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Use of a mixture of lignocaine and bupivacaine vs lignocaine alone for male circumcision under local anaesthesia in Rakai, Uganda

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Study Type – Therapy (case control)
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OBJECTIVE

- To assess self-reported pain control during and after surgery with a mixture of lignocaine and bupivacaine compared with lignocaine alone among male circumcision (MC) service recipients in Rakai, Uganda.

PATIENTS AND METHODS

- The two formulations of local anaesthesia for MC were used alternatively at weekly intervals in 360 patients; 179 received lignocaine alone and 181 received the lignocaine and bupivacaine mixture (LBmix).
- The proportions of men reporting pain during or after surgery, and the need for additional anaesthesia during surgery were determined for the LBmix vs lignocaine using Poisson adjusted rate ratios (RRs).
- Characteristics including age, weight, surgeon (medical officer vs clinical officer), surgical method and duration of surgery were compared between the arms using two-sample t-tests and chi-square tests.

What's known on the subject? and What does the study add?
Local anaesthetic drugs block the generation and the conduction of nerve impulses, presumably by increasing the threshold for electrical excitation in the nerve by slowing the propagation of the nerve impulse, and by reducing the rate of rise of the action potential. Lignocaine/Lidocaine has a rapid onset action and an intermediate duration of efficacy whereas Bupivacaine has a slower onset of action with a long duration of efficacy. A combination of the two drugs creates a mixture that has a short onset of action together with a long duration of action both of which are desirable qualities in provision of effective local anaesthesia.

Documenting whether use of lignocaine alone predisposes men to more pain during and after surgery will inform policy makers on the type of local anaesthesia to recommend for male circumcision, especially as circumcision programs roll out. This is important since pain has been associated with reduced acceptance of the male circumcision procedure and therefore can negatively influence male circumcision roll out programs.

RESULTS

- Patient and provider characteristics were comparable between the two anaesthetic groups.
- A higher proportion of patients reported pain during surgery in the lignocaine group (adjusted RR 11.6, 95% confidence interval [CI] 3.5–37.9, $P < 0.001$), required additional anaesthesia (adjusted RR 4.8, 95% CI 1.4–17.1, $P = 0.015$), and were more likely to report pain during the immediate postoperative period (adjusted RR 3.4, 95% CI 2.3–5.0, $P < 0.001$).
- These differences were particularly marked among patients with MC times longer than the median (adjusted RR 13.4, 95% CI 3.1–57.0, $P < 0.001$).

CONCLUSION

- The LBmix significantly reduced pain associated with MC and the need for additional anaesthesia during MC.

KEYWORDS

male circumcision, local anaesthesia, lignocaine, bupivacaine, pain control, anaesthetic mixture

TABLE 1 Number and P values for selected characteristics by anaesthetic type

Characteristic	*N*	Lignocaine, *n* (%)	LBmix, *n* (%)	*P*
All	360	179 (49.7)	181 (50.3)	
Age, years:				
12–19	112	57 (31.8)	55 (30.4)	0.397
20–29	169	88 (49.2)	81 (44.8)	
>30	79	34 (18.99)	45 (24.9)	
Weight, kg:				
≤60	220	114 (63.7)	106 (58.6)	0.319
>60	140	65 (36.3)	75 (41.4)	
Cadre of provider:				
Medical officer	131	60 (33.5)	71 (39.2)	0.260
Clinical officer	229	119 (66.5)	110 (60.8)	
Surgical method:				
Sleeve	152	79 (44.1)	73 (40.3)	0.465
Dorsal	208	100 (55.9)	108 (59.7)	

INTRODUCTION

Male circumcision (MC) has been shown to reduce the risk of HIV acquisition by 50–60% [1–3] and the WHO now recommends it as one of the proven methods for HIV prevention [4]. Several programmes in sub-Saharan Africa have initiated MC implementation. For MC to be effective at a community level there is need to achieve high MC coverage, and modelling suggests that the higher the prevalence of MC the greater the impact on HIV incidence [5]. One reason consistently cited by men for not accepting MC is fear of pain during surgery [6–10]. Our experience in Rakai is that when men are offered MC, only a few men initially come for surgery, and the majority, fearing pain, wait to hear the experiences of men who have had surgery. Once the circumcised patients share their experience of pain-free surgery, the numbers of men willing to accept MC exponentially increase (PC KG). Pain control during MC and the immediate postoperative period is therefore important for the uptake of MC.

Pain control during MC is achieved by local anaesthesia, and in Uganda, lignocaine is routinely used because of its low cost. We conducted a randomized controlled trial of MC for HIV prevention, using a mixture of lignocaine and bupivacaine for local anaesthesia [3], which provided good pain control and qualitative studies suggested that men were motivated to accept surgery after hearing about pain-free experiences from their peers.

