

A Proposal for a Cost-Effective National HIV/AIDS Clinical Policy

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In the last two years, the world has witnessed the effectiveness of the triple combination of antiretroviral drugs i.e. two nucleoside analogues and protease inhibitor in reducing the morbidity, hospitalization and mortality of AIDS. Treatment with single nucleoside analogue is now obsolete. Even combination of two nucleoside analogues has shown to be suboptimal because suppression of HIV is incomplete. Sooner or later the HIV will develop resistance to both nucleoside analogues and the HIV load will increase further. However, this triple combination of antiretroviral drugs come at a high cost, even the rich country might not be able to afford the enormous expense for her sick people.

Thailand is a developing country with a limited resource. Currently, we have an estimated number of one million persons infected with HIV. HIV/AIDS has created tremendous human suffering in term of quality of life and economy. In the wake of this new advance in antiretroviral drugs and its high cost we have to face this problem with reality and develop our own clinical policy instead of following Western countries (1).

Most of the Thai HIV-infected patients seek medical attention at a later stage of the disease when they are symptomatic from opportunistic infections (O.I.), i.e. tuberculosis (TB), *Pneumocystis carinii* pneumonia (PCP), cryptococcosis, penicilliosis etc. It is humane to treat the opportunistic infections as aggressive as we can, particularly TB because among the O.I., TB is the only communicable disease that will affect the entire non-HIV population. Once patients have been treated for the original O.I. they should receive secondary prophylaxis for that O.I. and primary prophylaxis for the other endemic infectious diseases of Thailand namely TB, PCP, and cryptococcosis but not MAC or CMV indefinitely. By preventing the opportunistic infections, AIDS patients will have a better quality of life and improved survival (2).

Not only TB is a highly endemic disease in Thailand, we also have a high prevalence of INH-resistant organism. All HIV-infected patients in any stage of infection are at a high risk for developing TB. Since HIV-infected patients can develop clinical tuberculosis through exogenous recent infection, reactivation of old TB infection and exogenous reinfection, INH prophylaxis (300 mg/day) should be given to all HIV-infected patients indefinitely rather than 1 year in order to prevent exogenous infection after active TB has been ruled out. There is an on-going study evaluating the effectiveness of INH in preventing tuberculosis in Thailand (personal communication). We are looking forward to the result of this study. So far we do not know whether combination of wide spread use of INH prophylaxis and poor compliance of taking medicine will lead to even more INH-resistant organisms.

Multiple studies convincingly document the benefit of cotrimoxazole in preventing PCP. Cotrimoxazole should be the first-line agent because it is cheap and also effective in preventing nocardia and toxoplasmosis. If AIDS patients are allergic to cotrimoxazole, dapsone 100 mg/day is the alternative.

Besides obvious clinical picture of advanced AIDS, CD4 cell count is helpful to determine who should receive primary prophylaxis. Cotrimoxazole and fluconazole should be started when CD4 cell count falls below 200 and 100/mm³ respectively. The recommended dosage of cotrimoxazole is 1-2 tab/day. Recently, 200 mg of fluconazole 3 times a week has been shown to be effective as a primary prophylaxis for cryptococcosis (3). Since body weight of Thai AIDS patients is much lower than American, we believe even smaller dose should remain effective in preventing cryptococcosis. We propose the randomized controlled trial study conducted in Thailand to determine the lowest effective dosage of fluconazole (for example

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50 mg/day) (4).

Since cotrimoxazole, dapsone and INH are cheap, no health policymaker will quibble over this small part of expenditure in taking care of AIDS patients. They would argue why fungal prophylaxis with oral anti-fungal agent is needed. Fluconazole is expensive. Even in the U.S. fluconazole is not recommended for cryptococcal prophylaxis. We should only look at our own experience. In the last few years we are seeing a staggering number of cryptococcal meningitis patients admitted to hospitals. Emergency room and out-patient department of some public hospitals are crowded with cryptococcal patients waiting to receive intravenous amphotericin B.

