

Monthly antibiotic chemoprophylaxis for reducing incidence of HIV-1 and Sexually transmitted infections

CITATION

Kaul R, Kimani J, Nagelkerke N, et al for the Kibera HIV Study Group. Monthly antibiotic chemoprophylaxis and incidence of sexually transmitted infections and HIV-1 infection in Kenyan sex workers: a randomised controlled trial. *JAMA* 2004;291:2555-2562

RESEARCH QUESTION

Does monthly antibiotic chemoprophylaxis reduce the incidence of sexually transmitted infections (STIs) and HIV-1?

THE STUDY DESIGN

Randomized double blind placebo controlled trial

STUDY SETTING

Kibera, urban slum area of Nairobi, Kenya
Ethics approval obtained.
May 1998 – July 2002

PARTICIPANTS

Included: self-identified female sex workers; negative HIV-1 at baseline; current engagement in sex work; age 18 years and older; expected residence in Nairobi for at least 2 years; no history of adverse drug reaction to macrolide antibiotics.

INTERVENTIONS

All participants received HIV prevention services

- peer and clinic counselling on reducing high risk behaviour for HIV-1 infection
- provision of free male condoms
- prompt treatment of any symptomatic STI
- screening and treatment of asymptomatic STIs every 6 months

Intervention group: 1g oral azithromycin per month

Control: matching placebo

Administered as directly observed therapy; 2 years.

OUTCOMES

Primary: Incidence of HIV-1 infection

Secondary: Incidence rates of bacterial STIs (*N Gonorrhoea*; *C Trachomatis*; *Trichomonas vaginalis*; *Treponema pallidum*; *Haemophilys ducreyi* and *bacterial vaginosis*)

RISK OF BIAS (Risk Scale: Low – Moderate – High)

SELECTION BIAS: Low - moderate

Self identified female sex workers were block randomised in groups of 50. Clinic staff assigned study numbers consecutively at enrolment. Allocation concealment not reported. Baseline characteristics including risk-taking behaviour (determined using behavioural questionnaire) for HIV-1 and other STIs were generally matched for treatment and placebo groups, but not so between those declining enrolment and enrolees.

PERFORMANCE BIAS: Low

(ie: *What else happened that may have affected the result?*)

All participants received HIV prevention services. Placebo controlled trial. Intervention or placebo was administered as directly observed therapy from numbered containers that were packaged,

labelled and shipped by the Misericordia General Hospital pharmacy. Neither the study staff nor the participants were aware of group assignments. All participants compensated for travel expenses and lost revenue - US \$1.65 – 2.48 per study visit.

DETECTION BIAS: Low - moderate

Do not mention whether laboratory staff was unaware of assignment.

Outcome measured using laboratory tests – validity of tests not reported.

- Blood tested for HIV-1 using ELISA and for syphilis using RPR (Rapid plasma reagen)
- Urine and cervical swabs tested for *N Gonorrhoe* (NG) and *C Trachomatis* (CT) using PCR and culture (NG)
- *Trichomonas vaginalis* (TV) detected through In Pouch culture, *Bacterial vaginosis* (BV) using Nugent score and *Candidiasis* using gram stain.

Seroconversion occurring between enrolment & first 3-month follow-up visit was assumed to be due to HIV-1 infection acquired prior to enrolment. STI defined as incident when preceding test had been negative and as incident syphilis when RPR titre increased from < 1:8 to 1:8 and greater.

ATTRITION BIAS: Low-moderate

	Azithromycin	Placebo
Started	230	236
Completed 2 years follow-up	169	172
Discontinued early*	61	64
Primary analysis	205	211

* Of those who discontinued early 75 attended at least one 3-month clinic visit for repeat HIV-1 serologic testing and no follow-up serology results were available for the remaining 50.

STUDY FINDINGS

890 screened - 251 HIV-1 +ve - 173 declined = 466 randomised.

Because of the large number of censored observations (50/466), rates calculated with CATmaker would be incorrect. Incidence rates, rate ratios (RR) and confidence intervals from the paper are presented.

Outcome	Treatment	Incidence rate per 100 person-years	RR (95%CI)
HIV - 1	Azithromycin	4	1.2
	Placebo	3.2	0.6-2.5
NG PCR	Azithromycin	2.6	0.46
	Placebo	5.7	0.31-0.68
CT PCR	Azithromycin	6.3	0.38
	Placebo	14.5	0.26-0.57
TV	Azithromycin	11.3	0.56
	Placebo	20.4	0.40-0.78
Syphilis	Azithromycin	3.9	1.02
	Placebo	3.8	0.54-1.95
BV	Azithromycin	53	0.91
	Placebo	57.4	0.77-1.10

ADVERSE EVENTS

GIT related adverse events with no significant difference between two groups.

COMMENTS

Chemoprophylaxis reduced the incidence of some STIs but did not reduce HIV-1 incidence. Need further exploration of HIV transmission dynamics.

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