Cut and Puncture Accidents Involving Health Care Workers Exposed to Biological Materials

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The first report of occupational acquisition of HIV appeared in 1984, and, by June, 1997, the Centers for Disease Control and Prevention (CDC) had reported 52 documented cases of sero-conversion following occupational exposure to HIV-1 by health care workers of those cases. 47 (90.3%) were exposed to blood. The most frequent type of accident reported was percutaneous needlestick injury. Prospective studies have estimated that the risk of HIV transmission following percutaneous exposure to infected blood is 0.3% (Confidence Interval 95% = 0.2% to 0.5%). Following a mucous membrane exposure, the risk is 0.09% (CI 95% = 0.006% to 0.5%). The risk of hepatitis B acquisition ranges from 6% to 30%, and hepatitis C acquisition, 3% to 10%. Since 1992, the São Paulo Hospital's Hospital Infection Prevention and Control Service (SPCIH) has notified and treated all workers exposed to accidents involving biological materials. In the last six years, we have handled approximately 1,300 cases of reported accidents, of which 90% were percutaneous, most involving needlesticks. Such cases were frequently caused by the inadequate disposal and recapping of needles. In these accidents, 20% of the source patients were HIV positive, 10% were hepatitis C positive, and 7.6% were hepatitis B positive. This review summarizes the guidelines for a standardized response when dealing with accidents involving health care workers. Transmission of hepatitis B and HIV can be reduced if adequate preventive measures are taken in advance. If proper prophylaxis is not being done, it should be initiated immediately.

Key Words: HIV chemoprophylaxis, occupational injuries, needlestick injuries, health care workers, injuri prevention.

Measures taken to prevent occupational exposure to HIV and hepatitis B and C, such as the use of individual protective equipment, proper disposal of needles without recapping, and continuous education for health care workers, are still the most effective and safe methods for preventing the hospital acquisition of these diseases.

Health care workers (HCW) are defined here as medical students, laboratory technicians, nurses, doctors, housekeepers and all others whose activities involve contact with patients, blood, or other body fluids [1,2].

Received on 5 May 2000; revised 4 October 2001.

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The Brazilian Journal of Infectious Diseases 2001;5(5):235-242

1413-8670

Exposure to a body fluid is characterized by a percutaneous injury caused by a contaminated needle or other sharp object, contact with mucous membranes or non-intact skin, or contact with intact skin when involving extensive areas for a long period of time [1,2]. Blood, any organic fluid containing visible blood, vaginal secretions, and semen are biological materials involved in HIV transmission [1, 2]. Organic fluids such as amniotic, peritoneal, synovial, and pericardial fluids are considered of unknown risk for HIV transmission, unlike sweat, tears, feces, urine, and saliva, which do not present a risk [3] and for which cases chemoprophylaxis and serum monitoring are not recommended [4, 5].

The first occupational acquisition of HIV was reported in 1984, and by June, 1997, the CDC had reported 52 documented cases of sero-conversion following occupational exposure to HIV; one by a

HCW. Of those, 47 cases (90.3%) were exposed to blood. The most frequent type of accident involved percutaneous needlestick injuries.

Prospective studies have estimated that the risk of HIV transmission following a percutaneous exposure to infected blood is 0.3% (CI 95% = 0.2% to 0.5%). Following a mucous membrane exposure, the risk is 0.09% (CI 95% = 0.006% to 0.5%).

The risk of hepatitis B acquisition ranges from 6% to 30%, and hepatitis C acquisition, 3% to 10%. Transmission of hepatitis B and HIV can be significantly reduced if adequate preventive measures are taken in advance. Therefore, prophylactic measures must be considered a medical emergency.

Given the importance of this problem, since 1992, the São Paulo Hospital's Hospital Infection Prevention and Control Service (SPCIH) has notified and treated all HCWs exposed to accidents involving biological materials. A professional, trained by the SPCIH, is alerted by a pager that operates 24 hours a day, 7 days a week, and gives advice based on the type of accident involved.

