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ORIGINAL ARTICLE

EFFECTIVENESS OF ORAL SUCROSE IN DECREASING PAIN DURING ROUTINE INFANT IMMUNIZATION INJECTIONS IN AN URBAN HOSPITAL IN JOS, NIGERIA

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ABSTRACT

Background: Routine immunization injections are the most common painful procedure of childhood, for healthy infants beyond the neonatal period. This is frequently performed without analgesia, probably because of the belief that infants do not experience pain with the same intensity as adults. However, newborns have the anatomical and functional components required for perception of painful stimuli, and unmanaged pain can affect central nervous system development and may ultimately affect neurologic function. Oral sucrose, which is inexpensive, short acting, non-sedating and easily administered has been shown to be a safe and effective method of pain relief during routine immunization in young infants.
Objective: To determine whether oral sucrose decreases pain response during routine infant immunization injections, with the overall purpose of recommending its use in hospitals.
Methods: This was a randomized, double blind interventional study; comparing pain scores between infants who received oral sucrose and control group who received placebo before immunization injections at 6 and 14 weeks of age. Infants 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 immunization. Acute behavioural pain response was quantified using the Neonatal Infant Pain Scale [NIPS] and results compared between the two groups.
Results: The control and the intervention group were similar with regards to mean weight (4.67±0.5kg versus 4.66±0.7kg, p=0.922), head circumference (39.42±0.3cm versus 39.50±0.2cm, p=0.665), and length (56.41±0.3cm versus 56.34±0.7cm, p=0.343). Infants who had oral sucrose before immunization injections had lower mean NIPS score compared to the control group (5.39 ±0.9 versus 6.90 ±0.3*, P = 0.001)*. Also, they had smaller decreases in transcutaneous oxygen levels, from 96.82±2.2 to 93.71±2.9, compared to the control group, from 96.97±1.6 to 91.74±3.1. They also had smaller increases in heart rate compared to the control group, from 134.74±3.5 to 137.27±7.8 beats per minute versus, from 133.42±7.3 to 145.00±8.6 beats per minute; and respiratory rates, from 44.29±2.4 to 46.17±4.5 compared to from 46.53±1.3 to 50.62±5.4 in the control group.
Conclusion: Infants receiving oral sucrose before the immunization injections experienced significantly less pain, smaller decreases in transcutaneous oxygen levels, smaller increases in heart rate and respiratory rate than controls.

INTRODUCTION

The invention and administration of immunizations are among the major achievements in medical practice, and their impact on disease prevention and reduction of human suffering cannot be over-emphasized.[1] Hundreds of millions of cases of illness and millions of deaths have been prevented by these agents. To provide this protection, the National Programme on Immunization schedule recommends many separate injections before the age of two years. The number of immunizations now recommended, necessitates that multiple injections be administered at the same visit. Despite the proven benefit of immunizations, the pain associated with the multiple frequent injections is a source of great concern and distress for, not only the children themselves but also their families and even the health care providers.[1,2]

Infant injection-related pain remains largely untreated despite increased focus on pain assessment and management in Family Practice. Injection-related pain in infants deserves attention because untreated pain has immediate and measurable negative effects, most notably child and parental distress.[3] Whenever a child received multiple injections at a single visit during routine immunization, the primary concern of both physicians and parents was reported to be pain.[5] Although the long-term consequences of pain and stress in human infants are unknown, evidence from animal trials indicate that pain and stress suffered early in life permanently alter the central nervous system.[3-5] Long-term effects of unmanaged pain in human infants have also been shown to include permanent impairment of cognitive development, including learning, memory, and behaviour in childhood.[1,4] The plasticity of the developing brain and the changes that occur in response to painful stimuli also contribute to altered perceptions of pain later in life.[5] Early painful experiences affect children's future response to analgesia.[6] Also, inadequate analgesia in young children during initial

procedures diminished the effects of adequate analgesia during subsequent procedures.[4-6]

Although children are vulnerable and are entitled to special consideration, inadequate prevention and relief of pain in children is still widespread. This failure largely reflects shortcomings in recognizing children's ability to perceive, respond to and be harmed by pain.[1,7]

For healthy infants beyond the neonatal period, routine immunization injections are the most common painful procedure of childhood. Analgesics for this routine intervention must therefore be effective, safe, practical, and easy to use.[7] Currently, pain associated with immunization is managed by acetaminophen, ibuprofen or topical anaesthetics, but these treatments may not provide the best relief or are not always practical for use on a routine basis.[8]

