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CLINICAL MANAGEMENT OF HIV/AIDS INFECTION USING ANTIRETROVIRAL DRUGS IN A NIGERIAN ENDEMIC SETTING

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Abstract

Current HIV/AIDS treatment strategies aim at maximal suppression of virus load levels (the number of free virus particles in the blood plasma) over long periods. Aside from inducing strong side effects, the long term effectiveness of HAART is also limited by the evolution of drug-resistant variants. Even in patients with viral load levels suppressed below detectable limits (50 copies/ml), ongoing viral replication can be found in a variety of tissues and cell types. Persistent virus production is facilitated by sub-inhibitory drug levels in infected cells or by host immune failure. Therefore, pre-existing or newly produced drug resistant mutants can emerge that have a selective advantage under drug pressure.

These mutants become dominant in the virus population and lead to viral rebound and therapy failure. The protease inhibitors are potent antiviral drugs because the protease activity is absolutely essential for production of infectious viruses. The newest class of drugs is the fusion inhibitors that block virus entry into cells.

Introduction and Background Information

Research on HIV/AIDS have provided convincing evidence of the beneficial impact of combination regimen of antiretroviral (ARV) therapy on the morbidity and mortality from HIV infection.[1,2,3,4,5,6,7,8,9]. It has been documented that the use of a suitable combination of antiretroviral drugs achieved a sustainable suppression of viral replication in the infected patient. The drug combination also achieved a sustainable suppression of viral replication in the infected patient. The drug combination also achieved significant improvement in the immune status of the patient through the reversal of the immunodeficiency that is characteristic of HIV infection. The antiretroviral therapy had indeed helped HIV infected patients to have productive lives and have prevented premature deaths. These reported benefits encouraged the use of antiretroviral therapy in the management of HIV infections in several developed countries. However, with the recent availability of cheaper generic drugs, some of the developing countries have initiated national antiretroviral programmes.

In January 2012, the Federal Government of Nigeria launched a National antiretroviral programme under which 10, 000 adults infected with HIV were to be treated with a combination of three antiretroviral drugs.
Currently over 12,000 patients are on treatment under the national programme. In addition, some state Government, Non -Governmental Organizations, and faith-based organizations have also started implementing antiretroviral programmes in the country. in the IHO planned programme of expanded access to treatment whereby more than 3 million patients are expected top be on treatment in Africa, Nigeria is likely to scale up its ARV programme to accommodate over 3 million patients. This will result in extensive use of antiretroviral drugs in the country by both public and private sectors.

The implementation of the President Bush's initiative (PEPFAR) is expected to put many more people on ARV treatment in Nigeria.

It is pertinent to note that for the desired results to be achieved, the ARV must be properly used otherwise the consequences can be very grievous at both National and Global levels. The ARVs are a new set of drugs with various degrees of potencies and side effects. The drugs must be used in defined combinations and under set guidelines. If the relevant healthcare providers are not properly knowledgeable on ARVs, the tendency is that the rate of misuse will be high and this will lead to high rate of treatment failure. Under this situation, drug resistant strains will emerge with the potential danger of rendering the present combination of ARVs used in Nigeria ineffective. The emergence of a new epidemic of drug resistant HIV will obviously have enormous devastating impact globally. It is therefore important that the relevant health care providers must have very good knowledge of the ARVs to be able to administer the drugs correctly on the patients. Apart from managing the HIV infection, it is important to also treat the associated opportunistic infections. These constitute the main causes of death amongst the HIV infected patients. Equally the response of the patients to the antiretroviral treatment needs to be monitored by laboratory tests.

There is need for more coordinated and sustained effort at all levels to train the relevant health personnel on what ARVs are and their proper use in developing countries. This very important gap needs to be bridged urgently especially now that these countries are poised to scale up their ARV programmes significantly. The health personnel to implement the ARV programme at various levels in the country need to be further trained on the proper use of ARVs, the various treatment options for opportunistic infections (OIs) and the relevant laboratory monitoring tests. [10, 11.]

