International Journal of Contemporary Pediatrics
Kavthekar S et al. Int J Contemp Pediatr. 2016 Nov;3(4):1375-1379
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20163681

Original Research Article

Comparison of analgesic effect of 24% sucrose and breast milk in healthy infants less than 2 months of age

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Received: 05 August 2016
Accepted: 13 September 2016

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ABSTRACT

Background: Many newborns undergo painful procedures like heel pricks, venepuncture and intramuscular injection for immunization. The medical and paramedical staffs usually ignore pain felt during these procedures. The aim of this study was to compare analgesic activity of 24% sucrose solution with breast milk during 1st DPT vaccination using sterile water as placebo.
Methods: This double blind, randomized placebo controlled trial was conducted in 150 healthy infants undergoing for their 1st DPT vaccination. Infants were randomized in to three groups of 50 each and received sterile water, 24% sucrose and breast milk 2 minutes prior to vaccination. The outcome variables were total duration of cry, first cry, change in heart rate and modified facial coding score (MFCS).
Results: Mean total cry was significantly lower in 24% sucrose babies 36.3 (25.34) seconds and breast milk babies 42.1 (26.13) seconds as compared to sterile water 137.2 (20.31) seconds. Mean first cry was significantly lower in 24% sucrose 18.2 (14.12) seconds and breast milk babies 25.1 (13.67) seconds as compared to sterile water 94.3 (23.26) seconds. Mean rise in heart rate (beats/min) at 3 minutes was significantly lower with 24% sucrose 3 (2.3)and breast milk 7.4 (4.6) as compared to sterile water 18.2 (4.61).Change in MFCS at 1min and 3 min was significantly lower in 24% sucrose and breast milk babies. Maximum reduction in total cry, first cry, lower rise in heart rate and low MFCS was with 24% sucrose as compared to breast milk group.
Conclusions: 24% sucrose and breast milk had analgesic activity in infants less than two months of age undergoing DPT vaccination. The analgesic effect was better for 24% sucrose as compared to breast milk.

Keywords: Analgesia, Breast milk, Infants, 24% Sucrose

INTRODUCTION

The myth regarding neonatal pain suggests that because of neurological immaturity, neonates do not experience pain. However, studies have shown that pain pathways as well as cortical and subcortical centres, necessary for pain perception are well developed late in gestation and physiological and behavioural responses to pain are well documented in neonates.[1] Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. It is difficult to assess pain in infants, as infants cannot verbalise their pain ,as they are dependent on others to recognize it, intervene it, treat it.[2] Many newborn babies undergo painful procedures like heel pricks, venepuncture and intramuscular injection for immunization, such procedures inflict distinct physiological, behavioral, hormonal and metabolic changes.[3] Moreover painful experience very early in life can promote somatization later in life.[4] Dextrose and sucrose in varying concentration have been shown to relive pain during venepuncture or intramuscular injection.[5-12] Breastfeeding or expressed breast milk have

also been shown to be effective for treating and preventing mild to moderate procedural pain.[13-17] Vaccination is the most common procedure performed in infancy, although parents might have significant concerns regarding the pain associated with routine vaccinations. The medical and paramedical staffs usually ignore pain felt during these procedures. This study was done to compare analgesic activity of 24% sucrose with breast milk during 1st DPT vaccination, using sterile water as placebo.

METHODS

This double blind, prospective, randomized placebo controlled trial was carried out in the immunization clinic of department of paediatrics, Dr. D.Y Patil Medical College, Kolhapur, Maharashtra, India. Written informed consent was taken from the parents and ethical clearance was taken from ethical committee of college. Healthy term infants less than two months of postnatal age who were on exclusive breast feed and attended the immunization clinic for first DPT vaccine were included. The following babies were excluded: preterm deliveries (<37 week of gestation), intrauterine growth retardation, birth asphyxia (Apgar score <5), infants who had required hospital admission for more than 48 hours, developmental delay with neurological deficit.

The babies were randomized into three groups of 50 each through computer generated random numbers and put in serially numbered opaque sealed envelopes (SNOSE method). The person generating random numbers and placing them serially in sealed envelope was not involved in the study. The name, age, sex, weight, length and head circumference were recorded in a pre-structured proforma. Babies were brought to the room where vaccination was to be done. At the recruitment, one person opened the sealed envelope and administered the allotted intervention in all the babies.

Randomized babies group

Sterile water group (placebo)

2 ml sterile water for injection was given orally by a sterile syringe 2 minutes prior to intramuscular vaccination.

24% sucrose group

Oral sucrose (Arbineo 24% w/v oral solution by Raptakos, Brett and co. Ltd) 2 ml was given orally by a sterile syringe 2 minutes prior to intramuscular vaccination.

Breast milk group

Babies in breast milk group were breastfed starting 2 minutes prior to vaccination till intramuscular vaccination.