Moreover, recent randomized controlled trials on the effect of paracetamol on the immunology of vaccines concluded that prophylactic paracetamol at the time of infant vaccination reduces the risk of fever but also significantly reduces the resulting post vaccine antibody response.[9,10]

The American Pediatric Society, Canadian Paediatric Society, and the American Pain Society recommend the use of sucrose for minor painful procedures in neonates.[7,11]

Sucrose has been examined for its effectiveness in calming distressed term newborns and for its analgesic properties in term and preterm infants for pain associated with venepuncture and heel lance. A meta-analysis revealed that a dose of 1 to 2ml of a 24% sucrose solution administered approximately two minutes before a minor procedure was effective in treating pain from mild, brief procedures.[11] It has been shown to be an effective, short acting, easily administered method of procedural analgesia in young infants in a number of clinical trials.[11-13]

The mechanism underlying the analgesic effects of sugars is thought to involve the activation of lingual sweet taste receptors and release of endogenous brain opioids.[13]

Although the analgesic properties of various amounts and concentrations of oral sucrose for procedure-related pain have been tested, the optimal dose of oral sucrose has not been established. Summaries of randomized, controlled trials (RCTs) suggest that a single dose of 0.5 to 2.00 mL of 12% to 50% sucrose delivered by nonnutritive sucking (NNS) via a pacifier for two minutes before a painful event is safe and effective in decreasing physiologic (e.g. heart rate, respiratory rate, and oxygen saturation) and behavioural pain indicators (e.g. crying, facial expression, and motor activity), and in reducing overall composite pain scale scores among hospitalized neonates at 32 to 40 weeks of gestation.[11]

Assessment and relief of pain, as in any other routine observation or examination should become a priority for professionals involved in the treatment of infants 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 infants.[4] For example, high internal consistency and reliability was demonstrated for the University of Wisconsin Children's Hospital (UWCH) Pain Scale.[4]

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] scores, 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.[15]

The Neonatal Infant Pain Scale [NIPS] was used for this study because it is a proven, objective and replicable tool for assessing pain responses in children less than one year of age. Its validity and high internal consistency have previously been demonstrated.[15]

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 infants who received oral sucrose and those who received placebo before immunization injections at 6 and 14 weeks of age. Infants at 6 weeks and 14 weeks of age were chosen for this study because a minimum of two injections are given at this age according to the National Programme on Immunization schedule. 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 routine immunization. A total of 154 infants were randomly assigned to the two groups; oral sucrose group and placebo group. Computer generated random numbers were prepared and sealed in opaque unmarked envelopes containing group assignments. Mothers were asked to pick the envelop which assigned the infants to either receive 2ml of 50% sucrose solution (wt/vol) or sterile water before the immunization.

The sample size 70 infants in each group was calculated using the formula.[16]

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

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 study in Sweden,[17] gave

$s = 2.5$

The expected size of the difference in the mean pain scores to be detected in the two groups, d = 0.6 at 80% power and 95% confidence interval (alpha = 0.05).
Therefore, minimum sample size in each group,

$$N = 4(2.5)^2/(0.6)^2$$
$$= 4(6.25)/(0.36)$$
$$= 69.44$$

An assumption of 10% drop out rate to account for participant disenrollment or incomplete data sets was made. The sample size was therefore placed at 154 infants, 77 in each group.
For each infant, a full physical examination was done including weight, heart rate, respiratory rate, oxygen saturation, length and head circumference. Infants were then randomly assigned to either treatment or control arm by asking the mothers to pick opaque unmarked envelopes containing computer generated random numbers which assigned the infant to either receive 2ml of 50% sucrose solution (wt/vol) or sterile water.
The test solutions were prepared fresh by dissolving 50 grams of table sugar in 100ml of sterile water inside coded bottles and administered by 2ml syringe to the front of the infant's tongue, slowly over one minute. The nurse and parents were blinded to the nature of the solutions throughout the study. The principal investigator conducted the consultation including data collection, preparation of the test solutions and other health advice. A nurse assistant administered all the test solutions given by mouth using 2ml syringe. Polio immunization was given by mouth first, followed by the test solution. Infant injections were given in the thigh by another nurse two minutes after taking the test solution in a separate room. Hepatitis B immunization was administered in the left thigh and immediately after, DPT vaccine was administered in the right thigh. All infants were in the awake state at the time of the procedure and there was no additional cost to the patient for the analgesia.
Acute behavioural pain response was quantified using the Neonatal Infant Pain Scale [NIPS].[18] It consists of six behavioural components with composite scores of 0 to 7. Each behavioural indicator is scored with 0 or 1 except "cry", which has three possible descriptors therefore, being scored with a 0, 1 or 2. A NIPS score of < 3 is interpreted as "No pain" a score of 3 to 5 is interpreted as mild to moderate pain and a score of 6 to 7 is interpreted as severe pain. Physiological changes such as heart rate, respiratory rate and oxygen saturation were also measured.
Data analysis was conducted using SPSS 21 (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 infants who received oral sucrose with those who received placebo before the immunization injections**.** The level of significance was set at P-value of less than 0.05.