This review evaluates the clinical management of HIV/AIDS in a Nigerian endemic setting which will provide knowledge of the HIV/AIDS clinical management techniques to the relevant health personnel in both the private and public health facilities in resource-poor settings which in turn improve and enhance the quality of their ARV programmes significantly.

Baseline demographic, clinical and biological characteristics used in the clinical management of HIV patients

The data on baseline characteristics obtained from the HIV/AIDS patients that are used for their management includes demographic data values like sex (male/female) , age (median /IQR) , biological data like CD4 cell count x 10^{6}/l(<200, 200-350, median and IQR) values, and plasma HIV RNA(copies/ml(median (log), IQR) values.

Clinical data values like stage of infection (%), WHO classification (stage 1, 2, 3, 4), Karnofsky's score (%), (<70, 70, 80, 90, 100), Body mass index ((kg/m^2) median, IQR), treatment regimen (3TC + d4T + NVP), profile of opportunistic infections (OIs) of the patient i.e. data on percentage of patients who presented with opportunistic infections (baseline (time) week), frequency of single or multiple opportunistic infections amongst the patients (%) like respiratory tract infections, gastroenteritis, sexually transmitted diseases, cutaneous infections, oral candidiasis and Kaposi sarcoma.

Data is also obtained on the follow-up of the patients over time like tolerated drugs with no side effects (%), experience of some degree of drug associated side effect and loss to follow-up (%).
A profile of drug associated side effects are also recorded for the patient. These side effects include skin rashes, insomnia, generalized weakness, uriticaria, abdominal discomfort, parasthesia, flatulence and diarrhea. Data on changes in plasma HIV RNA level of patients during treatment are also recorded , (Box-and-whiskers plot) HIV RNA level (log_{10} copies/ml (time weeks) baseline data).
Data is also obtained on the changes in body mass index of the patient during treatment. (Box-and-whiskers plot) body mass index (kg/m^2) time (weeks) (baseline 12 and 24).
Data on changes in CD4 cell counts and viral load are also obtained from the patient (Box-and-whiskers plot) (Baseline 12 and 24) time (weeks) CD4 cell count (x10 cells/1).

Effect of quality and quantity of CD4 + cells on clinical management of HIV/AIDS infection

Qualitatively, there is inability of the CD4 cells to respond to antigens as the CD4-HIV complex becomes internalized and the T-cell no longer expresses CD4 molecules. This depletion of the $CD4^{+}$ T-cell leads to

progressive impairment of the immune system. Monocytes and macrophages are now known to express CD4 and are also infected by HIV. An estimate of the $CD4^+$ count expressed as absolute counts, or percentage of the total lymphocytes is therefore not an absolute prognostic criterion. However unlike $CD4^+$ T-cells, monocytes are relatively refractory to the cytopathic effects of HIV. The normal range of the $CD4^+$ is 500-1400 cells/ml. They constitute 34-54% of the lymphocytes and are present in about 80% of thermocytes. Immunophenotyping of lymphocytes especially T-lymphocytes is a standard laboratory test in patients with HIV/AIDS.

In the quantification of $CD4^+$, T-cells, flow cytometry in combination with automated blood cell analyzers and the use of monoclonal antibodies are used to quantitate directly the various T- lymphocyte sub-types such as CD4 and CD8. Most centers in Nigeria, unfortunately do not have flow cytometry and other sophisticated methods and so resort to the use of manual kits for these tests either based on enzyme Immunoassay (EIA) or Rosetting techniques. Direct count using Coulter counting chamber is often employed and is fairly reliable.

The $CD8^+$ cells are the suppressor cells. They switch off the immune system and also have some immune enhancing effects. The normal range is 200-600 cells/nil. They constitute 12-28% of the thymocytes. The T4/T8 ratio usually has a normal range of 1.4-3.7 but in HIV/AIDS where there is selective $CD4^+$ cell depletion, the ratio may be inversed. As this ratio drops below 1.0, there is a correlation to a decline in immune function due to a destruction of T4s and an increase in T8 cells. These counts are useful prognostic markers which could be used to predict the stage of the disease, decide treatment option and assess the effect of treatment.

