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ORIGINAL ARTICLE

COMPARISON OF PAIN RESPONSE DURING NEONATAL CIRCUMCISION WITH OR WITHOUT A TOPICAL ANAESTHETIC FORMULATION IN AN URBAN HOSPITAL IN JOS, NIGERIA

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Keywords: EMLA, Local Anaesthesia, Male Circumcision, Pain Measurement.

ABSTRACT

Background: Circumcision is the commonest surgical procedure performed in male neonates, usually without anaesthesia. Recent research had shown that new-borns have the anatomical and functional components required for perception of painful stimuli, and that unmanaged pain can have long-lasting effects on neurological function. A topical application of eutectic mixture of local anaesthetics (EMLA) has been shown to be a safe and effective method of pain control during neonatal circumcision.
Objective: To determine whether topical anaesthesia (EMLA) decreases pain response during neonatal circumcision, with the overall purpose of recommending its use in Hospitals.
Methods: This was a randomized, double blind intervention study that compared pain scores between neonates who had circumcision with or without topical anaesthesia. Neonates were randomly assigned to either treatment or control group. A full physical examination was done, with weight, heart rate, respiratory rate, oxygen saturation measured before and after the circumcision. Acute behavioural pain response was quantified using the Neonatal Infant pain scale [NIPS] and results compared between the two groups.
Results: The mean age of the neonates in the study was 12 ±2 days. The mean of the weight for the intervention group was 3.7±0.5kg and that of the control group was 3.6±0.7kg. Also the mean of the head circumference in the intervention group was 38.4±0.3cm and that of the control group was 38.5±0.2cm. The mean of the length in the intervention group was 53.4±0.3cm and that of the control group was 53.3±0.7cm. The control and the intervention group were similar with regards to the physical characteristics. Neonates who had topical anaesthesia before circumcision had statistically, significant lower mean NIPS score compared to the control group (4.56 ±0.9 versus 5.94 ±0.2*), P = 0.001*. Also, they had smaller decreases in transcutaneous oxygen levels, from 96.11±1.8 to 93.3±3.2, compared to the control group, from 95.97±1.8 to 89.83±2.2. They also had smaller increases in heart rate compared to the control group, from 139.67±5.4 to 142.19±3.6 beats per minute versus, from 139.42±5.26 to 152.3±6.3 beats per minute; and respiratory rates, from 48.22±1.9 to 49.1±3.0 compared to from 48.28±1.9 to 53.2±2.9 in the control group.
Conclusion: Neonates receiving topical anaesthesia before the circumcision experienced significantly less pain, smaller decreases in transcutaneous oxygen levels, smaller increases in heart rate and respiratory rate than controls.

INTRODUCTION

The International Association for the Study of Pain (IASP) defines pain as an unpleasant sensory and emotional experience, associated with actual or potential tissue damage, or described in terms of such damage.[1]

Pain, a sensory experience, begins with the transmission of an impulse by the sensory receptors in the skin and other body tissues. Pain impulses are transmitted from sensory receptors in the skin via C- and A-delta fibres in the peripheral nerves to the dorsal horn in the spinal cord, then to the brain stem, the thalamus, and finally to the cerebral cortex. Ultimately, a process known as descending modulation assists to dampen specific pain impulses, presumably as a protective mechanism to modulate severe pain.[2] Neuroanatomical data indicate that this descending modulation is immature in newborns. Therefore, human newborns have anatomical and functional components required for the perception of painful stimuli, and younger children often report equivalent events as being more painful.[3-6]

Despite increased focus on pain assessment and management in Family Practice, neonatal circumcision, a painful surgical procedure, is often performed without analgesia. Circumcision-related pain in neonates deserves attention because newborns not only experience pain and stress, but their pain responses may even influence their subsequent social and behavioural development.[7] Repetitive painful stimuli have been associated with behavioural and emotional problems during childhood, major psychosis, altered responses to pain, and intractable pain states in later life.[7] The plasticity of the developing brain and the changes

that occur in response to painful stimuli contribute to altered perceptions of pain later in life.[8] Early painful experiences also affect children's future response to analgesia.[9]

The American Academy of Paediatrics (AAP) states that analgesia is safe and effective in reducing the pain associated with circumcision.[5] Studies have shown that babies who are circumcised without anaesthesia tend to develop higher heart and respiratory rates, skin flushing, vomiting, changes in sleep cycle, more crying, and less responsiveness to parents.[10]

