Male circumcision: Africa and beyond?

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Purpose of review

Male circumcision has become an important component of HIV prevention strategies in Africa. Results of recent trials have renewed interest in this ancient procedure and its potential application in the reduction of sexually transmitted infections (STIs). With renewed interest comes controversy, which has always been a close companion to circumcision.

Recent findings

Following the three randomized trials in Africa demonstrating the protective effects of male circumcision on HIV infection, studies have reported other benefits of circumcision including protection from certain STIs, including human papillomavirus and herpes simplex virus 2. With data accumulating on the public health benefits of circumcision and the endorsement of circumcision from WHO, investigators have begun to evaluate the feasibility, safety and cost of implementation of large-scale circumcision programs. Limitations of circumcision have also been explored.

Summary

Male circumcision will likely play an important role in HIV/STI prevention programs in Africa; the inclusion of circumcision in the health policy of developed countries will require further investigation.

Keywords

HIV, male circumcision, prevention, sexually transmitted infections

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Introduction

Male circumcision has been practiced for many centuries, with historical record of the procedure going as far back as the late dynastic period of ancient Egypt [1]. Circumcision originated as a religious and symbolic procedure, and medical uses eventually followed [1]. Perhaps because scientific data supporting circumcision arrived somewhat late in the timeline of the procedure and the data often lacked robustness, or perhaps because of its sociopolitical and religious origin, the practice of circumcision has been, and continues to be plagued by controversy. Despite valid concerns from anticircumcision factions, clinical evidence supporting the medical benefits of male circumcision continue to accumulate.

Any review of recent scientific data on the medical benefits of circumcision must mention the three randomized controlled trials conducted in South Africa, Kenya and Uganda that renewed interest in the application of circumcision in disease prevention. These studies randomized men to control and intervention groups and calculated protection against HIV infection, finding the protective effect of male circumcision to be up to 60% [2–4]. Auvert *et al.* [3] randomized 3274 uncircumcised men in South Africa aged 18–24 years to immediate or delayed (end of follow-up) circumcision. HIV incidence was 0.85 per 100 person-years in the intervention group and 2.1 per 100 person-years in the control group [relative risk (RR) 0.40, 95% confidence interval (CI) 0.24–0.68%; $P < 0.001$] [3]. Bailey *et al.* [4] performed a similar study in Kenya; they randomized 2784 men aged 18–24 to immediate or delayed circumcision. The RR of HIV infection in circumcised men was 0.47 (0.28–0.78) [4]. In Uganda, 4996 uncircumcised, HIV-negative men aged 15–49 years were randomized to immediate or delayed (24 months) circumcision [2]. Over 24 months, HIV incidence was 0.66 cases per 100 person-years in the immediate circumcision group and 1.33 cases per 100 person-years in the delayed circumcision group (estimated efficacy of intervention 51%, 95% CI 16–72; $P = 0.006$) [2]. These studies confirmed findings of observational studies and led to a recommendation by the WHO to use male circumcision for HIV prevention, along with HIV testing and counseling services, treatment of sexually transmitted infections (STIs), promotion of safer sex habits and correct and consistent condom use [5]. Risk compensation or increased HIV risk behavior was not a significant consequence of circumcision in these trials [6].

Sexually transmitted infections

Studies on the protective effects of circumcision on STIs followed the HIV prevention trials. Tobian *et al.* [7••] randomized 5534 HIV-negative uncircumcised male individuals aged 15–49 years in two trials of male circumcision for the prevention of HIV and other STIs. At 2 years, the cumulative probability of herpes simplex virus type 2 (HSV-2) seroconversion was 7.8% in the intervention group and 10.3% in the control group (adjusted hazard ratio in the intervention group, 95% CI, 0.56–0.92; $P = 0.008$) [7••]. The prevalence of high-risk human papillomavirus (HPV) genotypes in the intervention group and control group were 18.0 and 27.9%, respectively (adjusted risk ratio, 0.65; 95% CI, 0.46–0.90; $P = 0.009$) [7••]. The incidence of syphilis was not significantly different between the two groups (adjusted hazard ratio, 1.10; 95% CI 0.75–1.65; $P = 0.44$) [7••].

