Abstract # 1089

Potential Protection from HIV transmission by Penile Cuttings in Papua New Guinea

INTRODUCTION

Randomized clinical trials have shown that male circumcision reduces HIV-1 acquisition by approximately 60% (1-3). However, there has yet to be a scientific consensus on the protective mechanisms. The hypotheses are based around the reduction of the inner foreskin.

1. The inner foreskin barrier: inner foreskin removal exposes the inner foreskin that leads to the formation of a primary barrier equivalent to the outer foreskin.
2. Target cell density: higher cell density reduces the infective force.

The WHO/UNAIDS have heavily invested in male circumcision as a viable HIV prevention strategy, implementing a massive rollout of male circumcision programs. Present estimates for voluntary male circumcision are 5 million with 20 million variable estimates for full circumcision required. The number of male circumcision procedures varies, with 20 million estimated at the end of 2016 (1,4). Thus understanding how circumcision is protective is crucial.

Ethnographic studies in Papua New Guinea (PNG) have demonstrated insufficient non-medical motivation for circumcision unique to PNG. Cultural cutting (47%), especially the dorsal slit (DS), is more common than full circumcision (10%), the latter has yet to be assessed in PNG. Cultural cutting is not recorded by the national program, which has yet to be assessed.

The DS is a single longitudinal cut made across the foreskin. This leads to exposure of the inner and outer foreskin and provides a unique opportunity to study a scenario where the inner foreskin is exposed but not removed.

METHODOLGY

Research to investigate the potential protective effects of longitudinal cuts on HIV-1 acquisition is essential given the scale of dorsal slit penile cuttings in PNG. This unique cohort may also define how circumcision increases protection.

We present results from a cohort study assessing histological changes to this skin that may aid in preventing both circumcised and dorsal slit men.

AIM

To determine the histological changes that occur in the foreskin after dorsal slit we set out to answer the following questions:

• Is the keratin layer of the outer foreskin thicker than the keratin layer of the inner foreskin without and with penile cuttings?
• What is the distribution of target cells in the inner and outer foreskin in healthy men with and without penile cuttings?
• What are the histological changes that occur in the foreskin after dorsal slit? Are dorsal slits as protective as full circumcision in HIV transmission?

RESULTS

1. Keratin Thickness

• The epithelium obtained from dorsal slit men had significantly thicker keratin than circumcised men.
• Men with DS had significantly thicker keratin at the outer foreskin that was significantly greater than the inner foreskin (p<0.001).

2. Epithelial Surface Area

• Thinner primary barriers were seen at the outer foreskin that led to the formation of a primary barrier equivalent to the outer foreskin.

3. Epidermal to Dermal contact

• The interdigitation index of the outer foreskin was significantly greater at the outer than inner foreskin, (p<0.001)
• Overall greater epithelium surface area and epidermal to dermal contact in the outer than inner foreskin regardless of circumcised status.

4. Target cell analysis by Immunofluorescence (IF)

• Preliminary observations show lymphoid aggregates of CD4+ cells that may predispose them to HIV infection after mechanical injuries due to close proximity to the dermal and epidermal border.

CONCLUSIONS

Epithelial Surface Area Quantification

The outer foreskin keratin is significantly greater than the inner foreskin keratin as assessed by circumcised men and those undergoing dorsal slit penile cuttings. The data shows that dorsal slit men have significantly greater keratin at the outer foreskin compared to circumcised men.

Epidemiological evidence is compelling, suggesting that male circumcision reduces HIV-1 acquisition by approximately 60% (1-3). However, there has yet to be a scientific consensus on the protective mechanisms. The hypotheses are based around the reduction of the inner foreskin.

CONCLUSION

In conclusion, it is not known whether the outer foreskin displays a tissue structure phenotype that is a protective mechanism against the transmission of HIV from infected men. Different methods may be required to elucidate the protective role of the outer foreskin in reducing the transmission of HIV.

Acknowledgements

This work was supported by NHMRI project grant APP 443930.