

Compendium Report - Guidelines for Diagnosis and Treatment of HIV/AIDS

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Abstract

Since the first antiretroviral drug - zidovudine being created, several other drugs, including nucleoside reverse-transcriptase inhibitors (NRTIs), non-nucleoside reverse-transcriptase inhibitors (NNRTIs), and protease inhibitors (PIs), were developed. More and more antiretroviral drugs were marketed, which makes the therapy for HIV/AIDS more complicated. Besides the drug efficacy, the side effect, drug interaction, and high medical fees should put into consideration. Proper medical therapy for HIV-infected patients has become a specialized knowledge.

No common consensus for HIV/AIDS medical therapy was formed in Taiwan Before. The fees for HIV/AIDS medical therapy was drawn back into public budget since 2005. Taiwan authorities invited clinical experts to compile a "Guidelines for diagnosis and treatment of HIV/AIDS " for references for clinical medical staffs. Recently, many new drugs were developed and the therapy guidelines were also renewed successively. Thus, Taiwan authorities, once again, invited Taiwan AIDS Society and clinical experts to revise this guideline, renew existed chapters, including "Recommendation for antiretroviral therapy for HIV-infected patient in Taiwan", "Guideline for viral load, cell counts of CD4

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lymphocyte and related examinations for adult HIV-infected patients”, “Guidelines for prevention and treatment for opportunistic infections in adult HIV-infected patients”, “Guidelines for prevention and treatment of mother-to-child transmission”, and “Clinical signs, diagnosis and therapy of HIV-infected children and teenagers”. New chapters, including “Procedures for possible HIV-infected infant examination”, “Standard procedures for HIV post-exposure of on-duty medical care staffs”, “HIV prevention education for clinicians taking care of HIV-infected patients in outpatient service” and “Harm Reduction Program ”, were added. We wish that we could improve therapeutic quality through revising these guidelines.

Keyword: HIV, AIDS, HAART, opportunistic infection, HIV post-exposure

Introduction

According to the World Health Organization (WHO) and United Nations AIDS (UNAIDS), there were about 33.2 million existed HIV-infected patients in the world in 2007. 2.5 million new patients were recorded and 2.1 million patients passed away in the same year. This disease has huge effects on human health, economy, and social stabilization, and it is also a highly concerned issue in the world.

The first HIV-infected patient in Taiwan was found in 1984. Till the end of 2007, there are 15,011 HIV-infected patients recorded in our country. 4,250 patients progressed to AIDS and 1,870 patients died. The main transmission routes are injecting drug users, unsafe homosexual and heterosexual activities.

The mortality of HIV-infected patients is decreased and the life quality is increased since the “highly active antiretroviral therapy (HAART)” been created and introduced into Taiwan in 1997, and this disease has been considered as a

chronic disease. As the progress of medical technology and antiretroviral agents, the therapy schedules should be standardized to be able to decrease the viral load in the infected patient and to prevent the disease diffusion.

Applicable condition and patient

The “Guidelines for diagnosis and treatment of HIV/AIDS” is an important reference for health authorities, medical staffs and almoner providing to possible HIV-infected infants, HIV post-exposed medical staffs, and drug-addicted patients.

Recommendation for each chapter

1. Recommendation for antiretroviral therapy for HIV-infected patient in Taiwan:

The antiretroviral drugs are divided into 3 main categories, including nucleoside reverse-transcriptase inhibitors (NRTIs), non-nucleoside reverse-transcriptase inhibitors (NNRTIs), and protease inhibitors (PIs). HAART indicates the therapy method of 2 NRTIs combining 1 NNRTIs or 1 to 2 PIs.

Opportunistic infections, severe clinical signs or CD4 cell counts and virus load should be considered before using any antiretroviral drugs. The indications for initial antiretroviral therapy in HIV-infected patients is listed as follow (Table 1.).

Besides, the new edited chapter added the characteristics of each antiretroviral drugs, groups for specific drugs, recommendation and opportunity of combining anti-TB and antiretroviral drugs, and immune rebuilt syndrome as a reference for medical staffs choosing the suitable antiretroviral drugs and possible side effects. However, the patients should be informed the types and routes of each drug, the willing of taking medicine should be respected, and the health consultation should be provided, especially safe sexual behavior, needle-syringe

program, and methadone therapy, to decrease the spread of HIV and venereal diseases as well as the risk of antiretroviral drug resistance virus infection(as Table.1).

