AFAO POLICY ON POST EXPOSURE PROPHYLAXIS

AUSTRALIAN FEDERATION
OF AIDS ORGANISATIONS INC.

PO BOX 51
NEWTOWN
NSW 2042 AUSTRALIA

PH +61 2 9557 9399
FAX +61 2 9557 9867

HIV Health Information Line
1800 803 806

Email:
afao@afao.org.au

Internet:
http://www.afao.org.au

1. Definition

Post Exposure Prophylaxis (PEP) is the provision of HIV antiretroviral drugs to persons who have recently been exposed to HIV. The premise underlying PEP is that it may prevent initial cellular infection and subsequent replication of HIV, and thus allow the host immune defences to eliminate the virus.

2. Scientific Evidence

There is substantial scientific evidence that supports the use of PEP. A multi-centre case controlled study of health care workers showed a 79% reduction in the odds of infection for those who received PEP - in this case ZDV (AZT) monotherapy.[1] A clinical trial in the United States showed ZDV monotherapy reduces maternal-foetal transmission from 25% to 8%[2].

Several animal studies have been conducted. Many have shown AZT does not prevent infection, although two have demonstrated PEP efficacy.

One of the conclusions of the PEP studies has been the recommendation that optimally, PEP should be given 2-4 hours after exposure (From one case report and from animal studies)[3]

There are limits to these studies, and there has been scientific debate about the accuracy of the analysis in the first study. Further, the studies are based on AZT monotherapy, which has been long discarded as optimal therapy.

It is likely that combination therapy will increase the efficacy of PEP. Indeed, some commentators and scientists have suggested it may be more economic and just as effective to delay commencement of “treatment” until a positive antigen test is obtained. This hypothesis has not been tested, and AFAO believes it would be unethical to withhold PEP against the wishes of the individual while waiting for HIV antigenaemia to be established.

3. The Issue

The availability of PEP greatly advances the opportunity for individuals to interrupt infection with HIV. Its availability has triggered international debate about appropriate policy responses, and about its potential impact on adherence to safe behaviours.

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[1] (MMWR, 1995; 44:929-33).

[2] Connor EM, Sperling RS, Gelber R Reduction of Maternal-Infant Transmission of Human Immunodeficiency Virus Type 1 with Zidovudine Treatment New England Journal of Medicine 1994; 331:1173-1180

[3] Jeffries DJ Zidovudine After Occupational Exposure to HIV British Medical Journal 1991; 302:1349-1351

Initially the United States Center for Disease Control (CDC) issued guidelines for appropriate use of PEP in non occupational settings[4]. The CDC have now decided that PEP should not be made available to people exposed in non occupational settings except in instances of sexual assault[5]. Meanwhile, communities, scientists, health professionals and researchers in America are still debating the pros and cons of PEP[6].

Australia has not yet finalised its policy response to the issues of PEP availability. The Clinical Trials and Treatments Advisory Committee (CTTAC) is currently in the process of developing PEP policy. Some states have commenced developing guidelines for the administration of PEP. AFAO calls for a coordinated national policy response to the issues.

4. Policy Development

A previous advice for members paper on PEP has been developed by AFAO, exploring the key issues and nominating the problems inherent in PEP availability.

AFAO has consulted widely with its members and others with expertise in the area. The following policy directions are a result of those consultations, and are based on a collaborative multisector approach to the issues.

5. The Current Situation

PEP has been made available in a limited capacity through some major hospitals in some large Australian cities. The cost of PEP has been met by the hospitals. (Guidelines for possible PEP availability are currently being developed by a working group of the NSW Ministerial Advisory Committee on HIV/AIDS.)

PEP is also being made available by some general practitioners with high HIV caseloads. These GPs are using drugs on hand (which have been returned by patients, have been stockpiled for emergencies etc.), or the cost is met by the patient.

Thirdly, it is possible that some people could be obtaining HIV antiretrovirals for PEP purposes from people with HIV. The scenario of a HIV negative partner in a serodiscordant relationship using their partner's HIV antiretrovirals for PEP purposes after a condom breakage is not an unlikely one.

From the consultations conducted by AFAO, it is estimated that there is currently a low (eg 1-2 per month per individual doctor) 'demand' for PEP through the first two avenues. Little is known about the third possible means of access to HIV antiretrovirals for PEP purposes.

