Update Article

SURGEON AND HIV INFECTION

Post Exposure Prophylaxis : Need of the hour

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ABSTRACT

HIV infection in HCW is an occupational hazard requiring policy decisions by the health care administrators. In this article we have outlined a post exposure prophylaxis protocol following HIV exposure in HCWs. By determining the HIV status code of the source and the HIV exposure code of the HCWs, recommendations for PEP are forwarded. Occupational exposures should be considered urgent medical and surgical concerns to ensure timely administration of PEP. At the end, an algorithm is provided to guide exposed health-care workers in deciding when to consider PEP.

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KEY WORDS : Acquired immunodeficiency syndrome (AIDS); Antiretroviral therapy; Health care worker (HCW); HIV infection; Needle stick injuries; Occupational exposure; Post exposure prophylaxis (PEP).

Introduction

Of the 688,200 persons who reported with AIDS in United States through December 31, 1998, 21,267 had been employed in health care. These cases represented 5.1 percent of the 417,885 adult AIDS cases reported to Centre for Disease Control (CDC) about whom occupational information was known. The type of job is known for 20,071 (94 percent) of the 21,267 reported health care workers with AIDS. The specific occupations were as follows : 1,664 physicians, 111 surgeons, 4,698 nurses, 446 dental workers, 402 paramedics, 2817 technicians, 985 therapists and 4,553 health aides. Overall, 75 percent of the health care workers with AIDS, including 1,303 physicians, 85 surgeons, 3,521 nurses, 359 dental workers, and 289 paramedics, were reported to have died [1].

Because the disease is blood borne and transmissible, and because of the nature of surgical work, a concerned surgical community has become involved and has offered leadership in developing improved surgical techniques and procedures, and enhanced sterile surgical barriers. Surgeons are at risk of exposure to the HIV virus in their daily endeavours and are concerned about this risk. The prospect of acquiring HIV through occupational exposure is a fear most surgeons confront. Percutaneous injuries with HIV contaminated sharps are not uncommon, occurring in as many as 1 in 40 emergency room surgeons or nurses annually at hospitals serving areas with a high HIV

seroprevalence [2].

Occupational exposure to blood borne pathogens, including HIV, hepatitis B, and hepatitis C, is a major concern among surgeons, with exposure to HIV the most feared consequence. The risk of HIV transmission from a single percutaneous exposure to blood or bloody fluid is estimated at 0.3% (95% confidence interval {CI}=0.2%-0.5%) [3] and after a mucous membrane exposure is 0.09% (95% CI=0.006%-0.5%)[4].

Although preventing blood exposures is the primary means of preventing occupationally acquired human immunodeficiency virus (HIV) infection, appropriate postexposure management is an important element of workplace safety.

Post Exposure Management

a) *Exposure Report* - The health care workers should be educated to report occupational exposures immediately after they occur, particularly because post exposure prophylaxis (PEP) is most likely to be effective if implemented as soon after the exposure as possible.

b) *Occupational exposure* - means a percutaneous injury (e.g. a needle stick or cut with a sharp object), contact of mucous membrane or nonintact skin (eg. when the exposed skin is chapped, abraded, or afflicted with dermatitis) or contact with intact skin when the duration of contact is prolonged (i.e. several

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minutes or more) or involves an extensive area, with blood, tissue, or other body fluids. Body fluids include (i) semen, vaginal secretions, or other body fluids contaminated with visible blood that have been implicated in the transmission of HIV infection [5,6] and (ii) cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids, which have an undetermined risk for transmitting HIV [5].

c) *Wounds and skin sites* that have been in contact with blood or body fluids should be washed with soap and water; mucous membranes should be flushed with water. There is no evidence that the use of antiseptics for wound care or expressing fluid by squeezing the wound further reduces the risk of HIV transmission. The application of caustic agents (e.g. bleach) or the injection of antiseptics or disinfectants into the wound is not recommended [7].

d) *Evaluation and testing of an exposure source* - The person whose blood or body fluids are the source of an occupational exposure should be evaluated for HIV infection. Information available in the medical record at the time of exposure (e.g. laboratory test results, admitting diagnosis, or past medical history) or from the source person may suggest or rule out possible HIV infection (Fig. 1).

e) *HIV - antibody testing* of an exposure source - should be performed as soon as possible. Repeatedly reactive results by enzyme immunoassay (EIA) or rapid HIV-antibody tests are considered highly suggestive of infection, whereas a negative result is an excellent indicator of the absence of HIV antibody.

f) *Clinical Evaluation and Baseline Testing of Exposed Surgeon* - Exposed surgeon should be evaluated for susceptibility to bloodborne pathogen infections. Baseline testing (i.e. testing to establish serostatus at the time of exposure) for HIV antibody should be performed (Fig. 2).