A topical application of eutectic mixture of local anaesthetics (EMLA) has achieved considerable popularity for its ability to diminish pain associated with circumcision.[11] A systematic review demonstrated that the increase in heart rate (a primary marker of pain response in newborns) is 12 to 27 beats per minute lower in infants undergoing circumcision when they are anaesthetized with topical EMLA, compared with placebo.[12]

Assessment and relief of pain, as in any other routine observation or examination should be a priority for any professional involved in the treatment of neonates at any point in their transit through the healthcare system. Recent evidence suggests that multivariable instruments that include physiologic, behavioural, and contextual indicators yield composite pain scores that are predictive and valid measures of pain in neonates.[13]

Eyelade and colleagues in their study on convergent validity of pain measuring tools among Nigerian children, in Ibadan, Nigeria reported that the Oucher Observer Pain Scale, Visual Analogue Scale (VAS) and the Numeric Rating Scale (NRS) pain scales are reliable pain measuring tools that can be used to assess pain in Nigerian children.[14] Several other objective scales have been studied including Neonatal Infant Pain Scale[NIPS], which scores facial expression, cry, breathing patterns, arm and leg reflexion and state of arousal; CRIES, which scores crying, requirement of oxygen saturation, increased vital signs, facial expression and sleeplessness. Others include Neonatal Pain Agitation and Sedation [N-PASS], Neonatal Facial Coding System [NFCS], Pain Assessment Tool [PAT], Scale for Use in Newborns [SUN], and Post-operative Comfort Scale which scores post-operative pain in infants.[15,]

A study demonstrated that premature infants have a lower pain threshold than term infants, indicating a more intense transmission of painful stimuli via the spinal cord, which can be further intensified with repeated painful stimulation. The heel stick procedure can be used as an example of the reaction and response to pain: An infant senses the lance and immediately withdraws the foot. In the preterm infant this withdrawal reflex may be less dramatic because of less muscle strength compared with the term newborn. Following the withdrawal reflex, the infant cries and responds with the classic cry face, squeezed eyes, marked nasolabial folds, and gaping mouth. This response, commonly witnessed by health care providers during circumcision and venepuncture are examples of an intact sensory pathway that transmits painful stimuli.[16, 17]

Ethical consideration

Approval for the study was obtained from the hospital's ethical committee, written informed consent was obtained from the mothers of all subjects.

METHODOLOGY

The study was conducted at the Bingham University Teaching Hospital, Jos. The hospital is owned by the Evangelical Church Winning All (ECWA) situated in Jos, the capital of Plateau State, north central Nigeria. It was a randomized, double blind intervention study; comparing pain scores between neonates who received topical anaesthesia and those who received placebo before circumcision. Approval for the study was obtained from the Research and Ethics committee of Bingham University Teaching Hospital, Jos, and written informed consent was also obtained from mothers of consecutive subjects presenting for circumcision.

The sample size was calculated using the formula.[18]

$$N = 4s^2/d^2$$

Where N = minimum sample size in each group.

s = standard deviation of pain scores from a previous study.

d = size of the difference in mean to be detected (i.e. precision of estimates).

A previous U.S. study,[19] gave

$$s = 0.9$$

The expected size of the difference in mean pain scores to be detected in the 2 groups, d=0.3 at 80% power and 95% confidence level (alpha=0.05).

Therefore minimum sample size in each group,

$$N = 4(0.9)^2/(0.3)^2 = 36.$$

Thus, 72 neonates, 36 in each group participated in the study.

A full physical examination was done including weight, heart rate, respiratory rate, oxygen saturation, length and head circumference. Neonates were then randomly assigned to either treatment or control arm. Acute behavioural pain response was quantified using the Neonatal Infant Pain Scale

[NIPS][20] The scale consists of five behavioural components with composite scores of 0 to 6. Each behavioral indicator is scored with 0 or 1 except "cry", which has three possible descriptors therefore, being scored with a 0, 1 or 2. Physiological changes such as heart rate, respiratory rate and oxygen saturation were also measured.

