Effectiveness and comparison of various Non-Pharmacological methods of analgesia in newborns

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Running Title: Comparison of various non-pharmacological methods of analgesia in newborns
Abstract

Background: Pain during the developmental period has potential to adversely affect developing neuronal pathways and cause adverse neurodevelopmental, cognitive and behavioural effects in later life. Immunization e.g. Hepatitis B vaccine (HBV) at birth is a painful experience to which neonates are subjected universally.

Purpose: We aimed to study and compare the effectiveness of the various non-pharmacological method of pain management in newborns so that the safe and effective analgesic methods can be evolved in newborns.

Methods: It was a prospective study conducted at a tertiary care hospital in the Himalayan region. 300 term healthy enrolled neonates were divided into 6 groups each of 50 newborns. 1-5 groups were intervention groups and received one of non-pharmacological intervention, breastfeeding, non-nutritive sucking, rocking, 25% sucrose and distilled water before intramuscular HBV. Group 6 was a control group who received no intervention. Pain response in each group after HBV was assessed and compared using Duration of cry and Douleur Aigue Nveau-ne (DAN) score which is behavioural acute pain rating score for newborn.

Results: Duration of cry was reduced in all the intervention groups but was significant in sucrose (19.90sec), breastfeeding (31.57sec) and non nutritive sucking (36.93sec) when compared with controls (52.86sec). DAN scores showed a significant decrease (pvalues<0.05) at one or more points i.e. at 30 seconds or 60 seconds or 120 seconds in breastfeeding and 25% intervention groups when compared with controls.

Conclusion: Oral sucrose and non-nutritive sucking are simple yet underutilized non-pharmacological interventions which effectively reduce the pain in newborns.

Keywords: Non-pharmacological methods, Analgesia, Newborn, Hepatitis B vaccine (HBV).
**Key message:**

Pain is neglected aspect of sick and healthy newborn care which has adverse short and long term effects on newborn health.

In our study, Sucrose, breast feeding and NNS have shown to significantly reduce the pain caused by the painful event of intramuscular HBV vaccination at birth.

Sucrose and Breastfeeding are the safe and cheap potential modalities of analgesia which can be used during mild to moderate pain in newborns.
Introduction

Pain is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage\(^1\). Newborns are especially vulnerable to pain and its deleterious effects. Babies have larger receptive fields for nociceptive impulses and possibly a higher density of nerve endings and concentration of substance P receptors\(^2,3\). The density of proprioceptive nerve ending is equal to the adult\(^4\). In neonates, the harmful effects of pain include irritability, fear, sense of mistrust towards caregiver, disturbed sleep and wakefulness cycle, delayed wound healing, altered immunological functions, biochemical alterations in energy metabolism. Negative effects on the developing brain also include long-term adverse effects like subtle behavioural changes that may persist up to childhood. Neonates are exposed to various types of painful stimuli in the indoor and outdoor settings. Hence it is very important to have effective tools for the assessment and management of pain. The responses to pain in a newborn are nonverbal which include physiological, behavioural, biochemical, autonomic change and body movements\(^5\). These parameters are used for pain assessment in various scales\(^6\).

These can be used by the health functionaries to assess pain and evolve strategies to prevent, reduce or eliminate pain. There have been many pharmacological and non-pharmacological methods which are being evaluated in the recent past for effective management of the pain in newborns. The pharmacological agents like paracetamol, opiates, and local anaesthetic agents can be useful for severe pain management\(^7\). While non-pharmacological methods can be effective for the mild to moderate intensity pain relief. Various non-pharmacological methods mentioned in literature non-nutritive sucking, glucose solution, breastfeeding, kangaroo position, rocking, music therapy, massage therapy and distilled water\(^8,9,11\). These methods are low cost, simple and benign and have been found effective. Pain assessment in newborns is a special challenge due to the physiological handicaps of neurological and developmental functions. Various methods used for pain assessment are Neonatal Infant Pain
Scale (NIPS), Premature infant pain profile (PIPP), Revised FACES pain scale and DouleurAigue du Nouveau-ne (DAN). DAN score designed in 1997 is acute pain rating scale in neonates. DAN score is a reliable and valid method of pain assessment in the procedural pain. It is based on the three parameters; facial expression, limb movements and vocal expression. The score is assigned on these parameters depending upon the response of newborn to the painful stimulus. Total of the scores on three parameters is used to quantify pain experienced by the newborn.\(^6\)

Vaccination during the neonatal period is one of the most common mild to moderate painful experience to which newborns are subjected to universally.\(^{12}\) So it will be worthwhile to find the effectiveness of various non-pharmacologic methods in reducing the pain in newborns during the vaccination. So, we planned this study to find and compare the effectiveness of various non-pharmacological methods in the newborn pain management during the vaccination.