g) *Drug Treatment* - It is reasonable to initiate a two-drug post exposure prophylaxis (PEP) regimen i.e. Zidovudine 300 mg bid and lamivudine 150 mg bid. Add indinavir 800 mg tid or nelfinavir 750 mg tid for high-risk exposures-large-volume blood and high titer HIV. Treat for 4 weeks. The addition of lamivudine and indinavir to zidovudine provides 2 theoretical advantages. Combination antiretroviral therapy leads to reduction in viral load compared to single-drug regimens. Furthermore, given the growing number of people living with AIDS, the emergence of resistant viral strains in the setting of long-term antiretroviral therapy is significant. Therefore, a 3 - drug antiretroviral regimen appears to be justified in the

Fig. 1 : Determining the HIV status code (HIV SC)

Fig. 2 : Determining the HIV exposure code (HIV EC)

setting of highest risk exposures. Highest-risk exposures are defined as exposures involving both a large volume of blood (as in the case of a deep injury or a large-diameter needle) and a source patient with high viral titers (such as those that occur in end-stage AIDS or during the acute retroviral syndrome). A 2- or 3-drug regimen would be considered for exposures that constitute high risk. Such risk would include percutaneous exposure to blood that either is large volume or contains a high viral titer (Table-1). If the source patient's HIV status is unknown, decisions regarding PEP must be considered on a case-by-case basis, based on the probability of HIV infection in the source patient and the type of exposure. In a recent analysis of 51 seroconversions in HCWs, the estimated median interval from exposure to seroconversion was 46 days (mean: 65 days), an estimated 95% seroconverted within 6 months after the exposure [8]. In a retrospective case-control study of HCW, after controlling for other risk factors for HIV transmission, the risk for HIV infection among HCWs who used ZDV as PEP

was reduced by approximately 81% [9].

TABLE 1
Determining the recommendation for PEP

HIV EC	HIV SC	PEP recommendation
1	1	PEP may not be warranted
1	2	Consider basic regimen
2	1	Recommend Basic regimen
2	2	Recommend expanded regimen
3	1 or 2	Recommend expanded regimen
—	Unknown	Consider PEP basic regimen

Considerations for the use of antiretroviral drugs in pregnancy include their potential effect on the pregnant women and on her fetus or neonate. Some of the antiretroviral drugs are known to cross the placenta, but data for humans is not yet available for others (particularly the Protease Inhibitors). In addition, data is limited, on the potential effects of antiretroviral drugs on the developing fetus or neonate [10]. The dose of ZDV for pregnant women is the same as that in nonpregnant persons, and ZDV appears safe and well tolerated in both women and their infants who have had a follow-up period of several years [11]. There is limited data on use of 3TC alone or in combination with ZDV in late gestation in pregnant HIV-infected women. As with ZDV, the pharmacokinetics and dose of 3TC appear to be similar to those for non pregnant persons. The drug appears safe during pregnancy for women and infants, although long-term safety is not known. No data are available regarding pharmacokinetics, safety, or tolerability of any of the Protease Inhibitors in pregnant women. The use of Protease Inhibitors in HIV-infected persons has been associated with hyperglycaemia; it is not known whether the use of these agents during pregnancy will exacerbate the risk of pregnancy associated hyperglycaemia.

Zidovudine has been associated with headache, nausea, fatigue, rash, anaemia, neutropenia, thrombocytopenia, myositis and rarely hepatitis. Lamivudine (3TC) is generally well tolerated and in combination with ZDV has not been associated with any adverse events not seen in those receiving ZDV alone. Indinavir administration has been associated with gastrointestinal intolerance, changes in taste and indirect hyperbilirubinemia, which is usually not clinically significant. One of the most serious adverse effects of indinavir is nephrolithiasis caused by accumulation of the drug in the renal collecting system. Nephrolithiasis has been reported in approximately four percent of patients in clinical trials of indinavir. Patients taking

indinavir should consume 48 ounces of water daily in an attempt to prevent nephrolithiasis and not skip doses. The Nelfinavir (NEL) is available as a suitable protease inhibitor compared to indinavir due to its nephrotoxicity.

h) *PEP* should be started as soon as possible after the exposure (i.e. within a few hours rather than days). If there is a question about which antiretroviral drugs to use, or whether to use two or three drugs, it is probably better to start ZDV and 3TC (lamivudine) immediately than to delay PEP administration. Animal studies have demonstrated the importance of starting PEP within hours after an exposure [12-14].