Although quantifying $CD4^+$ cells have been used in staging HIV disease, care has to be exercised in using it or as a surrogate marker of the clinical benefits anti-retroviral drugs especially in areas with high Human T-cell lymphotrophic virus type 1 (HTLV1) prevalence. HTLTV has also been found to deplete the number of $CD4^+$ cells. Other diagnostic criteria for progression of infection or response to treatment that could be used, though available at only few centers, include serum Beta 2-microglobulin level using an automated micro-particle enzyme immunoassay and Neopterin (a product of activated macrophages) level, using a commercial radioimmunoassay. They are both elevated by HIV infection.

Both viral blood and $CD4^+$ count are still considered useful markers and where available should be used together, to monitor HIV/AIDS disease progression. It is suggested that plasma HIV RNA litres are the best predictor of long term clinical outcome while CD4 count is the best predictor of immediate or short-term risk of developing a new opportunistic disease process. The use of antiretroviral agents lower cell associated infectious litres of HIV plasma litres of viral RNA, and levels of neopterin and beta 2-microglobulin and raise the $CD4^+$ cell counts.

Clinical management of HIV/AIDS infection

There is need to build global and national advocacy to highlight the effects of HIV/AIDS and to stimulate concrete, effective action to mitigate its impact.
Efforts should be focused on preventing new HIV infections, promoting equal access to treatment and addressing legal inequalities and mitigating the effects of HIV/AIDS.
HIV attracts the body's immune system rendering it incapable of fighting of infections and certain cancers because of their companied immune system, persons with AIDS can suffer from infections and diseases that do not can be non-existent or easily mistaken for other viral, parasitic bacterial infection.
The AIDS problem in Nigeria has recently assured an alarming dimension as the incidence of new cases continues to grow at a geometric progression rate.
Hence the trend in HIV/AIDS management ahs to shift from symptomatic relief/supportive care to active management with antiviral drugs.

The therapeutic objectives for intervention at the early stage is to decrease plasma HIV-RNA levels and increase $CD4^+$ T-cell counts. Shorten duration of acute syndrome, reduce rate of clinical progression of the disease and to improve the chances of survival of the patient.
Intervention at the advanced stage includes the above and also includes the objective to decrease the incidence of opportunistic infections, alleviate/manage the symptoms of AIDS, boost the immune system and improve the quality

of life of the patients. AIDS is now a major cause of illness and death in Nigeria. For health care providers, the challenge is to provide medical, nursing, psychological care and support for people with HIV/AIDS.
Health services, in the present form are unable to meet these challenges. The clinical management of HIV infection requires a detailed history and physical examination which focuses attention on factors related to the mechanism of acquisition of infection, findings that are useful in staging the disease and medical conditions that require immediate intervention. Prevention, diagnosis and treatment of opportunistic infections are paramount. It is now proven that treatment with a combination of antiretroviral drugs greatly reduces illness and death and progression to AIDS. To achieve good clinical management of HIV/AIDS. There is need to find the best combination which effectively lowers the viral load without excessive side effects. Develop a policy on the management of HIV/AIDS patients to include pregnant women and children.

- Document the opportunistic infections in our environment and develop guidelines for management using cost effective drugs.
- Develop cost effective treatment guidelines which can be used at primary, secondary and tertiary health care levels.
- Outline appropriate procedures for referral of patients between and among institutions and community facilities at all levels.
- Ensure that antiretroviral drugs are available and affordable to many Nigerians who are HIV positive.
- Train health care workers in the skills for providing clinical management and care
- To provide guidelines to reduce risk of transmission in health settings
- Develop indicates to be used at various levels for monitoring of care
- Provide social, psychological support and counseling to people living with AIDS (PWAs) and their families at the levels.