Table 1. The indications for initial antiretroviral therapy in HIV-infected patients

Clinical classification	Lymphocyte (CD4)	Viral load in plasma (HIV RNA)	Recommendation
AIDS-related opportunistic infection or tumor; or severe clinical signs	Any value	Any value	Start therapy procedures
No clinical signs	CD4 < 200 cells/mm ³	Any value	Start therapy procedures
No clinical signs	200 < CD4 < 350 cells/mm ³	Any value	Provide therapy recommendation for patients after discussing the advantages and disadvantages
No clinical signs	CD4 > 350 cells/mm ³	HIV RNA ≥ 100,000 copies/mL	Most clinicians may delay antiretroviral drug usage; some clinicians may choose medical therapy
No clinical signs	CD4 > 350 cells/mm ³	HIV RNA < 100,000 copies/mL	Delay antiretroviral drug usage

2. Guideline for viral load, cell counts of CD4 lymphocyte and related examinations for adult HIV-infected patients :

The most important laboratory examinations are CD4 lymphocyte and viral load level after confirming patients being infected. The cell count of CD4 lymphocytes may be used to evaluate the immune condition. The viral load may indicate the situation of virus replication for evaluating the prognosis of this disease as well as the reaction of medical therapy. These 2 results play very important roles in clinical therapy and monitoring. This new guideline also added the routine examinations and other first evaluations for adult HIV-infected patients to provide more complete medical care based on the

overall clinical data. The examination indication for CD4 lymphocyte and viral load is listed in Table 2.

Table 2. The examination indication for plasma CD4 lymphocyte and viral load

Clinical classification	Viral load in plasma (by RT-PCR)	CD4
The CD4 lymphocytes, viral load, and clinical situation were not recommended for medical therapy or the patient was not prepared for medical therapy	Examine every 3 to 6 months recommended	Examine every 3 to 6 months recommended
Medical therapy procedure newly started patients	First examination before medical therapy Second examination after 1 month of medical therapy Examinations are taken every 3 to 6 months during the first year of medical therapy Repeat examination every 6 months recommended	First examination before medical therapy Second examination after 1 month of medical therapy Examinations are taken every 3 to 6 months during the first year of medical therapy Repeat examination every 6 months recommended
Medical therapy stable and the viral load undetectable (lower than 50 copies/mL) over 1 year	Repeat examination every 3 to 6 months recommended	Repeat examination every 3 to 6 months recommended
Medical therapy stable, the virus load is undetectable (lower than 50 copies/mL) and the cell counts of CD4 lymphocyte recovered. Medical therapy stopped under clinician recommendation	Repeat examination every 3 to 6 months recommended	Repeat examination every 3 to 6 months recommended
Medical therapy not expected*, the viral load elevated after medical therapy, or drug-resistance virus suspected	Genotypic resistance tests before changing antiretroviral drugs** Re-examination 1 month after changing antiretroviral drugs Re-examination every 6 months	Re-examination 1 month after changing antiretroviral drugs Re-examination every 6 months
Examination item	Clinical significance and recommendation	
Genotypic resistance	This test is recommended for those patients who had used antiretroviral drugs with no or fail to control the viral load which may be a referral for choosing other antiretroviral drugs	

* Medical therapy not expected: the viral load is still detectable after 6 months of regular usage of antiretroviral drugs.

** Genotypic resistance tests are available from: 1. Dr. Wing-Wai Wong, Taipei City Hospital Kunming branch (+886-2-25703739 ext. 1010); 2. Professor Shu-Yuan Chang, National Taiwan University Hospital (+886-2-23123456 ext. 6908); 3. Dr. Hsi-Hsun Lin, E-Da Hospital (+886-7-3468299)

3. Guidelines for prevention and treatment for opportunistic infection in adult HIV-infected patients:

The opportunistic infection of HIV and the mortality of this disease are decreased since HAART was created. In Taiwan, the authorities provide free HAART for HIV-infected patients, however, opportunistic infection may still be found in the patients with late stage of this disease or in the patients with decreased immunity caused by not following doctor's advice.

Some recommendations therapy for opportunistic infection were provided in this section. When an HIV-infected patient with intercurrent tuberculosis using rifamycin drugs for therapy, it should be aware that rifampin increases CYP450 3A4 (a hepatic enzyme) activity as well as PIs metabolism (except ritonavir), which may increase drug resistance of HIV to PIs. A substitute drug, rifabutin, is recommended for this condition due to less effect to CYP450 3A4. On the other hand, ritonavir is a strong inhibitor for CYP450 3A4. Combining rifabutin and ritonavir causes 4 times increase of rifabutin in the blood and, thus, dose regulation should be careful. Except TB, this section also provide recommendations for other diseases in opportunistic infection, such as *Mycobacterium avium* complex infection, *Pneumocystis* pneumonia, cryptococcal meningitis, Penicilliosis. cytomegalovirus diseases, and *Toxoplasma gondii* encephalitis.

4. Guidelines for prevention and treatment of mother-to-child transmission:

Mother-to-child transmission is recently focused by UNAIDS and international. The portion for female patients is increasing in the newly reported patients. HIV test is listed in the routine prenatal examinations since 2005 in Taiwan. This section provides recommendations for opportunity of medical therapy, antiretroviral drug selection and delivery method selections for pregnant

HIV-infected women to decrease the risk of mother-to-child transmission.

These recommendations are listed as Table.3.