Human papillomavirus

Two complementary randomized trials conducted in Rakai, Uganda evaluated the reduction of the incidence of multiple high-risk HPV infections (high-risk HPV) with circumcision in HIV-infected and HIV-negative men. Gray *et al.* [8] randomized HIV-negative, uncircumcised men aged 15–49 years to immediate circumcision (intervention arm) or delayed circumcision (control arm) [8]. HPV detection was performed by sampling the coronal sulcus and glans of the penis with moistened Dacron swab samples and transporting in Digene specimen medium [8]. HPV genotyping was performed using the Roche HPV Linear Array (Roche Diagnostics) [8]. High-risk HPV incidence for the intervention group and control group were 19.7 cases per 100 person-years and 29.4 cases per 100 person-years, respectively (RR, 0.67; 95% CI, 0.51–0.89; $P = 0.006$) [8]. The incidence of multiple high-risk HPV infections was 6.7 cases per 100 person-years in the intervention group and 14.8 cases per 100 person-years in the control group (RR, 0.45; 95% CI, 0.28–0.73), although there was no significant difference for single infections (RR, 0.89; 95% CI, 0.60–1.30) [8]. The clearance of pre-existing high-risk HPV infections was 215.8 cases per 100 person-years in the intervention group and 159.1 cases per 100 person-years in the control group (adjusted RR, 1.39; 95% CI, 1.17–1.64) [8]. Clearance was identified in men with pre-existing high-risk HPV whose tests were negative for that genotype at a subsequent sequential study visit [8]. Similar benefits of circumcision were found in HIV-infected men. Serwadda *et al.* [9] randomized HIV-positive, uncircumcised men aged 15–49 years to immediate circumcision (intervention arm) or delayed circumcision (control arm). At 24 months, high-risk HPV prevalence was 55.3% in the intervention group and 71.7% in the control group (RR, 0.77; 95% CI, 0.62–0.97) [9]. The prevalence of multiple high-risk HPV infections was 22.4% in the intervention group and 42.5% in the control arm (RR, 0.53; 95% CI, 0.33–0.83) [9]. The incidence of high-risk HPV was 42% in the intervention group and 57% in the control group (RR, 0.74; 95% CI, 0.54–1.01; $P = 0.06$) [9]. The incidence of multiple high-risk HPV infections was 9.9% in the intervention group and 24.7% in the control group (RR, 0.40; 95% CI, 0.19–0.84; $P = 0.01$) [9]. In their editorial commentary, Viscidi and Shah [10] cautioned that although significant, the decrease in HPV infections owing to circumcision in these trials is modest, pointing out that the prevalence of HPV in HIV-negative, circumcised men was still greater than 20%, and the prevalence of HPV in HIV-positive, circumcised men was still greater than 55%.

Auvert *et al.* [11] reported similar findings on the effect of circumcision on high-risk HPV infections from Orange Farm, South Africa. In an intention-to-treat analysis, the prevalence of high-risk HPV was 14.8% in the intervention group and 22.3% in the control group (prevalence rate ratio of 0.66; 95% CI, 0.51–0.86; $P = 0.002$). Hernandez *et al.* [12] found that although there was no difference in HPV acquisition by circumcision status, clearance of the HPV infection was slower in the glans/coronal sulcus of uncircumcised men compared with circumcised men, 154 days and 91 days, respectively ($P = 0.04$).

Assessment of implementation

With the identification of circumcision by WHO as a strategy for global HIV prevention, feasibility, safety and cost-effectiveness studies have also been conducted. Implementing large-scale circumcision programs in sub-Saharan Africa will require training programs for a large number of surgeons. Kiggundu *et al.* [13] used data from their randomized trial in Rakai, Uganda to determine the number of procedures required to achieve optimal competence with male circumcision. During their randomized trial, 3011 men were circumcised using the sleeve method. The mean surgical time was 40 min for the first 100 procedures and declined to 25 min for the subsequent 100 procedures [13]. The rate of adverse events (moderate and severe) was 8.8% for the first 19 unsupervised procedures after training, 4.0% for the next 20–99 procedures and 2.0% for the last 100 (P for trend, 0.003) [13].

