MANAGEMENT OF OCCUPATIONAL EXPOSURE TO THE HUMAN IMMUNODEFICIENCY VIRUSES

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Abstract

By the end of the year 2002, the World Health Organisation estimated that 42 million people have been infected with the Human Immunodeficiency Viruses (HIV). Though sexual transmission is the commonest mode of transmission, transmission to the health care personnel (HCP) who are exposed to blood and blood products remains an increasing risk. Because there is no cure or effective vaccine for HIV infection, optimal post-exposure care, including the administration of antiretroviral drugs to prevent HIV infection, remains a high priority for protecting health care personnel. Factors that should be considered in the choice of treatment for an exposed health care worker include the risk of HIV infection associated with the exposure, the expected benefit of antiretroviral treatment, the risks associated with the proposed treatment, and the probability that the infecting strains will be susceptible to the antiretroviral regimen used. U.S. public health guidelines recommend that a four-week regimen of two drugs be started as soon as possible after most cases of HIV exposure through percutaneous or mucosal routes. If the source person is found to be HIV-negative treatment should be discontinued. When the injury involves an increased risk of HIV transmission, the regimen should be expanded to include a third drug. Since post-exposure prophylaxis is not 100% effective, prevention strategies through safer practices, barrier precautions, safer needle devices, and other innovations, remain the best way to prevent occupational infection by HIV and other blood borne pathogens.

Key Words: HIV, occupational exposure, post-exposure prophylaxis

Introduction

By the end of the year 2002, the World Health Organisation estimated that 42 million people have been infected with the Human Immunodeficiency Viruses (HIV). 1 In that year alone, 5 million new infections occurred, with 75% of these infections occurring in sub-Saharan Africa. 1 Though sexual transmission is the commonest mode of transmission, transmission to the health care personnel (HCP) who are exposed to blood and blood products remains an increasing risk more so in sub-Saharan Africa, where medical manpower and facilities are grossly inadequate and over stretched. Because there is no cure or effective vaccine for HIV infection, optimal post-exposure care, including the administration of antiretroviral drugs to prevent HIV infection, remains a high priority for protecting health care personnel.

Strategies for management of occupational exposure to HIV

Factors that should be considered in the choice of treatment for an exposed health care worker include the risk of HIV infection associated with the exposure,

the expected benefit of antiretroviral treatment, the risks associated with the proposed treatment, and the probability that the infecting strains will be susceptible to the antiretroviral regimen used.²

Risk for occupational transmission of HIV

In prospective studies of HCP, the average risk of HIV transmission after a percutaneous exposure to HIV-infected blood has been estimated to be approximately 0.3% (95% confidence interval [CI] = 0.2%--0.5%) ³ and after a mucous membrane exposure, approximately 0.09% (95% CI = 0.006%--0.5%). 4 Injury with a hollow-bore needle is by far the commonest mode of infection. ² Although episodes of HIV transmission after non-intact skin exposure have been documented, 5 the average risk for transmission by this route has not been precisely quantified but is estimated to be less than the risk for mucous membrane exposures. ⁶ The risk for transmission after exposure to fluids or tissues other than HIV-infected blood also has not been quantified but is probably considerably lower than for blood exposures.

Epidemiologic and laboratory studies suggest that several factors might affect the risk of HIV transmission after an occupational exposure. In a retrospective case-control study of HCP who had

percutaneous exposure to HIV, the risk for HIV infection was found to be increased with exposure to a larger quantity of blood from the source person as indicated by a) a device visibly contaminated with the patient's blood, b) a procedure that involved a needle being placed directly in a vein or artery, or c) a deep injury. ⁸ The risk also was increased for exposure to blood from source persons with terminal illness, possibly reflecting either the higher titer of HIV in blood late in the course of AIDS or other factors (e.g., the presence of syncytia-inducing strains of HIV). A laboratory study that demonstrated that more blood is transferred by deeper injuries and hollow-bore needles lends further support for the observed variation in risk related to blood quantity. ⁹

A patient whose blood or other potentially infectious body fluid is involved in an occupational exposure should be evaluated to determine the likelihood of HIV infection, in accordance with relevant regulations and local policies. The interval between the onset of viremia and the detection of HIV antibody, with the use of current enzyme immunoassays for HIV, is a few days at most. ¹⁰ Hence, if the result of a reliable HIV test in the source patient is negative, the risk of transmission is assumed to be zero, unless the patient has risk factors for infection and the clinical findings are compatible with acute HIV infection (e.g., fever, pharyngitis, rash, lymphadenopathy, and malaise). ¹¹

