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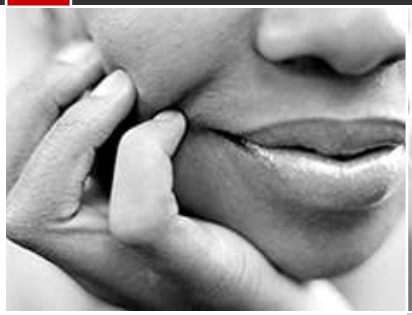

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All doctors with urgent requests such as patient registration, treatment changes, motivations etc. should phone and speak to our interventionists for prompt action. Non urgent communication may still be faxed

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Abacavir and the risk of myocardial infarction

In the previous AfA newsletter we discussed the evidence from cohort studies showing that there was an increased risk of myocardial infarction in patients on protease inhibitors[1] and the nucleoside reverse transcriptase inhibitors (NRTIs) abacavir (ABC) and didanosine (ddI).[2] The strength of the association with myocardial infarction and the NRTIs was stronger for ABC than ddI.

A sub-analysis of the SMART study (which randomised patients to interrupt or continue ART) has just been published showing that ABC, but not ddI or other NRTIs, was associated with myocardial infarction and other atherosclerotic complications.[3] Interestingly, in the SMART study patients on ABC had higher concentrations of inflammatory markers associated with increased risk of myocardial infarction (including CRP) compared with patients on other NRTIs. Finally, the SMART study also found that myocardial infarctions occurred mostly in patients with other cardiovascular risks.

By contrast, a conference presentation at the 2008 International AIDS Conference reported no increased risk in 54 ABC clinical trials.[4] Generally data from randomised controlled trials trumps that from cohort studies. But in most of the randomised controlled trials follow up was short term and selection bias may have excluded patients at risk of myocardial infarction.

Clinicians need to address modifiable risk factors in all patients on ART. As per our prior recommendation, if modifiable risk factors exist, it may be prudent to avoid ABC.

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New insights in infant feeding – breast versus formula

Infant feeding continues to be an area of controversy and concern for HIV-exposed and infected infants. Under optimal circumstances, in adequately resourced homes, replacement feeding is recommended as it is safe and does not transmit HIV. However, breast-feeding protects against diarrhoeal disease.

There are circumstances where breast-feeding is preferable. It must be given exclusively for the first 4 to 6 months of life, after which supplemental feeding is essential. New data has shown, in resource poor settings (rural Kwazulu-Natal), both exclusive breast-feeding and replacement can be safely given, provided that the caregivers are adequately supported and educated.[1] In an intriguing study by the same team, mixed feeding with solids was associated with far higher transmission than when breast milk was given with formula.[2] New data from Zambia shows that early abrupt weaning is of no benefit.[3] The viral load in breast milk of mothers increases dramatically after abrupt weaning[4], probably due to engorgement and mastitis and could facilitate transmission of HIV should the mother breast feed again during this period.

An emerging concept is the use of antiretrovirals to prevent breast-feeding transmission. Giving breast-fed, HIV-exposed uninfected infants nevirapine for 14 weeks, resulted in significant, but not absolute protection, which waned as breast-feeding continued.[5] The other strategy is to give HAART to breast-feeding mothers for the duration of breast-feeding. A number of prospective non-randomized studies have shown benefit, probably reducing transmission 3- fold when compared to historical data.[6, 7] For infants infected despite prophylaxis, the likelihood of resistance is extremely high, unfortunately.

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New Southern African HIV Clinicians Society Guidelines for Postexposure Prophylaxis

New guidelines for PEP management have recently been published in the winter 2008 edition of the South African Journal of HIV Medicine. Conceived specifically for the Southern African region, these represent a significant departure from previous guidelines.

