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Original Article

Paediatrics Section

Comparative Study between Analgesic Effect of Breast Feeding and Oral Sucrose in Full Term Newborns

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ABSTRACT

Introduction: Non-pharmacological measures like oral sucrose and breast feeding are recommended modalities to treat acute procedural pain in newborns. Birth dose of hepatitis B vaccine exposes newborns to pain of intramuscular injection which is preventable. The present study has been carried out to assess the severity of pain and the effect of breast feeding and oral sucrose.

Aim: To study the pain profile and the effects of breast feeding and oral sucrose solution on pain, in full term newborns.

Materials and Methods: A prospective interventional case control study was carried out in the Department of Paediatrics and Post natal ward of Obstetrics and Gynaecology associated Gandhi Memorial Hospital. Randomly selected 150 full term vaginally delivered healthy newborns were enrolled in the study. Recruited newborn infants were grouped into three arms and each arm had 50 newborns. Group I as control group, and group II and III as intervention groups. A 1 mL of 25% oral sucrose solution was given two minutes before the vaccination in group II. Breast feeding was started 2 minutes before vaccination and continued till the end of injection in group III. The primary outcome of the study was to assess pain by Premature Infant Pain Profile (PIPP) score. PIPP score was compared by using ANOVA test and student's t-test was used to compare continuous variables and two tailed Fisher-exact test or Chi-square test was used to compare categorical variables. The critical levels of significance of the results were considered at 0.05 levels i.e., $p<0.05$ was considered significant.

Results: Mean PIPP scores were lower in group III (8.36) than in group II (11.06) and difference was significant ($p<0.0001$). The pain profile of newborns ranged from 9 to 18 with mean of 14.26 in group I, from 5 to 12 with mean of 11.06 in group II and from 1 to 12 with mean of 8.36 in group III respectively.

Conclusion: Intramuscular injection produces moderate to severe pain response in group I and mild to moderate pain responses in group II and III. Breast feeding provides superior analgesia to oral sucrose and reduces moderate to severe painful response to mild to moderate grade in term newborns.

Keywords: Intramuscular injection, Pain, Vaccination

INTRODUCTION

The anatomical, physiological and neurochemical structures that convey pain are well developed at 24 weeks of gestation and thereafter foetus experiences pain [1]. Assessment of pain and its management is an integral part of care in neonatal intensive care unit. Non-pharmacological measures like pacifier, oral sucrose and glucose, swaddling, skin to skin contact with mother, massage and acupuncture therapy are recommended modalities to treat acute, transient or mild pain and as adjunctive therapy for moderate to severe pain [2]. Intramuscular injection produces acute transient pain in newborns. Breast feeding [3-7], Expressed Breast Milk (EBM) [8], oral sucrose [9,10] and glucose [10,11] has analgesic effect on acute procedural pain. Most of these studies examined effect on pain caused by heel sticks, venipuncture, eye examination and circumcision. Limited studies have examined the effect of oral sucrose, skin to skin contact and kangaroo mother care on newborns pain during intramuscular injections [12-16]. Only one study has examined the effect of breast feeding on newborns pain during intramuscular injection [17]. Pain scale used by investigator had limited reported clinical utility [18]. American Academy of Paediatrics (AAP) recommends nine commonly used pain assessment scales for acute procedural pain [19]. PIPP scale has established adequate psychometric properties (validity, reliability) and clinical utility for use in the infants [20]. The present study has been carried out to assess severity of pain and effect of breast feeding and oral sucrose in healthy full term newborns on birth dose of hepatitis B vaccine.

MATERIALS AND METHODS

This prospective interventional case control study was carried out in the Department of Paediatrics and Post natal ward of Obstetrics and Gynaecology, associated Gandhi Memorial Hospital over a period of one year from July 2010 to June 2011. The inclusion criteria were vaginally delivered, breastfeed, full term newborns with mean age of 40 hours and weight ranged from 2.59 to 2.732 kg. Exclusion criteria were sick newborn, formula fed, and those newborn whose mother received general anaesthesia and opiods during delivery. Informed and written consent was taken from parent/guardian and ethical committee approval was obtained before starting the study.

