Updates for your practice… April 2014, Volume 4, Issue 27

TLALELETSO

UPDATES FOR YOUR PRACTICE

TREATMENT AS PREVENTION

The Partners study confirms earlier research – Being on antiretrovirals is protective against transmission!

Take Home Message: Results from a large international observational study – the PARTNER study – estimate the risk of HIV transmission within HIV sero-different couples who do use condoms to be VERY LOW when the HIV positive partner is on ART and has an undetectable viral load.

The results were presented at the recent international HIV conference in Boston. They enrolled almost 1,100 couples, none of whom were routinely using condoms and determined how many of the HIV negative individuals acquired HIV when the partner was on treatment.

The main finding was that there were no transmissions within couples from a partner with an undetectable viral load, in what was estimated as 28,000 sexual encounters. Although some of the HIV-negative partners became HIV positive (exactly how many will be revealed in later analyses), genetic testing of the HIV revealed that in all cases the virus came from someone other than the main partner. These results do not prove the safety of having sex without a condom when viral load is undetectable. However, they do provide the most reliable evidence to date on the level of risk for people who have already been having sex without condoms. Other factors affecting risk, including genetic disposition to HIV infection and STIs could make the risks higher on an individual rather than a population-based level.

Reference: Rodger A et al. *PARTNER study.* 21st Conference on Retroviruses and Opportunistic Infections, Boston, abstract 153LB, 2014

Tlaleletso is a monthly publication produced by the Botswana UPenn Partnership, in response to your expressed need for accessible, digestible clinical information. In this issue we focus on new and important research that has been recently published and is relevant to clinical practice in Botswana.

Editor Mike Reid

Abacavir increases risk of heart attack…

New data supports old data that patients on abacavir have significantly increased risk of cardiovascular disease.

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Long acting ARVs may help prevent HIV

Monkey study strengthens evidence that long acting antiretroviral can be used to prevent HIV.

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HIV drugs: hope for drug resistance HIV

Two new drugs – one acting by a novel mechanism offer options to patients with multidrug resistant disease

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Abacavir linked to risk of heart attack: new data, old news

New research supports existing data that abacavir increases the risk of heart disease, especially when prescribed in patients with pre-existing risk of ischaemic heart disease.

In the study, complicated statistical analyses were performed to compare cardiovascular disease and abacavir (ABC) use in a large cohort of HIV-infected patients from over 7 different countries. The researchers found that individuals prescribed abacavir had a 98% increase risk of myocardial infarct (RR 1.98; 95% CI: 1.7-2.3). There was no difference after adjusting for other cardiovascular risk factors (such as hypertension and dyslipidemia).

These findings are important for Botswana because of the types of patients that get started on abacavir in our setting. Note that ABC is a second line drug reserved for patients with chronic kidney disease and anemia. Given that both of these conditions also increase the risk of heart disease, prescribers need to be aware of the risks of CVD in patients on ABC and manage those risks appropriately.

Reference: Sabin C et al. 21st CROI, 3-6 March 2014, Boston. Poster abstract 747 LB

New drugs: MK-1439 and BMS-068. Its always good to have options

Doravirine (MK-1439) is a once daily NNRTI in development that was presented at the recent HIV conference in the USA. It is an important development because it has activity against HIV even when virus has developed resistance mutations that render Efavirenz and Nevirapine ineffective.

BMS-663068 is an attachment inhibitor that works by a novel mechanism to prevent HIV binding to host cells. Early results suggest that it might have a role in patients who have failed all other therapies. Neither of these drugs are available in Botswana yet – and may be prohibitively expensive for some time to come.

MONKEY STUDY SHOWS INJECTABLE PREP POTENTIAL

This recent study measured how long was the protective effect of a injectable antiretroviral –GSK733LA- in monkeys exposed to simian HIV (sHIV). Researchers gave monkeys three injections of GSK733LA a month apart, while also giving them frequent low-dose challenges with simian HIV. They found that no treated monkey became infected over the 12 week period of the study whereas all six untreated monkeys were infected within 11 weeks, and all but one within five weeks.

The researchers stated that while the vaginal levels of the drug were lower than the serum levels, the protection offered may be systemic as well as loca/, ie not totally dependent on drug levels in the vagina.

