Stress and discomfort in the care of preterm infants: A study of the Comfort Scale and the Newborn Individualized Developmental Care and Assessment Program (NIDCAP®) in a Dutch level III NICU

Wielenga, J.M.

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Chapter 3

Ventilation and stress in preterm infants; high frequency ventilation is not an additional stressor

Joke M. Wielenga, Bert J. Smit

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ABSTRACT

Aim To study the hypothesis that high frequency ventilation (HFV) is an additional stressor compared to conventional ventilation (CV).

Methodology A prospective explorative cohort study in a consecutive sample of 50 preterm infants (<37 gestational age) with Respiratory Distress Syndrome admitted to a Level III Neonatal Intensive Care Unit. During the first three days of ventilation stress was assessed by means of the Comfort scale (CS).

Results 35 Infants received HFV and 15 CV. The HFV group was significantly younger (p = 0.003), had a significant lower birth weight (p = 0.017) and were significant more severely ill (p < 0.0001). Stress scores between groups were comparable, adjustment for baseline differences revealed no differences in scores during the first 3 days of ventilation. Of all CS assessments, 34.0% in the HFV group and 35.6% in the CV group indicated stress (score ≥ 20).

Conclusion Stress during the first three days of mechanical ventilation using the CS did not reveal any difference between high frequency and conventional ventilated preterm infants. Routine use of sedatives seems insufficient to prevent high stress scores.
INTRODUCTION

Medical technology within Neonatology has strongly and rapidly developed the last two decades. A wider range of intense medical treatment became available and current ways of treatment are being improved and refined. The technical possibilities, such as mechanical ventilation strategies, often result in rather aggressive medical and nursing interventions. The period of mechanical ventilation can be described as a very uncomfortable and stressful period. Notwithstanding the fact that it is difficult to prove that mechanical ventilation is painful or stressful in itself, mechanical ventilation is accompanied by a lot of potential painful interventions like (re)intubation, endotracheal suctioning, skin lesions as a result of punctures for blood samples, and change of adhesive materials. The less mature the infant the more likely the infant will be dependent of mechanical ventilation and the less mature the infants the more stress and painful procedures are performed. Infants of lower gestational age (GA) are known to be more sensitive to stress and pain. Repetitive pain may lead to increased cell death in the immature brain, poor neurological outcome, abnormal behaviour as adolescents or adults and increased vulnerability to stress, anxiety and psychiatric disorders. For all these reasons stress and pain should be prevented and minimized as much as possible.

Stress and pain are often used interchangeable in clinical practice as well as in literature. It is stated that all pain is stressful but not all stress is painful.

With the introduction of high frequency ventilation (HFV) in the Neonatal Intensive Care Unit (NICU) of the Emma Children’s Hospital / Academic Medical Center (EKZ/AMC), nurses reported an increase in stress in newborn infants. Nurses described stress in terms of discomfort, distress, agitation, restlessness, increase in pain and decrease in sleep time. Nurses had the impression that the constant vibrations of the HFV were an additional source of stress for preterm infants. Consequences of this constant vibration of the body are unknown.

In the last two decades the number of ventilated infants increased from 27% for an average time of 4 days to 40% for an average time of 8 days. We wanted to study if HFV could be labelled as an additional stressor compared to conventional ventilation (CV) in preterm infants, during the first 3 days of ventilation.

METHODS

An explorative prospective cohort study with a convenience sample was performed. Infants born before 37 weeks of gestational age admitted to the level III NICU of the EKZ/AMC in Amsterdam, the Netherlands were consecutively included after informed consent. They were mechanical ventilated due to respiratory distress syndrome (RDS) confirmed by X-ray. Infants with congenital or neurological abnormalities and infants who
were ventilated later than 72 hours after birth were excluded. The study was approved by the Research and Ethics Committee of the hospital.