In the last six years, we have handled approximately 1,300 reported accident cases, 90% of which were percutaneous, most involving needlestick injuries. Such cases were frequently caused by inadequate disposal and recapping of needles. In these accidents, 20% of the source patients were HIV positive, 10% were hepatitis C positive, and 7.6% hepatitis B positive.

We developed the following guidelines in order to standardize responses when dealing with accidents involving HCW and biological materials at São Paulo Hospital.

Guidelines

Guidelines to follow when an accident involving biological materials occurs

The hospital's HCW have been informed about the SPCIH and its goal to prevent accidents involving biological materials. Educational lectures are given and posters are displayed in each sector considered to be at risk, including the number of the SPCIH's pager. That way, HCW involved in accidents know about the service and the need to contact the SPCIH immediately.

Initial guidelines for managing HCW exposure are listed in Table 1.

Guidelines when the source patient is HIV positive

Chemoprophylactic measures must be studied on a case-by-case basis according to the type of exposure, the body fluid involved, and the immunological status of the source patient. The most recent guidelines issued by the Centers for Disease Control and Prevention (CDC), in 1998, do not distinguish between considering and recommending a basic regimen. In our experience, this confuses the exposed HCW who seeks clear and objective information, and contributes to the practical difficulty of dividing cases into high and low risk categories.

In order to provide better care for HCWs without endangering their health, we believe that they should receive an anti-retroviral regimen only when they are at high risk, and, when this regimen is deemed appropriate, it should always be prescribed in conjunction with a protease inhibitor (PI). High risk situations include cases involving large amounts of blood characterized by deep wounds caused by puncturing/cutting objects, the presence of visible blood on the penetrating object, accidents involving needles used in the veins or arteries of the source patient, and accidents involving large-bore needles and those in which there is greater viral inoculation involving a source patient with advanced stages of AIDS or acute HIV infection (extremely high viremias) (see Table 2). Alternative regimens should be evaluated individually by specialists when there is a possibility of a source patient's involvement with multi-resistant viruses.

HCWs who are pregnant, or believed to be pregnant, must be informed that, to date, the only safe option for the fetus is zidovudine (AZT), although other anti-retrovirals may be recommended depending on the severity of exposure.

Table 1. Initial guidelines for managing health care worker exposures

Treat exposure site: Immediately after an accident involving percutaneous or cutaneous exposure, wash the site with running water and antiseptic solutions such as PVPI, 2% chlorhexidine or 70% alcohol. There is no evidence that expressing fluid by squeezing the wound reduces the risk of HIV transmission (CDC 1998). Following exposure to mucous membranes, rinse thoroughly with water or physiologic solution. Never use irritating solutions such as ether, hypochlorite, or glutharaldehyde, as they can increase the exposed area.
Inform: The Head of the service will inform the Personnel Department so that it can produce a Work Accident Bulletin that will be sent to the occupational health doctor for legal purposes.
Collect: Blood samples must be collected from the source patient with his/her permission to conduct serological tests for HIV, hepatitis B and C. The use of rapid tests to detect anti-HIV antibodies permits us to determine the immunological status of the source patient in up to 30 minutes, thereby avoiding the initiation or maintenance of anti-retrovirals. This test must not be considered definitive. Confidentiality must be assured.
Collect: Blood samples must be collected from the exposed HCW and serological tests conducted for HIV, hepatitis B and C immediately after the accident.
Inform: The exposed HCW must be informed about the risk of acquiring these diseases and the importance of follow-up by the team until the final results of serological tests are obtained. The HCW should be advised to use condoms, avoid getting pregnant and not to donate blood during the follow-up period.

When appropriate, chemoprophylaxis should be started as quickly as possible, ideally within 1 to 2 hours after the accident. Animal studies suggest that chemoprophylaxis is not effective when started 24 to 36 hours after an accident. Starting medication after longer intervals (1 to 2 weeks) should be considered only when exposure involves a high risk of HIV transmission. Chemoprophylaxis lasts for 4 weeks. Adverse effects and drug interactions may occur during prophylaxis (see Table 3).

Serological anti-HIV monitoring (ELISA) must be carried out at the time of the accident and repeated after 6 weeks, and 12 weeks, and at least 6 months. A HCW who tests anti-HIV reactive at the time of the accident should be informed that this result was not caused by the accident and be referred for specific medical care.