**Aims and objectives:**

1. To study the effectiveness of various non-pharmacological methods i.e. (1) Breastfeeding (2) Non-Nutritive Sucking (3) Rocking (4) 25\% Sucrose (5) Water in reducing the pain in newborns induced during the first dose of intramuscular Hepatitis B vaccine.

2. To compare the effectiveness of various non-pharmacological methods i.e. (1) Breastfeeding (2) Non-Nutritive Sucking (3) Rocking (4) 25\% Sucrose (5) Water in reducing pain on the duration of cry after vaccination and DAN score at 30, 60 and 120 seconds.
Methods

Cases

Inclusion criteria:

1. Newborns (0-28 days) receiving Hepatitis B vaccination.
2. Parents consenting to take part in the study.

Exclusion Criteria:

1. Preterm (<37 weeks of gestation) newborns
2. Sick newborns
3. Birth weight <2.5 kg or >4.0 kg
4. Newborns suffering from any major congenital anomaly
5. Newborns on any drug

This study was conducted in the tertiary care hospital of hilly state of Himalayan region from October 2016 to March 201. Ethical approval from the Institution Ethical Committee- IGMC Shimla was obtained. Three doses of hepatitis B vaccine are administered at birth within 24 hours of life, six weeks and fourteen weeks of life under national immunization program in our country (India). 1697 newborns received Hepatitis B vaccine at birth within 24 hours under national immunization program during our study period and 597 among them met the study criteria. Out of 597 eligible newborns, parents of only 300 newborns consented to take part in the study. These 300 newborns constituted our study group. While obtaining consent, parents were explained regarding the various intervention and also explained that their baby could get any of the intervention. Demographic and personal information of each enrolled newborn was recorded as per case record form.

The enrolled neonates were randomized using sequentially numbered, opaque sealed envelopes (SNOSE) method which is an easy, cheap, effective and reliable method of maintaining allocation concealment, which was maintained by the using sequentially numbered, opaque, sealed envelopes\textsuperscript{12,13}. Enrolled cases were divided into six groups of 50
each using SNOSE method. The person performing randomization was not involved in the study beyond this. The first observer opened one sealed envelope for each baby and recruited that baby to one of six groups depending upon the group mentioned in that envelop.

Six groups mentioned above along with their suggested mechanism of action are as:

**Breastfeeding (BF) Group 1:** Newborns in this group were started on breastfeeding two minutes before the vaccination and continued until 120 seconds. BF produces analgesia through multisensory stimuli like skin to skin contact, sucking and glucose present in the breast milk.

**25% Sucrose (25% S) Group 2:** 2ml of 25% dextrose solution was given through mouth with sterile dropper two minutes prior to vaccination. A sweet taste of 25%S sensation stimulates cortical areas related to the pleasure which helps in the release of endogenous opioids and endorphins which modulate the transmission of painful signals acting on dorsal horn interneuronal gateway regions.

**Distilled Water (DW) Group 3:** 2ml of DW was given through mouth with sterile dropper two minutes prior to vaccination. It reduces pain by distracting attention and reducing anxiety.

**Non-Nutritive Sucking (NNS) Group 4:** A sterile silicon pacifier (Bonny Baby Care Ltd) was held gently to stimulate sucking. Vaccination was given two minutes after the newborn started sucking and it was continued till 120 seconds.NNS decrease hyperactivity promotes calmness and regulates newborns’ discomfort.

**Rocking (R) Group 5:** Newborns in this group were given gentle rocking movement by lifting the head on the palm of the hand. Rocking started two minutes before vaccination and continued till120 seconds. Positioning and tucking reduce pain by distraction, comforting the baby, reducing anxiety and stimulating the vestibular system.

**None (N) Group 6:** In this, no intervention was used.

Groups 1-5 were subjected to one or other intervention and constituted intervention groups while group 6 constituted control group as it was subjected to no intervention.
Newborns were brought to immunization room from the postnatal ward which is around 100 meters from the same, no strict restrictions were imposed to keep the baby nil per orally and most babies were breastfed within 1 hour prior to immunization, with waiting time of about 15 minutes at immunization room. The babies in the breastfeeding group were given breastfeed in the immunization room itself during immunization session. Newborns were held in the mother's lap in the warm well lighted vaccination room. All the newborns were in stage 3 or 4 of alertness and with DAN score of zero before they were subjected to one of the interventions. The intervention decided was given by the same trained health worker. Hepatitis B vaccination administered through intramuscular route at anterolateral aspect of the thigh.

