Male circumcision for prevention of heterosexual acquisition of HIV in men (Review)

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ABSTRACT

Background

Male circumcision is defined as the surgical removal of all or part of the foreskin of the penis and may be practiced as part of a religious ritual, as a medical procedure, or as part of a traditional ritual performed as an initiation into manhood. Since the 1980s, over 30 observational studies have suggested a protective effect of male circumcision on HIV acquisition in heterosexual men. In 2002, three randomised controlled trials to assess the efficacy of male circumcision for preventing HIV acquisition in men commenced in Africa. This review evaluates the results of these trials, which analysed the effectiveness and safety of male circumcision for preventing acquisition of HIV in heterosexual men.

Objectives

To assess the evidence of an interventional effect of male circumcision for preventing acquisition of HIV-1 and HIV-2 by men through heterosexual intercourse

Search strategy

We formulated a comprehensive and exhaustive search strategy in an attempt to identify all relevant studies regardless of language or publication status (published, unpublished, in press, and in progress). In June 2007 we searched the following electronic journal and trial databases: MEDLINE, EMBASE, and CENTRAL. We also searched the electronic conference databases NLM Gateway and AIDSearch and the trials registers ClinicalTrials.gov and Current Controlled Trials. We contacted researchers and relevant organizations and checked reference lists of all included studies.

Selection criteria

Randomised controlled trials of male circumcision versus no circumcision in HIV-negative heterosexual men with HIV incidence as the primary outcome.

Data collection and analysis

Two review authors independently assessed study eligibility, extracted data, and graded methodological quality. Data extraction and methodological quality were checked by a third author who resolved differences when these arose. Data were considered clinically homogeneous and meta-analyses and sensitivity analyses were performed.
Main results

Three large RCTs of men from the general population were conducted in South Africa (N = 3,274), Uganda (N = 4,996) and Kenya (N = 2,784) between 2002 and 2006. All three trials were stopped early due to significant findings at interim analyses. We combined the survival estimates for all three trials at 12 months and also at 21 or 24 months in a meta-analysis using available case analyses using the random effects model. The resultant incidence risk ratio (IRR) was 0.50 at 12 months with a 95% confidence interval (CI) of 0.34 to 0.72; and 0.46 at 21 or 24 months (95% CI: 0.34 to 0.62). These IRRs can be interpreted as a relative risk reduction of acquiring HIV of 50% at 12 months and 54% at 21 or 24 months following circumcision. There was little statistical heterogeneity between the trial results ($\chi^2 = 0.60; df = 2; p = 0.74$ and $\chi^2 = 0.31; df = 2; p = 0.86$) with the degree of heterogeneity quantified by the $I^2$ at 0% in both analyses. We investigated the sensitivity of the calculated IRRs and conducted meta-analyses of the reported IRRs, the reported per protocol IRRs, and reported full intention-to-treat analysis. The results obtained did not differ markedly from the available case meta-analysis, with circumcision displaying significant protective effects across all analyses.

We conducted a meta-analysis of the secondary outcomes measuring sexual behaviour for the Kenyan and Ugandan trials and found no significant differences between circumcised and uncircumcised men. For the South African trial the mean number of sexual contacts at the 12-month visit was 5.9 in the circumcision group versus 5 in the control group, which was a statistically significant difference ($p < 0.001$). This difference remained statistically significant at the 21-month visit (7.5 versus 6.4; $p = 0.0015$). No other significant differences were observed.

Incidence of adverse events following the surgical circumcision procedure was low in all three trials.

Reporting of methodological quality was variable across the three trials, but overall, the potential for significant biases affecting the trial results was judged to be low to moderate given the large sample sizes of the trials, the balance of possible confounding variables across randomised groups at baseline in all three trials, and the employment of acceptable statistical early stopping rules.

Authors’ conclusions

There is strong evidence that medical male circumcision reduces the acquisition of HIV by heterosexual men by between 38% and 66% over 24 months. Incidence of adverse events is very low, indicating that male circumcision, when conducted under these conditions, is a safe procedure. Inclusion of male circumcision into current HIV prevention measures guidelines is warranted, with further research required to assess the feasibility, desirability, and cost-effectiveness of implementing the procedure within local contexts.

Plain Language Summary

Male circumcision for prevention of heterosexual acquisition of HIV in men

Results from three large randomised controlled trials conducted in Africa have shown strong evidence that male circumcision prevents men in the general population from acquiring HIV from heterosexual sex. At a local level, further research will be needed to assess whether implementing the intervention is feasible, appropriate, and cost-effective in different settings.