Data analysis was conducted using SPSS 16 (SPSS Inc., Chicago, IL, USA). Mean values for NIPS score, heart rate, oxygen saturation and respiratory rate were initially analyzed separately for each of the two groups. A secondary analysis was performed using Student t-tests to compare the mean values of NIPS score, heart rate, oxygen saturation and respiratory rate of the neonates who received topical anaesthesia with those who did not receive topical anaesthesia before the circumcision. The level of significance was set at P-value of less than or equal to 0.05.

RESULTS

Out of the 98 neonates seen during the study period, 26 were excluded for various reasons. A total of 72 neonates were recruited and completed the study. Majority (61.1%) of the neonates were in the 9-15 day age group. All the neonates in the experimental and the control groups studied were comparable with regards to age, weight, head circumference and length. (See Table 1).

Table 1: Physical characteristics of the neonates

			Treatment allocation		
			EMLA (n = 36)	Placebo (n = 36)	p-value
		Total	N (%)	N (%)	
Age (Days)	2-8	11	6 (16.7)	5 (13.9)	0.961
	9-15	44	21 (58.3)	23 (63.9)	
	16-22	8	5 (13.9)	4 (11.1)	
	23-29	8	4 (11.1)	4 (11.1)	
Weight (kg)	2.5-3.0	17	9 (25.0)	8 (22.2)	0.972
	3.01-3.50	17	8 (22.2)	9 (25.0)	
	3.51-4.50	25	13 (36.1)	12 (33.3)	
	> 4.50	13	6 (16.7)	7 (19.4)	
Head circumference	30-35	18	8 (22.2)	10 (27.8)	0.538
	36-40	53	27 (75.0)	26 (72.2)	
	> 40	1	1 (2.8)	0 (0)	
Length (cm)	40-45	5	2 (5.6)	3 (8.3)	0.867
	46-50	25	12 (33.3)	13 (36.1)	
	51-55	37	19 (52.8)	18 (50.0)	
	56-60	4	2 (5.6)	2 (5.6)	
	> 60	1	1 (2.8)	0 (0)	

The physiological indicators of pain in the neonates recorded before the circumcision were as shown in Table 2 below and they were comparable with regard to heart rate, respiratory rate and oxygen saturation.

Table 3: Physiological indicators of pain in the neonates recorded before the circumcision at baseline.

Parameters	Treatment allocation		p-value
	EMLA Mean ± SD	Placebo Mean ± SD	(0.05)
Heart rate	139.67±5.4	139.42±5.26	0.843
Respiratory rate	48.22±1.9	48.28±1.9	0.900
Oxygen saturation	96.11±1.8	95.97±1.8	0.748

Table 4: Physiological changes due to pain in the neonates during circumcision

Parameters	Treatment allocation		p-value
	EMLA Mean ± SD	Placebo Mean ± SD	
Heart rate	142.2±3.6	152.3±6.3	0.001
Respiratory rate	49.1±3.0	53.2±2.9	0.001
Oxygen saturation	93.3±3.2	89.8±2.2	0.001

The pain scores recorded during the circumcision are shown in Table 5. None of the neonates had a pain score of less than 3 during the circumcision. The experimental group (EMLA) had statistically, significantly lower pain scores than the control group (placebo).

Table 5: Pain scores (NIPS) recorded during circumcision

Pain scores	Total	Treatment allocation: EMLA (n = 36) N (%)	Placebo (n = 36) N (%)	p-value
< 3	0	0 (0)	0	
3	6	6 (16.7)	0	
4	10	10 (27.8)	0	
5	16	14 (38.9)	2 (6.0)	
6	40	6 (16.7)	34 (94.0)	0.0005

The pain scores recorded during the circumcision showed that the difference in the NIPS scores was statistically significant for the arms movement and cry parameters

Table 6:Pain scores (NIPS) during circumcision by parameter.

Parameter	Treatment allocation: EMLA	Placebo	p-value
Facial expression	36	36	0.500
Cry	28	71	0.000
Breathing pattern	36	36	0.500
Arms movement	29	35	0.013
State of arousal	36	36	0.500

Results from the independent t-test indicated that there was a significant mean pain score (NIPS) difference between the intervention (EMLA) and the control (placebo) groups, t = 8-360, p = 0.001 (p < 0.05); the mean values were 4.56 ±0.9 for intervention group and 5.94 ±0.2 for control group, meaning that the control group had a significantly higher mean value of NIPS score than the intervention group.