All the babies received the intervention from one investigator only another two investigators would then come in the immunization room. Whole DPT vaccine, 0.5 ml by a 2 ml disposable syringe with 23 G" needle was given on the anterolateral aspect of thigh (left/right) after cleaning the skin with spirit, in the mother's lap by single nursing staff, so that duration and depth of needle insertion should remain apparently same in all babies. All events were recorded by audio video camera (Sony camcorder DCR SX 63) by the investigator for total duration of three minutes from the insertion of needle. A different investigator analysed the outcome variables from the audio video recordings in all babies. Three investigators were blinded to the pharmacological interventions given to the babies however none was blinded to the intervention of breastfeeding.

The outcome variables were total duration of cry, first cry, change in heart rate from base line and Modified facial coding score (MFCS).[15] Crying time was defined as the number of seconds the baby had distressed vocalization after needle insertion within the first 3 minutes. Duration of first cry was defined as duration of continuous crying before a quiet interval of 5 seconds. The MFCS was calculated immediately and after one and three minutes of needle insertion. This was a composite score obtained from the sum of the following: brow bulge, eye squeeze, nasolabial furrow, and open mouth, chin quiver and trunk movement. Each parameter was scored "0" if absent and "1" if present and the total score was obtained. One observer was responsible for giving the scores in all the babies. During breastfeeding, only one half of the face was visible; thus all facial parameters of MFCS were based on facial side which observer could see. Heart rate in beats/min was counted just before and after vaccination at 3 minutes by same investigator to avoid interpersonal error.

Every effort was made to ensure that the infant was awake before vaccination. The mothers were allowed to hold, talk or rock the baby during procedure in all groups. Non-nutritive sucking was not done during the procedure. All tests were performed between 10 am to 1 pm to avoid diurnal variation in pain response. All babies had been fed within three hours prior to the interventions but had not received a feed in the previous 30 minutes. All data was analysed by analysis of variance (ANOVA) test for multiple comparisons except MFCS which was analysed by Kruskal Wallis test in which $P < 0.05$ was significant.

RESULTS

150 babies were randomized into 3 groups of 50 babies each. The postnatal age, weight, sex and time since last breast feed was comparable in all three groups (Table 1).

Mean total duration of cry was significantly lower in 24% sucrose fed babies 36.3 (25.34) seconds and breast milk babies 42.1 (26.13) seconds as compared to babies given sterile water 137.2(20.31) seconds.

Mean duration of first cry was significantly lower in 24% sucrose babies 18.2 (14.12) seconds and breast milk babies 25.1 (13.67) seconds as compared to babies given sterile water 94.3(23.26) seconds (Table 2). Mean change i.e. rise in heart rate (beats/min) from base line was significantly lower in 24% sucrose fed babies 3 (2.3) and breast milk babies 7.4 (4.6) as compared to babies given sterile water 18.2 (4.61) (Table 3). Change in MFCS at 1 and 3 minutes was significantly lower with 24%sucrose and breast milk group as compared to sterile water group (Figure 1). Maximum reduction in total duration of cry, first cry, less rise in heart rate and lower MFCS at 1and 3 min was significant with 24% sucrose group as compared to breast milk group.

Table 1: Baseline characteristics of the study groups. mean (SD).

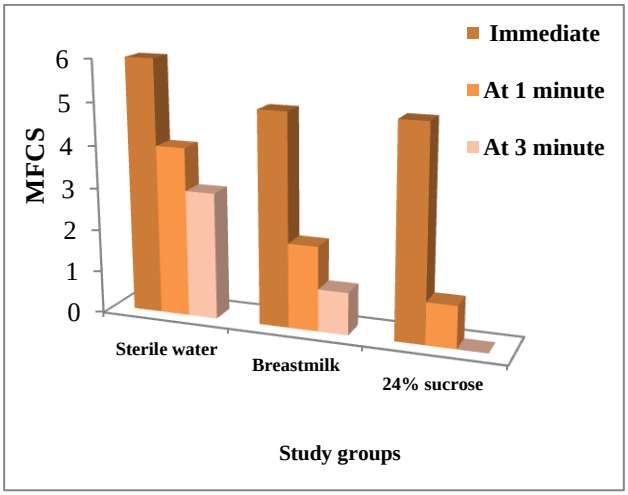
Parameter	Sterile water (n = 50)	Breast milk (n = 50)	24% sucrose (n = 50)
Age (weeks)	6.2 (2.2)	6.1 (2.2)	6.2 (2.4)
Weight (kgs)	4.1 (0.4)	4.2 (0.5)	4.1 (0.4)
Time since last fed (m/n)	47 (9.2)	42 (4.3)	44 (8.4)

Table 2: Duration of cry in each minute, total duration of cry and duration of first cry in seconds in study groups after DPT vaccination mean (SD).