Clinical characteristics
Infant characteristics were collected on GA, birth weight, gender, and Apgar score at five minutes. Data on illness related characteristics included cerebral ultrasound findings (subependymal / intraventricular haemorrhage ≥ grade 1), air-leak syndrome (confirmed by X-Ray), sepsis (clinical symptoms and positive blood culture) or death. Treatment related characteristics were measured as therapy-based severity-of-illness by the Neonatal Therapeutic Intervention Score System (NTISS). Infant characteristics, illness, and treatment related characteristics and the mode of ventilation were taken from the medical and nursing charts.

Procedure
Infants were ventilated in a CV mode (Dräger Babylog 8000) or in a HFV mode, either high frequency flow interruption (Dräger Babylog 8000) or high frequency oscillation mode (Sensor Medics 3100A). The choice of ventilation mode was made according to existing unit protocols; infants with a gestational age <30 weeks were preferably ventilated in the high frequency mode. Infants of ≥30 weeks gestational age were, if CV had reached a peak pressure of >24 cm H_{2}O, treated with HFV as rescue therapy. All ventilated infants were given a standard loading dose of 0.1 mg/kg morphine i.v. followed by a continuous i.v. infusion of 0.25 mg/kg/day morphine as analgesic therapy.

Outcome
Data on stress were collected during the first 3 days of ventilation by means of the Comfort scale, originally an instrument to measure distress in ventilated infants and children. Scores on the Comfort scale are the observed variation of 8 items (alertness, calmness/agitation, respiratory response, physical movement, blood pressure, heart rate, muscle tone and facial tension) on a 1 to 5 scale. The total score is the sum of the 8 separate item scores (maximum 40), the higher the score the more stress. Prior to this study we tested the Comfort scale for its reliability and validity as well as its clinimetric properties in measuring stress in ventilated preterm infants. The criterion validity of the COMFORT scale was good (Pearson’s r of 0.84). Inter observer reliability of each item varied from good to almost perfect (weighted kappa 0.64 to 1.00). The reliability of the total COMFORT scale score was satisfying (intra class correlation coefficient [ICC] of 0.94). Based on the receiving operator characteristic (ROC) a score of 20 (giving a sensitivity of 100% and a specificity of 77% with an area under the curve of 0.95) was decided to represent the cut off point for stress. The Comfort scale is administered (duration ± 3 minutes) after a 2-minute observation of the premature infant.
The first measurement of stress with the Comfort scale took place immediately after receiving informed consent. Next measurements of stress took place twice a day, before daily care procedures, during 3 days or less if mechanical ventilation was no longer needed. No interventions or handling one hour prior to stress measurement were performed. Observations were performed by observers trained in the Comfort scale.

Statistical Analyses
Results are expressed as means, standard deviation (SDs) for normally distributed variables and as medians and ranges in case of non-normal distributions. Chi-square statistics or the Mann Whitney U-test, when appropriate, were applied for group comparison. Subsequently stepwise multivariate linear regression analysis was employed to adjust the effect of mode of ventilation on Comfort scale scores for differences in clinical characteristics at inclusion. As numbers were small, only clinical characteristics that differed significant between both groups were introduced as independent variable next to mode of ventilation. All statistical analyses were performed using SPSS 12.0 software (SPSS, Chicago, IL, USA).

RESULTS
In the study period 65 of the 74 infants of < 37 weeks of gestation admitted to the NICU were eligible for the study. Parents of 56 infants were asked for participation; nine infants were missed due to an estimated short period of ventilation so informed consent could not be arranged before extubation. Six parents refused permission for various reasons; overwhelmed by the premature birth (2), the infant was too sick or too small (3), no reason mentioned (1). In total 50 parents gave permission by written informed consent.

