Epidemiology, Economic Burden, and Risk Factors of Chronic Viral Diseases

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ABSTRACT

OBJECTIVE: To outline the epidemiology of the human immunodeficiency virus (HIV) and hepatitis B virus (HBV) epidemics and their economic burden.

SUMMARY: The global epidemics of HIV infection (40 million) and HBV infection (400 million) overlap so that approximately 4 million individuals worldwide are co-infected with HIV and HBV. Generally about 5%-10% of HIV-infected individuals are co-infected with HBV, but the numbers depend on the specific patient population.

In the most recent published comparison of costs of treating chronic viral infections, HIV accounts for higher medical expenses than HBV. The overall costs of treating HIV in the United States in 1997 were about $4.5 billion (in 1997 U.S. dollars), while the overall cost for treating hepatitis B in 1997 was $51.4 million. However, HBV complications are expensive.

Treatment options for HIV and HBV have evolved differently. In HIV treatment, the high pill burden and dietary restriction of early highly active antiretroviral therapy (HAART) have been replaced with simpler more potent combination regimens that combine several agents in a single oral dose taken once or twice daily. For HBV infection, the issues are somewhat different: sequential monotherapy rather than combination therapy is the usual management approach. A substantial number of individuals are co-infected with HIV and hepatitis viruses, including HBV, which complicates clinical management because some antiviral agents have activity against both HIV and HBV.

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Introduction

This supplement to the Journal of Managed Care Pharmacy addresses key issues in the management of 2 important chronic viral diseases that sometimes affect the same patient: human immunodeficiency virus (HIV) infection, hepatitis B virus (HBV) infection, and HIV-HBV co-infection. Relevant evidence-based guidelines and current therapeutic options are outlined in the following articles, which include an extensive discussion of patient adherence in long-term therapy for chronic viral infection, current treatment options, and management of drug formularies.

Epidemiology

The global epidemics of HIV infection (40 million) and HBV infection (400 million) overlap so that approximately 4 million individuals worldwide are co-infected with HIV and HBV.1-3 HIV and HBV are transmitted via exchange of body fluids (i.e., blood, sexual fluids). Unequally distributed, the 2 epidemics overlap in certain regions of the world. For example, HIV prevalence in injection drug users is 40% or higher in North America (especially in the United States and Canada), Eastern Europe, and Asia (including Russia and other states from the former Soviet Union, but not India where it is reported to be less than 10%).4 The prevalence of chronic HBV is more than 8% in most of southern Asia (including southeast Asia and Indonesia, but excluding both India and the former Soviet Union), sub-Saharan Africa, and the circumpolar regions in North America.5 Excluding India, Asia and African regions show the most potential for epidemic overlap in HIV and HBV.

Although HBV has been vaccine-preventable since 1981,6 it remains a significant problem in southeast Asia and southern Africa; in the United States, more people are infected with HBV than with HIV. Based on serological measures from the third National Health and Nutrition Examination Survey (NHANES III), an estimate from the Centers for Disease Control and Prevention (CDC) suggests that there are 1,250,000 HBV cases in the United States with approximately 128,000 new cases per year.7 Another report from the CDC notes that in 2006, 4,758 cases of HBV were reported to the CDC, but the actual number of new infections was about 46,000.8 About one third are transmitted via exchange of blood, and two thirds are transmitted sexually.7 By comparison, there are an estimated 800,000 diagnosed cases of HIV in the United States (perhaps an additional 25% are undiagnosed bringing the total to 1 million), with an estimated 41,000 new cases per year.9

Generally, about 5%-10% of HIV-infected individuals are co-infected with HBV, but the numbers depend on the specific patient population. For example, in the Strategic Management of Antiretroviral Therapy (SMART) study, which enrolled nearly 5,500 HIV-infected individuals with CD4 cell counts more than...
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<table>
<thead>
<tr>
<th>TABLE</th>
<th>Leading Causes of Death by Age and Rank, United States, 2005</th>
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<tbody>
<tr>
<td>Rank</td>
<td>1-24 Years</td>
</tr>
<tr>
<td>1</td>
<td>Accidents</td>
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<td>2</td>
<td>Homicide</td>
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<td>3</td>
<td>Suicide</td>
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<td>4</td>
<td>Cancer</td>
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<td>Heart disease</td>
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<td>6</td>
<td>Flu/pneumonia</td>
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<td>7</td>
<td>COPD</td>
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<tr>
<td>8</td>
<td>Stroke</td>
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<td>9</td>
<td>Septicemia</td>
</tr>
<tr>
<td>10</td>
<td>HIV infection</td>
</tr>
</tbody>
</table>