Circumcision devices have been evaluated for their potential role in large-scale circumcision programs. One promising device is the Shang Ring, developed in China and currently being evaluated in clinical trials in multiple sites in Africa. The device consists of two concentric plastic rings that clamp the foreskin and allow for removal of the foreskin without suturing. Cheng *et al.*

[14] developed a standardized training protocol for performing the Shang Ring circumcision. They circumcised 328 men with the Shang Ring with mean operative time of 4.7 ± 1.3 min and postoperative complication rates were 0.6% for infection, 0.6% for bleeding, 0.6% for wound dehiscence and 4.9% penile edema [14].

Bollinger *et al.* [15] used the Joint United Nations Programme on HIV/AIDS (UNAIDS)/WHO Decision-Makers' Program Planning Tool to estimate the cost and impact of male circumcision in Bostwana. They found that scaling up adult and neonatal circumcision to 80% coverage by 2012 would avert almost 70 000 new HIV infections through 2025, at a net cost of US$47 million [15]. The average cost per HIV infection averted was US$689. Pushing back the target year to 2015 would still avert about 60 000 new HIV infections through 2025 [15].

The UNAIDS/WHO/South African Centre for Epidemiological Modelling and Analysis Expert Group on Modelling the Impact and Cost of Male Circumcision for HIV Prevention reviewed the outcomes of six simulation models and found that one HIV infection could be averted for every five to 15 male circumcisions performed in low male circumcision and high-HIV prevalence settings [16]. The costs to avert one HIV infection ranged from US$150 to US$900 using a 10-year time horizon [16]. The models also predicted that risk compensation will have only small population level effect [16]. Furthermore, the male circumcision worked synergistically with other HIV prevention strategies, and may indirectly benefit women by reducing HIV prevalence [16].

Binagwaho *et al.* [17] performed a cost-effectiveness study of male circumcision in Rwanda. They developed three hypothetical cohorts, newborns, adolescents and adult men, and found that neonatal male circumcision is less expensive than adolescent and adult male circumcision (US$15 vs. US$59 per procedure) and is cost saving. The cost per infection averted was US$3932 for adolescent male circumcision and US$4949 for adult male circumcision [17]. They concluded that Rwanda should scale up circumcision across a broad range of ages, with neonatal circumcision having the most potential to maximize the reduction of HIV incidence [17].

Sansom *et al.* [18] addressed a similar question in the USA. They calculated the cost-effectiveness of newborn circumcision in reducing lifetime HIV risk among all males, and found a 15.7% reduction of lifetime HIV risk in the base case analysis, ranging from 7.9% for white men to 20.9% for black men. The net cost of neonatal circumcision per quality-adjusted life years saved was US$87792 for white men [18]. Overall, neonatal circumcision reduced the 1.87% lifetime risk of HIV for all men by 16% [18].

Out of Africa

Although the three randomized trials conducted in South Africa, Kenya and Uganda reported significant protective effects of male circumcision against HIV infection, how applicable are the results of these trials to men in other parts of the world, with different biological, socioeconomic, cultural and political contexts? Xu *et al.* [19] posed this very question in the USA. The authors cautioned that there were significant differences between Africa and the USA, such as age at circumcision, dominant mode of HIV transmission, biological factors, HIV transmission dynamics and healthcare system factors [19]. For example, the studies in Africa had a minimum age requirement of 15 years, whereas most American men are circumcised at birth. A direct comparison of the effects of circumcision is difficult to make in these disparate age groups. Another important distinction is the dominant mode of HIV transmission. Whereas heterosexual contact is the most common mode of transmission in the three African countries, penile–anal sexual contact is the most common mode of transmission in the USA [19]. Therefore, the effects of circumcision on male-to-male HIV transmission would be an important component of circumcision policy recommendations in the USA, a transmission mode that was not addressed in the trials in Africa. The effect of circumcision on male-to-female HIV transmission is another question that remains unanswered.

In the many articles that have been published in the last few years on male circumcision and HIV prevention, one recurring theme is that circumcision programs have the most impact on regions with low circumcision and high-HIV prevalence. Although many countries in sub-Saharan Africa fit this description, the USA has a relatively high circumcision and low HIV prevalence. HIV prevalence among adults and adolescents in the USA was about 0.14% in 2005 [19,20], compared with 6.2–7% in Uganda and Kenya and almost 25% in South Africa [19,21]. The lower prevalence of HIV in the USA would increase the number of circumcisions needed to avert one new HIV infection and raise the cost per averted infection [19].