Cryptococcosis is an endemic fungal disease in Thailand as in sub-Saharan Africa. The incidence of cryptococcal infection in Thailand is 20-25 percent which is at least 2.5-3 times that of U.S.A. Among the O.I., cryptococcosis is one of the highest-cost complication of AIDS. Cryptococcal-infected patients occupy many hospital beds, consume our limited resource, time and energy. Of all the O.I., cryptococcal meningitis carries the highest mortality despite of therapy. We believe primary prophylaxis against cryptococcosis in Thailand is cost-effective especially if we can use the lowest dosage of fluconazole and its clinical benefit outweighs the risk of emergence of fluconazole-resistant candidiasis.

The question is where the money will come from in this era of cost containment. At the present time there is a budget for a government subsidized double nucleoside analogues to selected HIV/AIDS patients. We advocate the moratorium on free supply of suboptimal regimen. We should learn from the tuberculosis treatment. An ineffective regimen is worse than no treatment at all. It will create multi-drug resistant HIV which is a special health concern to the others.

The funding of double nucleoside analogues should be transferred to primary fungal prophylaxis program. Part of savings from cutting hospitalization cost with fluconazole can be diverted to funding the program for post exposure prophylaxis for HIV with triple combination of antiretroviral drugs to health care workers with needle stick injuries and to those unfortunate Thai citizen who are raped by HIV infected person.

It is obvious that we can not offer viral load measurement and give free supply of triple combination therapy to all HIV/AIDS patients for life. We may select a small group of patients in their earliest stage of infection i.e. primary HIV infection. According to the mathematical model if we give the most potent antiretroviral combination in this

early stage we can eradicate the HIV in a few years. If the hypothesis turns out to be correct, treating primary HIV infection with antiretroviral drugs for a few years will be cost effective. Otherwise we should give the effective combination i.e. two nucleoside analogues and protease inhibitor only to those HIV-infected patients who can afford the high price and commit to take medicine for life.

AZT or other better drugs program for HIV-infected mother to prevent transmission of HIV from mother to baby should be continually supported. Part of the AIDS budget should be reserved for palliative care of terminal AIDS patients. Last but not least prevention through educational program should remain number one policy in combating the HIV disease.

In summary, we propose (A) the Thai government should give free supply of antiretroviral drugs only to these selected group of patients.

A.1 Triple therapy to prevent HIV infection in health care worker from occupational exposure to HIV patients.

A.2 AZT or better regimen to prevent perinatal transmission from HIV-infected mother to baby.

A.3 Triple therapy to treat primary HIV infection.

All other HIV/AIDS patients must pay for the antiretroviral drugs out of their own pockets.

(B) The Thai government should give free supply of the following medicine as primary prophylaxis against PCP, TB and cryptococcosis indefinitely to all HIV/AIDS patients with the above criteria.

B.1 Cotrimoxazole 1-2 tab/day (dapsone 100 mg/day is the alternative agent in case of intolerance to cotrimoxazole).

B.2 INH 300 mg/day (result of study in Thailand is pending).

B.3 Fluconazole (smallest effective dosage to be determined in Thailand).

This recommendation may change when the new inexpensive treatment become available in the future. Until then we believe this is one of the most cost effective clinical policy for Thailand. Our health economist will have to look into this pharmacoeconomic policy and come up with the calculation if this recommendation is to be implemented whether it will save or escalate cost. We welcome a debate and input from all concerned physicians in this form of rationing of our limited health budget.

References

1. Selwyn PA. HIV therapy in the real world. *AIDS* 1996;10:591-93.
2. Clumeck N. Primary prophylaxis against opportunistic infections in patients with AIDS. *N Engl J Med* 1995;332:739-40.
3. Singh N, Barnish MJ, Berman S, et al. Low-dose fluconazole as primary

prophylaxis for cryptococcal infection in AIDS patients with CD4 cell counts of $\leq 100/\text{mm}^3$. Demonstration of efficacy in a prospective, multicenter trial. Clin Infect Dis 1996;23:1282-6.

4. Guidelines on issues of clinical and public health importance. Managing HIV/AIDS with limited resources. J Infect Dis Antimicrob Agents 1997;14:53-54.