DISCUSSION

Circumcision is the commonest procedure performed in the neonatal population.[21] This procedure is often done without the benefit of anaesthesia. This is probably because of the general belief that neonates do not experience pain with the same intensity as adults. Physicians may also be reluctant to use anaesthesia for circumcision of neonates because of concern regarding efficacy and safety. In the study environment, there are only few studies describing the benefits of anaesthesia for neonatal circumcision especially with objective outcome measures like the NIPS. Hence, this study hypothesized that topical anaesthesia is effective in decreasing the pain response during neonatal circumcision and this can be objectively measured using the NIPS.

The mean age of the neonates in the study was 12 ±2 days. Generally, the common age for neonatal circumcision is 2 to 30 days.[22] Osifo and colleagues in a similar study in Benin city, Nigeria reported a mean age of 7.6 ±4.2 days.[23] Osuigwe and colleagues reported a mean age of 8 days and Okeke et al in Ibadan found a mean age of 9 days.[24,25] This could be reflective of the reasons for the circumcision which is mainly sociocultural in many parts of Nigeria. It is believed to be a commandment in the Holy Books of both the Bible and the Quran for a male child to be circumcised on the eighth day or after one week of birth. In this study, the mean age of the circumcised neonates was 12 ±2 days. This is probably because circumcision is usually done only on Mondays of every week in the research centre.

In this study, the mean of the weight of the neonates was 3.7±0.5kg, while in a similar study in Israel, Dollberg et al reported a mean weight at circumcision of 3.3 ±0.6kg.[26] Also the mean of the head circumference in this study was 38.4±0.3cm, and the mean of the length of the neonates was 53.3±0.7cm. The control and the intervention group were similar with regards to the physical characteristics and this was in consonance with the findings of the study by Dollberg and colleagues in an Israeli population. These similarities may be reflective of the age at circumcision which was almost the same in the two countries.

In this study, the mean oxygen saturation for those that received topical anaesthesia before the circumcision was 93.3±3.2 compared to 89.83±2.2 in those who were not anaesthesized. Crying and

increased intra-thoracic pressure is believed to have caused the desaturation. Perrin and colleagues state that neonates experiencing pain usually show a decrease in oxygenation.[27] The mean heart rate for those that received topical anaesthesia before the circumcision was 142.19±3.6 beats per minute compared to 152.3±6.3 beats per minute in those who did not receive topical anaesthesia. In this study also, neonates who did not receive topical anaesthesia before the circumcision had higher respiratory rate compared to those who received topical anaesthesia before the circumcision. The infants in both groups began to cry at the onset of the painful stimulus and they started breathing more quickly. However, the mean respiratory rate was less in those that received topical anaesthesia before the circumcision compared to the control group. These differences in the mean oxygen saturation, mean heart rate and the mean respiratory rate between the two groups were statistically significant. This result is similar to that of other studies done previously.[22,28]

In this study, the use of topical anaesthesia during circumcision is associated with an average NIPS score of 4.56 ±0.9 while an average NIPS score of 5.94 ±0.2 was found in those infants who did not receive topical anaesthesia before the circumcision. This difference in the average NIPS score between the two groups was statistically significant.

Overall, this shows that topical anaesthesia significantly decreases the pain responses during circumcision as evidenced by decreased physiological and behavioural response associated with the procedure. Other previous studies also reported similar findings as in this study.[12,13]

CONCLUSION

Neonates show objective evidence of significant pain during neonatal circumcision. Those neonates receiving topical anaesthesia before circumcision experienced significantly less pain, as evidenced by reduction in their mean NIPS score, smaller decreases in transcutaneous oxygen levels, and smaller increases in heart rate and respiratory rate, than neonates who received a placebo before the circumcision. This calls on clinicians involved in neonatal circumcision to modify their practices and include safe analgesia.

