

From: Janet Giddy [jgiddy@hebron.za.net]
Sent: 02 September 2005 10:08 AM
To: Doctor's Dialogue
Subject: [mailadoc] Lactic Acidosis Alert

For those of you working in the ART field:

At McCord's ART clinic, we are becoming increasingly concerned about the problem of lactic acidosis in our patients on HAART. We are seeing increasing numbers of patients with this problem, as we have more people on HAART for longer (over the last 5 years we have started about 1500 patients on ART and at present have about 1200 on treatment).

So, far we have had over 20 documented cases (there may be more who have died at home or in other hospitals, who we do not know about) in the last year. We have a high index suspicion of the condition and we keep all records of patients who develop lactic acidemia or acidosis. We have been doing an analysis of the cases and there are clear trends emerging. All of the patients were on a D4T containing regimen e.g. 1a / 1b (D4T, 3TC, EFV / NVP), or DDI / D4T (from GP's), all but 2 of the patients were female, and most have a raised BMI. The majority have been on ART for 6-12 months. The mortality appears to be around 40% (The most distressing case was of a senior staff member working in the hospital who died about 3 days after being admitted in the ICU of the Inkosi Albert Luthuli Academic hospital).

The concern we feel about D4T as a drug is shared by other clinicians - we discussed this at the National AIDS conference with people like Francois Venter, who works for RHRU, based in JHB. Apart from lactic acidosis, we see a lot of peripheral neuropathy, some hepatitis as well as some lipodystrophy. Of all these conditions, lactic acidosis concerns us the most as it is unpredictable and often fatal.

As a result of this growing problem and our concern about it, we feel we need to highlight the problem to the KZN Dept of Health as well as other clinicians working with patients on ART.

We had a meeting with Chris Jack and Thilo Govender (KZN DoH) and some of the other ART sites on 19/8/05. The issue was definitely taken very seriously by the DoH. We are not the only site to have picked up the problem, we just happen to have collected the data for a useful case series.

The immediate concern is to validate the findings and collect more evidence. We spent time discussing a provincial pharmacovigilance strategy which would also incorporate reporting on serious adverse events, by certain sentinel sites. Members of the group were tasked with developing case definitions and forms to be used for this reporting. There will be a follow up meeting on 27th September, to take the process forward. So, sites in KZN, expect to hear something about reporting adverse events soon.

The point was made by a visiting ART expert that in future we will need to select patients for ART regimens more carefully according to certain profiles, and that we will need some flexibility, nuance and choice in regimens.

At McCords, after a lot of discussion amongst the clinicians, we have decided to try and prevent lactic acidosis by NOT starting female patients with a BMI > 28 on regimen 1a/b, if possible. We plan to use combivir (AZT / 3TC) and EFV or NVP, in women with a BMI > 28 if they have an Hb > 9. We are also starting to switch patients with this risk profile who are now on regimen 1a to combivir. This decision is not in line with the present Dept of Health protocols. However, we did inform others at the meeting that this is what we are doing and no objection was raised.

We are concerned about any extra adverse publicity about ART, considering all the panic in South Africa about toxicity. However we are balancing this reality against our concerns about patients and the need to inform medical colleagues. We have presented this information at the SA HIV Clinician's Society meeting in Durban in August.

In the long run, I think that the Dept of Health is going to have to make more ARV's available (e.g. tenofovir) and probably restrict the use of D4T.

I hope this is of help for those of you in the ART business. We have developed protocols and guidelines (and Francois Venter also has some) about the issue of lactic acidosis, if anyone is interested.

Have a good weekend
Janet