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Comparision of Analgesic Effect of oral 25% Dextrose, 12% Sucrose,24% Sucrose and Placebo During 1 St Dpt Vaccination in Healthy Term Infants

KEYWORDS: Sucrose, 25% dextrose, DPT vaccination, Pain.

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ABSTRACT *Objective: To compare analgesic effect of 12% sucrose, 25% dextrose, 24% sucrose and placebo during 1st DPT vaccination in healthy term infants.*

Design: Double blind, randomized placebo controlled trial.

Setting: Immunization clinic of Department of Paediatrics, Dr. D.Y Patil Medical College, Kolhapur

Participants: Infants coming for their 1 st DPT vaccination were randomized in to four groups of 50 each.

Interventions: Infants in interventional group received sterile water, 12% sucrose, 25% dextrose, 24% sucrose.

Outcome measures: The primary outcome variables was the duration of cry after vaccination. Secondary outcome variables were change in heart rate from base line and change in behavioural state score according to Glad man at three minutes after vaccination.

Result: Mean total duration of cry was significantly lower in 24% sucrose fed babies36.3(25.34) seconds, 25% dextrose fed babies 67.1(38.53) seconds and 12% sucrose fed babies 101.11(34.13) seconds as compared to babies given sterile water 137.2(20.31)seconds. Mean rise in heart rate(beats/min) at 3 minutes after vaccination was significantly lower with 24% sucrose 3(2.3), 25% dextrose (5.6), 12% sucrose 13.4(4.6)as compared to sterile water 18.2(4.61). There was no rise in behvioural state score only with 24% sucrose fed babies.

Conclusion: 24% sucrose has better analgesic activity than 25% dextrose in infants less than 2 months of age undergoing DPT vaccination.

Introduction :

Till recently the management of pain in the newborn was hampered by the lack of awareness among healthcare professionals that the neonate is capable of perceiving pain(1,2). Many newborn babies undergo painful procedures like heel pricks, venepuncture and intramusclar injection for immunisation, such procedures inflict distinct physiological behavioural, hormonal and metabolic changes. Great emphasis is being laid in minimizing pain during these minor procedures in neonates(3,4). Vaccination is the most common procedure performed in infancy, although parents might have significant concerns regarding the pain associated with routine vaccinations. Moreover, painful experiences very early in life can promote somatization later in life(5). Non pharmacological methods have also been shown to be effective for treating and preventing mild to moderate procedural pain (6-9). Dextrose and sucrose in varying concentration have been shown to relive pain during venepuncture or intramusclar injection (10-17). There are very few studies which directly compare analgesic effect of glucose and sucrose in infants(18,19). We planned a study with the objective to compare the efficacy of different sucrose concentration 12% sucrose and 24% sucrose and 25% dextrose, 2 minutes before DPT vaccination, using sterile water as placebo.

MATERIALS AND METHODS:

This double blinded, prospective, randomized placebo controlled trial was carried out in the immunization clinic of Department of Paediatrics, Dr. D.Y Patil Medical College, Kolhapur, Maharashtra. 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(IUGR), asphyxia (Apgar score <5) or delayed cry (>5 min)if born at home, infants who have required hospital admission for more than 48 hours , developmental delay (developmental age lags behind past conceptional age by 1 months),previous surgery ,with neurological deficit .The subjects were randomized into four 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 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. ***Placebo group***: 2ml sterile water for injection as given orally by a sterile syringe 2 minutes prior to intramuscular vaccination ***12% Sucrose group:*** Arbineo 24% w/v oral solution 1ml added with sterile water for injection making total volume of 2 ml i.e. 12% oral sucrose solution, given orally by a sterile syringe 2 minutes prior to intramuscular vaccination. ***25% dextrose group:*** 2 ml of 25% Dextrose was given orally by a sterile syringe 2 minutes

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prior to intramuscular vaccination .***24% Sucrose group:*** Oral sucrose (Arbineo 24% w/v oral solution) 2ml orally by a sterile syringe2 minutes prior to intramuscular vaccination. All the babies received the intervention from one investigator only another two investigators would then come in the immunization room. Behavioural state score(0-4) in the infant was scored by observing the baby for 15 seconds before intramuscular vaccination according to Gladman scale (20). 0: Non rapid eye movement, sleep, no movements, and regular breathing. 1: Regular eye movement sleep, small movement, irregular breathing.2: Quiet awake, eyes open, slight limb movement. 3: Active awake, eyes open, moderate limb movement. 4: crying and vigorous limb movements. Heart rate in beats /min before intramuscular vaccination was counted. Whole DPT vaccine, 0.5 ml by a 2ml disposable syringe with 23 G" needle was given on the anterolateral aspect of thigh (left/right) after cleaning the skin with spirit, by single same nursing staff, so that duration of needle insertion, depth ,should remain same in all the groups. The injection was given with the baby in the mother's lap with thigh exposed, after calling aloud 'in' when the needle was inserted, and 'out' when the needle was removed. The two investigators were blinded to the Pharmacological interventions given to the baby.