When the MC trials ended, we started using lignocaine alone for local anaesthesia as was the standard of care in Uganda, and observed that men were more likely to report pain during and after MC, and to require more anaesthesia than when the lignocaine and bupivacaine mixture (LBmix) had been used. The field team also noted that the number of men coming for MC was lower than expected in communities in which lignocaine alone was used.

Because of the potential importance of pain control in uptake of MC, we assessed self-reported pain control with lignocaine alone compared with the LBmix.

PATIENTS AND METHODS

The study was conducted in Rakai, Uganda among males aged 13–49 years who requested circumcision as a service. In all, 360 patients were included in the study 179 of whom received lignocaine 1% alone and 181 received a mixture of lignocaine 1% and bupivacaine 0.25% prepared by drawing equal amounts of bupivacaine 0.5% and lignocaine 2%. Patients were assigned to receive either lignocaine alone or the LBmix on alternative weeks. Thus, the study allocation was not randomized.

All men were offered voluntary HIV counselling and testing before surgery. They received group health education on HIV prevention and individual counselling to address questions and provide clarification on issues that they may not have clearly understood.

All patients were then screened for contraindications for MC by a clinical or medical officer through history and examination. Those with medical contraindications (e.g. penile infections) were treated and re-screened before MC. Eligible men provided consent for surgery and adolescents aged <18 years provided assent and were required to have parental or guardians consent for surgery. MC was performed by either medical or clinical officers who had been trained in MC, and two surgical procedures, sleeve or dorsal slit were used for MC.

We recorded the type of anaesthesia given, the provider performing the surgery (physician/clinical officer), the time anaesthesia was given, the time surgery was started and completed, pain experienced during the operation, whether additional anaesthesia was needed and self-reported level of the pain felt. Postoperative pain was graded as level 1 (mild or moderate) if pain was controlled by routine analgesia with acetaminophen, level 2 (severe) if pain was controlled by additional analgesia, and level 3 (very severe) if pain was not controlled by additional analgesia. Patients were monitored in the recovery room for self-reported postoperative pain, the severity of pain and the need for additional postoperative analgesia.

The provision of surgery was funded by the USA President's Emergency Plan for AIDS Relief (PEPFAR) and the assessment of anaesthesia was separately funded by the Bill and Melinda Gates Foundation. The assessment of anaesthesia was approved by the Uganda Virus Research Science and Ethics Committee and the Uganda National council of Science and Technology.

The characteristics of patients were assessed at enrolment. The chi-square test was used to compare distributions of age, weight, cadre of provider and surgical procedure. We used a two sample *t*-test to compare mean time from administration of anaesthesia to end of surgery.

We determined the proportion of patients reporting pain during and/or after surgery and the proportions requiring additional

TABLE 2 Self-reported pain and RRs (95% CIs) of occurrence of pain by type of anaesthesia and duration of MC

Characteristic	*N*	Yes, *n* (%)	Unadjusted RR (95%CI)	Adjusted RR (95%CI)	*P*
Pain during surgery					
All	360	34 (9.4)			
Anaesthetic type:					
Lignocaine	179	31 (17.3)	10.5 (3.3–33.6)	11.6 (3.5–37.9)	<0.001
LBmix	181	3 (1.7)	ref		
Duration of surgery:					
≤ median duration 26 min	185	11 (6.0)	0.5 (0.2–0.9)	0.4 (0.2–0.8)	0.007
> median duration 26 min	175	23 (13.1)	ref		
Duration of surgery ≤26.0 min					
Lignocaine	102	10 (9.8)	8.13 (1.1–62.3)	8.14 (1.0–63.6)	0.046
LBmix	83	1 (1.2)	ref		
Duration of surgery >26.0 min					
Lignocaine	98	21 (27.3)	13.4 (3.2–55.3)	13.4 (3.1–57.0)	<0.001
LBmix	77	2 (2.0)	ref		
Additional anaesthesia required					
All	360	15 (4.2)			
Anaesthetic type					
Lignocaine	179	12 (6.7)	4.0 (1.2–14.1)	4.8 (1.4–17.1)	0.015
LBmix	181	3 (1.66)	ref		
Duration of surgery:					
≤ median duration 26 min	185	2 (1.1)	0.2 (0.03–0.6)	0.1 (0.03–0.6)	0.006
> median duration 26 min	175	13 (7.4)	ref		
Pain during recovery					
All	360	157 (43.6)			
Anaesthetic type:					
Lignocaine	179	122 (68.2)	3.5 (2.6–4.8)	3.4 (2.3–5.0)	<0.001
LBmix	181	35 (19.3)	ref		
Cadre of provider:					
Medical officer	131	46 (35.1)	0.7 (0.6–1.0)	0.8 (0.5–1.1)	0.176
Clinical officer	229	111 (48.5)	ref		
Pain during surgery:					
Yes	34	23 (67.7)	1.7 (1.3–2.2)	1.1 (0.7–1.8)	0.670
No	326	134 (41.1)	ref		
Duration of surgery:					
≤ median duration 26 min	185	89 (48.1)	1.2 (1.0–1.6)	1.0 (0.7–1.4)	0.943
> median duration 26 min	175	68 (38.9)	ref		

anaesthesia during surgery or requiring additional postoperative analgesia. We estimated unadjusted rate ratios (RRs) and 95% CIs of these parameters in patients receiving lignocaine alone relative to the LBmix using Poisson regression. Statistical associations were assessed using chi-square tests.