The clinical expression of HIV infection is not only very diverse, but may also vary in different populations according to the relative frequency of other endemic and potential opportunistic infections. The clinical features therefore depend on the stage of the disease and the presence of opportunistic infections or AIDS associated malignancies.

History and physical examination should focus attention on factors related to mechanism of acquisition of infection, findings that are useful in staging the disease and medical conditions that require immediate intervention.
Attention should be paid to those anatomical sites that are likely to show significant changes and prove useful in management including staging e.g. lymph nodes, funduscopic examination, oral cavity, careful kin examination, abdominal examination for hepatosplenomegaly, genital examination for Sexually Transmitted Disease (STD), pelvic examination in women, neurological examination, psychological evaluation and nutritional assessment. Women with HIV infection have been known to show high rates of gynaecological complications such as recurrent or refractory vaginal candidiasis which is a relatively early manifestation, cervical dysplasia which is increased 8-11 fold and pelvic inflammatory disease which is also a common presentation. The Centers for Disease Control and Prevention [12] recommends that gynaecological evaluation and pap smear should be carried out annually or six monthly. Women with HIV infection also need specialized counseling as appropriate for testing and care of children, reproduction and abortion. The neurological examination should include evaluation of HIV associated dementia, which is seen in late stages with advanced immune suppression. In the WHO clinical case definition of AIDS in resource limited settings. AIDS is an adult is defined by the existence of at least 2 major signs associated with at least minor sign in the absence of known causes of immune suppression such as cancer or severe malnutrition or other recognized etiologies. However the presence of generalized Kaposi Sarcoma or *Cryptococcal meningitis* is sufficient by itself for the diagnosis of AIDS.

The major signs of AIDS are weight loss >102 of the body weight, chronic diarrhea > 1 month, prolonged fever > 1 month (intermittent or constant). The minor signs are persistent cough < 1 month, generalized pruritic dermatitis, recurrent herpes zoster, orophanyingeal candidiasis, chronic progressive and disseminated herpes virus infection and generalized lymphadenopathy.

It is WHO clinical definition of AIDS in adults when diagnostic resources are scarce [13] has been evaluated in several countries. The specificity has been put at 90% while the sensitivity was 59% with a positive predictive value of 74%.

As a result of low sensitivity WHO addressed these issues in 1989, and a draft proposal on clinical staging of HIV infection was developed. Regular of Relese 1 observations that can be made at this stage includes cognitive defects such as problems with concentration, mental showing and memory, motor dysfunction such as unbalance in co-ordination or difficulty with complex motor tasks, neuropsychological abnormalities like slowed verbal response and difficulty with complex sequencing. Nutritional assessment is very important as wasting is a very common feature in the late stage of the disease. Contributing factors are increased metabolic requirements, reduced intake (depression, anorexia, oral/aesophageal lesbiory) and mal-absorption.

An important component of the evaluation is staging/classification of HIV infection based on the medical findings and where possible CD4 cell count. The purpose of staging is to determine at what point in the disease process the patient presents and to follow the rate at which immunosuppression progresses.

These findings dictate management strategies and prognosis. Different classification system have been proposed. These include the Walter Reed classification and the center for disease control (CDC) classification most of these require AIDS-type abnormalities to be shown in laboratory tests and such definitions may not be applicable in most African countries, where laboratory facilities are lacking.

WHO therefore proposed the clinical case definition for AIDS in adults and children where diagnostic resources are lacking. In this proposal, clinical conditions were correlated with laboratory markers already known to reflect disease progression such as CD4 counts.

Studies in 907 HIV positive patient collected in 26 clinical centers all over the world were done. The results were reviewed in 1990and proposal was developed for the clinical stages of the disease.
Individual stage 1, the patients is asymptomatic and has persistent and generalized lymphadenopathy, performance scale 1; the patient is asymptomatic with normal activity.