For sample size calculation we did a pilot study on 20 newborns and was found that mean PIPP score was 11 after giving 1 mL of 25% oral sucrose. So on assuming that there is 15% decline in mean PIPP score in breast feeding group, with power of study 90% and with alpha error of 0.05, a sample size of 51 newborns was required.

Intervention

Recruited newborns were divided into control (group I) and intervention groups (group II and group III). Newborns were vaccinated on mother's lap without any intervention in group I. A 1 mL of 25% oral sucrose was given two minutes prior to vaccination in group II. Breast feeding was started two minutes prior to vaccination and continued till the end of injection in group III.

Newborns were attached with BPL ACCURA MPM5553 multipara monitor using a neonatal probe. One lady attendant/Staff nurse along with mother was present when breast feed newborns were vaccinated. With all aseptic precautions, 0.5 mL hepatitis B vaccine

S. No	Baseline characteristics	Group I	Group II	Group III	p-value
1	Males	22 (44.0%)	29 (58.0%)	23 (46.0%)	0.318$
2	Females	28 (56.0%)	21 (42.0%)	27 (54.0%)	0.318$
3	Birth weight, mean (gram) SD	2597 (282)	2732 (341)	2641 (214)	0.056#
4	Length, mean (cm) SD	47.74 (1.54)	48.73 (2.22)	48.4 (1.30)	0.019#
5	Head circumference, mean (cm) SD	33 (0.92)	33.94 (1.25)	34.06 (0.71)	<0.001#
6	Mean age of vaccination (hrs) SD	46 (8.5)	42 (8.8)	44 (7.9)	0.06#
7	Heart rate, mean, SD	126.88 (12.47)	128.76 (12.28)	136.76 (13.89)	<0.001#
8	Oxygen saturation, mean (%), SD	96.30 (1.54)	96.86 (1.49)	95.66 (2.20)	0.004#
9	Heart rate[1], mean, SD	27.35 (9.28)	16.58 (7.89)	13.47 (7.32)	<0.001*
10	Oxygen saturation[2], mean, SD	4.19 (2.11)	2.07 (3.23)	2.33 (2.91)	<0.001*

[Table/Fig-1]: Neonatal infant baseline characteristics.
[1]. Mean increase in heart rate from baseline to 30 sec. after vaccination
[2]. Mean decrease in oxygen saturation from baseline to 30 sec. after vaccination
$Chi-square test was use to calculate the p-value
#One-way ANOVA parametric was use to calculate the p-value
*Wilcoxon signed rank test was use to calculate the p-value

was administered intramuscularly on anterolateral aspect of mid thigh to all neonates by auto disposable syringe. Position of baby (mother lap), the vaccinator, brand of vaccine and syringe used was the same throughout the study. Two observers were present during vaccination session, one for recording of facial expression of baby, and second observer was recording heart rate and oxygen saturation. Sucrose was administered in the absence of the observers and within two minutes, the intervention was done.

Gestational age was calculated by new Ballard score and behavioural state of newborns was assessed 15 seconds prior to vaccination, along with baseline recording of Heart Rate (HR) and SpO_2. The maximum HR and minimum oxygen saturation were noted between 0-30 seconds. Cry time was defined as the total duration of audible cry, and calculated by using the video time bar at 30 seconds, 60 seconds and 90 seconds and 120 seconds after vaccinations. The facial expression component of PIPP score was analysed by recording, the first 30 seconds of clipping by third observer. The primary outcome of the study was the PIPP score. It is a validated pain measure that includes contextual (behavioural state and gestational age), behavioural (brow bulging, eye squeezing and nasolabial furrowing) and physiological (heart rate and oxygen saturation) indicators of pain. Each indicator is scored in a 4 point scale (0-3) and total scores vary from 18 to 21 depending on the infant's gestational age. In mild to moderate grade pain total score would be 6 to 12 and scores more than 12 indicates moderate to severe pain in newborns [21,22].

