Circumcision May Lower HIV Risk, Survey Finds

BY ED SUSMAN

CAPE TOWN, SOUTH AFRICA — Circumcision appears to exert a protective role among men who have sex with men, according to survey findings from nearly 400 men in Soweto, South Africa.

The evidence suggests that circumcision lowers the risk of infection with HIV for men who nearly exclusively practice insertive anal intercourse or receptive anal intercourse, according to a presentation at the International AIDS Society Conference on HIV Pathogenesis, Treatment, and Prevention.

The risk of HIV infection in an uncircumcised man who practiced insertive sex with other men was 4.5 times higher than in a circumcised man.

However, a clinical trial to prove the effectiveness of circumcision will be required, according to the study's lead investigator, Tim Lane, Ph.D., assistant professor in medicine at the Center for AIDS Prevention Studies at the University of California, San Francisco. During his poster presentation, Dr. Lane added that "the acceptability and ethical implications of male circumcision in the men who have sex with men must be assessed prior to initiating clinical trials."

Dr. Lane and colleagues recruited 363 men who lived in Soweto between February and August 2008. The men completed a one-time behavioral survey, focusing particularly on their sexual behavior with their last five most recent partners in the previous 6 months.

HIV status was determined through rapid antibody testing; the prevalence of HIV infection was 13%. A total of 36% of the men were circumcised.

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A circumcised man who practiced receptive sex with other men had a nonsignificant 1.4 times greater risk of HIV infection than a circumcised man who practiced insertive sex.

Uncircumcised men who practiced receptive sex with other men were at 7.5 times the risk of HIV infection than circumcised men who practiced insertive sex.

In the population studied, the vast majority of men who had sex with men practiced either insertive or receptive sex exclusively, Dr. Lane said. "Only 14% of the men said they practice both insertive and receptive sex," he said. "About 40% of the men said they also had sex with women."

"This study may open the door for other studies," said Dr. Naomi Bock, medical officer at the Global AIDS Program, at the Centers for Disease Control and Prevention, Atlanta.

However, the study findings are limited by the fact that the information was self-reported and because most of the men said that they engaged in either receptive or insertive sex.

The Soweto Men's Study was supported by the National Institute of Mental Health; the Peninsula Community Foundation; the Hurlbut-Johnson Fund; the UCSF Research Institute Jesse Miller Memorial Fund; United States Agency for International Development; and the President's Emergency Plan for AIDS Relief. The researchers did not disclose any financial conflicts. The International AIDS Society does not require financial disclosures. ■

Vaginal Microbicide Provides 24-Hour Protection in Study

BY KATE JOHNSON

MONTREAL — A single application of a vaginal microbicide gel resulted in persistently protective levels 24 hours later, with no significant side effects, reported Dr. Katherine Bunge of Magee-Womens Hospital in Pittsburgh.

This preliminary safety and persistence information "justifies daily dosing," she said at the annual meeting of the Infectious Diseases Society for Obstetrics and Gynecology.

The phase I, single-center trial of the nonnucleoside reverse transcription inhibitor UC-781 randomized 60 healthy women at a ratio of 2:1 to either treatment or placebo, explained Dr. Bunge, who had no disclosures to declare.

The women (mean age 26 years) also were randomized to product exposure durations of either 2, 4, or 8 hours. They received a physician-administered dose of vaginal gel and were then required to stay in the research facility for their assigned time period, after which specimens were collected by cervicovaginal lavage (CVL) and vaginal swabs. The subjects then returned 1 day, 1 week, and 1 month later for follow-up.

Urogenital irritation was assessed by pelvic exam and symptoms, microscopic genital changes were assessed by colposcopy, systemic safety was assessed by history and laboratory parameters, vaginal flora was quantified, and cervical cytokines were measured.

"These are fairly typical safety measures in any phase I trial of a microbicide, but what we attempted to do that hadn't really been looked at before was to figure out a way to determine the persistence of this vaginally applied drug that we didn't really expect to be absorbed," she said.

To that end, plasma drug levels were measured both immediately after the patients' timed exposure and then again a day later; drug levels were measured in CVL and vaginal swab specimens, which also were collected at those two time points, Dr. Bunge explained.

