Male circumcision offers significant protection to men against the acquisition of HIV during heterosexual sex. The conclusions of this review would be applicable to all under-resourced settings, especially where circumcision is already practised and where the heterosexual HIV transmission is predominant.

RHL Commentary by Bamigboye AA and Igberase GO

1. INTRODUCTION

In 2008, 33.4 million people worldwide were living with HIV/AIDS. HIV infection continues to be a global pandemic and a scourge of our generation, with 2.7 million new infections and 2.1 million AIDS deaths in 2008 (1). Sub-Saharan Africa remains the worst hit region, accounting for 67% of the global burden of HIV prevalence (1). In this region HIV is spread predominantly via heterosexual intercourse (1).

Male circumcision is the complete or partial surgical removal of the foreskin of the penis, and is one of the oldest known surgical interventions carried out for religious, societal or medical reasons (2). Male circumcision has been promoted for a variety of reasons: as a manifestation of faith; a method of improving hygiene (3); for initiation into manhood; and as a method of preventing sexually transmitted and (4) urinary tract infections and discouraging masturbation (5).

The present review (6) is the October 2009 update of the previous version (September 2008) that had included over 35 observational studies conducted since the 1980s. In the previous version, the authors had observed a protective effect of between 38% and 66% for male circumcision with regard to the acquisition of HIV by heterosexual men, although the results were deemed inconclusive owing to heterogeneity between the studies (6). Following the publication of three large randomized controlled trials since 2005, the review (6) was updated to assess the effect of male circumcision for preventing the acquisition of HIV-1 and HIV-2 by men through heterosexual intercourse.

2. METHODS OF THE REVIEW

On 14-15 June 2007, the review authors searched MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials for published papers and trials. The authors also searched databases of conference abstracts and searched reference lists of articles and contacted the authors of included studies as required. The authors conducted a careful assessment of the quality and potential source of bias in the identified studies. The authors present in the review a stratified analysis of the effect of male circumcision by study...
quality for each study design. The search and quality control methods used were comprehensive and appropriate.

The titles, abstracts and descriptor terms of all downloaded materials from electronic searches were read independently by two review authors and papers not conforming to the inclusion criteria were discarded. The studies were reviewed for relevance based on study design, types of participant and exposure, and outcome measures. The primary outcome measure was incidence of HIV-1 and HIV-2 infection in men confirmed by laboratory tests. Secondary outcomes included behavioural outcomes such as sexual activity, having two or more sexual partners, having sex with a non-marital partner, last casual sex contact, inconsistent or no condom use, any unprotected sex, sex under the influence of alcohol, and transactional sex. The outcomes were assessed at time points common to all trials (12 months) and at end points of trials (21 or 24 months).

3. RESULTS OF THE REVIEW

The three new randomized controlled trials included in the updated review were conducted among men in the general population in South Africa (3274 men), Uganda (4996 men) and Kenya (2784 men). Circumcision was done using common surgical techniques (the Forceps-Guided technique and the Sleeve Resection method) under local anaesthesia. All three trials had commenced in 2002 and ended in 2005 or 2006.

None of the trials described clearly the method used for generating the random sequence, but it appears that the sequence was generated using a computer. Allocation of concealment was unclear in one of the trials, which may have introduced a moderate to a high risk of bias in the results. In two trials, blinding of outcome assessors was poorly described and was graded by the authors as unclear. The authors judged the risk of bias as likely to be low. The important primary end point was laboratory-confirmed seroconversion (presence of HIV antibody).

All three trials were prematurely terminated after they had met the statistical requirements for early discontinuation. At 12 months, the incidence risk ratio (IRR) of acquiring HIV in circumcised heterosexual men in all the three trials combined was 0.50, with the 95% confidence interval (CI) being 0.34–0.72. At 21 or 24 months follow-up, the IRR was 0.46 (CI 0.34–0.62). This translates into a reduction in HIV acquisition by 50% at 12 months and 54% at 21 or 24 months following circumcision. All trials were statistically homogenous.

Sensitivity analysis was done by conducting a meta-analysis of the reported IRRs, the reported IRRs as per protocol, and the reported full intention-to-treat analysis. The overall effect of circumcision was protective and statistically significant in most cases. When analysing secondary outcomes, the mean number of sexual contacts at the 12th-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 21st-month visit (7.5 versus 6.4, p=0.0015).

Overall, the number of all adverse events reported was 1391 in the intervention group and 1320 in the control group (56% versus 52%, p=0.083%). Of the events in the control group, none was considered to be related to the trial, whereas 87% of events in the circumcision group were considered to be trial-related.

4. DISCUSSION

4.1 Applicability of the results

The authors conclude that male circumcision offers a protective benefit against the acquisition of HIV by heterosexual men. Since all trials were carried out in low-income countries, the conclusions of the review would be applicable to all under-resourced settings, but especially those where circumcision is already practised and where heterosexual HIV transmission is predominant. Application of this intervention may
pose a greater challenging in terms of persuading men to undergo circumcision in areas where religious or
cultural beliefs do not permit circumcision of men, as well as in underprivileged populations in under-
resourced settings owing to the cost of the procedure.

4.2 Implementation of the intervention

Because of the high costs of this intervention, male circumcision may have to be funded partly or completely
by the government or donor agencies. Moreover, intensive awareness programmes will need to be instituted
to educate people in the target communities. Significant amounts of funds will be needed to train health-care
personnel and procure surgical materials for male circumcision.

In settings where male circumcision is also provided by traditional practitioners, the rates of morbidity and
mortality associated with the procedure are often high. In such settings it would be risky to introduce this
intervention without ensuring that men who wish to be circumcised have easy access to a safe operation in a
medical setting. A secondary objective of providing safe medical circumcision for HIV prevention should
also be to reduce the morbidity and mortality associated with circumcisions performed by traditional
practitioners. In settings where circumcision is currently not practiced, clinicians and programme managers
would need to be informed about how best to deal with resistance from groups opposed to male circumcision.

4.3 Implications for research

Further topics for research include: behavioural research on people's perceptions regarding the procedure
and factors that hinder or facilitate its uptake; better understanding of the differences in the shedding of HIV
by rectal versus vaginal mucosa; assessment of the risk of an increase in unsafe sex after circumcision; and
communication strategies for influencing health policy-makers regarding the advantages to the society of
male circumcision and how to design effective models for delivery of male circumcision services.

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This document should be cited as: Bamigboye AA, Igberase GO. Male circumcision for prevention of
heterosexual acquisition of HIV in men : RHL commentary (last revised: 1 January 2010). The WHO