All data were entered into excel sheet and analysed by using SPSS version 16. PIPP score were compared by using ANOVA test, student's t-test was used to compare continuous variables and two tailed Fisher-exact test or Chi-square test was used to compare categorical variables. The critical levels of significance of the results were considered at 0.05 levels i.e., p<0.05 was considered significant.

RESULTS

Out of 150 newborns, 74 were males and 76 were females. The neonatal characteristics like, mean birth weight, length, head circumference, mean age of vaccination and baseline heart rate and oxygen saturation were comparable between the groups [Table/Fig-1]. Mean PIPP scores were lower in group III (8.36) than in group II (11.06) and difference was significant (p<0.0001) The pain profile of newborns ranged from 9 to 18 with mean of 14.26 in group I, from 5 to 12 with mean of 11.06 in group II and from 1 to 12 with mean of 8.36 in group III respectively [Table/Fig-2]. Total duration of cry was lower in group III (23.8 sec) than group II (26.36 sec) and difference was not significant (p>0.05). The mean of heart rates were 13.47, 16.58 and 27.35 respectively in group III, group II and group I [Table/Fig-1]. The mean difference of increasing heart rate between group I and group II was 10.76, and between group I and group III was 13.88, and between group II and group III was 3.11 respectively. The difference was significant when compared with group I, II and III (p 0.001) and it was not significant between group III and group II (p 0.526) [Table/Fig-3].

Variable	Group I	Group II	Group III	p-value
PIPP scale, mean (range)	14.26 (9 to 18)	11.06 (5 to 12)	8.36 (1 to 12)	PIPP score t ½ (0.0001) t 1/3 (0.0001) t 2/3 (0.0001)
Total duration of cry, mean (second).	61.38 (15-135)	26.36 (7-76)	23.8 (0-90)	Total duration of cry t ½ (0.001) t 1/3 (0.0001) t 2/3 (>0.05)

[Table/Fig-2]: Comparative analysis of outcome variables in this present study.

Physiological Parameters	Group	Group	Mean Difference	Std. Error	p-value
HR_DIFF	Group I n=50	Group II	10.76607*	2.28791	<0.0001
		Group III	13.88189*	2.28791	<0.0001
	Group II n=50	Group III	3.11582	2.28791	0.526
SpO_2_DIFF	Group I n=50	Group II	2.11866*	0.70678	0.010
		Group III	1.86032*	0.70678	0.028
	Group II n=50	Group III	-.25834	0.70678	1.000

[Table/Fig-3]: Comparative analysis of mean difference of heart rate and SpO_2.
*The mean difference is significant at the 0.05 level.

The mean of oxygen saturation were 2.33, 2.07 and 4.19 respectively in group III, group II and group I [Table/Fig-1]. Difference in means of oxygen saturation between group I and group II was 2.11, between group I and group III was 1.86 and group II and group III was -0.25 respectively. The difference was significant when compared with group I (p 0.01) and it was not significant between group III and group II (p=1) [Table/Fig-3]. Minimum level of desaturation was observed in group II.

DISCUSSION

The observations of this study were, intramuscular injection produced moderate to severe pain response, breast feeding has superior analgesic effect than oral sucrose and physiological parameters (HR, SpO_2) and duration of cry were significantly lower in group II, and group III than group I, change in physiological parameters were not significant in group II and group III.

Analgesic effect of skin to skin contact, non nutritive sucking, kangaroo mother care, 24% oral sucrose, and 25-30% oral glucose were done in past by different researchers on pain induced by intramuscular injection in first 48 hours of life. The results are compiled in [Table/Fig-4]. Most of the studies mentioned in the table investigated the analgesic effect of skin to skin contact, and oral sucrose or glucose and found that skin to skin contact was superior to 25% glucose in reducing NFCS and NIPS (p=0.045) and NIPS score was lower in 30% glucose than water (p=0.001). A study by Moddares M et al., found that DAN score was lower in breastfeeding than control (p<0.001) [17]. None of the studies described the pain profile and comparison between analgesic effect of breast feeding

and oral sucrose. In the present study, it was found that pain intensity was mild to moderate in group II and III that means breast feeding or oral sucrose alone is not able to bring down the pain score below non treatable levels. There was equal effect shown by breast feeding and sucrose on increase in heart rate and decrease in oxygen saturation similar results were found by other researchers mentioned in [Table/Fig-4] [12-17,23,24]. Author had assumed that 15% lower score in group III than group II during pilot study in 20 newborns for sample size calculation, but this difference was 25%.

