Use of HIV Postexposure Prophylaxis in Healthcare Workers after Occupational Exposure: A Thai University Hospital Setting

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Background: *PostExposure Prophylaxis (PEP) is widely used after exposures to Human Immunodeficiency Virus (HIV) to reduce the risk of infection in the healthcare setting. Few data are available on the safety and tolerability of Anti Retro Viral drugs (ARV) among Health Care Workers (HCWs) who are prescribed prophylaxis.*
Objective: *To collect information about the safety and compliance of taking ARV for HIV PEP among HCWs.*
Material and Method: *Retrospective review on registry data regarding occupational HIV exposures, the PEP regimens used, and the adverse events associated with PEP was performed.*
Results: *During a five year-period, 820 episodes with occupational blood or body fluid exposures were reported. Nurses (27%) were the largest group at risk. The most common type of exposure was percutaneous injuries (82%). Only 125 (15%) HCWs had occupational exposures to HIV, 64 HCWs were prescribed HIV PEP and 32 (50%) HCWs did not complete the PEP regimen as initially prescribed. The commonly prescribed ARV was zidovudine (38%), lamivudine (33%), and indinavir (11%). Overall, 18 (28%) HCWs reported symptoms while on PEP, such as nausea (89%), vomiting (55%), and dizziness (39%). None of the HCWs had HIV seroconversion.*
Conclusions: *Adverse effects from HIV PEP were very common. Clinicians prescribing HIV PEP need to discuss with HCWs about PEP efficacy and side effects. Education efforts aimed at occupational exposure prevention are still important issues.*

Keywords: *HIV, Postexposure prophylaxis, Health care worker, Antiretroviral drug, Adverse event*

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Health Care Workers (HCWs) are at risk for acquiring Human Immunodeficiency Virus (HIV) following an occupational exposure to HIV-contaminated blood. Although universal infection control precautions, safer use of needles, and other innovations may substantially reduce the incidence of occupational exposures, this risk cannot be eliminated completely[1]. The average risk of acquiring HIV infection after percutaneous and mucous membrane exposure to HIV-infected blood had been estimated as 0.3% and 0.09%, respectively[2,3]. Antiretroviral Post Exposure Prophylaxis (PEP) is widely used after exposures to HIV to reduce the risk of infection in the healthcare setting[4]. Despite current practice, few data are available on the safety and tolerability of Anti Retro Viral drugs (ARV) among HCWs who are prescribed prophylaxis.

Ramathibodi Hospital (an 800 bed-teaching hospital, Bangkok, Thailand) has adopted a policy to

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ensure HCWs against work-related HIV infection since 1991. The house staff have a responsibility to develop and implement protocols for managing HCWs who are occupationally exposed. The authors aimed to analyze safety and compliance of taking ARV for HIV PEP in the hospital setting.

Material and Method

All HCWs were required to report the incidents immediately to their works supervisors who could then act as witnesses to the accident having occurred. They were then required to consult an infectious disease expert or a chief medical resident on duty as soon as possible to determine the need for antiretroviral prophylaxis. If in doubt, the physicians who evaluated the HCW and exposure initially were authorized to prescribe HIV PEP for a few days before a full evaluation was performed by an infectious diseases specialist.

The information obtained at baseline included age and gender of HCWs, exposure information, HIV source-patient information, and HIV PEP regimen initiated. HIV serological status of HCWs and source patients were determined by gel particle agglutination and ELISA test within a few hours of exposure. HIV serology of HCWs was repeated at six weeks, three, and six months after exposure in order to establish that the HIV infection was caused by occupational exposure. The follow-up HIV status was obtained from the follow-up incident report form as completely as possible. Routine laboratory monitoring was left to the discretion of the healthcare provider. All the results including the incidence report forms were confidentially reported to infection control staff.

The authors reviewed the registry data on characteristics of occupational HIV exposures, the PEP regimens used, and the side effects associated with PEP. The study had been approved by the institutional review board committee.

