Rakai STD Control for AIDS Prevention Project

Project Summary, May 1995

The Rakai STD Control for AIDS Prevention Project is a community trial to assess the effects of intensive, population based STD control, via mass treatment, on STD incidence/prevalence and HIV transmission.

RF 91079
A31

Project hypotheses:

1. Reductions in STD prevalence and incidence will result in reductions in HIV transmission and acquisition.
2. Reductions in STD prevalence and incidence can be accomplished by population-based mass treatment, coupled with active surveillance.

Study design:

The goal of this single blinded, population-based intervention trial, is to enroll a population of 5,200 adults (approximately 4,200 of whom are HIV seronegative) into each of two study arms.

Treatment arm subjects, reside in 29 communities, which have been grouped into 5 "superclusters" each comprised of 5 to 6 communities. The superclusters have been designed to encompass social/sexual networks. All adults aged 15-59, resident in the treatment communities, are eligible for study enrolment. All consenting eligible persons are offered mass treatment in the home, twice yearly, whether symptomatic or not. The STD mass treatment has been designed around a highly effective, single oral dose therapeutic regimen, and consists of azithromycin 1 gram, ciprofloxacin 250 mg, metronidazole 2 grams, with supplementary IM benzathine penicillin offered to persons with serological evidence of syphilis. The regimen is modified for pregnant women, who receive azithromycin 1 gram, cefixime 400 mgs and IM penicillin prn. The drugs are delivered in the home over a two day period, in order to reduce potential GI side effects and to increase compliance.

Adults in 29 equivalent communities grouped into 5 superclusters are being enrolled as a control population, receiving a twice annual regimen of anthelminths and multivitamins.

All consenting subjects in both the treatment and control arms are visited twice yearly for treatment. During each of these two annual home visits, they are also administered a sociodemographic/behavioral/health survey, and are asked to provide a venous blood sample (for HIV-1, syphilis, HSV-2 and *H.ducreyi* serology) and urine (ligase chain reaction testing for *C.trachomatis* and *N.gonorrhoeae*). In addition, women provide a self-administered vaginal swab for BV gram stain and *T.vaginalis* culture (InPouch TV™ technique). All interviews and sample collection occurs in the home.

Preliminary results:

As of the end of May, 1995, the project will have fully enrolled 8,700 of the projected cohort of 10,400 persons (evenly divided between treatment and control arms). As of early May, the HIV-1 prevalence rate was just over 17% overall. We thus have approximately 7,100 HIV- persons fully enrolled, versus our target of 8,000 (evenly divided between the two arms). At current rates of accrual, enrolment of the entire cohort will be completed in June, as described in the original schedule. (Full enrolment refers only to those permanent subjects on whom questionnaire and a

serological sample have been collected. Another 850 bloods and truncated questionnaires have been collected on "transients": persons present in the household at the time of the survey, but who indicate they reside in the community less than 6 months of every year. Such persons also receive mass treatment. Some proportion of these transients will become permanent residents and will be folded into the main study in subsequent rounds.)

Compliance with sample collection has been excellent during the baseline round. In both treatment and control communities, among persons eligible for enrolment (ie., persons aged 15-59, permanently resident in study communities), 91% have consented to enrolment. Among consenting subjects, 90% have provided a serological sample (for HIV, HSV-2, *H.ducreyi* and syphilis) and 94% have provided a urine sample (*C.trachomatis* and gonorrhea). In addition, 96% of women have correctly provided a self-administered vaginal swab for trichomonas culture and BV gram stain.

Treatment compliance has also been high. In treatment arm communities, 94% of enrolled persons have accepted the first day treatment (azithromycin and ciprofloxacin for non-pregnant subjects; azithromycin alone for pregnant women). Just over 95% of persons with serological evidence of syphilis accept penicillin IM on day 2. Approximately 90% of non-pregnant subjects accept second day treatment (metronidazole 2 grams), and 92% of pregnant subjects have accepted second day cefixime (400 mg). In the control arm, we have had a 96% compliance with anthelminth and multivitamin treatment.

Preliminary lab data suggests high baseline levels of STDs, and good comparability between study arms. As of late April, HIV prevalence in the Treatment arm was 18.0%, compared to 17.4% in the control. Syphilis serology was running 15.3% and 17.0% in treatment and control arms, respectively; trichomonas culture was positive in 23% of treatment arm women and 25% in the control arm.

Of the first 200 BV slides read (obviously a small subsample to date), 52% had evidence of BV, and 12.9% was grade 9 or 10. Urinary LCR testing is currently in progress; serological samples are being sent to the CDC and Johns Hopkins for *H. ducreyi* and HSV-2 testing. (Early results suggest an 8% prevalence of chlamydia in pregnant women.)

The project will begin the second survey/sample collection/treatment round in July, 1995, and STD prevalence and incidence in treatment and control arms will be assessed.

With Rockefeller and MotherCare funds, we have initiated supplementary data collection on pregnant women and their offspring, in order to determine the effects of intensive STD control on reproductive health. We have also initiated Adverse Experience reporting, are carrying out a systematic 10% survey of all subjects regarding reported side effects, and are conducting a substudy of short term effects of mass STD treatment on vaginal flora. To date, approximately 10% of treatment arm subjects report limited GI upset (as predicted), with no serious side effects noted.

Preliminary conclusions:

The mass STD treatment strategy is feasible in the Rakai district setting. Sample collection in the home is also feasible, and preliminary results suggest high prevalence of STD.

Other accomplishments

We have published a letter in Lancet regarding trichomonas culture from self-administered vaginal swabs for the assessment of community trichomonas prevalence, have had two abstracts accepted for the August STD meetings in New Orleans, and are preparing additional abstracts for the International African AIDS/STD Conference to be held in Kampala in December, 1995.