

UPDATES IN HIV:

AGING & HIV

Tlaleletso is a monthly publication produced by the Botswana UPenn Partnership, in response to your expressed need to have accessible, digestible clinical information.

*Each issue will summarize new scientific evidence and highlight recommendations in a user-friendly format. This month's Tlaleletso provides an introduction to the topic of **HIV and Aging**.*

For a more detailed review of the literature in this field, please check out www.clinicaloptions.com. This website is an invaluable resource for doctors managing HIV patients.

*Next month Tlaleletso will discuss the **Management of Acute Respiratory Distress**. If there are other topics you would like it to cover, please send us your feedback— either on content or format.*

Respectfully, Mike Reid

The number of older (ie, aged 50 years or older) HIV-infected patients has greatly increased since the advent of effective combination antiretroviral therapy.^{1,2} In Botswana, 21% of all HIV-infected patients are older than the age of 50 years. Furthermore over 22% of all Botswana between the ages of 50 and 64 years are HIV infected.³

With the increased availability of antiretrovirals, people infected with HIV in their youth are living longer and there is an increasing number of Botswana on ARVs living well into later life. Increased rates of new HIV infection in older individuals are also being recognized in other areas of Africa, with one study suggesting that 17% of mortality in Kenya among persons older than 50 years of age may be HIV related.^{4,5}

There are significant important challenges to managing older individuals with HIV.

Evidence from North America and Europe suggest that rates of bacterial pneumonia, stroke, myocardial infarction, diabetes mellitus and non-AIDS-defining malignancies are significantly higher for older HIV-infected individuals (older than 50 years of age) than in younger patients.

In this edition of Tlaleletso we summarize how older people are affected by HIV and suggest management strategies for improving quality for such patients.

NATURAL HISTORY OF UNTREATED HIV INFECTION IN OLDER PATIENTS

Studies have clearly demonstrated that when older people get HIV, their average viral load levels after sero-conversion are much higher compared to younger people. In addition, CD4 cell counts are 40 cells/mm³ lower in individuals aged 40 years or older compared with individuals younger than 40 years of age. Subsequently, older persons have faster rates of CD4+ cell count decline and more rapid progression to AIDS and death^{6,7}. One big study in North America demonstrated that for every 10 years of increased age, there was a 32% increased risk of developing AIDS and a 47% greater risk of death⁶.

UPCOMING LECTURES

October

Guidelines Update:
Acute Respiratory Distress

November

Topics in HIV
HIV and Cancer

December

Holiday Quiz 2012!

CLINICAL MANIFESTATIONS AND COMPLICATIONS OF HIV IN OLDER PATIENTS

Among the AIDS-defining diagnoses, HIV-associated dementia (HAD) and, to a lesser degree, HIV-associated esophageal candidiasis and wasting are more frequent in older compared to younger individuals^{8,9}. A recent study demonstrated that HIV associated dementia occurred nearly twice as frequently in older (50 years of age or older) compared to younger (20-39 years of age) HIV-infected individuals. Although the mechanism by which HIV contributes to HAD is uncertain, one study suggests that blood flow in the brains of HIV-infected patients is reduced to levels typically observed in individuals 15-20 years older¹⁰. Older HIV-infected patients are also more likely to develop comorbid conditions such as non-AIDS-defining malignancies, diabetes, hypertension, and liver, pulmonary, vascular, and renal disease¹¹⁻¹³.

TREATMENT EFFICACY IN OLDER HIV-INFECTED PATIENTS

Clinical Response to Therapy

Combination antiretroviral therapy provides substantial benefit to older patients^{15,16}. Nonetheless, studies have clearly demonstrated that the risk of AIDS and/or death after the initiation of combination antiretroviral therapy remains greater in older compared to younger patients.^{15,17} In one study, compared with 30-39 year olds, the risk of developing an AIDS-defining condition was 18% higher in those aged 55-59 years and 32% higher in those 60 years or age or older even after correcting for the latest CD4+ cell count¹⁸. Compared with younger persons, older people are also less likely to have a significant improvement in their CD4 count, even if their viral load is suppressed on HAART¹⁹. On average, for every 10-year increase in age, patients with consistent virologic suppression gain on average 35 fewer