Benefits of chemoprophylactic treatment

Information about primary HIV infection indicates that systemic infection does not occur immediately, leaving a brief window of opportunity during which antiretroviral intervention post-exposure modify or prevent viral replication. In a primate model of simian immunodeficiency virus (SIV) infection, infection of dendritic-like cells occurred at the site of inoculation during the first 24 hours following mucosal exposure to cell-free virus. Over the subsequent 24-48 hours, migration of these cells to regional lymph nodes occurred, and virus was detectable in the peripheral blood within 5 days. 12 Theoretically, initiation of antiretroviral PEP soon after exposure might prevent or inhibit systemic infection by limiting the proliferation of virus in the initial target cells or lymph nodes. 2 Data from clinical of prophylaxis against perinatal trials transmission have consistently demonstrated that antiretroviral treatment can prevent HIV infection after exposure, even among neonates who are not treated until after birth. $^{13-18}$ The relevance of this clinical situation to occupational exposure is not known.

Although these data are encouraging, it is clear that, whatever benefit is afforded by post-exposure treatment, the protection is not absolute. Twenty-one cases of HIV infection have been reported in health care personnel in the United States and elsewhere, despite post-exposure antiretroviral treatment, which

included two or more antiretroviral drugs in some cases. ^{2, 19, 20} A variety of factors may have contributed to the treatment failure, including an intrinsic lack of efficacy of prophylactic antiretroviral treatment and resistance to antiretroviral drugs. ¹⁰

Risks of prophylactic anti-retroviral therapy

All antiretroviral agents are associated with adverse events, especially gastrointestinal symptoms. Data from the National Surveillance System for Health Care Workers and the HIV Post-exposure Prophylaxis Registry of the United States indicate that nearly 50 percent of health care personnel report adverse events while taking antiretroviral drugs prophylactically, and about one third stop taking the drugs as a result. All Most of these symptoms are not serious and can be managed. Prophylactic regimens that include three drugs are more likely to result in adverse events and early discontinuation of treatment than are two-drug regimens.

Antiretroviral drug resistance

Resistance to antiretroviral drugs is a growing problem for all patients especially so in sub-Saharan Africa where erratic supply of anti-retroviral drugs is a major concern. ¹ In the health care setting resistance to antiretroviral drugs is most likely in patients with clinical progression of disease, increasing quantitative plasma HIV RNA titers, a decline in the CD4 T-lymphocyte count, or a combination of these findings. ²² Unfortunately, clinical data alone are not reliable in detecting resistance, and data from genotyping or phenotyping assays are rarely available in time to guide decisions about empirical post-exposure treatment. For this reason, two or more antiretroviral drugs are usually used for prophylaxis after occupational exposure. ²

Antiretroviral drugs for HIV post-exposure prophylaxis

U.S. public health guidelines recommend that a fourweek regimen of two drugs be started as soon as possible after most cases of HIV exposure through percutaneous or mucosal routes. ² If the source person is found to be HIV-negative treatment should be discontinued. Therapy is not indicated for contact between intact skin and blood or other body fluids contaminated by HIV. 11 When the injury involves an increased risk of HIV transmission (e.g., an injury caused by a large-bore needle, associated with a deep puncture, or caused by a device visibly contaminated with blood or a device in a patient's artery or vein), the regimen should be expanded to include a third drug. Indinavir or nelfinavir is recommended as a good option when a third drug is indicated. Efavirenz, a non-nucleoside analogue, and abacavir are also considered potentially useful drugs when an expanded regimen is indicated. Routine use of three drugs is not

recommended for all exposed persons, because adding a third drug increases the probability that adverse events will occur and that the four-week course of treatment will not be completed. 2,21 Table 1 lists the

regimen used in HIV post-exposure prophylaxis, their dosages and side-effects while Table 2 summarizes the current recommendations for post-exposure prophylaxis according to the source person.

Table 1: Basic and expanded regimens of post-exposure prophylaxis against human immunodeficiency virus infection. 10