The clinical stage 2 is characterized by weight loss > 10% of body weight, minor mucocutaeneous manifestations (seborhoeic dermatitis, prurigo, fungal infections, recurrent oral ulcerations), Herpes zoster within the last 5 years, recurrent upper respiratory tract infections, and performance scale 2 i.e. symptomatic but normal activity.
The clinical stage 3 features weight loss > 10% of body weight, unexplained chronic diarrhea for more than one moth, unexplained prolonged fever (intermittent or constant) for more than one moth, oral candidiasis (thrush), oral hairy leukoplakia, pulmonary tuberculosis within the past year, severe bacterial infection (pneumonia, pyomyositis) and performance scale is 3: Bedridden 50% of the day during the last month.

The clinical stage 4 is characterized by HIV wasting syndrome, pneumocysts carinic pneumonia, toxoplasmosis of the brain, cryptococcosis with diarrhea for more than one month, cryptococcosis extra pulmonary, cryptococcosis disease of an organ other than liver, spleen or lymph node, Herpes virus infection, mucocutaneous for more than one month or visceral for any duration, progressive multifocal leuko encephalopathy, any disseminated endemic mycosis (histo plasmosis, coccidiomycosis), candidiasis of the oesophagus, trachea, bronchi or lungs, a typical mycobacteriosis, disseminated, non typhoid salmonella, septicaemia, extra pulmonary tuberculosis, lymphoma, laposis sarcoma, HIV encephalopathy, performance scale is 4, and patient is bed ridden 50% of the day during the last month. Both definitive and presumptive diagnosis are acceptable at this stage.

A further refinement of the system is the laboratory axis which sub divide each clinical category into 3 strata A, B, C depending on the number of $CD4^+$ lymphocytes (500, 200 - 500, <200). If $CD4^+$ counts are not available, absolute lymphocytes should be done as an alternative laboratory marker, also in 3 different strata (>2000, 1000 – 2000, <1000).

In patients classified as 1A, 1B etc a suffix will be used to indicate if classification is based on $CD4^+$ © or lymphocyte counts L. If laboratory ◯ values are not available, patients should be classified as 1x, 2x, 3x, 4x or simply 1, 2, 3, 4.

The laboratory axis of the classification is as follows:

STRATA	**LYMPHOCYTES**	**CD4**
	Per mm3	Per mm3
A	2000	500
B	1000-2000	200-300
C	1000	200

The clinical axis of the classification is as follows:

STRATA	**1**	**2**	**3**	**4**
	Asymptomatic	Early	Intermediate	Late
A	1A	2A	3A	4A
B	1B	2B	3B	4B
C	1C	2C	3C	4C

The optimal approach to treatment of patients with HIV disease requires the identification and treatment of active infection in patients who already manifest severe immune deficiency. Primary and secondary prophylaxis are used to prevent new or recurrent opportunistic infections.

The treatment of primary HIV infection is used to slow immunological deterioration using antiretroviral drugs.
The asymptomatic patients receive counseling about their sero status. Family members nominated by the patient should also be informed and counselled on prevention, transmission and healthy living. Patients should be followed up at regular intervals and be advised to seek prompt treatment for any infection or symptoms. Confidentiality should be maintained. It has been shown that antiretroviral drugs is of benefit at this stage of the disease.
In symptomatic patients, certain clinical symptoms are common in HIV-infected persons in sub-Saharan Africa including Nigeria. These are chronic diarrhea, wasting (slim disease), chronic fever with or without an obvious localizing source, pulmonary disease, fungal and parasitic infections. Isosporiasis, crytosporiduosis and microsponriasis have been identified as causative agents of chronic diarrhea in some areas. The main stay for chronic diarrhea treatment is rehydration. All patients will require oral rehydration therapy (ORT) 3-4 L/day. Some patients will require intravenous fluids due to severe dehydration. Diagnosis is also carried out to identify the cause of diarrhea. This may be unlikely to be always possible.

All patients should receive clotrimazole for 7 days combined with metronidazole for presumptive amoebic infections. The same drug could be used to treat *Giardia lamblia*, another cause of chronic diarrhea. Antimotility agents such as loperimide or codeine can also be used.