Author (reference), N	Comparison Group	Outcome measures and Main results
Kostandy R et al., [24]; n=72, Term infant	Skin to skin contact (SSC) No intervention	SSC neonates cried less compared to control (23 vs 32 seconds) and trend towards more rapid heart rate rise.
Liaw JJ et al., [12]; n=165, gestational age >36 week	Non nutritive sucking (NNS), 20% oral sucrose Routine care	Pain was significantly lower among infants in the NNS (p<0.001) and sucrose (p<0.001) groups than that in controls. Infants in the NNS and sucrose groups also had significantly lower mean heart and respiratory rates than the controls. Cry duration of infants receiving sucrose was significantly shorter than those in the NNS (p<0.001) and control groups (p<0.001).
Present study, n=150, term infants	Breastfeeding 25% oral sucrose No intervention	Mean Premature infant pain profile (PIPP) scores were lower in group III (8.36) than in group II (11.06) and difference was significant (p<0.0001). Total duration of cry was lower in group III (23.8 sec) than group II (26.36 sec) and difference was not significant (p>0.05). Breast feeding provides superior analgesia to oral sucrose and reduces moderate to severe painful response to mild to moderate grade in term newborns.
Chermont AG et al., [13]; n=640 term infants	Skin to skin contact and 25% glucose No intervention	Lower NFCS, NIPS and PIPP scores for skin-to-skin contact and 25% glucose group compared with each intervention alone and no intervention group (p<0.001 for each comparison). Skin to skin contact superior to 25% glucose group in reducing NFCS and NIPS (p=0.045).
Taddio A et al., [14]; n=240 gestational age >36 week	24% sucrose Placebo	PIPP score did not differ significantly between the sucrose and placebo groups for newborns of diabetic or non diabetic mothers.
Kashaninia Z et al., [15]; n=100, term infants	Kangaroo mother care (KMC) No intervention	The cumulative NIPS score immediately after injection in the intervention group was significantly lower (p<0.001) than in the control group.
Golestan M et al., [23]; n=90 term infants	50% glucose Water No intervention	No significant differences in HR between glucose and the other groups. Reduced crying time for glucose group compared with no intervention (p=0.0001) but not compared with water (p=0.191).
Moddares M et al., [17]; n=130 term infants	Breast feeding No intervention	The mean of pain severity (DAN score) in case group was 3.5 and in control group was 6.7 and it shows significant difference according to Mann-Whitney U test (p<0.0001).
Sajedi F et al., [16]; n=64 term infants	30% glucose Water	Lower NIPS scores for glucose group compared with water (p=0.001). No significant differences in HR between groups.

[Table/Fig-4]: Comparative analysis of different studies with present study [12-17,23,24].

LIMITATION

The limitation of present study was lack of blinding because in breastfeeding group it is not possible to blind. Four or more investigators were blinded for pharmacological intervention; intervention was given by first investigator alone and then other investigators entered the immunization room, one administered vaccine after calling aloud in when the needle was inserted and when the needle was removed. Other investigator recorded all events on a digital camera from the removal of the needle, and fourth investigator analysed the outcome variable from the recording. Following this protocol three investigators were blinded to the pharmacological intervention. We could not study the role of the different component of breast feeding or the mechanism behind the analgesic effect of sucrose. The strength of study was use of PIPP score to assess pain because scale is validated and proven to discriminate painful from non painful stimuli, and we compared the analgesic effect of breast feeding and oral sucrose on pain response induced by intramuscular injection within 48 hours of life.

CONCLUSION

Intramuscular injection produces moderate to severe pain response in newborns, and breast feeding provides superior analgesia to oral sucrose and reduces moderate to severe painful response to mild to moderate grade in term newborns.

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