Primary outcome variable was duration of cry (in seconds) after vaccination, which was counted by digital electronic watch. 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. As crying time was counted only for 3 minutes, the babies who were still crying even after 3 minutes, the duration of cry was noted as 180 seconds only.

Secondary outcome variable was change in heart rate (beats/minutes) from baseline and behavioural state score (0-4) of a baby. Heart rate (beats/min) was counted and behavioural state score was observed at 3 minutes after intramuscular vaccination, by same investigator ,who recorded it before intramuscular vaccination to avoid interpersonal error.

In order to avoid confounding by other pain relieving methods, the following steps were ensured. All babies were held in the mothers lap during vaccination. The mothers were allowed to hold, talk to or rock the baby during procedure in all groups .Non-nutritive sucking was not done during the procedure. All the test was performed between 10 am to 1 pm to avoid diurnal variation in pain response. The time since last breast feeding of all babies kept apparently same. All the data except behavioural state was analysed by analysis of variance (ANOVA) test with Postdoc Tukey's least significance difference (LSD) method for multiple comparisons. Analysis of Behavioural state score was analysed by Wilcoxon signed Ranks Test. Level of significance was fixed at $P < 0.05$.

RESULTS:

A total 240 babies were approached, of which 40 were excluded (25 not meeting exclusion criteria; 15 refusal to participate).200 babies were randomized into 4 groups of 50 babies each. The postnatal age, weight and sex ratio was comparable in all four groups. ***(Table I)***

Mean total duration of cry was significantly lower in 24% sucrose fed babies 36.3 (25.34) seconds, 25% dextrose fed babies 67.1(38.53) seconds, and 12% sucrose fed babies 101.11(34.13) seconds as compared to babies given sterile water 137.2(20.31) seconds. Mean duration of first cry was significantly lower in 24% Sucrose fed babies 18.2(14.12) seconds, 25% Dextrose fed babies 34.2(23.67) seconds, 12% sucrose fed babies 58.1(24.28) seconds as compared to babies given sterile water 94.3(23.26) seconds. ***(Table II)***

Mean change i.e. rise in heart rate (beats/min) from base line was significantly lower in 24% sucrose fed babies 3(2.3), 25% dextrose fed babies11 (5.6), 12% sucrose fed babies 13.4(4.6) as compared to babies given sterile water 18.2(4.61) [F statistics 101.85, LSD 2.29, $P<0.01$](***Figure I)***

There was significant change i.e. rise in behavioural state score after intramuscular vaccination in sterile water fed babies, 12% sucrose fed babies and 25% dextrose fed babies, as compared to no significant rise in 24% sucrose fed babies ***(Table III)***

Discussion

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, they are dependent on others to recognise it, intervene it and treat it (21). Various behavioural, physiological and biological responses present in neonate can be used to assess pain (22). 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. It should be noted that without direct verbal corroboration from the infants, we cannot be extremely sure that any of the above outcome measures actually reflect degree of pain. In this study three easily detectable parameters were first cry, total duration of cry, change in heart rate from baseline and Gladman's behavioural state score were used to assess pain while doing intramuscular injections in infants. First cry following pain is most sensitive to noxious stimuli. Duration of cry has been widely used in various studies as marker of severity of pain (3, 4).

In our study, infants demonstrated significantly shorter duration of first cry, total duration of cry and lower rise in heart rate at 3 mins with 24% sucrose, 25% Glucose, 12% sucrose fed babies as compared with 24% sucrose fed babies. There is significant change in behavioural state score at 3 min i.e. no rise in score only with 24% sucrose fed babies. Fusun Okan etal (23) demonstrated significant reduction in first cry and total duration of cry with 20% sucrose and 20% glucose fed babies after heel prick. Hourai etal (24) 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. Their study showed maximum effect with 50% sucrose solution. Blass etal (25), Ramenghi etal (26), Stevenes etal (27) showed reduction in crying time using sucrose solution. Jatana etal (28), P Thalkar etal (29) also showed reduction in crying time using glucose solution. When results for change in heart rate were pooled Funsun Okan etal, Jatana etal, Skogsdal Y etal(30), reported similar effect as in our studies, during painful procedures in neonates using either sucrose or glucose solution. Hourai etal found no significant difference with change in heart rate using sucrose solution. Rushforth etal (31) observed no rise in behavioural score with sucrose solution.