The study group consisted of 50 preterm infants, 35 infants (20 boys) in the HFV group and 15 infants (12 boys) in the CV group (Table I). The HFV group infants had a statistically significant lower mean gestational age 28.7 ± 1.4 weeks, CV group infants were 31.3 ± 2.9 weeks (p = 0.003). Mean birth weight of HFV infants was statistically significant lower compared to CV infants, 1171 ± 337 grams versus 1585 ± 598 grams (p = 0.017). The HFV infants had a statistically significant higher mean NTISS score 27.6 points compared to 22.4 points of the CV infants (p < 0.0001). No significant differences were seen in Apgar score or gender. Illness related complications and medication were comparable between both ventilation groups (Table I).

Scores on the Comfort scale were comparable HFV and CV group infants at the start of ventilation, HFV mean 16.6 ± 3.6 vs. CV mean 17.7 ± 3.9, or at any of the separate ventilation days or moments (Table II). Comfort scale scores and the change over time of the scores are visualized in Figure I. A total of 274 Comfort scale scores were assessed during the study period of which 34.5% resulted in a score ≥ 20 points, indicating stress.
for the infant at that moment (Table II and Figure I). No significant differences were seen in percentages of scores ≥ 20 points HFV and CV ventilation, respectively 34.0% versus 35.6%.

Taking the significant clinical variables into account in multivariate analysis, no difference in stress was between both ventilation (mean difference [95%CI] HFV vs. CV: -0.40 [-1.52 to 0.71] points, p = 0.475).

**DISCUSSION and CONCLUSION**

This study showed no differences in stress of preterm infants between HFV and CV. HFV was primarily given to lower birth weight, lower GA and sicker infants. Adjustment for these differences revealed also no differences in Comfort scale scores.

Research in the comparison of HFV with CV concerned the acute phase treatment, complications during treatment, long-term effects and refinement of the method and
Table II Comfort scale scores and percentage of infants with stress during first three days of ventilation

<table>
<thead>
<tr>
<th>Time of Assessment</th>
<th>HFV N*</th>
<th>HFV CS mean ± SD</th>
<th>HFV stress†</th>
<th>CV N*</th>
<th>CV CS mean ± SD</th>
<th>CV stress†</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start of ventilation</td>
<td>35</td>
<td>16.6 ± 3.6</td>
<td>11.4%</td>
<td>15</td>
<td>17.4 ± 3.9</td>
<td>26.7%</td>
<td>0.237</td>
</tr>
<tr>
<td>Ventilation Day 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 12 hours of ventilation</td>
<td>33</td>
<td>17.5 ± 3.6</td>
<td>30.3%</td>
<td>12</td>
<td>17.3 ± 4.7</td>
<td>16.7%</td>
<td>0.699</td>
</tr>
<tr>
<td>After 24 hours of ventilation</td>
<td>32</td>
<td>20.7 ± 4.0</td>
<td>59.4%</td>
<td>11</td>
<td>20.1 ± 2.5</td>
<td>45.5%</td>
<td>0.685</td>
</tr>
<tr>
<td>Ventilation Day 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 36 hours of ventilation</td>
<td>31</td>
<td>19.3 ± 3.8</td>
<td>41.9%</td>
<td>10</td>
<td>20.3 ± 2.8</td>
<td>60.0%</td>
<td>0.344</td>
</tr>
<tr>
<td>After 48 hours of ventilation</td>
<td>29</td>
<td>18.3 ± 4.2</td>
<td>35.7%</td>
<td>6</td>
<td>17.4 ± 1.6</td>
<td>40.0%</td>
<td>0.434</td>
</tr>
<tr>
<td>Ventilation Day 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 60 hours of ventilation</td>
<td>27</td>
<td>18.6 ± 3.9</td>
<td>33.3%</td>
<td>4</td>
<td>21.3 ± 4.0</td>
<td>33.3%</td>
<td>0.200</td>
</tr>
<tr>
<td>After 72 hours of ventilation</td>
<td>26</td>
<td>18.0 ± 2.9</td>
<td>26.9%</td>
<td>3</td>
<td>18.7 ± 1.5</td>
<td>33.3%</td>
<td>0.613</td>
</tr>
<tr>
<td>Total ventilation period</td>
<td>18.5 ± 2.1</td>
<td>34.0%</td>
<td>35.6%</td>
<td>18.7 ± 2.1</td>
<td>35.6%</td>
<td>0.766</td>
<td></td>
</tr>
</tbody>
</table>