Table.3 Recommendation for antiretroviral drug use by HIV-infected pregnant women and prevention of mother-to-child transmission in Taiwan

ZDV using time	Prescription
Prenatal	Patient condition should be understood and taken antiretroviral therapy, including zidovudine, is recommended after 12 weeks of pregnancy.
Delivery period	During delivering, initial dose of zidovudine (2 mg/kg) slow IV for 1 hour should be given, and then 1 mg/kg/hour for maintenance till child born. Patients with no HAART should be given 200 mg nevirapine PO when labor pains started.
Postnatal	6 to 12 hours after birth, zidovudine syrup should be given to the new born every 6 hours with the dose of 2 mg/kg for 6 weeks. * §

* IV 1.5 mg/kg zidovudine every 6 hours can be provided to a 1-month old infant who can not tolerate PO medicine. IV 1.5 mg/kg or PO 2 mg/kg of zidovudine (twice daily) can be given to infants with <35 weeks of pregnancy. IV or PO medicine every 8 hours should be provided to 2 weeks old infant IV or PO medicine every 8 hours should be provided to 4 weeks old infant born with less than 30 weeks of pregnancy.

§ Each CDC branch provides zidovudine syrup if it is not available in the hospital.

5. Procedures for possible HIV-infected infant examination:

The mortality in HIV-infected children, as well as opportunistic infection caused by decreased immunity, is decreased since HAART is proceeded. Less than 2% infant may be infected by HIV under the prevention procedures. This section provides recommendation for monitoring, examinations, medical and daily care, and rule in/out HIV infection for the infants born by those who are confirmed or HIV-suspected patients.

In the examination and medical care procedures for possible HIV-infected infants in Taiwan, the infants less than 18 months old should be monitored for HIV examination at 48 hours old, 1 to 2 months old, 4 to 6 months old, 12 months old, and 18 months old to prevent mother-to-child transmission and for proper medical therapy. Free antiretroviral drugs and breast milk substitute for the first 6 weeks of life are provided by authorities after full communication

between public health office and care taker, and authorization letter signing by the legal representative (biological parents, guardian, or family members).

6. Clinical signs, diagnosis and therapy of HIV-infected children and teenagers:

The number of children HIV-infected patient is increasing following the increase of female HIV-infected patient. 25 mother-to-child transmission cases were recorded till February, 2008. HIV infections in children may reflect the HIV epidemiologic situation in female patients. 90% of children HIV cases are caused by mother-to-child transmission, which is also the main resource of new children HIV cases.

HIV examination is based on antibody tests in adult patients. However, newborns may be detected maternal HIV antibody before 18 months old. Thus, HIV examination in less than 1-year-old child should be based on HIV DNA PCR, HIV RNA tests and viral cultures.

The progress in children patients is fast and it is difficult to predict the progress by CD4 lymphocyte and viral load tests. Furthermore, opportunistic infections, such as pneumocystic pneumonia, are common and may cause high mortality. Thus, HAART is highly recommended after confirming a children HIV case. It is very important to aware that drug resistance may occur while the drug concentration is lower than the effective concentration. Complete communication and evaluation of patient willingness are necessary.

7. Standard procedures for HIV post-exposure of on-duty medical care staffs:

The risk of HIV infection, caused by needle puncture or cut wound by sharp equipment, of on-duty medical care staffs is increasing due to more and more HIV infection cases. This section is added for proper handling and monitoring examinations after exposure of HIV.

The routes of exposure, or even infection, of HIV include: A. cutaneous wound

(caused by needle or sharp equipment); B. mucosal exposure; C. contact with blood, tissue fluid or other infective body fluid by cutaneous wound. The infective body fluid indicates body fluid with visible blood, semen, vaginal discharge, CSF, synovial fluid, thoracic fluid, ascites and amniotic fluid. Feces, nasal discharge, saliva, sputum, tears, sweat, urine and vomit are not considered as infective fluid if there is no visible blood.

No direct contact with patient's blood and body fluid is the main handling principle. Medical care staffs should attend the designated medical institutions for HIV antibody examination (as a baseline) and continuous monitoring examinations at 6 weeks, 3 months and 6 months after exposure. The clinician should consult with Taiwan CDC toll free consultation line (+886-1922) for evaluation of post-exposure prophylaxis (PEP).

8. HIV prevention education for clinicians taking care of HIV-infected patients in outpatient service:

The clinical medical team, including clinicians, nurses, social workers, volunteers, and case managers, plays a very important role in prevention for dangerous behavior of HIV-infected patients. HIV medical care team can process a simple risk evaluation for dangerous behavior, as well as proper health education and transferring, may effectively and persistently decrease the patients' dangerous behavior. This procedure may decrease the risk of transmission and re-infection to ensure the clinical therapeutic effectiveness.

9. Harm Reduction Program:

Harm Reduction Program is an omnibearing program for reducing narcotic damages to individual, family and society. The procedures include: A. expanding the HIV examinations and monitoring for drug-addiction patients for timely therapy and transmission prevention; B. providing needle-syringe program,

monitoring, guidance, and rehabilitation consultation to prevent further infection of type B and C hepatitis and HIV; C. providing alternative therapy. Oral low-damage substitute is provided to the patients replacing high-damage IV route. Further monitoring, consultation, health education and transferring are also recommended.

1,173 needle-syringe service sites are available in Taiwan, including pharmacy, local health center and medical laboratories, and 73 medical institutes provide methadone therapy. Detail information is available on the Taiwan CDC website or toll free consultation line (+886-1922).

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