Variables significant at $P < 0.2$ and variables likely to influence pain control or the duration of surgery (e.g. type of surgical procedure (sleeve vs dorsal slit methods) and cadre of provider (physician vs clinical officers), were included in a multivariable Poisson regression models to adjust for potential confounding.

RESULTS

In all, 360 patients were included in the analysis; 181 received the LBmix and 179 men received lignocaine alone.

Table 1 shows a comparison of age, weight, cadre of provider and surgical procedure by anaesthetic type. All characteristics were comparable by anaesthetic type ($P > 0.05$).

The mean (SD) time from administration of anaesthesia to completion of surgery was significantly longer for the LBmix 27.7 (5.9) min compared with 25.5 (6.8) min in the lignocaine group, ($P < 0.001$.)

Table 2 shows the proportions reporting pain and RRs of occurrence of pain during surgery, the need for additional anaesthesia and pain during the immediate postoperative period. Compared with the LBmix group, a higher proportion of men reported feeling pain during the operation in the lignocaine group (1.7% vs 17.3%, respectively, adjusted RR 11.6, 95% CI

3.5–37.9, $P < 0.001$), required additional anaesthesia during surgery (1.7% vs 6.7%, respectively, adjusted RR 4.8, 95% CI 1.4–17.1, $P = 0.015$), and were more likely to report postoperative pain while in recovery (19.3% vs 67.7%, respectively, adjusted RR 3.4, 95% CI 2.3–5.0, $P < 0.001$). There was no difference between the groups in reported pain during recovery among those in whom the duration of surgery was less than the median duration of 26 min. Patients with durations of surgery shorter than the median were less likely to report pain during MC compared with those whose duration of MC was more than the median (adjusted RR 0.4, 95% CI 0.2–0.8), and less likely to require additional anaesthesia during MC (adjusted RR 0.1, 95% CI 0.02–0.46, $P = 0.006$). However, the LBmix provided better analgesia than lignocaine alone, irrespective of the duration of MC. For MCs requiring less than the median duration, pain was reported by 1.2% of patients receiving LBmix and 9.8% of those receiving lignocaine (adjusted RR 8.14, 95% CI 1.0–63.6, $P = 0.05$). Among MCs requiring more than the median time, pain was reported by 2.0% of patients receiving the LBmix and 27.3% of those receiving lignocaine alone (adjusted RR 13.4, 95%CI 3.1–57.0, $P < 0.001$). After adjusting for provider, pain during surgery and duration of surgery, lignocaine was associated with a significantly higher rate of self-reported pain during recovery (adjusted RR 3.4, 95% CI 2.3–5.0, $P < 0.001$).

DISCUSSION

The present findings indicate that use of lignocaine alone significantly increases rates of self-reported pain and the need for additional anaesthesia during MC, and postoperative pain (Table 2). Fear of pain is a deterrent to acceptance of MC, therefore, achieving pain control is critical in motivating men to accept MC, so programmes should consider using the LBmix despite the slightly higher cost. In Uganda the cost of a 20-mL vial of lignocaine 2% is ≈USA $1.00 while the cost of a 20-mL vial of bupivacaine 0.5% is ≈$5.00. Use of equal volumes of 10 mL lignocaine 2% and 10 mL bupivacaine 0.5% costs $3.0 and provides better analgesia.

We observed that despite the longer interval between administration of local anaesthesia and completion of surgery (2.2 min) in the LBmix group, the proportion of men reporting pain or requiring additional anaesthesia was less than in the lignocaine group. This is because lignocaine requires a shorter time to achieve anaesthesia sufficient to start surgery but analgesia wears off faster than with the LBmix, resulting in more surgical pain and the need for additional anaesthesia during surgery.

The present findings indicate that lignocaine can be used by surgeons who require less time for MC (i.e. take less than the median duration of surgery of 26 min), with moderate complaints of pain during surgery. However, patients were more likely to report postoperative pain if lignocaine was used alone and therefore required additional analgesia while in recovery.

In summary, use of the LBmix significantly improved pain control during and after MC and reduced the need for additional anaesthesia during surgery and postoperative analgesia. This is of programmatic importance, as pain-free surgery can positively influence uptake of MC.

CONFLICT OF INTEREST

None declared.

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