At 24 hours post exposure, two patients had detectable levels of UC-781 in their plasma, but in both cases the levels were considered below the limits of quantification, she said.

In contrast, "the most important and interesting data" showed persistence of the drug in the vagina, she said. Eight hours after treatment, 100% of the women had detectable drug levels in CVL specimens and 90% had detectable levels in vaginal swab specimens. At 24 hours post exposure, 93% had detectable levels after a second CVL, and 42% showed detectable levels after a second vaginal swab.

Dr. Bunge pointed out that even after 24 hours, the median concentration of UC-781 in CVL specimens was 4,965 pmol/mL. "The inhibitory concentration of UC-781 is 2 pmol/mL, so in fact at 24 hours after washout, the median concentration of detectable drug in CVL samples was a thousand times the inhibitory concentration."

Among the 197 adverse events (121 in the treatment group and 76 in the placebo group), 85% were classified as mild. There were four severe events but all were deemed not related or probably not related to treatment, said Dr. Bunge.

"There was no difference between groups in terms of concentration of microorganisms at every time point, or proinflammatory cytokines—and most importantly in the treatment group, there was no shift in these concentrations," she said. A total of 18 patients had new colposcopic findings on follow-up, but all were considered superficial. ■

Earlier HIV Therapy Would Save Lives, Model Shows

BY MICHAEL SMITH

CAPE TOWN, SOUTH AFRICA — In South Africa, starting anti-HIV treatment earlier than recommended in current World Health Organization guidelines for the developing world would save lives and reduce opportunistic infections.

Such a change in clinical practice would also be cost effective, according to Dr. Rochelle Walensky of the Massachusetts General Hospital in Boston and colleagues.

The conclusions are based on a mathematical model of the HIV epidemic in South Africa and are intended to guide clinical practice until several formal clinical trials studying the issue are complete, Dr. Walensky and colleagues reported (Ann. Intern. Med. 2009; 151).

The researchers also reached similar conclusions using data from Cote d'Ivoire and presented them in a poster at the International AIDS Society Conference on Pathogenesis, Treatment, and Prevention.

The current standard for starting HIV treatment in South Africa followed WHO guidelines for the developing world: A patient is eligible for treatment when his or her CD4-positive T-cell count falls below 200 per cubic millimeter of plasma or when there is an AIDS-defining illness.

But guidelines in the developed world now suggest starting at a higher level—350 cells per cubic millimeter—and some recent studies have suggested that clinical outcomes would be even better if the threshold were set to 500 cells or more.

Clinical trials are underway in Africa to settle the issue, but they won't report for another 5 years. In the meantime, Dr. Walensky and colleagues said, their model may provide guidance to clinicians.

They explained that the bottom line is that in all cases, starting therapy at the 350-cell threshold saved more lives, prevented more disease, and cost more, compared with a threshold of 250 cells.

The researchers estimated that such a threshold would mean 4.7 million people would be eligible for therapy in South Africa over the next 5 years.

Under the assumption that 10% of those patients would be identified and given care using the 350-cell threshold would result in 1,599,900 deaths, compared with 1,622,000 for the lower level, the investigators said.

There would also be 1,664,500 opportunistic infections, compared with 1,689,700 using the lower threshold.

On the other hand, costs would increase by $141,977,100 (U.S.), using the higher threshold, they said. At the other extreme, if all eligible patients were identified and linked to care, the higher threshold would avert 221,000 opportunistic diseases and 253,000 deaths.

The additional costs in that scenario would rise to $1.4 billion, the researchers said.

Either scenario would increase long-term survival by at least 7.9 years, with an average per-person life expectancy of 3.8 years with no therapy and 12.5 years at the 350-cell threshold.

Compared with the 250-cell threshold, starting at the 350-cell threshold had an incremental cost-effectiveness ratio of $1,200 per year of life saved, the researchers said.

"It is probably both effective and cost effective" to allow therapy to start at the higher level, the researchers said.

The study was supported by the National Institute of Allergy and Infectious Diseases and the Doris Duke Charitable Foundation.

The researchers did not report conflicts. ■