Editor's comment: This data provides evidence to support a role for long-acting anti-retrovirals to prevent HIV, (in the same way that depo-provera is used to prevent pregnancy). The first human study to gauge efficacy, HPTN 077, is now planned to start soon.

Reference: Radzio J (CROI), Boston, abstract 40LB, 201

CANCER AND HIV: New study results….

A new study has shed light on risk factors for cancers. The researchers were particularly interested in those cancers which are sometimes caused by viruses and which are not considered to be AIDS-defining illnesses. These include anal cancer (linked to human *papillomavirus*, HPV), Hodgkin's lymphoma (linked to Epstein-Barr, a type of herpes virus) and liver cancer (often caused by hepatitis B or C).

Most people are infected with one of these viruses, but they don't usually cause problems. And while cancer rates are higher in people with HIV than in the general population, we need to remember that only a minority of HIV-positive people go on to develop cancer.

In this study, in a group of just under 10,000 Americans living with HIV, there were 65 diagnoses of these cancers in around four years of follow-up. People with a low CD4 cell count were more likely to have cancer. However, what was more important was the way the CD4 count changed after starting to take treatment – people who had a rapid rise in CD4 cell count were *less* likely to have a cancer later on, while people whose CD4 count did not improve much were at greater risk.

This underlines the importance of good adherence to HIV treatment. The researchers also recommend that people living with HIV whose CD4 counts stay low after starting treatment should have more frequent screening for these cancers.

Ref: Yanik EL et al. *Relationship of immunologic response to antiretroviral therapy with non-AIDS defining cancer incidence.* AIDS 28: 979-97, 2014.

PREDICTING KIDNEY DISEASE IN HIV

Without HIV treatment, people with HIV can develop kidney disease. Some antiretroviral drugs have also been linked with increased rates of kidney disease, including tenofovir (also in the combination pills *Truvada and Atripla*).

Tools which can help people living with HIV and their doctors assess the risk of kidney problems would be useful when choosing which antiretroviral drugs to take.

Based on analysis of over 20,000 male patients in the United States, the researchers identified risk factors for kidney disease. They then developed a simple way for doctors to score an individual's risk.

Kidney problems were more likely to occur in men who were over the age of 40, had high levels of glucose or triglycerides (fat) in their blood, had protein in their urine, had high blood pressure, had hypertension or had a low CD4 cell count.

This confirms existing practice in Botswana to screen for kidney disease in all patients before initiating HAART. However, it also provides valuable insight into which patients may subsequently develop kidney problems on HAART at some point in the future.

Ref: Scherzer R et al. *A chronic kidney disease risk score to determine tenofovir safety in a prospective cohort of HIV-positive male veterans.* AIDS, 2014

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Maternal tenofovir and newborn bone mineral content

Maternal tenofovir use is associated with reduction in bone mineral content in neonates in the US….

Tenofovir is currently recommended for pregnant women in Botswana and WHO guidelines. However, little is known about the effect on infant bones with this strategy. Data was recently presented from a study conducted to compare the bone mineral content of newborns exposed and not exposed to tenofovir in utero.

This study enrolled two groups of HIV-exposed, uninfected newborns of at least 36 weeks gestational age at sites in the US and Puerto Rico. The TDF group included infants whose mothers received this drug for at least 8 weeks or more in the third trimester. The non-TDF group included infants whose mothers did not receive TDF in pregnancy at any time. Bone density testing was performed on all infants within 4 weeks of birth.

The study demonstrated that the body bone mineral content was significantly lower in the TDF group. The effect persisted even after controlling for other variables

Editors comment: The big question is what does this data mean? On their own the data are probably not enough to change current recommendations for TDF use in pregnancy. However, it is the first study to address the long-standing concerns about the effect of maternal TDF on infant bones and provides some evidence that these concerns may have been well placed. For right now, we do not know whether this research – from the US – is relevant to Botswana. More research is underway, including one study that will look at bone health and kidneys in infants of women on TDF. It includes several sites in Africa. Results should be available in 2016

Ref: Siberry et al. Lower newborn bone mineral content associated with maternal use of tenofovir disoproxil fumarate. 21st CROI. 3-6 March 2014. Boston. Oral abstract 71.

THIS IS GOODBYE FROM ME! After almost 3 great years in Botswana, my family and I are leaving Gaborone at the end of May. It has been a pleasure working with you. Thank you! Please do keep in touch:

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