Results

From January 1998 through December 2003, a total of 820 episodes of 816 HCWs were registered after a recent exposure event that carried a risk for HIV transmission. Nurses (27%) were the largest group of HCWs at risk, followed by medical students (21%), and nurse aids (17%). The rest of the HCWs were physicians (10%), housekeepers (8%), laboratory technicians (7%), nurse and nurse aids students (6%), and others (4%). None of HCWs were pregnant women. For all exposures, the source-patient was known in 642 (78%) of the episodes. Of the known source-patients, One-hundred-and-twenty-five (15%) patients were known to be HIV-positive at the time of exposure. The exposures were percutaneous, 676 (82%), mucous membrane 103 (13%), and skin exposures 41 (5%). Of the percutaneous exposure, 474 (70%) involved hollow-bore needle and the remainder involved suture needles, razor, knife, and other sharp instruments.

Of the exposed patients, 64 HCWs were prescribed HIV PEP. The majority (70%) of HIV PEP regimens consisted of two drugs (Fig. 1). The initial prescribed ARV were zidovudine (38%), lamivudine (33%), indinavir (11%), didanosine (10%), nevirapine (1%), ritonavir (1%), and nelfinavir (1%). The most common ARV combinations were zidovudine plus lamivudine together with or without indinavir. Of these, 32 (50%) completed all of the drugs in regimens as initially prescribed. Antiretroviral regimen was changed in four (6%) HCWs because of adverse drug events.

Of the 32 HCWs who discontinued all ARV earlier than the intended duration of prophylaxis, 13 (36%) did so because the source-patient turned out to be HIV-negative and 12 (33%) had adverse effects attributed to ARV. The rest of the reasons were physicians' decision (22%), patients' decision (6%), and infectious diseases staff re-evaluation (3%). Overall, 18 (28%) HCWs reported some symptoms while on ARV. The most frequent adverse effects were nausea (89%), vomiting (55%), and dizziness (39%) (Table 1). Two HCWs were reported to have serious adverse effects and were hypersensitivity to nevirapine and haematuria and frank pain from indinavir. None of the

Table 1. Adverse events on human immunodeficiency virus postexposure prophylaxis: symptoms reported in 18 health care workers

Adverse events	Number of HCWs* (%)
Nausea	16 (89)
Vomiting	10 (55)
Dizziness	7 (39)
Fatigue	6 (33)
Diarrhea	3 (16)
Rash	1 (5)
Hepatitis	1 (5)
Haematuria	1 (5)
Abdominal pain	1 (5)
Headache	1 (5)
Anorexia	1 (5)
Flu-like symptoms	1 (5)

* HCWs may have experienced more than one event

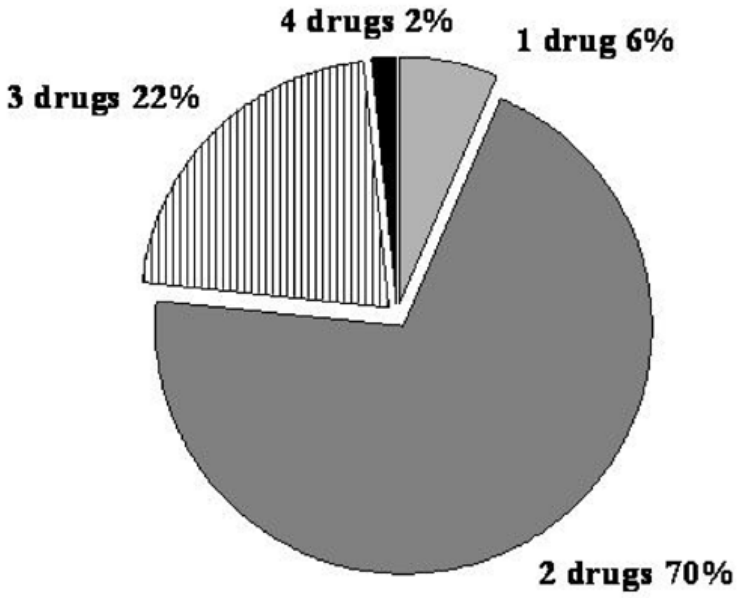

Fig. 1 HIV postexposure prophylaxis regimens in 64 health care workers

HCWs was reported to have HIV seroconversion during the period of study.