| Regimen | Doses | Primary adverse effects | |
|--|---|---|--|
| Basic | | | |
| Zidovudine plus lamivudine; | 600mg of zidovudine daily in two or three divided doses; 150mg of lamivudine twice daily | Zidovudine: aneamia, neutropenia, nausea, headache, insomnia, muscle weakness and pain. Lamivudine: abdominal pain, nausea, diarrhoea, rash, pancreatitis. | |
| Stavudine plus lamivudine | 40mg of Stavudine (30mg if body weight is <60kg). twice daily. 150mg of lamivudine twice daily | Stavudine: Peripheral neuropathy, headache, diarrhoea, nausea, insomnia, anorexia, pancreatitis, elevated liver enzyme values, anaemia, neutropenia Lamivudine: as above | |
| Didanosine plus Stavudine | 400mg of Didanosine daily, taken on an empty stomach if a buffered tablet is used, or 250mg daily if a delayed-release capsule is used. | Didanosine: Pancreatitis, lactic acidosis, neuropathy, diarrhoea, abdominal pain, nausea. Stavudine: as above. | |
| Expanded (basic regimen plus one of the following) | • | | |
| Indinavir | 800mg every 8hr, taken on an empty stomach | Nausea, abdominal pain, nephrolithiasis, indirect hyperbilirubineamia. | |
| Nelfinavir | 750mg three times daily, with a meal or snack, or 1250mg twice daily with a meal or snack. | Diarrhoea, nausea, abdominai pain, weakness, rash. | |
| Efavirenz | 600mg daily, at bedtime | Rash (including Stevens-Johnson syndrome), insomnia, somnolence, dizziness, trouble concentrating, nightmares. | |
| Abacavir‡ | 300mg twice daily | Nausea, diarrhoea, anorexia, abdominal pain, fatigue, headache, insomnia, hypersensitivity reactions. | |

[†]Available as a combined formulation Combivir®, the recommended dose is one tablet twice daily.

Management of the exposed person and follow up
The exposed person should receive immediate first
aid and post-exposure counseling with emphasis on
the minimal risks of infection, the need for immediate
HIV testing and the available resources for postexposure prophylaxis.

HIV testing of exposed persons is recommended as soon as possible after exposure (to establish that the infection was not already present) and periodically during the first six months after the exposure (to detect occupational transmission). Testing after six months is not usually indicated, but if the exposure posed an especially high risk or if the exposed worker needs further reassurance, additional testing may be helpful. An enzyme immunoassay for HIV antibody is the appropriate test for detecting new infections.

Laboratory monitoring, including a complete blood count and tests of renal and hepatic function, is

[‡] Available as a combined formulation with zidovudine and lamivudine (Trizivir®).

recommended at base line and at two weeks. The use of additional tests depends on the specific regimen acquired hepatitis C virus infection from the exposure be followed for 12 months, because anecdotal evidence indicates that they may be at risk for delayed HIV seroconversion. ² All exposed persons, regardless

used and the medical condition of the source patient. The guidelines also recommend that persons who have of the post-exposure treatment regimen, are advised to return for immediate evaluation if symptoms or signs that might be attributable to acute HIV infection appear.

Table 2: Recommendations for prophylaxis against human immunodeficiency virus (HIV) infection after percutaneous injury, according to the infection status of the source person.¹⁰

| Risk posed by exposure† | | | Infection status of source person‡ | | |
|-------------------------|---|---|---|---|------------------------------|
| Lower | HIV Positive, Class 1 | HIV Positive, Class 2 | Unknown Status | Unknown Source Person | HIV-Negative |
| | Basic 2-drug prophylaxis recommended | Expanded (3-drug) prophylaxis recommended | Generally, prophylaxis not warranted, but basic 2-drug prophylaxis can be considered if source person has risk factors for infection§ | Generally, prophylaxis not warranted, but basic 2-drug can be considered in settings where exposure to HIV-infected is likely | Prophylaxis not warranted |
| Higher | Expanded (3-drug) prophylaxis recommended | Expanded (3-drug) prophylaxis recommended | As above | As above | As above |

[†] Injuries caused by solid needles and superficial injuries pose a lower risk of infection, and those involving a large-bore hollow needle, a deep puncture, a device visibly contaminated with blood, or a needle used in a patient's artery or vein pose a higher risk of infection.

Conclusion

Post-exposure prophylaxis for HCP exposed to HIV infection is not a trivial undertaking as antiretroviral drugs are associated with serious, and rarely lifethreatening, adverse effects; an assessment of the risks of benefit and harm should be made in all cases. Management of the HCP exposed to HIV infection is medical emergency. Where post-exposure prophylaxis is indicated, it should be instituted as soon as possible after exposure, preferably within hours. Since post-exposure prophylaxis is not 100% effective, prevention strategies through practices, barrier precautions, safer needle devices, and other innovations, remain the best way to prevent occupational infection by HIV and other blood borne pathogens.

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[‡] A class 1 positive status is defined by asymptomatic HIV infection or a low viral load (e.g., <1500 RNA copies per milliliter); a class 2 positive status is defined by symptomatic HIV infection, the acuired immunodeficiency syndrome, acute seroconversion or a high viral load.

[§] If the source person has risk factors for HIV Infection, prophylaxis is optional and should be based on an individualized decision made jointly by the exposed person and the treating physician. If prophylaxis is administered and the source person is subseuently determined to be HIV-negative, prophylaxis should be discontinued.

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