To maintain uniformity and avoid the subjective variation during vaccination the vaccine was administered by the same health worker and needle of the same size (24G) and same make was used. After vaccination, the following variables were recorded

(B) Duration of cry by the second observer

(C) DAN score at 30 sec, 60 seconds and 120 seconds after the vaccination by the third observer. DAN score is totally objective based on behavioural assessment, so the point of having interobserver variation seems remote. In addition to that single observer throughout who was familiar with the scoring system will have a more accurate assessment of the score and hence single observer was employed. Single observer, DAN score is pain assessment scale employed in children of 0-2 years of age. It is based on three parameters: facial expression, limb movements, and vocal expression. Each parameter is assigned a score on three parameters: facial expression (0-4), limb movements (0-4), and vocal expression (0-3) depending upon the behaviour observed. Sum of the three scores gives the intensity of the pain. DAN score of 0 signifies no pain perceived and 11 as the maximum.
Statistical analysis:

All calculations were performed using SPSS ver. 20.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean+standard deviation. One way analysis of variance (ANOVA) test and student test for continuous variables were used for comparisons between groups. The Pearson chi-square test was used for categorical variables. A p value of<0.05 was considered statistically significant. Data were analyzed to look for any statistically decrease in pain during vaccination in various intervention groups.
Results

300 new-born were studied over a period of six months. There were 159 males (53.1%) and 141 females (46.9%). The demographic profile of the new-born enrolled in the study under various groups was comparable (Table 1). Comparison of mean duration of cry in different intervention groups with the control group using unpaired T-test showed that there was a decrease in duration of cry in all the intervention groups after vaccination in comparison to control group (p<0.05) (Table: 2). The difference observed in Breastfeeding, Non-Nutritive Sucking and 25% sucrose groups was statistically significant (p value) while in Rocking and Distilled Water groups, the difference was not significant. The difference was statistically highly significant in the group receiving 25% sucrose & breastfeeding (p<0.000). ANOVA was conducted to compare the difference in analgesic effect of various interventions groups namely Breastfeeding, Non-nutritive sucking, rocking, 25% sucrose and distilled water in reducing pain assessed by DAN scores at 30, 60 and 120 seconds. It was observed that there was significant difference of DAN (30 sec) at p < 0.05 between different interventions [F (5, 294) = 5.049, p = <0.000]. Post Hoc comparison using Tukey HSD indicated that mean DAN (30 sec) score for sucrose intervention (M = 3.10, SD = 1.875) was significantly different from the DAN (30 sec) score in BF (M = 4.54, SD = 1.727), NNS (M = 4.64, SD = 1.526), rocking (M = 4.58, SD = 2.139) and Control (M = 5.00, SD = 2.283). While ANOVA exhibited no significant effect of DW intervention (M = 3.97, SD = 2.025) on DAN (30 sec) score. Similarly It was observed that there was significant difference of DAN (60 sec) at p < 0.05 between different interventions [F (5, 294) =8.8081, p = 0.000].on post hoc comparison using tukey HSD mean DAN(60sec) score for sucrose intervention (M=.58, SD=0.8) was significantly different from NNS(M=1.9, SD=1.5), rocking(M=2.23, SD=2.3), DW(M=1.65, SD=1.7) and control(M=2.82, SD=2.3) while ANOVA exhibited no significant effect when compared with breastfed group (P>0.05)
means these intervention are equally effective in reducing pain scores after 60 sec of painful stimuli. For DAN (120 sec) scores found to be significantly different in sucrose(M=0.05,SD=0.22) and rocking(M=1.04,SD=2.05) intervention (p<0.05) while no significant difference was observed with other interventions. DAN score was reduced in all the intervention groups at 30, 60 and 120 seconds in comparison to control except at 30 seconds for Distilled Water group. However, this decrease was significant (p<0.05) only in 25%Sucrose at 30, 60 and 120 seconds and at 60 and 120 seconds in Breastfeeding group. In intergroup comparison, a significant difference was observed for DAN (30 sec) at p < 0.05 between sucrose and other interventions. On post Hoc comparison using Tukey HSD indicated that mean DAN (30 sec) score for sucrose intervention was significantly lower than breastfeeding.