RESULTS

Out of the 186 infants seen during the study period, 32 were excluded for various reasons. A total of 154 neonates were recruited and completed the study. All the infants 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 infants

			Treatment allocation		
			Oral Sucrose (n = 77)	Sterile Water (n = 77)	p-value
		Total	N (%)	N (%)	
Age (Weeks)	6 weeks	76	38 (49.35)	38 (49.35)	0.564
	14 weeks	78	39 (50.65)	39 (50.65)	
Weight (kg)	2.5-3.0	22	12 (15.58)	12 (15.58)	0.922
	3.01-3.50	24	10 (12.98)	14 (18.18)	
	3.51-4.50	40	20 (25.97)	20 (25.97)	
	4.51- 5.0	58	30 (38.97)	28 (36.36)	
	>5.0	10	5 (6.49)	5 (6.49)	
Head circumference	30-35	12	7 (9.09)	5 (6.49)	0.665
	36-40	106	54 (70.12)	52 (67.53)	
	> 40	36	16 (20.77)	20 (25.97)	
Length (cm)	40-45	4	0 (0)	4 (5.19)	0.343
	46-50	17	9 (11.68)	8 (10.38)	
	51-55	56	30 (38.96)	26 (33.76)	
	56-60	66	32 (41.58)	34 (44.15)	
	> 60	11	6 (7.79)	5 (6.49)	

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

Table 2: Physiological indicators of pain in the neonates recorded at baseline.

	Treatment allocation			p-value
		Oral Sucrose (n =77)	Sterile Water (n = 77)	
	Total	N(%)	N (%)	
Heart rate (beats/minute)				
<120	13	6 (7.8)	7 (9.1)	0.901
121-130	53	28 (36.4)	25 (32.4)	
131-140	64	31 (40.3)	33 (42.9)	
141-150	16	9 (11.6)	7 (9.1)	
>150	8	3 (3.9)	5 (6.5)	
Respiratory rate (breath/minute)				
<40	14	9 (11.7)	5 (6.5)	0.539
41-45	66	34 (44.2)	32 (41.6)	
46-50	56	27 (35.1)	29 (37.7)	
51-60	18	7 (9.0)	11 (14.2)	
Oxygen saturation (%)				
90-92	4	3 (3.9)	1 (1.3)	0.962
93-95	49	24 (31.2)	25 (32.4)	
96-98	64	31(40.2)	33 (42.9)	
99-100	37	19 (24.7)	18 (23.4)	

The physiological changes due to pain recorded before and after the immunization included heart rate, respiratory rate, and oxygen saturation. These are presented in Tables 3 and 4 below.

Table 3: Physiological indicators of pain in the infants recorded before immunization at baseline.

Parameters	Treatment allocation		p-value (0.05)
	Oral sucrose Mean ± SD	Sterile Water Mean ± SD	
Heart rate	134.74±3.5	133.42±7.3	0.722
Respiratory rate	44.29±2.4	46.53±1.3	0.623
Oxygen saturation	96.82±2.2	96.97±1.6	0.949

Table 4: Physiological changes due to pain in the infants after immunization injections

Parameters	Treatment allocation		p-value
	Oral Sucrose Mean ± SD	Sterile Water Mean ± SD	
Heart rate	137.27±7.8	145.00±8.6	0.001
Respiratory rate	46.17±4.5	50.62±5.4	0.001
Oxygen saturation	93.71±2.9	91.74±3.1	0.001

The pain scores recorded after immunization are shown in Table 5. None of the infants had a pain score of less than 4 after the immunization. The experimental group (Oral Sucrose) had statistically, significantly lower pain scores than the control group (Sterile Water).