6. Key Policy Issues Arising from Consultations

6.1 Availability

Across the board, there is agreement amongst AFAO's constituency that PEP should be available to those individuals that have probably been exposed to HIV. Most people consider that this access to PEP needs to by necessity be restricted to individuals who have been accurately assessed for risk, and are informed and consenting to the drug regimens involved

[4] Centers for Disease Control and Prevention Update: Provisional Public Health Service Recommendations for Chemoprophylaxis After Occupational Exposure to HIV Morbidity and Mortality Weekly Report 1996; 44(22):468-472

[5] AIDS Alert. CDC Won't recommend Non-Occupational PET. February 1998 (17-18)

[6] Dahir M. Hard to Swallow- The morning after morning after morning after pill. Poz Magazine. March 1998

in PEP. However, there is considerable debate about what constitutes an accurate risk assessment, and the most useful information about risk depends on information about the 'source'. This raises many potential ethical and practical problems.

Indeed, in the absence of information about the 'source', and given the current seroprevalence levels in Australia, then it is possible that the costs of PEP may be very difficult to calculate.

6.2 Non occupational versus occupational

Generally, the AFAO constituency believes that it is unethical to make distinction between occupational and non-occupational exposure. AFAO supports the concept of *individuals* placed at risk regardless of the environment in which possible transmission may have occurred. To this end, someone who may be exposed to HIV infected matter in a surgical procedure should have the same access to PEP as a person who experiences a condom breakage with a person who is infected with HIV. AFAO also believes that there should be a non moralistic 'non fault' approach to PEP, allowing equitable access for everybody regardless of the risk episode.

While AFAO recognises that there are legal and ethical reasons why PEP needs to be made available in occupational settings and cases of sexual assault, we see no reason that this should be at the exclusion of people exposed in other settings. While such distinction exists, there will be a continuing perception of discrimination, and that HIV can be guiltily or innocently acquired.

In many instances, systems have been established to optimise access to PEP in occupational settings. AFAO believes these systems could be adapted and expanded for non-occupational exposure.

6.3 Economic Viability

Researchers in the United States have attempted to estimate the cost of PEP should it become widely available. There is a general consensus that the cost of preventing an infection with HIV is reasonable when comparing it with the cost of treatment for a person infected with HIV[7]. Even when PEP treatment consists of three of the more expensive HIV antiretrovirals, the cost is still estimated as acceptable, particularly when compared to other medical technologies.

The move from monotherapy to combination therapy for PEP was considered by another study to be within the bounds of cost effectiveness[8].

Another 'cost' that must be considered is the cost to the individuals engaging in PEP treatments that may cause debilitating side effects. The Centre for Disease Control in America estimates that for a hypothetical group of 10000 who present for PEP, 18 infections will be prevented.[9]. For the other 9988 people, infection either occurred or their was no initial infection to begin with. ie. the 'source' was HIV negative. For these people, 299460 potential days of illness could be caused due to PEP drug side effects. The economic cost of this induced illness is yet to be estimated.

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[7] Li R., Wong J. New England Journal of Medicine 1997 Vol 337/7

[8] Pinkerton S., Holtgrave D., Pinkerton H. Cost Effectiveness of Chemoprophylaxis after Occupational Exposure to HIV Archives of Internal Medicine. 1997 Vol 157/17

[9] Pinkerton S., Holtgrave D., Pinkerton H. Cost Effectiveness of Chemoprophylaxis after Occupational Exposure to HIV Archives of Internal Medicine. 1997 Vol 157/17

AFAO strongly supports accurate risk assessment and appropriate case management to limit the economic cost of PEP as well as the health costs to the individual.

6.4 Official Availability

There are a number of concerns about the current covert means of obtaining PEP for non-occupational exposure. From the consultations, it is believed that PEP is currently being made available for non-occupational exposure to individuals from a variety of sources. Concerns about the covert nature include :

- It is by necessity non-equitable
- Doctors have concerns about the legality of administering PEP
- It makes systems for monitoring PEP impossible
- It makes it less likely that individuals will obtain access to PEP within the optimum timeframe
- It puts pressure on individuals to be dishonest about the nature of their exposure

A more overt system of making PEP available to those in the Australian population who require it is being proposed. There are complex issues associated with PEP being more overtly available, and systems of monitoring and evaluation need to be put in place.