i) *Follow up* - Patients with occupational exposure to HIV should receive follow-up counselling, postexposure testing and medical evaluation regardless of whether they receive PEP. HIV antibody testing should be performed for at least 6 months postexposure (eg. at 6 weeks, 12 weeks, and 6 months), HIV testing should be performed on any HCW who has an illness that is compatible with an acute retroviral syndrome, regardless of the interval since exposure. HIV antibody testing using EIA should be used to monitor sero-conversion. The routine use of direct virus assays (eg. HIV p24 antigen EIA or polymerase chain reaction for HIV RNA) to detect infection in exposed HCWs generally is not recommended [8]. Use sexual abstinence or condoms to prevent sexual transmission during the first 6-12 weeks after the exposure when most HIV infected persons are expected to seroconvert.

j) *Counselling and Education* - Although HIV infection following an occupational exposure occurs infrequently, the emotional impact of the exposure often is substantial. A 4 week regimen of PEP is recommended and they are asked to commit to behavioral measures (i.e. sexual abstinence or condom use, to avoid pregnancy; and refrain from donating blood, plasma, organs, tissue, or semen) to prevent secondary transmission, all of which influence their lives for several weeks to months [15,16].

Thus to summarize, although much attention and energy has been focused on PEP, it should be recognized that this is really only one component of exposure management. Prevention of exposures should remain the major focus. Recommendations for PEP are a basic 4 week regimen of two drugs (zidovudine and lamivudine) for most HIV exposures and an expanded regimen that includes addition of a protease inhibitor, indinavir 800 mg every 8 hourly on empty stomach and increased fluid consumption or nelfinavir 750 mg

three times a day with meals for HIV exposures that pose an increased risk for transmission or where resistance to one or more of the antiretroviral agents recommended for PEP is known or suspected. At the end, we recommend that all cases requiring postexposure prophylaxis should be reported and monitored regularly by the central HIV registry maintained at Department of PSM, Armed Forces Medical College Pune, India.

References

1. CDC. Reported cases of AIDS and HIV Infection in Health Care Workers. Divisions of HIV/AIDS. Prevention Centres for Disease Control and Prevention. May 13, 1999
2. Marcus R, Culver D, Bell DM et al. Risks of human immunodeficiency virus infection among emergency department workers. *Am J Med* 1993;94:363-70.
3. Bell DM. Occupational risk of human immunodeficiency virus infection in healthcare workers an overview. *Am J Med* 1997;102:9-15.
4. Ippolito G, Puro V, De Carli G. The Italian study Group on Occupational Risk of HIV Infection. The risk of occupational human immunodeficiency virus infection in health care workers. *Arch intern Med* 1993;153:1451-8.
5. CDC. Recommendations for prevention of HIV transmission in health-care settings. *MMWR* 1987;36(suppl no.2S).
6. Update: universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus, and other bloodborne pathogens in health-care settings. *MMWR* 1988;37:377-82 & 387-8.
7. Public Health Service Guidelines for the Management of Health-Care Worker Exposures to HIV and Recommendations for Postexposure Prophylaxis May 15, 1998/47(RR-7);1-28.
8. Busch MP, Satten GA. Time course of viremia and antibody seroconversion following human immunodeficiency virus exposure. *Am J Med* 1997;102:117-24.
9. Cardo DM, Culver DH, Ciesielski CA, et al. A case-control study of HIV seroconversion in health care workers after percutaneous exposure. *N Engl J Med* 1997;337:1485-90.
10. CDC. Public Health Service task force recommendations for the use of antiretroviral drugs in pregnant women infected with HIV-1 for maternal health and for reducing perinatal HIV-1, transmission in the United States. *MMWR* 1998;47(no. RR-2).
11. CDC. Birth outcomes following zidovudine therapy in pregnant women. *MMWR* 1994;43:409, 415-6.
12. Martin LN, Murphey-Corb M, Soike KF, Davison-Fairburn B, Baskin GB. Effects of initiation of 3'-azido, 3'-deoxythymidine (zidovudine) treatment at different times after infection of rhesus monkeys with simian immunodeficiency virus. *J Infect Dis* 1993;168:825-35.
13. McClure HM, Anderson DC, Ansari AA, Fultz PN, Klumpp SA, Schinazi RF. Non human primate models for evaluation of AIDS therapy. In: *AIDS: anti-HIV agents, therapies and vaccines*. Ann N Y Acad Sci 1990;100:616:287-98.
14. Bottiger D, Johansson N-G, Samuelsson B, et al. Prevention of simian immunodeficiency virus, SIVsm, or HIV-2 infection in cynomolgus monkeys by pre-and postexposure administration of BEA-005. *AIDS* 1997;11:157-62.
15. Gerberding JL, Henderson DK. Management of occupational exposures to bloodborne pathogens: hepatitis B virus, hepatitis C virus, and human immunodeficiency virus. *Clin Infect Dis* 1992;14:1179-85.
16. Armstrong K, Gorden R, Santorella G. Occupational exposure of health care workers (HCWs) to human immunodeficiency virus (HIV): stress reactions and counselling interventions. *Social Work in Health Care* 1995; 21:61-80.