Patients can also have oral or oesophageal candidiasis. This illness occur at an early stage of the disease and can cause mild to moderate disability. The disease may compound the effect of dehydration caused by diarrhea because the oral and oesophageal thrush makes swallowing painful. First line treatment of oral or oesophageal candidiasis is gentian violet. This is cheap and fairly effective but does cause blue staining around the mouth, which may be unacceptable. Nyastatin tablets or mixture can also be used. Ketoconazole is also good but expensive. Nyastatin pessaries and cream, are also used to treat vulvo-vaginitis, which occurs in female HIV patients. Other anti-fungal agents e.g. clotimazole, miconazole are expensive.

Respiratory conditions is the commonest in HIV/AIDS patients. *Pneumocystis carinii* common in western countries is not easily diagnosized although there are clinically identified one or two patients on the basis of chest x-ray and other clinical findings. Other pneumonia occur and therefore the use of broad-spectrum antibiotics is advisable. Sputum specimens should also be examined for acid-fast bacilli where feasible. Chest physiotherapy and breathing exercises may be needed in these patients.

Many people in Nigeria have suffered a primary infection of tuberculosis in childhood from which most recover. With the HIV infection, however, latent infection can be reactivated and many patients respond well to therapy.
The treatment is standardized and is intensive 9-12 months Rifampicin, Pyrazinamide and Isoniazid. Compliance is them problem here as the drugs expensive but is free under the WHO DOTS programme. Thiacetazone should not be used as many countries have reported frequent severe and sometimes fatal drug reactions.

Lymphadenopathy can be caused by many infections, lymphomas, or HIV itself or fungi. Except for syphilis which can be diagnosed with a simple serological test and can be cheaply healed, all other diagnosis require a laboratory support, and many of our surgeons are not keen to do a biopsy. A wide variety of abnormal skin conditions are seen in HIV. Infections with viruses, bacteria and fungi as well as allergic reactions are also inclusive. Most skin conditions present early in the course of HIV disease. For example, *Herpes Zoster* is almost diagnostic of HIV infection and may predate any other symptoms by many years. *Herpes Zoster* can be treated using an antiviral agent, acyclovir but it is expensive. Patients also need antiseptics, analygesics and treatment of super infection with antibiotics. Herpes Simplex can occur anywhere on the body but the most severe and disabling infection involve the genitals and buttocks. Treatment is with gentian violet or acyclovir.

Condyloma Acumionata are warty lesions in the genital areas. Podophyllin 20% solution or Trichloroacetic acid are used for treatment. Superficial bacterial skin infections such as furunculosis, impetigo, pyoderma and fulliculitis are common and require treatment with antibiotics. Fungal super infections are also common as well as allergic skin conditions like eczema. Severe prurigo may require treatment with anti-histamines or calamine.
The condition of Kaposi sarcoma is aggressive in HIV patients. The tumor, which is usually found in the skin may invade other organs e.g. brain, lungs, gut etc. commonly occurs at a fairly late stage of the disease. Histology is required but difficult to do and therefore clinical judgment is mostly used. Results with radiotherapy is not extensive and exciting. Other cancers are non-Hodgkins lymphoma and cervical cancer. All these require chemothopology and results are not encouraging, many patients present with severe headaches which could be a symptom of meningitis and amours. These need to be probably investigated and treated accordingly. Many patients present with fever which may be an indicator of an opportunistic infection and should always be taken seriously. Investigations should always be done to determine the origin. Pain is a very common compliant and need to be treated effectively with potent analgesics. Antidepressant drugs may also be needed.

Opportunistic infections should be prevented, Tuberculosis (TB) can be prevented with prophylaxis with Isoniazid (INH) which has been shown to reduce the incidence of TB reactivation in HIV positive patients. WHO recommends that INH be given to HIV infected persons without active TB for 6-12 months but the problems are cost implication, toxity, non-compliance and INH resistance.