6.5 Equitable Access

PEP should be made available without any hierarchical stratification due to knowledge, position in society, lifestyle, gender, sexuality, ethnicity or any other identifier.

6.6 Risk assessment

The literature researched refers to the following factors that impact on accurate risk assessment in cases of sexual exposure:

6.6.1. Information about the 'source' (may not able to be determined)
HIV-positive?
Viral load (Advanced HIV disease? Primary HIV infection?)
Viral strain (eg tropism for mucosal cells)
Uncircumcised
History of genital ulcers or STDs
Active menstrual flow
Treatment combinations and drug resistance factors

6.6.2. Factors about the activity
Type of activity (receptive anal or vaginal intercourse?)
Vigorousness of activity (cf sexual assault)

6.6.3. Factors about the 'exposed' individual
History of genital ulcers or STDs
Uncircumcised
Immune system features which may enhance or deter infection

6.6.4. In the absence of knowledge about the 'source'
HIV seroprevalence becomes a determining factor

Where a positive ‘source’ can be determined and the activity clearly involves high risk, then there is consensus that PEP is both scientifically and economically justifiable. However. in the absence of knowledge about the ‘source’, there is concern that the potential health benefits of PEP would be less than the negative effects of relatively well people taking a range of toxic drugs over a period of time.

Risk assessment in all likelihood will be undertaken by the clinician who has been approached for PEP. To this end, a training program needs to be developed for those clinicians who may be administering PEP. This training should be developed by skilled health practitioners in collaboration with HIV/AIDS organisations including AFAO, and workers in primary health care settings.

The need to obtain knowledge about the ‘source’ creates many ethical, practical and legal dilemmas, which unless addressed, make it improbable (and probably extremely unlikely) that such information can be obtained. Currently, each state and territory has laws relating to the transmission of HIV. The existence of these laws will be a major obstacle to the willing cooperation of people with HIV or AIDS. In the absence of law reform in this area, PEP management protocols need to guarantee (as far as they are able) absolute confidentiality and freedom from prosecution.

6.7 Case Management

AFAO supports the development of case management protocols for people engaging in PEP. This management extends beyond the four week period that a person takes HIV antiretroviral drugs, allowing for continuing support and follow up. The case manager may not necessarily be the clinician administering the PEP drugs, and may be a social worker, psychologist or outreach worker or other who has a pre-existing relationship with the person engaging in PEP. Ideally though, due to personal crisis associated with initial PEP administration, case management should be commenced by the doctor administering the HIV antiretrovirals for PEP purposes.

Attempts should be made to ensure that the PEP case management protocol developed fits with the lifestyle of the individual requesting it, rather than an expectation that all people will conform to a standard PEP protocol. Those who administer PEP will also need to remain aware of the needs of certain sub populations of people who may require PEP, but will have continuing difficulties with access.

The most difficult aspect of PEP case management will relate to obtaining information about the ‘source’. The problems that have been evident in developing national contact tracing guidelines indicate the complexity and difficulty likely to be associated with obtaining information about ‘sources’. AFAO recommends that an intersectoral national working party be formed to develop appropriate management protocols in relation to obtaining information about ‘sources’. In order to maximise the chances for success in this area, the active involvement of PLWHA organisations must be sought.

6.8 PEP and HIV prevention messages

There has been extensive international debate about the impact of PEP availability on safe behaviour maintenance. There is no consensus on the likely impact of PEP availability.

It is critical that there be a solid inter-relationship between PEP and prevention education messages. Information about PEP needs to be complementary to prevention messages rather than conflicting. Support must be given to community based organisations to develop

their education messages on PEP. AFAO also supports consistency of information about PEP throughout the country.

The impact of the availability of PEP also needs to be closely monitored through the use of appropriate evaluative mechanisms. If possible, PEP education messages should strengthen pre existing HIV prevention education messages.

6.9 Trialing PEP

AFAO supports and will advocate for a PEP trial to be set up, probably in Sydney and Melbourne. This trial must be the result of collaboration between researchers, communities, governments and health practitioners. If possible, the Australian trial should link into the San Fransiscan trial currently underway. The research agenda for the trial needs to be clearly articulated and agreed upon by the major stake-holders.