Similarly, a significant difference was observed for DAN (60 sec) at p < 0.05 between different interventions. Mean DAN score (60 sec) for sucrose intervention group was significantly lower than NNS followed by rocking and distilled water group while ANOVA exhibited no significant difference between 25% sucrose with breastfeeding group (p>0.05).

Further, DAN score (120 sec) found to be significantly lower in 25% sucrose in comparison to rocking intervention p<0.05 while it showed no significant difference with other interventions. The pain intensity was significantly lower at 30 seconds in breastfeeding & 25% sucrose group. Comparison of DAN scores at 30 seconds, 60 seconds and 120 seconds in intervention groups with control group have shown statistical significant reduction (p<0.05) at one or more point i.e. at 30 second or 60 seconds or 120 seconds in breastfeeding and 25% sucrose intervention group when compared with control(Table:3).
Discussion

The analgesic effects of various non-pharmacological methods in newborns have been studied in the past and their results are varying. However, there are no comprehensive and definite recommendations for their regular use in day to day clinical scenarios. Our study has been carried out for the same purpose. We have studied the effectiveness of five non-pharmacological methods during painful stimulus of HBV vaccination. We conducted our study over a period of months involving 300 newborns divided into six equal groups. Group 1-5 received one of the five non-pharmacological methods and constituted the intervention groups while the Group 6 acted as the control. Most of these studies done in this regard had quite a less number of the cases as compared to our study. Above this, most of them evaluated two or three methods in a particular study as compared to our study where we have evaluated the analgesic effect of five non-pharmacological methods simultaneously. Grey et al (2000) studied the analgesic effect of skin-to-skin contact during heel stick in newborns and found it to be potent intervention in reducing the pain\(^{14}\). Carbajal et al 2003 studied the effectiveness of breastfeeding and a combination of sucrose and pacifier in pain reduction and the result were comparable between two groups\(^{16}\). Gray et al 2002 found that newborns if put on breastfeeding before, during, and after the heel prick had reduced crying and grimacing and it also prevented an increase in heart rate\(^{16}\). Yılmaz et al (2002) reported that holding the baby in arms in the upright position decreased the duration of crying during painful stimulus of heel prick. Funda K recorded lower pain score and shorter crying duration in response to vaccination using music as an intervention\(^{17}\).

Our study has shown that all the intervention groups (1-5) lower mean duration of cry after vaccination as compared to control group. Mean duration of cry in three groups namely 25% S, BF and NNS was 19.90, 31.51 and 36.93 seconds respectively which was statically significantly lower as compared to control group which has the mean duration of the cry of
52.86 seconds. The mean duration of cry was lowest in 25% S group. The difference between BF and 25%S group was not significant.

The mean duration of cry in rocking and distilled water group was lower as compared to control but the difference was not significant. On serial observation of the DAN score at 30, 60 and 120 seconds after vaccination it was observed that DAN score was lower in all the intervention groups as compared to control group except DW group at 30seconds. Their results were same as found in our study and both the methods. Taddio et al studied analgesic effect of sucrose during various procedures in newborn and found that the effectiveness of sucrose was limited to venipuncture for the newborn and not during the intramuscular Vitamin K injection. Carbajal et al 2008 reported the analgesic effect of sucrose and pacifiers during venipuncture and found that the analgesic was even better when both used together. On intergroup comparison in various intervention groups, sucrose was found to be the best as it significantly reduced the pain as shown by the serial observations of DAN scores. Breastfeeding was the second-best option in pain reduction as it also reduced the pain intensity significantly at all the observations except DAN at 30seconds. NNS has reduced the duration of cry significantly after painful stimulus but the decrease in DAN scores was though seen but not significant. DW and rocking have shown to decrease the duration of cry and DAN scores but these observations were not significant. Above observations demonstrate that sucrose and NNS are the effective non-pharmacological means of reducing the pain during mild to moderate painful stimuli.

Sucrose has shown a better analgesic effect in comparison to BF only at DAN score at 30seconds. At the rest of the observations, both these interventions were comparable.

Breastfeeding is a physiological phenomenon and its great benefits to the newborn, mothers and community on various aspects are well established and beyond doubt. So it is recommended that BF is one of the effective and useful ways to decrease pain in newborns.
During non-availability of breastfeeding other methods like 25%, S or NNS can be employed in the pain management of newborns.

**Limitation of the study:**

Limitations in our study were: Blinding of observer doing DAN scoring and observing total duration of cry was not possible in various groups. Secondly during DAN scoring in the BF group only half of the face was visible to the observer.