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REFERENCES

1. Kumar H, Elavarasi P. Definition of pain and classification of pain disorders. Journal of Advanced Clinical & Research Insights. 2016; 3:87 - 90.
2. Hall RW, Anand KJS. Physiology of Pain and Stress in the Newborn. Neoreviews 2005; 6: 61.
3. Hatfield LA. Neonatal pain: What's age got to do with it? Surgical Neurology International. 2014; 5(13): 479 - 89.
4. Anand KJ. Pharmacological approaches to the management of pain in the neonatal intensive care unit. Journal of Perinatology. 2007; 27(1): 4-11.
5. Batton DG, Barrington KJ, Wallman C. Prevention and management of pain in the neonate: an update. *J Am Acad Pediatrics.* 2006; 118(5):2231–2241.
6. Fitzgerald M. The development of nociceptive circuits. Nat Rev Neurosci 2005; 6:507–520.
7. Williams HT, Alma MM, Colin JP. Pain during Mogen or plastibell circumcision. J Perinatology 2002; 22:214-218.
8. Lidow MS. Long-term effects of neonatal pain on nociceptive systems. *Pain.* 2002; 99:377-383.
9. Bhutta AT, Anand KJS. Vulnerability of the developing brain. Neuronal mechanisms. *Clin Perinatol.* 2002; 29(3):357–372.
10. Grunau RV, Holsti L, Peters JW. Long-term consequences of pain in human neonates *Semin Fetal Neonatal Med.* 2006; 11(4): 268–275.
11. Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. *Cochrane Database Syst Rev.* 2004; 4:CD004217.
12. Kaur G, Gupta p, Kumar A. A Randomized Trial of Eutectic Mixture of Local Anesthetics during Lumbar Puncture in Newborns. *Arch Pediatr Adolesc Med.* 2003; 157:1065-1070.
13. Taddio A, Olsson K, Ohlsson A. Lidocaine-prilocaine cream for analgesia during circumcision in newborn boys. Cochrane Database Syst Rev. 2003; 1:CD000496.
14. Eyelade OR, Oladokun RE, Fatiregun AA. Convergent validity of pain measuring tools among Nigerian children. *Afr J Med Med Sci* 2009; 38(4):333-336.

15. Bhutta AT, Anand KJS. Vulnerability of the developing brain. Neuronal mechanisms. *Clin Perinatol*. 2002; 29(3):357–372.
16. Hatfield AL, Gusic EM, Dyer Anne-Marie and Polomano CR. Analgesic Properties of Oral Sucrose during Routine Immunizations at 2 and 4 Months of Age. *J Am Acad Pediatrics*. 2008; 121:327-334.
17. Eyelade OR, Oladokun RE, Fatiregun AA. Convergent validity of pain measuring tools among Nigerian children. *Afr J Med Med Sci* 2009; 38(4):333-336.
18. Indrayan A, Satyanarayana L. Simple Biostatistics for MBBS, PG Entrance and USMLE. 2ND Ed. New Delhi. Academa: 2006; 177-179.
19. Gradin M and Schollin J. The Role of Endogenous Opioids in Mediating Pain Reduction by Orally Administered Glucose Among Newborns. J Am Acad Pediatrics 2005; 115: 1004-1007.
20. Gallo AM. The fifth vital sign: implementation of the Neonatal Infant Pain Scale. J Obstet Gynaecol Neonatal Nurs 2003; 32(2):199-206.
21. Ridings H, Amaya M. Male neonatal circumcision An evidence-based review. Journal of the American Academy of Physician Assistants. 2007; 20(2):32-6.
22. Taddio A, Ohlsson K, Ohlsson A. Lidocaine-prilocaine cream for analgesia during circumcision in newborn boys (Cochrane Review). In: The Cochrane Library, Issue 4, 2002.
23. Osifo DO, Osaigbovo EO. The prevalence, postnatal descent, and complications of undescended testes among children who underwent neonatal circumcision in Benin City, Nigeria. J Paediatric Surg. 2009; 44(4): 791-6.
24. Osuigwe AN, Ikechebelu JI, Okafor PIS. Circumcision-Related Complications in the Male: Experience among the Igbos of Southeast Nigeria. African Journal of Urology. 2005 10(4) ISSN: 1110-5704.
25. Okeke LI, Asinobi AA, Ikuerowo OS. Epidemiology of complications of male circumcision in Ibadan, Nigeria. BMC Urology 2006; 6: 21.
26. Stolik-Dollberg OC, Dollberg S. Bupivacaine versus lidocaine analgesia for neonatal circumcision BMC Pediatrics 2005, 5:12.
27. Perrin S, Meiser-Stedman R. The children revised impact of event scale (CRIES): Validity as a screening instrument for PTSD. Behavioural and cogtnitive psychotherapy. 2005; 33:487-498.
28. Nelson CP, Dunn R, Wan J, Wei JT. The increasing incidence of newborn circumcision: data from the nationwide inpatient sample. Journal of Urology 2005; 173 (3): 978981.