Malaria prophylaxis is advisable in malaria endemic area of HIV positive patients with depressed immunity are more susceptible to malaria and celebral malaria may be a complication.
Killed or attempted vaccines are considered safe for vaccinations in HIV positive patients but live viral and live bacterial vaccines like oral polio, yellow fever, cholera, BCG and live oral typhoid are not recommended.
In the administration of antiretroviral therapy on HIV positive patients, it is known that there is no initial dormant phase of infection. “Latent phase” is a misnomer. There is extensive viral replication (millions of viruses are produced daily) even in the early stage of the disease.
The quantity of total virus in plasma is a prediction of progression to AIDS.
There is a homogenous population of virus early in the disease compared to heterogenous population later which are due to mutations ionotherapy e.g. Zidovudine is effective in pregnancy where it lowers vertical transmission by 68%. The challenges then are to find the best combination of drugs which effectively lower the viral load without excessive side effects or complications and which are cost effective.
Two combinations are used. The first combination involves Lamivudine (EPIVIR) 150 mgbd and Zidovudine (Retrovir) 200 mgtds or 300 mgbd (Two nucleoside analogues).

The second combination involves Zalcitabine (Hivid) 0.75 mgtds and Saquinavir (Invirase) 600 mgs tds (One nucleoside analogues added to a proteinase inhibitor). 1 dealy three drugs are recommended i.e. two nucleoside analogues added to a proteinase inhibitor in many settings. Initial clinical symptoms and signs, CD4 cells count,

viral load, absolute lymphocyte counts, stage of the disease, opportunistic infections and baseline haematology and chemistry data are obtained from each patient and documented before treatment.

A client is any person seeking or receiving HIV counseling and/or testing. A care provider in the context of HIV/AIDS counseling is any provider who is trained to provide HIV/AIDS counseling services.
Enabling the client to cope with stress in the context of HIV/AIDS clinical management means providing the emotional support that will help a client to accept the reality or a possibility of a positive diagnosis of HIV or AIDS of oneself or one's loved one, helping the client to identify, explore and select the best options for handling stress and helping HIV positive clients plan for the future by identifying, exploring and selecting available resources in order to meet emotional, medical and social needs that may exist in the life of an individual after a diagnosis of HIV or AIDS.

Facilitation of preventive behavior means helping the client to identify, explore, select and practice behaviors which will eliminate or greatly reduce the risks or transmission of HIV. This will include helping the client to assess his/her personal risks of transmitting or acquiring HIV and helping the client to plan for a reduction of the risks.

HIV/AIDS treatment options and their implication

Therapeutic option of direct antiretroviral agents involves reverse transcriptase inhibitors (RTI's) and Protease Inhibitors (PI's) while that of supportive regimen includes antibiotics, antifungal and antituberculosis agents while immuno-stimulants and immuno-dilators includes growth factors and inter ferons.
RTI's includes Zidovudine (AZT): 200mg tid, Didanosine (ddl): 200 mg bd, ZXalcitabine (ddc): 0.75 mg tid, Lamivudine (3TC): 150 mg bd and Stavudine (d4T): 40 mg bd.
PI's includes Saquinavir: 600mg tid, Indinavir: 800 mg tid and Ritonavir 600 mg bd involves factors. Therapeutic strategy employed in Nigeria drug cocktails optimizing therapeutic regimen, and the Nigerian factor. In the use of drug cocktails factors taken into consideration are convergent, divergent, mono, double and triple combination as well as drug sequencing.

Drug naïve and drug experienced patients are also factors taken into consideration. In the optimization of therapeutic regimen, factors influencing drug bio availability, patients concomitant conditions, factors influencing toxicity, compliance and dosing schedule, counseling and monitoring are taken into consideration. The Nigerian factor involves socio-economic status of the patient and the health-care facilities that have extremely poor infrastructure, no strategic guidelines for drug management, no monitoring facility, limited therapeutic options, no data from structured and/or controlled clinical trails and no funds for research.

Conclusion

The benefits of the combination therapy of HIVID and INVIRASE is that it creates the option of adding another antiretroviral drug.