Discussion

HIV transmission in the healthcare workplace has prompted a more general awareness of the occupational hazards posed by all blood borne pathogens. Needle-stick, percutaneous, and mucous membrane exposures are frequent[5]. Underreporting is common.

The information that suggested the likely benefit of HIV PEP was obtained from three types of studies: animal models of retroviral infection[6], prevention of maternal-fetal transmission of HIV in humans[7], and a case-control study showing reduction of occupational HIV infection by using zidovudine[4]. These studies led to recommendations for ARV as PEP in various situations. Guidelines for the management of occupational exposure to HIV are now widely adopted[1,5,16]. Initiation of HIV PEP and the regimen is needed to be thoroughly assessed by physicians. These assessments should take into account the nature of the exposure, the likelihood of HIV infection in the source patient and, in cases of known infection, the level of HIV RNA, and possibility of drug resistance[8]. Currently, no data directly support expanded regimen apart from sole zidovudine to enhance the effective of the PEP regimens. However, combination regimens have proved superior to mono- or dual-therapy regimens in reducing HIV RNA in HIV-infected patients[9].

The toxicity profile of antiretroviral agents is a relevant consideration. All antiretroviral agents were associated with adverse effects, especially gastrointestinal symptoms[1]. Adverse effects of ARV have been reported for patients with HIV infection but may not reflect the experience of uninfected patients. Several authorities have expressed concern about the potential for serious toxicity associated with administering PEP to HCWs[10]. The presented data suggested that, although toxicity from antiretroviral PEP was frequently reported, it was rarely severe or serious. The most common adverse effect is gastrointestinal irritation.

Because PEP treatment duration influenced the success of chemoprophylaxis in an animal model[11], an important goal of PEP is to encourage and facilitate compliance with a four-week PEP regimen. Adverse effects of ARV were frequent reasons for the discontinuation or modification of therapy[12] thus compromising the treatment efficacy. Depending on the study, in 20% to 45% of these patients, the adverse effects were severe enough to cause discontinuation of PEP[13-15]. Data from the National Surveillance System for Health Care Workers and the HIV Postexposure Prophylaxis Registry showed that nearly 50% of HCWs reported adverse effects while taking antiretroviral PEP, and about one-third stopped taking the drugs as a result[16,17]. PEP regimens that included three drugs were more likely to result in adverse effects and earlier discontinuation

of treatment than are two-drug regimens[17]. The present report showed that overall adverse effects were approximately 30% and one-third of HCWs had to stop taking the drugs.

Severe toxicities are more common when these agents are used for the long term therapy of HIV-infected patients. The instances of severe toxicities associated with nevirapine administration for PEP had been reported. These included hepatotoxicity, skin reaction and rhabdomyolysis[18]. On the basis of these reports, the US Public Health Service now does not recommend using nevirapine for basic or expanded PEP regimens[16,18]. Although nevirapine hypersensitivity usually begins after the first few weeks of therapy[19], a presented case developed this reaction early after drug administration. The pathogenesis of hypersensitivity is still unknown[19].

Administration of protease inhibitors as part of a PEP regimen had been commonly associated with gastrointestinal side effects[12], and a few cases of nephrolithiasis have been reported[13,15]. Indinavir is poorly water-soluble and can crystallize in urine, causing urinary tract obstruction[19]. Drinking less than 1.5 L of water daily and hot weather were possible causes of adverse effects related to indinavir[19]. Gross haematuria and frank pain of the HCW may be caused by ureteric stone.

The presented registry data also reflected that PEP was rapidly initiated for high-risk exposures when the source-patient HIV status was unknown. When the source-patient HIV serology was found to be negative, the PEP regimen was discontinued in nearly one-third of the cases.

There were a number of limitations of the present study. First, this was a retrospective study, therefore there is missing data. Second, the authors did not prospectively collect laboratory monitoring, such as complete blood count and liver function test, at the second and fourth week of PEP period according to the recommendation[1,16]. Third, since there appeared to be a greater tendency to report adverse effects when HCWs had any symptoms, data may actually reflect underreporting of drugs toxicities.

