An unethical study?

May 18, 2010 By Joseph Sonnabend, MD

The combination of TB and HIV is devastating. Both are bad enough on their own, but together, each makes the other even more dangerous. This destructive combination is seen more frequently in South Africa than anywhere else in the world.

SAPIT is the name of a trial in South Africa that attempted to determine when treatment for HIV should be started in relation to TB treatment. The timing of the start of treatment for HIV can be a problem. When treatment for HIV is started it may temporarily make the manifestations of TB more severe as part of an immune reconstitution inflammatory syndrome - or IRIS. For these reasons trials had to be done to determine when best to start the anti-HIV drugs.

TB is treated with an intensive 2-3 month course of anti-TB drugs followed by a simplified 4-5 month continuation course. SAPIT looked at three time points for starting anti-HIV therapy. This was initiated together with anti-TB treatment either in the intensive phase or in the continuation phase. The third group started anti-HIV drugs after treatment for TB had been completed.

The study was stopped because there was a higher rate of death among those whose HIV treatment was delayed until after the completion of TB treatment. They had to wait on average about 9 months to receive their treatment for HIV with some waiting as long as 11 months. Most deaths occurred in patients who had less than 200 CD4 lymphocytes on study entrance.

While the study did show that early treatment for HIV during TB treatment is better than waiting, critics of the study contend that this result could have been obtained without allowing individuals with under 200 CD4 lymphocytes to wait for up to 11 months before being treated for HIV.

The ethical flaws of this study are described in a Hastings Center bioethics forum. The study report itself appeared in the New England Journal of Medicine last February.

Are the criticisms of SAPIT justified? It's unquestionably important to know when it's best to start anti-HIV treatment in a person treated for TB. At the same time it's unquestionably important to not allow a person with less than 200 CD4 lymphocytes to wait for up to 11 months to receive treatment for HIV.

Both of these imperatives could have been met. An answer could have been obtained without endangering the lives of people with fewer than 200 CD4 cells.

Francois Venter of the University of the Witwatersrand, the medical school in Johannesburg where I trained is reported to have said that he would not have allowed his patients to have entered the

trial.

Gary Maartens of the University of Cape Town was reported by Jon Cohen in Science to have said:

"We did not need a clinical trial to tell us that deferring lifesaving therapy for 8 months in patients with advanced disease results in higher mortality."

He also pointed out that an answer could have been obtained more safely by enrolling people with 200-500 CD4 lymphocytes.

The Principal investigator was a South African epidemiologist called Salim Abdool Karim, who was reported to have been stunned by the criticisms. So was Dr Wafaa El Sadr, who according to Jon Cohen, was flabbergasted. She said that SAPIT would be cited as one of the landmark studies in HIV/TB.

It may indeed be cited, but as a study in which people with under 200 CD4 lymphocytes were allowed to wait for up to 11 months before being treated.

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