Post-exposure follow-up for HCW must be conducted for 6 months after an accident involving materials contaminated with HIV, and in case of accidents involving unknown source patients. The HCW must be closely monitored for the first month following the accident, as 80% of cases of sero-conversion in HCW occur during this period through mononucleosis-like syndrome.

Before and during chemoprophylaxis, laboratory tests such as a full hemogram, transaminases, urea, and creatinine must be conducted to evaluate adverse effects. Side effects resulting from the use of anti-

Table 2. Recommended chemoprophylaxis following occupational exposure to HIV, per type of exposure and source of material

Type of exposure	Source	Prophylaxis	Regimen
Percutaneous	Blood	Recommended	ZCV + 3TC + PI (2)
	Fluid containing visible blood, infectious fluids (1) or tissue)	Recommended	ZCV + 3TC + PI
	Other fluids	Not recommended	
Mucous membrane (3)	Blood	Recommended	ZCV + 3TC + PI
	Fluid containing blood	Recommended	ZCV + 3TC + PI
	Other fluids	Not recommended	
Open Skin	Blood	Recommended	ZCV + 3TC + PI
	Fluid containing visible blood, infectious fluids (1) or tissue)	Recommended	ZCV + 3TC + PI
	Other fluids	Not recommended	

Source: Centers for Disease Control, 1998 [1].

Notes:

(1) Infectious fluids: vaginal secretions, cerebrospinal, synovial, pleural, peritoneal, pericardial or amniotic fluid.

(2) ZDV – Zidovudine (200 mg 3 times daily), 3TC – Lamivudine (150 mg 2 times daily), PI – Protease inhibitor (Indinavir 800 mg 3 times daily).

(3) These recommendations are applicable to large exposures to blood and fluids containing blood

The original standards issued by the Centers for Disease Control (1996) distinguish between recommending and offering. In our experience, these terms confuse exposed HCW seeking objective guidelines on what to do. Similarly, it is often difficult to rank accidents as low- or high-risk (from the conceptual standpoint). Therefore, we believe that infection risk situations and anti-retroviral therapy should be recommended using two reverse transcriptase inhibitors and a protease inhibitor. We also advise HCW about factors associated with a high risk of infection and the side effects of anti-retroviral drugs. Other variables, such as possible resistance of HIV to the prophylactic regimen (if the source is already using anti-retrovirals), should be studied on a case-by-case basis.

retroviral drugs frequently occur, but they are usually slight and transient. The HCW must be advised to adhere to the dosages, intervals of use, and duration of treatment. Drug therapy may not have to be interrupted if symptomatic medications, such as anti-emetic and gastric protector drugs, are included in the regimen.

Discussion of guidelines for dealing with HIV positive exposure

Factors that may increase the risk of sero-conversion include delayed initiation of chemoprophylaxis, high viral load of source patient, terminally ill source patient, the degree of inoculation, the type of body fluid involved, the extent of the injury, use of large-bore hollow needles, and factors inherent to the host.

Cardo, et al., carried out a retrospective case study to evaluate risk factors following percutaneous exposure to HIV-infected blood in HCW. They observed that when the object that caused the accident was visibly contaminated with blood, and/or had been used in a vascular procedure and associated with a deep cut, blood from a terminally ill source patient or a source with