CD4+ cells/mm³ during the first 12 months of therapy. The clinical consequences of incomplete recovery of CD4+ cell count include not only an increased risk for developing HIV-related opportunistic infections but also increased rates of non-AIDS-related morbidity and mortality caused by liver, cardiovascular, pulmonary or renal disease as well as by non-AIDS-defining malignancies.²⁰

Timing of Therapy

Because of the rapid progression of HIV in older patients, as well as the increased risk of comorbidities in older patients, in some settings HIV clinicians are recommending that an age of older than 55-60 years should be considered for earlier initiation of antiretroviral therapy regardless of CD4 count. Such recommendations have not been applied in Botswana. There remains insufficient evidence to justify starting ART at higher CD4 counts for older patients. However, older patients should be monitored closely and started on HAART as soon as they meet eligibility criteria of CD4 count of 350 or below, renal insufficiency, or a WHO stage 3 or 4 defining illness.

OPTIMAL MANAGEMENT OF HIV IN OLDER PATIENTS

Regardless of the cause, optimal management of older HIV-infected patients involves the following:

1. Recognizing that older HIV infected patients are at risk of developing other diseases and should be screened regularly for diseases such as diabetes, dementia, kidney disease.
2. Management of older persons requires close working relationship between clinicians and pharmacists. Older people are at increased risk of drug toxicity.
3. Team work is vital. Older people with HIV often need more health care support. It is important that doctors, nurses, social workers and adherence support staff work closely together when managing older HIV infected people.

SPECIFIC MEDICAL COMORBIDITIES

The complex relationship of HIV infection, antiretroviral therapy, and aging with the development and treatment of comorbidities makes the comprehensive care of older HIV-infected patients a challenging clinical endeavor.

Cardiovascular Disease. The available data indicate that the rate of heart attack is greater in HIV-infected persons than in persons not known to be HIV-infected and increases by 32% for every 5 years of additional age¹⁴. This risk is most marked in older individuals who are not on HAART²¹. However, certain antiretrovirals are associated with an increased risk of cardiovascular disease.

Data from North America suggest that among HIV-infected patients receiving antiretroviral therapy, use of lopinavir/ritonavir may be associated with an increased risk of myocardial

infarction²². As a consequence, all patients on lopinavir/ritonavir should be screened regularly for diabetes and dyslipidemia, risk factors for the development of cardiovascular disease.

Diabetes. The risk of new-onset diabetes among HIV-infected persons also increases with age; large multinational studies have demonstrated a 30% increase per 5 years of increased age^{23,24}. The observation that depletion of skeletal muscle mitochondrial content in older patients is associated with the development of diabetes may explain the association between use of agents that contribute to mitochondrial toxicity, specifically stavudine (D4T), zidovudine (AZT), and didanosine (DDI), and increased rates of diabetes among HIV-infected patients receiving antiretroviral therapy.²⁴

The risk of diabetes in people with HIV and the outpatient management of diabetes in such patients will be discussed in more detail in a future edition of *Tlaleletso*.

Because of the increased risk of diabetes, it is important that all HIV-infected patients be screened for diabetes at the initiation of HAART and then regularly thereafter. In South Africa, annual fasting blood glucose testing is recommended for all patients on HAART²⁵. In Botswana annual glucose monitoring is recommended for all patients on a PI based regimen. Given the increased risk of diabetes with age, these practices are particularly relevant to older patients.

Non-AIDS-Defining Malignancies. The incidence of a broad range of non-AIDS-defining malignancies is increased in HIV-infected individuals. In particular, the risks of Hodgkin's lymphoma and anal, cervical, lung, and oral/pharynx cancers are increased in HIV-infected persons with



Because of the increased risk of cervical cancer, it is particularly important that all older women undergo regular PAP smear screening. The Botswana guidelines recommend that all HIV infected women, sexually active and/or over 18 years of age, should be screened annually. If the initial PAP smear is normal then subsequent screening can be repeated every 3-5 years thereafter.