In conclusion, despite current practice, little is known regarding prescribing practices following accidental exposure to HIV. Appropriate counseling for the exposed worker is crucial, and the risk of infection should be weighed against the potential toxicity of antiretroviral agents. Finally, education efforts aimed at occupational exposure prevention are still important issues.

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การให้ยาป้องกันการติดเชื้อ HIV ในบุคลากรทางการแพทย์หลังได้รับอุบัติเหตุในขณะปฏิบัติงาน: ในโรงพยาบาลโรงเรียนแพทย์ในประเทศไทย

ศศิโสภิณ เกียรติบูรณกุล, บรรจง วรรณยิ่ง, ศิริรัตน์ ตันสุทธากูล, ปราณี เคหะจินดาวัฒน์, ศิริลักษณ์ อภิวาณิชย์, สมพร สมสกุล, กำธร มาลาธรรม

***ที่มา**: เนื่องจากมีการใช้ยาต้านเอชไอวีอย่างแพร่หลาย เพื่อลดการติดเชื้อเอชไอวีในบุคลากรทางการแพทย์ที่ได้รับอุบัติเหตุขณะปฏิบัติงาน แต่ยังมีข้อมูลไม่มากเกี่ยวกับผลข้างเคียงของยา ความปลอดภัย และความสามารถในการทนยา ของบุคลากรทางการแพทย์ที่ได้รับประทานยาต้านไวรัสในกรณีดังกล่าว*

***วัตถุประสงค์**: เพื่อให้ทราบข้อมูลเกี่ยวกับลักษณะของอุบัติเหตุขณะปฏิบัติงาน ผลข้างเคียงของยา ความปลอดภัย และการรับประทานยาในบุคลากรที่รับประทานยาต้านเอชไอวีเนื่องจากการเกิดอุบัติเหตุขณะปฏิบัติงาน*

***วัสดุและวิธีการ**: เป็นการศึกษาเชิงพรรณนา เก็บข้อมูลย้อนหลังจากทะเบียนประวัติ โดยเก็บข้อมูลเกี่ยวกับลักษณะของอุบัติเหตุที่เกิดขึ้น ยาต้านเอชไอวีที่ใช้ และผลข้างเคียงของยา*

***ผลการศึกษา**: ในระยะ 5 ปี มีบุคลากรรายงานอุบัติเหตุที่เกิดขึ้นทั้งหมด 820 ครั้ง กลุ่มที่พบมากที่สุดคือ พยาบาล (ร้อยละ 27) ลักษณะของอุบัติเหตุที่พบบ่อยที่สุดคือ การโดนเข็มตำ (ร้อยละ 82) บุคลากร 125 ราย (ร้อยละ 15) ได้รับอุบัติเหตุขณะปฏิบัติงานที่เกี่ยวข้องกับผู้ติดเชื้อเอชไอวี บุคลากร 64 ราย ได้รับยาต้านเอชไอวี ในจำนวนนี้บุคลากร 32 ราย (ร้อยละ 50) รับประทานยาไม่ครบตามที่แพทย์สั่ง ยาที่มีการใช้มากที่สุดคือ ซิโดวูดีน (ร้อยละ 38) ลามิวูดีน (ร้อยละ 33) และอินดินาเวียร์ (ร้อยละ 11) บุคลากร 18 ราย (ร้อยละ 28) มีผลข้างเคียงของยาคือ คลื่นไส้ (ร้อยละ 89) อาเจียน (ร้อยละ 55) และเวียนศีรษะ (ร้อยละ 39) ไม่มีบุคลากรรายใดมีการติดเชื้อเอชไอวี*

***สรุป**: พบผลข้างเคียงของการให้ยาต้านเอชไอวีสำหรับการป้องกันการติดเชื้อขณะปฏิบัติงานได้บ่อย ดังนั้นแพทย์ควรให้ข้อมูลเกี่ยวกับประสิทธิภาพและผลข้างเคียงของยาก่อนที่จะให้ยา การให้ความรู้แก่บุคลากรเกี่ยวกับการป้องกันอุบัติเหตุขณะปฏิบัติงานยังเป็นสิ่งที่สำคัญ*