Table 3. Drugs used in chemoprophylaxis and their adverse effects

Drug	Adverse Effects
Zidovudine (AZT) 100 mg capsules Dose: 300 mg 2 x day or 200 mg 3 x day	Anemia, neutropenia, leukopenia, low platelet count, nausea, vomiting, asthenia, malaise, headache, myopathy, insomnia, nail and mucous pigmentation, change in liver-function tests, hepatitis.
Ivudine (3TC) 150 mg tablet Dose: 150 mg 2 x day	Pancreatitis, diarrhea, abdominal pain, anemia, neutropenia.
Indinavir (IDV) 400 mg capsule Dose: 800 mg every 8 hours on empty stomach or low-fat diet (Drink 1.5 or more liters of liquids daily to prevent kidney stones)	Kidney stones (nephrolithiasis), hematuria, headache, insomnia, nausea, vomiting, asthenia, fatigue, palate disturbances, dry skin and mouth, abdominal pain, thrombocytopenia, indirect asymptomatic hyperbilirubinemia, increased triglycerides, increased cholesterol, hyperglycemia, diabetes.
Nelfinavir (NFV) 250 mg tablet Dose: 750 mg 3 x day, with food	Diarrhea (most common effect), skin eruptions, flatulence, nausea, muscular pain, weakness, increased triglycerides, increased cholesterol, hyperglycemia, diabetes.

Source: Centers for Disease Control, 1998 [1].

a high viral load, the risk of HIV-1 acquisition could surpass 0.3%. The use of AZT in this study appeared to be effective [8].

There is some evidence that the host's defense mechanisms can influence the risk of HIV transmission. A study demonstrated that HCW exposed to, but not infected by, HIV-1 showed an immune response mediated by HIV-1-specific cytotoxic T-lymphocytes which could be either a protective mechanism or simply a marker of exposure [9].

In an attempt to prevent sero-conversion after occupational exposure, in 1990, the CDC standardized the use of zidovudine (AZT) as chemoprophylaxis following exposure [10]. No data were published regarding the effectiveness of this measure until 1995, when a report documented the decreased risk of HIV-1 sero-conversion in HCW who used AZT in a prospective case study undertaken in France, the United Kingdom, and the United States of America [11]. Another retrospective case study found that the risk of acquiring HIV among HCW who used AZT was reduced by approximately 81% (CI 95% = 43% to 94%) [8].

Published data are still lacking on human studies to provide evidence that other anti-retrovirals associated with AZT are more effective than monotherapy as post-exposure prophylaxis. However, in theory, a combination of drugs that increases the anti-retroviral effect and works at different stages of the HIV-1 virus's replicative cycle should provide greater protection for exposed HCW [3,9].

Table 4. Recommended hepatitis B prophylaxis for health care workers

HCW's Status	HbsAg-Positive Source	HbsAg-Negative Source	Unknown Source
Incomplete vaccination	1 dose of hepatitis B immunoglobulin and vaccination	Complete vaccination	Complete vaccination
Complete vaccination	Known response with anti-HBs over 10U/ml – Intervention unnecessary	Intervention unnecessary	Intervention unnecessary
	Anti-HBs under 10U/ml – 1 dose of hepatitis B immunoglobulin and resume vaccination	Intervention unnecessary	If source shows high risk of positivity, handle as if HbsAg positive

Source: Centers for Disease Control, 1998 [1,2].

Based on these reasons, lamivudine (3TC) came to be recommended with a goal of covering AZT-resistant strains or delaying their emergence without considerably increasing toxicity. Similarly, a third drug – a protease inhibitor (PI) – should be associated with the regimen in cases of high-risk exposure. Indinavir was initially suggested, and more recently, nelfinavir. An animal study using rhesus monkeys demonstrated that, 24 hours after an intravaginal inoculation of HIV-1, infected cells were found near the inoculation site. Regional lymph nodes were infected 24 to 48 hours later, and, after 5 days, the virus was detected in peripheral blood [12]. Therefore, in theory, early initiation of chemo-prophylaxis could prevent systemic dissemination.

Estimates suggest that 10 billion HIV-1 virions are produced daily in patients with established infection [13], resulting in frequent genetic mutations including the mutations responsible for resistance to HIV-1. Genotypic HIV-1 resistance can be primary, which occurs in treatment-naïve patients, or secondary, as a result of the selective pressure of anti-retrovirals in treated patients.

The failure of AZT as a chemo-prophylactic following occupational exposure by HCW has been reported in at least 11 cases between 1990 and 1997. Ten cases involved percutaneous injury accidents, where AZT was started 30 minutes to 8 days after exposure, and taken for 8 to 54 days. Acute retroviral disease occurred 13 to 75 days after exposure in 10 cases. A possible explanation proposed by the authors is the possibility of the transmission of strains with diminished sensitivity to AZT. Other factors that may have contributed to this failure include inoculation involving extensive exposure, delayed initiation of chemoprophylaxis or short duration of therapy, and factors pertaining to the host [14].