OTHER COMORBIDITIES

Liver disease has become a leading cause of mortality among persons receiving antiretroviral therapy²⁶. Predictors of liver-related deaths in HIV-infected individuals include increased age as well as CD4+ cell count depletion, uncontrolled viremia, and active hepatitis B virus infection²⁰. While routine screening for hepatitis B is not recommended in Botswana, it is important to consider testing for hepatitis B, in all HIV infected individual with abnormal liver function tests.

Kidney disease. Independent risk factors for the development of renal impairment in HIV-infected patients include CD4+ cell count depletion, incomplete viral suppression as well as advanced age, diabetes, hyperlipidemia, hypertension, elevated baseline serum

creatinine, concomitant nephrotoxic medications, and low body weight.²⁷ Regimens containing tenofovir are still recommended as first line therapy in patients with a creatinine clearance of >60ml/min without other contraindications. However there is an increased risk for renal impairment in older patients, in those with hypertension, lower baseline eGFR and lower CD4+ cell counts, highlighting the importance of regular monitoring in these individuals. Because of the decreasing muscle mass in the elderly a creatinine clearance should be calculated to estimate the renal function more accurately prior to starting Tenofovir.

Lung disease. As well as indirectly causing pulmonary disease as a consequence of bacterial pneumonia and tuberculosis, HIV infection alone is associated with increased rates of chronic obstructive pulmonary disease and pulmonary hypertension²⁸. Given that older patients are at increased risk for pulmonary TB and other pulmonary complications of HIV disease, it is particularly vital that they are screened for TB and tobacco use at every visit.

Frailty. There is increasing evidence that older patients with HIV are at increased risk of ‘frailty.’ Researchers have used numerous terms to define this concept. In one recent study, frailty was defined as the presence of ≥ 3 factors including unintentional weight loss, exhaustion, low physical activity level, and slowness, to provide insight into the overall status of HIV-infected patients²⁹. While there is limited research assessing prevalence of frailty among older persons living with HIV in Botswana, it is very probable that the clinical phenomenon of frailty is more common among older HIV infected persons compared to uninfected persons. ‘

Emerging data suggests that ‘total body weakness’ (which maybe understood as similar to frailty) is a common presenting complaint among persons with HIV presenting for care in Botswana and maybe a useful predictor of poor prognosis.

Drug toxicity. Where possible, it is important to work closely with a pharmacist when prescribing drugs in the elderly. Increased age is also associated with decreased functioning of the liver enzymes that metabolism must drugs. With age there is also a reduction in kidney function. Age-related changes in body composition also influence drug pharmacokinetics by altering the volume in which medications are distributed. All of these contribute to the higher rates of adverse medication effects observed in older HIV-infected patients.³⁰ Furthermore, older people may also be taking multiple different prescriptions, prescribed by different doctors. Preexisting comorbidities also affect the tolerability of antiretroviral therapy. For these reasons, it is always essential to take thorough past medical history and a complete drug history when writing prescriptions for the elderly.

PREVENTION OF HIV INFECTION IN OLDER INDIVIDUALS

Many older patients do not consider themselves to be at risk for acquiring HIV infection. However, many older people are sexually active with multiple partners. It is therefore important that all older persons receive counseling about the importance of safe sex and regular HIV testing. This is especially important for older individuals who have become newly single because of divorce or death of their partners.



SUMMARY

Older persons infected with HIV have increased rates of disease progression before the initiation of therapy, decreased rates of immune reconstitution, decreased rates of survival after therapy is initiated, increased rates of comorbidities that are exacerbated by HIV infection and CD4+ cell depletion, and increased rates of AIDS-defining complications at higher CD4+ counts than those observed for younger patients.

Older patients are also more susceptible to the consequences of metabolic disturbances associated with antiretroviral therapy, to drug-drug interactions because of polypharmacy, and to adverse drug effects due to impaired hepatic and/or renal function.

It is important to employ a multi-disciplinary approach when managing older patients. Nursing and social work professionals can provide important input into addressing the social barriers to health for these patients. Working closely with pharmacy staff to optimize drug regimens and avoid drug interactions in such patients is also important.

Got a clinical question about a complicated medical patient

Or a patient with HIV?

Mike Reid

267 724 78 777

OR

Miriam Haverkamp

267 76516520

Want to read more? Check out the references below:

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