Recognising that the Sothern African region differs significantly from other parts of the world in terms of very high HIV and hepatitis B prevalence, the committee advocates PEP management strategies based on an increased appreciation of the high risk nature of HIV exposure in this region. While previous guidelines have separated Occupational (Health Care Worker) exposure and Non Occupational exposure (Sexual exposure, intravenous drug users, and other) the similarities in both risk and management are recognised, and guidelines are combined in the document. Finally, the need for simplified regimens and algorithmic management structures in the PEP scenario is identified. A large portion of the document deals with the prevention of exposure, particularly in the occupational setting. Strategies to reduce the need for PEP are highlighted.

Where PEP is felt to be justified, a 3 drug strategy is advocated, although the potential risk to optimal adherence is noted and strategies to maintain optimal adherence for a full 28 days are discussed. The role of counselling, side effect management, and aggressive follow-up strategies to ensure completion of full course PEP regimens are emphasised.

Cont.

ARV regimens for PEP are suggested as follows:

1. Nucleoside backbone:
    a. Stavudine + Lamivudine
    b. Tenofovir + Emtricitabine
    c. Zidovudine + Lamivudine

2. Third agents:
    a. Lopinavir/ ritonavir
    b. Efavirenz
    c. Atazanavir/ritonavir
    d. Saquinavir/ritonavir

The use of 3 drug regimens in previously assessed “low risk” settings such as occupational mucosal bloodsplashes and oral sex remains controversial, but in the absence of data to the contrary, the committee advocates 3 agents in these settings.

Further information pertains to the baseline and ongoing investigation of people on PEP, as well as the diagnosis and management of intercurrent illnesses and ARV side-effects. Co-morbidities (such as tuberculosis) affecting the choice of PEP are outlined. Management of Hepatitis B exposure is also addressed.

The guidelines represent a comprehensive approach to the management of HIV and other blood borne viral exposure.

Switching antiretrovirals for lipodystrophy

Lipodystrophy is a distressing complication of long term antiretroviral therapy (ART). Lipodystrophy consists of two separate abnormalities of fat distribution: fat loss (lipoatrophy) or fat accumulation. Some patients have only one abnormality of fat distribution whilst others have either lipoatrophy or fat accumulation.

Lipoatrophy is subcutaneous fat loss – it is best appreciated in the face, limbs & buttocks. Lipoatrophy is linked to the thymidine analogue nucleoside reverse transcriptase inhibitors (NRTI), stavudine (d4T) and zidovudine (AZT), particularly d4T. Switching to a non-thymidine NRTI will result in very gradual improvement of lipoatrophy – evidence for improvement has been shown for tenofovir and abacavir. Patients should be warned that improvement is very slow – they are unlikely to notice much change before about 2 years (but DEXA scans show improvement after a year). It is unclear whether lipoatrophy is fully reversible. Therefore it is important to recognise lipoatrophy early in order to switch, or to avoid thymidine analogue NRTIs if possible.

Fat accumulation occurs intra-abdominally, in the breasts and as the unsightly “buffalo hump”. There is a widespread belief that fat accumulation is due to protease inhibitors, but this is not the case. The risk is just as great with non-nucleoside reverse transcriptase inhibitors. There is also no data showing that any particular protease inhibitor is associated with a different risk of fat accumulation. Therefore there is as yet no scientific basis for switching antiretrovirals for fat accumulation. Patients need to be counselled about this. Cosmetic surgery may be an option for breast enlargement or “buffalo humps”, but few medical aid schemes will fund this. Exercise and diet have been shown to be effective for intra-abdominal fat accumulation. This visceral fat is associated with insulin resistance and dyslipidaemia, thus it is important to measure both lipids and glucose when intra-abdominal fat accumulation occurs. The increased cardiovascular risk associated with visceral fat accumulation is another good reason for promoting exercise and healthy diet. The only medical therapy that has shown promise for fat accumulation is growth hormone or its analogues, unfortunately long term therapy is required and growth hormone is unaffordable and the growth hormone analogues are not registered in South Africa.

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