
Received in revised form 25 October 2012
Accepted 1 November 2012
Available online 10 November 2012

Keywords:
Vaccines
Viral hepatitis
Africa
Control
Hepatitis A
Hepatitis B
Hepatitis C
Hepatitis D
Delta hepatitis
Hepatitis E

ABSTRACT

Background: At least five different types of viral hepatitis cause problems of significant public health importance in Africa, where together they constitute a huge burden of disease. But until now, efforts to control the infections have been largely piecemeal. Analysis of the strategies needed to control each virus, however, reveals major overlaps.
Proposal: We propose that the control of these infections in the WHO African Region should start with the common strategies rather than with each disease. But this approach presents potentially huge problems to overcome, such as the difficulty of integrating multiple health service elements – the track record for successful integration of such services is not good. This is despite encouraging rhetoric from donors and national leaders alike. And to succeed, disparate programmes must work closely together. But we believe that the time is right to create new opportunities for prevention and treatment of hepatitis, including increasing education, and promoting screening and treatment for more than 500 million people already infected with hepatitis B and C viruses.
Impact: The impact of these efforts on decreasing mortality and morbidity will be significant because of the high burden of disease from these infections, and also because the effect will spill over to benefit the control of other communicable diseases and health systems strengthening. Such a project will inevitably involve multiple strategies that will vary somewhat according to the epidemiology of the diseases and the location.

1. Introduction

The 2010 World Health Assembly adopted resolution 63.18, calling for the World Health Organization (WHO) to adopt a comprehensive approach to hepatitis prevention and control and to mark World Hepatitis Day on 28 July. The WHO African Region has already facilitated hepatitis B prevention through the introduction and rapid scale-up of infant hepatitis B immunization in almost all Member States. The Region is now addressing comprehensive viral hepatitis prevention and control through a regional strategy. Such a strategy involves multiple actions, such as providing safe drinking water, which may support control of more than one infectious agent. Is this strategy too difficult, a pipe dream, or is it a real possibility?

Hepatitis is a huge global problem that affects varying populations and age groups being made up of cases and deaths from hepatitis A (HAV), B (HBV), C (HCV), delta (HDV) and E (HEV). Worldwide, an estimated 350 million people are chronically infected with HBV and around 170 million are chronically infected with HCV. Together, viral hepatitis causes the deaths of some 1 million people every year, the overwhelming majority as a result of chronic infection complicated by cirrhosis and hepatocellular carcinoma (HCC) [1]. All of the above-listed hepatitis viruses can cause acute liver disease. HAV causes acute illness from food and water contamination, whereas HBV and HCV can cause chronic infections that remain silent for decades, placing infected persons at risk for premature death from cirrhosis or HCC in later life. The global burden of disease caused by acute hepatitis B and C viruses, and cancer and cirrhosis is high – about 2.7% of all deaths [2]. Those with chronic HBV infection have a 15–25% risk of dying prematurely from HBV-related cirrhosis or HCC. Those with chronic HCV infection are also at high risk for developing cirrhosis and

Abbreviations: MCH, maternal and child health services; NCD, non-communicable diseases; IDS, integrated disease surveillance; Socio-e, socioeconomic; i.v., intravenous.

* Corresponding author at: The University of Melbourne, Melbourne, Australia. Tel.: +61 3 9775 2931.
E-mail address: john@clem.com.au (C.J. Clements).

0264-410X/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.vaccine.2012.11.001

hepatocellular cancer. Even worse outcomes result in patients who are co-infected with HDV and HBV.

Exposure to blood through injections with non-sterile equipment or transfusion of infected blood or blood products is a common and preventable cause of HBV and HCV infections. Unsafe injection practices are estimated to be responsible for 21 million new HBV infections and two million new HCV infections a year. A significant proportion of the blood supply is either not screened at all for HBV or HCV, or not screened properly. The probability of transmission of HBV and HCV through transfusion of unsafe blood can be as high as around 70% and 90%, respectively, depending on the volume transfused and the viral load. Injecting drug use is the highest risk for HCV infection, with prevalence rates in people reporting this behaviour ranging between 30% and 60% [3]. HDV demands co-infection with HBV and therefore its epidemiology and control strategies are similar to those for HBV. HEV is transmitted mainly through contaminated drinking water, and has recently been shown to cause epidemics in Africa.

2. Burden of viral hepatitis in Africa

The African Region contributes significantly to the global burden of disease from hepatitis. The precise burden in the continent is difficult to quantify because of inaccurate statistical data and under-reporting. Estimates must be derived from serosurveys or other epidemiological investigations. Of the various agents causing viral hepatitis, data on HBV have been relatively more available and suggest that 15–60% of the normal population in many African countries may be positive for one or more of the serological markers for infection, whilst the corresponding values for patients with diagnosed HCC ranges from 49% to 80%. The prevalence of chronic HBV infection is high (more than 8%) in all of sub-Saharan Africa.