Our study concluded 24% sucrose has better analgesic activity than 25% Dextrose during 1st DPT vaccination in healthy term infants less than 2 months of age. A. Guala (19) concluded 33% and 50% glucose solution most effec-

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tive than sucrose in reducing pain. Fusun Okan etal demonstrated 20% sucrose and 20% glucose has same analgesic activity.

The analgesic effect of sucrose and glucose occurs by activation of central endogenous opioid system an action similar to that of opioid (e.g. morphine) analgesics. They also stimulate the release of endorphins from hypothalamus. Endorphins act by blinding to opioid receptors in the CNS to inhabit 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. Studies have attributed analgesic effect to the presence of sweet taste in the mouth; researchers have termed this as 'sweetness effect'(32). 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 (33).

Limitations of this study were, we have not used pain scales, and other physiological parameters apart from heart rate. We avoided using pulse oximeter, because pulse oximeters often do not give correct reading in crying and vigorous babies and it would feel stressful to the parents. No major adverse effects were found during or after administration of sucrose or glucose. Regarding the practical utility of different methods of analgesia for routine infant vaccination, lidocaine-prilocaine can be difficult to apply and maintain in place for the 30 minutes, oral analgesics have significant adverse effect, in contrast 24% sucrose readily available, safe and inexpensive, it should be used routinely in infants less than 2 months before intramuscular vaccination.

Tables and Figures:

Parameter	Sterile water (n=50)	12% sucrose (n=50)	25%dextrose (n=50)	24% sucrose (n=50)
Age (wks.)	6.2(2.2)	6.1(2.2)	6.2(2)	6.2(2.4)
Weight(kgs)	4.1(0.4)	4.1(0.5)	4.2(0.5)	4.1(0.4)
Time since last fed (m/n)	47(9.2)	45(8.2)	40(4.3)	44(8.4)
Duration of needle insertion	2.9(0.6)	2.8(0.4)	2.8(0.5)	3(0.5)

Table I: **Baseline Demographic characteristics of the study subject. Mean (SD)**

Duration of cry in seconds	Sterile water	12% sucrose	25% dextrose	24% sucrose	F statistics	LSD	P value
First minute	59.7 (1.09)	52.3 (8.24)	38.9 (14.45)	26.3 (12.94)	96.15	5.47	<0.01
Second minute	47.5 (9.99)	32.3 (15.39)	20.9 (15.61)	8.8 (11.68)	74.99	6.94	<0.01
Third minute	30.4 (14.11)	16.0 (15.56)	7.36 (12.06)	1.3 (3.34)	51.98	6.35	<0.01
Total cry	137.2 (20.31)	101.1 (34.13)	67.1 (38.53)	36.3 (25.34)	97.74	15.95	<0.01
First cry	94.3 (23.26)	34.1 (23.67)	34.1 (23.67)	18.2 (14.12)	122.73	11.27	<0.01

Table II **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)**

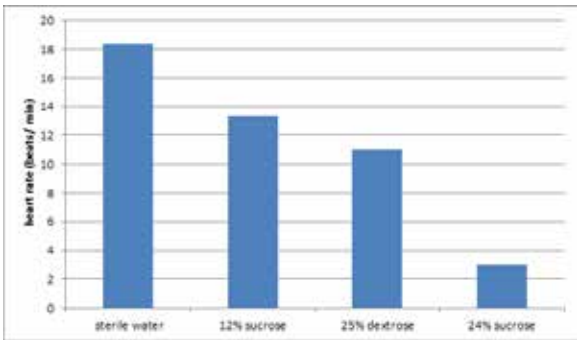

Figure I: **Mean change i.e. rise in heart rate (beats/min) from baseline after DPT vaccination at 3 minutes in study groups.**

Groups	Median behavioural state score (0-4)			
	Before intramuscular injection(range)	After intramuscular injection(range)	Z value	P value
Sterile water	1(0-3)	3(2-4)	6.15	<0.01
12% sucrose	1(0-3)	3(1-4)	6.09	<0.01
25% glucose	2(0-3)	3(0-4)	4.82	<0.01
24% sucrose	2(0-3)	2(0-4)	1.59	<0.05

Table III: Showing median behavioural state before and after (at 3 minutes) intramuscular vaccination in study groups.

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