COPD = chronic obstructive pulmonary disease; HIV = human immunodeficiency virus.

350 cells/cubic millimeter to evaluate an antiretroviral management strategy, about 5% were co-infected with HIV and HBV, while a somewhat larger percentage were co-infected with hepatitis C virus (HCV). Of the 5,472 HIV-infected individuals followed, 17% (922/5,472) were co-infected with a hepatitis virus (798 were co-infected with HCV only, 110 with HBV only, and 14 with both HCV and HBV). The mortality rate of the co-infected patients was 2.52 (95% confidence interval [CI] = 1.71-3.33) per 100 patient-years of follow-up, compared with 0.68 (95% CI = 0.48-0.90) for patients with HIV but without either HBV or HCV.

Economic Burden

In the United States, HIV is associated with higher medical expenses than HBV. In the most recent published comparison, the comparative costs of treating chronic viral infections (a December 1998 report from the Kaiser Family Foundation in the United States), HIV costs were about $4.5 billion (in 1997 U.S. dollars), while hepatitis B costs were $51.4 million (1997 dollars). However, this report did not include HBV complications, which are expensive. The average cost per hospitalization of a patient with liver inflammation was $8,464 (1999 U.S. dollars) and for cirrhosis $14,063 (1999 U.S. dollars). In young adults (aged 25-44 years), HIV infection and chronic liver disease are the sixth- and seventh-ranked causes of death. In children and young adults (aged 1-24 years), liver disease has not manifested itself, but HIV infection is the tenth leading cause of death. In older adults (aged 45-64 years) liver disease remains the seventh leading cause of death, but HIV is not among the top 10 causes of death (Table).

Treatments for HIV, HBV, and Dual HIV-HBV Infections

Treatment options for HIV and HBV have evolved differently. Therapy for HIV infection has changed as nucleoside analog reverse transcriptase inhibitors were supplemented with nonnucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), and finally nucleotide and acyclic nucleoside reverse transcriptase inhibitors (NRTIs). In addition, second-generation NNRTIs and PIs are now available along with drugs in new classes, including a fusion inhibitor, an integrase inhibitor, and a CCR5 co-receptor antagonist. The high pill burden and dietary restriction of early highly active antiretroviral treatment (HAART) regimens have been replaced with simpler more potent regimens that combine several agents in a single oral dose taken once or twice daily.

With these simple, potent antiretroviral regimens, HIV disease has become increasingly treatable, and mortality has decreased dramatically. However, as patients live longer, metabolic abnormalities, such as elevated lipids, which may affect long-term heart health, and lipodystrophy, which may cause disfiguring changes in the face and body, have emerged. These and other side effects of therapy decrease adherence. Suboptimal drug levels subsequent to pharmacokinetic issues or poor adherence, can promote viral drug resistance that leads to treatment failure.

As therapies for HIV disease have improved, medicines’ focus has shifted from considering HIV/AIDS as an aggressive terminal disease to considering HIV infection a treatable condition in which good treatment adherence improves survival and reduces morbidities. Effective HIV suppression with potent antiretroviral therapy must be continued indefinitely, because treatment interruptions and drug holidays result in negative outcomes. Any long-term therapy cost becomes an important consideration.

The issues are somewhat different for HBV infection. Several effective therapies to suppress HBV are available, but they are less advanced than those for HIV; sequential monotherapy rather than combination therapy remains the norm for treating HBV infection. Also, treatment of HIV-HBV co-infection is complicated by the fact that some antiviral agents have activity against both HIV and HBV.

REFERENCES