Table 5: Pain scores (NIPS) recorded during the immunization

Pain scores	Total	Treatment allocation		P - Value
		Oral Sucrose (N = 77) N (%)	Sterile Water (N = 77) N (%)	
< 4	0	0 (0)	0	
4	16	16 (28.8)	0	
5	26	26 (33.8)	0	0.0005
6	33	25 (32.5)	8 (10.4)	
7	79	10 (12.9)	69 (89.6)	

Results from the independent t-test indicated that there was a significant mean difference in NIPS score between the intervention (Oral sucrose) and control (sterile water) groups, (5.39 ±0.9 vs 6.90 ±0.3 p = 0.001)

DISCUSSION

Pain associated with immunization injections is a source of concern and distress for children receiving immunizations, their parents, and the providers who must administer them. Nevertheless, routine immunization is frequently performed without the benefit of analgesia. This is probably because of the general belief that infants do not experience pain with the same intensity as adults. In the study environment, there are few studies describing the benefits of analgesia for routine immunization. Hence, this study hypothesized that oral sucrose is effective in decreasing the pain response during routine immunization injections.

This study focused on infants presenting for routine immunization at 6 weeks and 14 weeks of age, because a minimum of two injections are given at 6 weeks and 14 weeks of age according to the National Programme on Immunization schedule. In a similar study by Hatfield and colleagues, infants at two months and four months of age were studied because multiple injections are given at that age in the American population.[4]

In this study, the mean of the weight of the infants for the two groups was 5.80±0.3kg, while the mean of the head circumference was 39.46±0.2cm, and the mean of the length of the infants was 56.38±0.5cm. The control and the intervention group were similar

with regards to these physical characteristics but this was overall lower than that reported by Hatfield and colleagues for an American population.[4] The infants in the American study were slightly older, but it could also be due to the fact that mothers were more affluent than their counterparts in the Nigerian population. The measurements in this study are however higher compared to other reports from a Nigerian population. Ukegbu and colleagues had previously reported a mean weight of 4.23±0.2kg, mean head circumference of 38.01±0.3cm and mean length of 53.21±0.4cm.[19] This variation could be because Ukegbu and colleagues' study was conducted in rural communities where their parents probably had lower socioeconomic status compared to this study which was conducted in urban setting.

The mean oxygen saturation for those infants that received oral sucrose before the immunization injections was higher than in those who received sterile water. Crying and increased intra-thoracic pressure is believed to have caused the desaturation. Perrin and colleagues stated that infants experiencing pain usually show a decrease in oxygenation.[20] The mean heart rate for those that received oral sucrose before the immunization injections was lower compared to the control group. In this study also, infants who took the placebo before the immunization had higher respiratory rate compared to the intervention group. The infants in both groups began to cry at the onset of the painful stimulus and started breathing more quickly. However, the mean respiratory rate was less in those that were given oral sucrose before the immunization injections 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 the study done previously by Sharek and colleagues.[21]

In this study, the use of oral sucrose during routine immunization is associated with a lower mean NIPS score compared to those infants who did not receive oral sucrose before the immunization injections. This difference in the average NIPS score between the two groups was statistically significant.

Overall, this shows that oral sucrose significantly decreases the pain score and pain responses during routine immunization injections as evidenced by decreased physiological and behavioural response associated with the procedure. Other previous studies also reported similar findings as in this study.[22-27]

CONCLUSION

Infants show objective evidence of significant pain during routine immunization. Those infants receiving oral sucrose before immunization injections 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 infants who received a placebo before the immunization. This calls on primary care physicians involved in immunization procedures to modify their practice based on current evidence from research.

Implication for policy makers

1. The National Programme on Immunization should ensure that the number of separate injections on a single visit during routine infant immunization is minimized.
2. Policy makers should ensure availability of effective, safe, practical, and easy to use analgesics for routine interventions like infant immunization injections.
3. Policy makers should take steps to integrate the use of oral sucrose during routine immunization injections.

Implication for clinical practice

1. Clinicians should always consider the use analgesia during routine infant immunization injections.
2. Clinicians should focus more on infant injection-related pain assessment, prevention and appropriate management
3. Use of pain scores for evaluation of pain as in any other routine observation or examination should become a priority for professionals involved in routine infant immunization injections.

Contribution of each author

1. Odekunle, Rotimi Raphael - Conceptualization, design of methodology, manuscript writing, literature search, data collection, analysis and presentation of findings and discussion.
2. Dankyau, Musa - Manuscript editing, contributed to the planning and final approval.

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