This addition help to reduce disease progression, increase CD4 cell count, reduce viral load, reduce resistance and has low risk of cross resistance. Patients have good safety profile and prolonged survival.
The cost management of opportunistic infections and lack of treatment or effective treatment is reduced.
Opportunistic infections includes chest (TB or pneumonia), skin, fungal and other viral infections malignancies in HIV/AIDS includes Kaposis sarcoma and lymphoma. Neutropenia is also involved.

In HIBVID and INVIRASE viral drug resistance, HIV exhibits high mutation rate, HIV reverse transcriptase does not correct reverse transcription error by proof reading.

Mutants are generated randomly during replication cycle. Some mutants are resistant to antiretroviral drugs. Resistance develops more rapidly in patients with lower CD4 cell counts and more advanced disease.
There is need for early antiretroviral therapy as combination therapy delays resistance. There is significant clinical benefit of HIVID + INVIRASE combination therapy over monotherapy of each ARV agent mortality and time to AIDS death is decreased and HIVID and INVIRASE combination is well tolerated by HIV/AIDS patients.

Roche drugs for treatment of associated condition in AIDS are Kaposis sarcoma (Roferon –A interferon- alpha), Lymphoma (interferon-Alpha), TB (Rimifon(INH), BACTRIM (Cotrimoxazole), Pneumonia (BACTRIM) and Neutropenia (NEUPOGEN). In Nigeria, there has been a significant antiviral and clinical response in patients on treatment reflecting the relative efficacy of the antiretroviral drug regimen administered to HIV/AIDS patients. Tolerability and adherence to the relatively simple drug regime is also quite high.

References

1. Carpenter C.C.J, Cooper D.A, Fischi M.A *et al* (2002). *Antimicrobials in adults: updated recommendations of the International Aids society, U.S.A panel. JAMA: 283: 381-390*
2. Patella F.J Jr, Delaney K.M, Moorman A.C *et al* (1998). *Declining morbidity and mortality among patients with advanced Human Immunodeficiency Virus Infection (HIV) outpatients study investigators, N. Engl. J. Med: 338: 853-860*
3. Vittinghoff E, Scheer S, O'malley P, Colfax G, Holmbery S.D, Buchbinder S.P (1999). *Combination antiretroviral therapy and recent declines in AIDS incidence and mortality, J. infect Dis 179: 717-720*
4. WHO/UNAIDS/IAS (2000*). Safe and effective use of antiretroviral treatment in adults with particular reference to resource limited settings. ED: Munderi, Praag and Bella. WHO/HIS (2000).04.2001 pp 1-31*
5. Centers for Disease Control and Prevention (2002). *Guidelines for using antiretroviral agents among HIV-infected adults and adolescents. Recommendations of the panel on clinical practices for Treatment of HIV. MMWR, %1: (No RR-7): 1-553*
6. Ho DD, Neumann A.H, Perelson A.S, Chen W, Leonard J.M, Markowitz M (1995). *Rapid turnover of plasma virioris and CD4 lymphocytes in HIV-1 infection Nature: 373: 123-126.*
7. Egger M, Hirschel B, Francioli P et al (1997). *Impact of new antiretroviral combination therapies of HIV infected patients in Switzerland: Prospective mullicenter study. Swiss HIV cohort study, BMJ, 315: 1194-1999*
8. Hogg RS, Health KV, Yip B et al (1998). *Improves survival among HIV-infected individuals following initiation of antiretroviral therapy. JAMA: 279: 450-454*
9. Lederman MM (2001). *Immune restoration and CD4 T-cell function with antiretroviral therapies. AIDS: 15(suppl 2): 511-515*
10. Nigerian Institute of Medical Research (2003). *Background document for the training modules on laboratory tests for diagnosis and monitoring of HIV infection, pp 5*
11. Nigerian Institute of Medical Research (2005). *Training manual for Doctors on the use of antiretroviraldrugs in Nigeria: pp X-XV.*