6.10 Double Combination Versus Triple Combination

Some guidelines developed in the United States differentiate treatment regimes according to estimated risk. While information about the 'source' (particularly any drug resistance information) will affect treatment regimes, AFAO believes that once a decision to administer PEP has been made, therapy should be the most optimal and independent of estimated risk. Further, AFAO believes that it is the individual's choice as to whether they take as their PEP regimen two drugs or three drugs. Health practitioners need to develop skills in assisting people choosing PEP to identify what their PEP needs may be.

6.11 Funding

In order for PEP to be made available, the approved indications for the relevant HIV antiretroviral drugs need to be updated. The relevant pharmaceutical companies should be encouraged to submit applications for revised indications.

Governments, both federal and state/territory have a responsibility for subsidising the funding of post exposure prophylaxis in this country, similar to the ways in which treatment costs are subsidised for HIV positive people. AFAO in no way endorses the subsidisation of PEP over the subsidisation of treatments for people with HIV/AIDS. Where possible, the expenses of PEP should be kept to a minimum through careful risk assessment and appropriate case management.

Implementation

Implementation of systems for PEP administration will be very complex and difficult. Occupational and non occupational exposure to HIV should be addressed by the same systems and given equal weighting.

Some of the challenges will be utilising mechanisms for working with 'sources' that are equitable and respectful of the privacy of PLWHAs, advocating effectively for access to PEP for people who have been exposed to HIV in a non occupational setting, training of all those involved in PEP, developing and operationalising appropriate risk assessment, effective case management, and securing adequate funding for equitable access to PEP.

Recommendations

1. That there be a coordinated national policy response to the issues of PEP availability.

2. That PEP be made available in Australia for those people who have been assessed as being at risk of becoming HIV infected, at no cost to them. In support of this, AFAO recommends that changes to the Therapeutic Goods Administration Act (TGA) and the Pharmaceutical Benefits Scheme (PBS) be made, updating the approved indications and funding criteria for the relevant drugs. The relevant pharmaceutical companies should be encouraged to submit applications for revised indications.

3. That PEP should be made available in an equitable manner, without any hierarchical stratification due to knowledge, position in society, lifestyle, gender, ethnicity, or any other identifier.

4. That current systems that exist for the management of PEP in an occupational setting be adapted and expanded for non-occupational exposure.

5. That appropriate systems for monitoring and evaluating PEP be put in place in the first instance.

6. That a training program be developed for those clinicians who may be administering PEP. This training should be developed by skilled health practitioners in collaboration with HIV/AIDS organisations including AFAO, and workers in primary health care settings.

7. That accurate risk assessment of people presenting for PEP is necessary to ensure that drugs are being administered to people who have been, in all probability, exposed to HIV.

8. That risk assessment be undertaken by the health practitioner approached for PEP, where possible in consultation with people with expertise in the area such as other health workers, social workers, outreach workers etc.

9. That administration of PEP be based on the informed choice of the person presenting for treatment, and not at the discretion of the health practitioner approached.

10. That PEP management protocols guarantee (as far as they are able) absolute confidentiality.

11. That case management protocols for people engaging in PEP be developed. This management extends beyond the four week period that a person takes HIV anti retroviral drugs, allowing for continuing support and follow up.

12. That an intersectoral national working party be formed to develop appropriate management protocols in relation to obtaining information about ‘sources’. The active involvement of PLWHA organisations in this working party should be encouraged.

13. That the central principle to PEP education be a solid and complementary inter-relationship between PEP and prevention education messages. Support must be given to community based organisations to develop their education messages regarding PEP. AFAO also supports consistency of information about PEP throughout the country.

14. That any PEP protocols that invade the privacy of, or impinge in any way on the lives of HIV positive people or people of unknown status are opposed by AFAO.

15. That AFAO supports the continuing role of HIV positive people in PEP protocol and policy development in Australia.

16. That there be a PEP trial in Sydney and Melbourne that is the result of collaboration between researchers, communities affected by HIV, health practitioners and government. Where possible this trial should link into, or be comparative with, the trial currently underway in San Fransisco. The research agenda for the trial needs to be clearly articulated and agreed upon by the major stake-holders.