**Conclusion:**

Pain has short term and long term negative effects in newborns. Various non-pharmacological methods are safe, simple, easily available and effective tools in pain management in newborn. Breastfeeding is a physiological phenomenon and along with its all other advantages, can be used as an effective tool to manage mild to moderate pain in newborns and during non-availability of breastfeeding other methods like 25%, S or NNS can be employed. Efficacy of non-pharmacological interventions in reducing mild to moderate procedural pain is already proven in many studies still there are no definite guidelines which method is superior. We comprehensively studied five parameters at the same time in contrast to the others studies in past who had studied one or two interventions. Moreover, we had a higher number of the subjects in each group in contrast to previous studies. In addition to breast feeding Hence our findings carry better meanings in the formulation of operational guidelines.
References


8. Taddio A, Shah V, Hancock R. Effectiveness of sucrose analgesia in newborns undergoing painful medical procedures. CMAJ. 2008;179:37


Table 1. Demographic profile of the newborns enrolled in the study

<table>
<thead>
<tr>
<th>Group no.</th>
<th>Intervention</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
<th>Mean age (hrs)</th>
<th>Mean wt (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Breast feeding</td>
<td>50</td>
<td>28</td>
<td>22</td>
<td>25.31 ± 11.01</td>
<td>3.0 ± .425</td>
</tr>
<tr>
<td>2.</td>
<td>25% Sucrose</td>
<td>50</td>
<td>29</td>
<td>21</td>
<td>34.36 ± 18.08</td>
<td>2.9 ± .427</td>
</tr>
<tr>
<td>3.</td>
<td>Distilled water</td>
<td>50</td>
<td>26</td>
<td>24</td>
<td>28.58 ± 26.21</td>
<td>3.0 ± .532</td>
</tr>
<tr>
<td>5.</td>
<td>Rocking</td>
<td>50</td>
<td>28</td>
<td>22</td>
<td>23.82 ± 14.80</td>
<td>2.8 ± .460</td>
</tr>
<tr>
<td>6.</td>
<td>None (control)</td>
<td>50</td>
<td>25</td>
<td>25</td>
<td>22.31 ± 11.12</td>
<td>3.0 ± .481</td>
</tr>
<tr>
<td></td>
<td>Total/mean</td>
<td>300</td>
<td>159</td>
<td>141</td>
<td>26.66±18.02</td>
<td>3.00± .483</td>
</tr>
</tbody>
</table>
Table 2. Total duration of cry in various intervention groups and their comparison with the control group:

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Mean duration of cry (sec)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breastfeeding</td>
<td>31.57 ± 22.26</td>
<td>0.000</td>
</tr>
<tr>
<td>Non nutritive sucking</td>
<td>36.93± 26.19</td>
<td>0.001</td>
</tr>
<tr>
<td>Rocking</td>
<td>51± 47.07</td>
<td>0.605</td>
</tr>
<tr>
<td>Sucrose</td>
<td>19.90± 12.84</td>
<td>0.000</td>
</tr>
<tr>
<td>Distilled water</td>
<td>38.42± 30.66</td>
<td>0.06</td>
</tr>
<tr>
<td>None (control)</td>
<td>52.86± 48.75</td>
<td></td>
</tr>
</tbody>
</table>
Table 3. Mean DAN Scores with various interventions and comparison with control

<table>
<thead>
<tr>
<th>Interventions</th>
<th>DAN 30 sec±S.D.</th>
<th>DAN 60 sec±S.D.</th>
<th>DAN 120sec±S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Breast feeding</td>
<td>4.54±1.72</td>
<td>1.28±1.31*</td>
<td>0.24±0.56*</td>
</tr>
<tr>
<td>2. 25% sucrose</td>
<td>3.10±1.87*</td>
<td>0.59±0.85*</td>
<td>0.05±0.22*</td>
</tr>
<tr>
<td>3. Distilled water</td>
<td>5.00±2.02</td>
<td>1.65±1.77</td>
<td>0.63±1.26</td>
</tr>
<tr>
<td>4. Non nutritive sucking</td>
<td>4.64±1.52</td>
<td>1.91±1.55</td>
<td>0.75±1.38</td>
</tr>
<tr>
<td>5. Rocking</td>
<td>4.58±2.13</td>
<td>2.23±2.32</td>
<td>1.03±2.05</td>
</tr>
<tr>
<td>6. Control</td>
<td>5.00±2.48</td>
<td>2.82±2.38</td>
<td>1.35±2.06</td>
</tr>
</tbody>
</table>

*p value<0.05

DAN score—Behavioural acute pain rating scale for Newborn