Transmission of zidovudine-resistant HIV-1 mutants through sexual relations was first described in 1992 [15]. The effectiveness of the regimen proposed by the CDC (AZT + 3TC or AZT + 3TC + Indinavir or Nelfinavir) for chemoprophylaxis following occupational exposure to HIV is uncertain, as there is a possibility that the source is resistant to these anti-retroviral regimens. At present, in occupational accidents, there is a growing risk of dealing with source patients who have had extensive prior exposure to anti-retrovirals and successive failures of such treatment plans. The mapping of the anti-retroviral sensitivity profile of these patients is essential for determining guidelines for the rational use of chemoprophylaxis following exposure.

What to do when the source patient is HBV positive

Occupational infection with HBV poses a serious threat for HCW. Before the advent of an HBV vaccine, nearly 10% to 25% of HCW showed evidence of HBV infection (compared with just 6% of blood donors). The risk of acquisition following occupational exposure depends on the nature and frequency of exposure to blood or fluids containing blood. The risk of infection would be at least 30% following a percutaneous injury involving blood from an *e* antigen-positive patient [16]. The vaccination of HCW during training and before exposure could increase the vaccination rates for HCW in training, which is the period when the risk of exposure is highest due to the learning process.

The serological tracing of professionals susceptible to HBV infection before vaccination is not advisable unless the institution considers such a procedure to be cost-effective. It is recommended that anti-HB antibodies be studied following vaccination in order to determine whether there is a post-vaccination response. For HCW who do not respond to the vaccine or fail to carry out the full regimen, we recommend repeating the vaccination regimen in three doses.

The antibodies induced by vaccination are gradually reduced over time, and nearly 60% of those who initially responded to vaccination will not show detectable anti-HBs for about 8 years [17]. Nevertheless, periodic booster shots are not recommended since the people who responded to the initial series are still protected against clinical hepatitis and chronic infection, even when anti-HBs levels are undetectable [18].

In case of accidents involving HBV-positive patients, the initial guidelines for HCW are the same as those shown in Table 1. The regimen of vaccination and/or use of immunoglobulins is appropriate depending on the HCW's vaccination status (see Table 4). It is important to note that hepatitis B immune globulin (HBIG), when indicated, should preferably be given within the first 24 hours or up to 72 hours after the accident. The effectiveness of HBIG following the first seven days after the accident is unknown [19].

The incubation period for HBV is 45 to 180 days (average 60 to 90 days). Therefore, after prophylaxis, we recommend monitoring with biochemical tests (liver enzymes) and serology for HBV 60 and 180 days after the accident.

What to do when the source is HCV positive

HCW also face a high risk of hepatitis C infection. Studies of seroprevalence among HCW show anti-HCV antibody positivity of 1% to 2%. Follow-up studies of HCW exposed to percutaneous injuries involving blood or fluid containing blood from an HCV-positive source showed that the sero-conversion rate is approximately 1.8% (ranging from 0 to 7%). In a study using polymerase chain reaction (PCR) methods, the HCV transmission rate was 10% [20].

In case of accidents involving an HCV-positive source, the HCW will be informed of the risks because we still lack vaccines for this virus and the use of immunoglobulins in such cases does not appear to be effective. An experimental study involving chimpanzees demonstrated that the administration of immunoglobulin one hour after exposure did not prevent infection or disease [21].

Initial procedures undertaken for exposed HCW are the same as those described in Table 1. The incubation period is 6 to 7 weeks. Therefore, monitoring should be conducted using biochemical tests (liver enzymes) and serological tests for HCV carried out 60 and 180 days after exposure. The use of antiviral agents (e.g. interferon) is not recommended as post-exposure prophylaxis [22].

Other serologies may be requested according to the epidemiological status of the source, including serology for Chagas's disease and HTLV 1. Cases where the source cannot be identified will be evaluated individually according to the degree of risk [1, 2].

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