Duration of cry in seconds	Sterile water	Breast milk	24% sucrose	F-statistics	Degree of freedom	P-value
First minute	59.7 (1.09)	30.3 (10.24)	26.3 (12.94)	182.45	149	0.000
Second minute	47.5 (9.99)	12.3 (13.39)	8.8 (11.68)	165.4	149	0.000
Third minute	30.4 (14.11)	5.2 (6.56)	1.3 (3.34)	147.77	149	0.000
Total cry	137.2 (20.31)	42.1 (26.13)	36.3 (25.34)	277.12	149	0.000
First cry	94.3 (23.26)	25.1 (13.67)	18.2 (14.12)	286.53	149	0.000

Table 3: Mean change in heart rate (beats/min) from baseline after DPT vaccination at 3 minutes in study groups.

Study groups	Mean heart rate (beats/min)		t-test			
	Before vaccination	After vaccination	Change in heart rate	't' value	Degree of freedom	'p' value
Sterile water	113.8 (9.2)	132.0 (9.4)	18.2 (4.61)	-9.784	98	0.000
Breast milk	111.4 (7.6)	118.8 (9.4)	7.4 (4.6)	-4.329	98	0.000
24% sucrose	110.9 (10.9)	113.9 (11.9)	3 (2.3)	-1.315	98	0.192



At 1 min: H = 40.891 with 2 degrees of freedom; P=0.000significant; At 3 min:H = 80.926with 2 degrees of freedom; P = 0.000significant.

Figure 1: Median change in MFCS in study groups.

DISCUSSION

Detection and quantification of pain in neonates and infants is difficult. Various behavioral, physiological and biological responses present in neonate can be used to assess pain.[18] Measures used to describe pain in infants include motor responses, facial expressions, cry and changes in physiological parameters like heart rate, blood pressure, oxygen saturation and respiratory rate. In this study four easily detectable parameters first cry, total duration of cry, heartrate and MFCS were used to assess pain. These are included because they are multidimensional and demonstrate evidence of reliability, validity and utility. However we have used MFCS pain score beyond neonatal age.

Present study demonstrated that babies who were given 24% sucrose or directly breast fed had significantly shorter duration of first cry, total duration of cry, lower rise in heartrate at 3 minutes and lower pain score at 1 minute and 3 minute as compared to placebo after

intramuscular vaccination. Hourai et al using oral sucrose as an analgesic agent found decrease in duration of first cry and total duration of cry in neonates given 12.5%, 25% and 50% sucrose solution with maximum effect for 50% sucrose.[8] Stevens et al, Hatfield et al, Blass et al, Ramenghi et al showed reduction in crying time using sucrose solution.[6,9-11] Upadhyay et al had demonstrated expressed breast milk significantly reduces pain in term infants prior to venepuncture.[15] Osinaike et al and Singh et al demonstrated similar effect for breast feeding while doing venepuncture and intramuscular injection respectively.[16,17] Goswami G et al compared analgesic effect of breast feeding and 25% dextrose and found that direct breast feeding is more superior than 25% dextrose.[19] No other previous study has directly compared analgesic effect for breast feeding and sucrose. Thakar P et al evaluated analgesic effect in newborns for combined use of sucrose and non-nutritive sucking while undergoing minor painful procedure.[20]

The analgesic effect of sucrose occurs firstly by activation of central endogenous opioid system an action similar to that of opioid (e.g. morphine) analgesic. They also stimulate release of endorphins from hypothalamus. Endorphins act by binding to opioid receptors in the CNS to inhibit the feeling of pain. Thus increasing and prolonging the relief from pain and promoting a sense of wellbeing in the neonate as demonstrated by reduced crying. Secondly because of presence of sweet taste in the mouth; researchers have termed this as 'sweetness effect'.[21] The peak response time of 2 minutes is the time needed for taste stimulation to activate the endogenous opioid system for the release of endorphins. The duration of action is 5-10 minutes.[22]

Efe E et al and Gray L et al hypothesized that following mechanisms could be attenuating the pain response while direct breast feeding the baby during the painful procedure.[23-24] Firstly, suckling at the breast stimulates the infant's oropharyngeal tactile and mechanoreceptor and focuses attention on the mouth, reducing outside influences. Secondly, sweet flavour of milk stimulates the release of opioids in mid brain of infants which act on receptor that decrease the perception of pain. Thirdly, breast feeding involves maternal skin to skin contact which stabilizes blood glucose level, body temperature and respiratory rate and reduces release of stress hormone. Fourthly, breast feeding involves intimate social interaction between mother and child and may release anti-stress hormone, oxytocin.

CONCLUSION

Oral 24% sucrose and breast milk had analgesic effect during intramuscular 1st DPT vaccination in infants less than two months. This effect was better for 24% sucrose as compared to breast milk. Both could be used simultaneously to enhance the analgesic effect.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Kavthekar S, Patil R, Kurane A, Bharati H. Comparison of analgesic effect of 24% sucrose and breast milk in healthy infants less than 2 months of age. Int J Contemp Pediatr 2016;3:1375-9.