CV= conventional ventilation, HFV= high frequency ventilation, CS = Comfort scale score
* CS scores were omitted after extubation
† CS score ≥ 20 indicates stress

Figure I Comfort scale scores during the first three days of ventilation

Box plot illustrates the median, the interquartile range and the range that contains the central 95% of the Comfort scale scores for the HFV and CV group
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The technique of HFV.18-22 Since we are the first to report on stress during HFV, comparison with other studies is not possible.

The present study concerned a non-randomized comparison. Differences in clinical characteristics were accounted for in multivariate analysis. Control for unknown confounders is not possible with multivariate analysis and therefore it can’t be ignored that they may have influenced study outcomes. This type of study can only be done as an observational study. The choice of ventilation mode is dependent on infant condition, and it is not ethical to randomize to one or another mode in order to study stress. However, stress could be included as a secondary outcome in a randomized study focusing on respiratory and or neurological outcomes.

Since study numbers were small, results need to be interpreted cautiously and need to be confirmed by larger studies. Next to a small sample size there was a wide range of gestational age, research in the field of stress is hampered by a still incomplete understanding of stress expression and behaviour in preterm infants of various gestational ages and factors that affect stress. Recently the Comfort scale has been modified to be used in for ventilated as well as non-ventilated infants with a gestational age of ≥ 35 weeks and a body weight of ≥ 1500g.23 This adapted version has also been validated as a pain scoring tool for infants between 28 to 37 weeks during capillary blood sampling with interrater reliability 0.62 to 0.84 (weighted kappa) and ICC 0.92 (95% CI 0.89 - 0.96).24 That study stratified for gestational age and found no differences in pain responses according to maturity.24 However, the Comfort scale is not yet extensively tested to measure stress in preterm infants, the Comfort scale scores seem to be unaffected by maturity of the infant or ventilation mode.17,24

Our study took the edge off the impression among nurses that the impressive vibrations of the tiny bodies were an extra source of stress for the infants. Using the Comfort scale showed us that our “clinical look”, concerning stress, was not accurate. Striking are the high percentages of scores ≥ 20 points (34.5%), meaning stress during the period of mechanical ventilation although this was not influenced by the choice of ventilation mode. The high percentage of stress could suggest an inadequate analgesic and sedation policy or could reflect the choice in cut off point.17 A cut off point with a sensitivity of 100% results in a low cut off point and more false positive findings. Routine sedative medication as used in this study may have interfered with the Comfort scale scores. As the current use of analgesics and sedatives seems insufficient to prevent high stress scores a more effective analgesic and sedative policy during ventilation is needed.

In the near future we plan to study mechanical ventilation and stress with a randomized allocation to routine use of morphine or morphine based on stress scores. Hopefully, that study will provide us with a more adequate analgesic and sedative protocol for preterm infants during the period of mechanical ventilation. In the mean time it is recommended to assess stress, by means of the (adapted) Comfort scale on a routine basis during mechanical ventilation and provide non-pharmacological pain interventions next to routine medication.
Next to measurement of stress, ways to prevent and reduce stress of preterm infants in a period of life in which the brain development is so important have to be explored.

A study on Newborn Individualized Developmental Care and Assessment Program (NIDCAP®) could be highly relevant and worthwhile. NIDCAP is known as a method to assess (stress) behaviour of the preterm infant at an individual level. Adjustment of care and the individual appropriate interventions are provided to prevent stress and to enhance comfort.

In conclusion; there is no difference in stress, as measured by means of the Comfort scale, during the first three days between HFV and CV in very preterm infants.

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REFERENCES