Liver disease was the third most common (12.1%) of all 4568 deaths on the medical wards of one hospital in Ibadan, Nigeria over a 14-year period. Of all causes of deaths from liver disease, HCC alone accounted for 42.5% while cirrhosis accounted for 21.1% of the deaths and, in both diseases, HBV was the commonest cause. HCC, which accounted for 491 out of 100,000 admissions in that teaching hospital, was the commonest malignancy on the medical wards and was the commonest cause of deaths from cancers in middle-aged and elderly Nigerians [4].

In the Gambia, HCC has been defined as the country's most common form of cancer [5], and HBV infection is endemic. A national cancer registry was established in 1986 and this continues to generate data on the incidence of all cancers in the country. HCC in the Gambia is the most common cancer in men and the second most common in women.

In high-risk situations in the region such as prisons, viral hepatitis may co-exist with other diseases such as HIV infection, syphilis or other sexually transmitted diseases. The high incidence of HBV and HCV in prisoners and prison officers suggests the need for institutionalized implementation of surveillance for viral infections, standard infection control practices, blood-borne infectious diseases risk reduction, mandatory screening for HBV and HCV upon employment, and promoting harm-reduction behaviour in prison inmates [6]. Measures to control infection or reduce harm for one disease are likely to have a positive effect on controlling the others as well.

2.1. Hepatitis A virus (HAV)

HAV has a high level of endemicity in the African Region and is transmitted via the faecal–oral route, either by direct contact with an infectious person or by ingestion of contaminated food or water. Persons with hepatitis A can shed the virus in their stool beginning several weeks before the onset of symptoms. Under favourable conditions, HAV may survive in the environment for months. As water and sanitation improve in some communities, the overall incidence of HAV infection decreases, leaving adults susceptible to increasing morbidity and mortality from HAV infection. Outbreaks can occur periodically in these areas that are experiencing an epidemiological transition. A number of hepatitis A vaccines are available that are safe and effective.

2.2. Hepatitis B virus (HBV)

HBV is transmitted by per-cutaneous and per-mucosal exposure to infected blood and other body fluids. The main ways of becoming infected with HBV are perinatally (from mother to baby around the time of birth); child-to-child transmission – a very important but incompletely understood route for African children [7–10]; through unsafe injections and transfusions; and having sex with an infected person. Although not yet proven, it seems possible that the virus could also be transmitted by traditional practices such as circumcision, scarification and *inyangas* (ritual amputation of a finger tip).

Humans are the only reservoir of HBV. The disease is highly endemic in Africa with a prevalence of surface antigen (HBsAg) of at least 8%. A considerable proportion (7–40%) of HBsAg-positive individuals may also be "e" antigen (HBeAg) positive, which is associated with high infectivity. Unless immunized at birth, the majority of children born to HBeAg-positive mothers become chronically infected [11,12]. A comprehensive approach to eliminating HBV transmission may also address infections acquired in the perinatal period and, most importantly, during early childhood, as well as those acquired by teenagers and adults.

As of 2011, in the WHO African Region, hepatitis B vaccine (HepB) was administered in 45 of 46 countries. Only Equatorial Guinea had not introduced the vaccine yet. None the less, in 2009, more than 4.2 million infants in the African Region did not receive three doses of the vaccine. This deficiency is not uniform, with around 75% of the under-vaccinated children coming from only 10 countries. Currently only 5 countries in the African Region (Algeria, Botswana, Cape Verde, The Gambia, and Nigeria) are reporting administering a birth dose, and the timeliness of these doses is unknown.

In the Gambia study, childhood vaccination status is being linked to those subjects with cancer to determine the effectiveness of the vaccine at preventing HCC – this result is expected in the next decade [13]. This framework has generated an extensive body of research on hepatitis viruses and cancer with more than 60 publications. In particular the proportion of HCC due to hepatitis B in this population has been carefully characterized, showing that hepatitis B-related HCC affects people at a median age of 40 years [5].

HBV/HIV and HCV/HIV co-infections are increasing problems in countries with concentrated HIV epidemics and among injecting drug users. For those co-infected persons who are being treated with highly effective antiretroviral medicines (HAART), underlying viral hepatitis is becoming a major cause of death.

It is estimated that perhaps 10% of the 40 million people infected with HIV worldwide are co-infected with HBV; the majority live in resource-constrained settings. As many as 3 million HIV/HBV co-infected persons live in Africa [14]. Although HBV infection appears to have a minimal effect on the progression of HIV, the presence of HIV markedly accelerates the progression of liver fibrosis, and may increase the risk of developing HCC and cirrhosis by accelerating the progression to these adverse consequences in many co-infected persons [15–17] (Fig. 1).

2.3. Hepatitis C virus (HCV)

HCV is present worldwide, but its distribution is directly related to the prevalence of persons who routinely share injection