Considerations for circumcision

Not everyone embraces the virtues of circumcision and there are a wide range of opinions and many points of contention. Some circumcision opponents question the removal of healthy tissue rich in nerve-endings and the potential detriment to sexual pleasure. Others dispute the true medical benefits of circumcision, contending

that even if it protects against certain infections and diseases, the low incidence (of neonatal urinary tract infections or penile cancer, for example) does not justify the costs of circumcision. As with any surgical procedure, male circumcision has the potential for complications. Complication rates for circumcision in the three randomized controlled trials in South Africa, Kenya, Uganda ranged from 1.7 to 8% [2–4] However, complication rates for male circumcision can be much higher, as seen in a study conducted in Bungoma, Kenya: 17.7% among clinical circumcisions (in hospitals, health centers, dispensaries or private clinics) and 35.2% among traditional circumcisions (in villages or household compounds) [22].

The article by Xu *et al.* [19] echoed some of the reservations held by the individuals and groups cautioning the implementation of circumcision programs. As discussed previously, the differences between the USA and other developed countries and Africa, where many of the recent studies reporting the benefits of circumcision were conducted, must be assessed before determining health policy. Perhaps the greatest limitations of male circumcision as a prevention strategy are the disappointing results in studies of male-to-female and male-to-male HIV and STI transmission.

The data demonstrating the protective effects of male circumcision in high-HIV prevalence regions in Africa are strong, and circumcision programs as part of a broader strategy along with counseling services, safe sex education and testing and treating for STIs and HIV will play an important role in Africa. With the increased media interest generated by positive results of recent studies, Wang *et al.* [23] assessed the content and accuracy of print media reports on male circumcision for preventing HIV infection among men in sub-Saharan Africa. They identified 15 key messages from the WHO-UNAIDS Montreux recommendations and a supplementary legal and ethical guidance document and found that the accuracy of the reports was good, but were few in number and often omitted important messages [23–25]. See the list below:

Key messages on male circumcision for preventing HIV infection. Reprint of box 1 in [23]:

(1) HIV testing is recommended for all men seeking male circumcision.
(2) Male circumcision should be provided after informed consent, with confidentiality and without coercion or discrimination.
(3) Based on current available evidence, male circumcision is not recommended for HIV+ men.
(4) Male circumcision provides only partial protection against HIV.
(5) Male circumcision is an addition to, not a substitute for, other proven methods for preventing HIV infection.
(6) Whether circumcision takes place in a clinic or traditional setting, it is important to ensure surgical safety and quality.
(7) Men should not resume sexual intercourse for at least 6 weeks after male circumcision.
(8) Ideally, sex should only recommence after a medical exam confirms the healing process is complete.
(9) All males, circumcised or not, should seek to reduce the risk of HIV infection by using condoms correctly and consistently.
(10) All males, circumcised or not, should seek to reduce the risk of HIV infection by limiting their number of sexual partners.
(11) Because of a lack of data, it is not known whether male circumcision reduces the risk of transmitting HIV to women.
(12) There is a lack of data on direct protection for either partner during anal sex.
(13) Male circumcision and female genital mutilation are very different things.
(14) No association has been found between male circumcision and risk compensation.
(15) As with any surgical procedure, there is some risk of complications with male circumcision.

Adapted from WHO-UNAIDS recommendations and a supplementary ethical and legal guidance document.

Interestingly, although the majority (56%) of articles were positive in their portrayal of circumcision, the negative articles were repeated 2.9 times more often, perhaps indicating the media's inclination for covering controversial viewpoints [23].

Conclusion

Male circumcision has been performed for many centuries. Although health benefits have been reported for many years, circumcision has once again garnered attention as a critical public health initiative. Circumcision appears to protect against certain STIs in addition to HIV and will likely be an integral part of HIV prevention programs in Africa. The broader application of this procedure to other areas of the world with different population, infrastructure and disease characteristics warrants further investigation.

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There are no conflicts of interest.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 537).

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