2014

Improved Growth and Development in Premature Infants Managed with Nasal Continuous Positive Airway Pressure

Susan L. Flesher M.D.
Marshall University, nine@marshall.edu

Renee S. Domanico M.D.

Recommended Citation

Flesher SL, Domanico RS. Improved growth and development in premature infants managed with Nasal Continuous Positive Airway Pressure. West Virginia Journal of Medicine. 2014;110(2):14-8.

Improved Growth and Development in Premature Infants Managed with Nasal Continuous Positive Airway Pressure

Susan Lee Flesher, MD, FAAP
Division of Neonatal Follow Up, Marshall University Medical Center, Huntington, WV

Renee S. Domanico, MD
Division of Neonatology and Neonatal Follow Up, Marshall University Medical Center, Huntington, WV

Corresponding Author: Susan L. Flesher, MD, Department of Pediatrics, Division of Neonatal Follow Up, Marshall University School of Medicine, Huntington, WV. Email: nine@marshall.edu

The authors would like to dedicate this article to Anna Dusick, MD, neurodevelopmentalist and researcher. Dr. Dusick was a passionate physician who dedicated her life to both research and clinical practice focused on improving neonatal outcomes. She was a mentor to Dr. Flesher, spending hours teaching the infant neurological exam and sharing years of best practice research. Dr. Domanico had recommended her for this mentoring role, having known her as a former colleague from residency.

ABBREVIATIONS

NCPAP	nasal continuous positive airway pressure
CV	conventional ventilation
ROP	retinopathy of prematurity
CLD	chronic lung disease
BINS	Bayley Infant Neurodevelopmental Screener
NICU	neonatal intensive care unit

Abstract

Objective: Our goal was to assess the association between the use of nasal continuous positive airway pressure (NCPAP) vs. conventional ventilation (CV) in premature infants and its effects on: 1) growth in the NICU and at follow up visits 2) neurodevelopmental outcomes measured by Bayley Infant Neurodevelopmental Screener (BINS) 3) the incidence of retinopathy of prematurity (ROP) and chronic lung disease (CLD).

Methods: A retrospective chart review of two groups of NICU patients was conducted. The first group was from 1/1999 – 12/2000 (n=140) and was managed by CV. The second group (n=168) was from 1/2003 – 12/2004 and was managed primarily by NCPAP. Categorical variables were analyzed using Pearson Chi Square. Mean numerical values were analyzed with the student t-test.

Results: There was no statistical difference between the groups in regard to 15 demographic and interventional variables. There were significant differences between the two groups in CLD ($p<0.05$) and ROP ($p<0.01$), mean weight at one month ($p<0.05$), 9-12 months ($p<0.01$) and 15-18 months ($p<0.01$), length at 4-6 months ($p<0.05$), 9-12 months ($p<0.05$), 15-18 months ($p<0.01$), and 2 years ($p=.05$), and in BINS scores at 9-12 months ($p<0.01$) and 15-18 months ($p<0.01$).

Conclusions: Managing babies with NCPAP therapy when compared with CV, significantly increased the weight at one month which was sustained at the 9-12 month and 15-18 month visits, increased length at all follow up visits, increased BINS scores at the 9-12 month and 15-18 month visits, and decreased the incidence of ROP and CLD.

Introduction

Studies over the past twenty years have shown an improvement in neonatal mortality but unfortunately have not shown the same for morbidity. Fanaroff et. al prospectively studied the mortality and morbidity of infants 501-1500 grams from 1990 to 2002 at twelve centers of the National Institute of Child Health and Human Development Neonatal Research Network. While it was found that mortality decreased in subsequent cohorts, survival with one or more morbidities increased slightly. In the EPIcure Study in the UK (2000), of infants 23-26 weeks, fewer than half were neurologically intact. Similar neurodevelopmental outcomes have been reported in the US in studies by Hack and Fanaroff (2000) and Vohr, Wright, and Dusick (2000). While these studies have considered effects of such treatment modalities as antenatal and postnatal steroids and antibiotics, to our knowledge no one has studied the effect of NCPAP on neurodevelopmental outcomes.

Use of NCPAP in premature infants has gained favor. Children's Hospital of New York – Columbia University has become known for the use of NCPAP which has resulted in significantly lower rates of chronic lung disease. The association of decreased chronic lung disease with NCPAP was reported by Avery et. al, and has been confirmed in a survey of 11 other American centers. While NCPAP is now being used more routinely, there still remain questions and the body of knowledge regarding its use is still growing. One issue is it is very resource-intensive, requiring skilled and experienced staff to ensure success of the treatment. Additional research regarding benefits of NCPAP will increase universal acceptance and make centers less likely to stop NCPAP and begin conventional ventilation with onset of apnea, skin irritation or nurse frustration with correct NCPAP positioning. Some studies have also shown an increased risk of pneumothorax and necrotizing enterocolitis.[8] Most importantly regarding the need for our research is the fact that recent studies acknowledge long term consequences including neurodevelopmental outcomes of CPAP remain undetermined

Table 1. Group Demographic and Intervention Variables.

Variable	CV	CPAP	p Value
Male (%)	49	52	0.51
Gestational Age (mean)	29.5	29.3	0.40
Birth Weight (mean)	1140	1148	0.79
Birth Head Circ (mean)	26.5	26.5	0.88
Birth Length (mean)	37.2	37.6	0.34
1 min Apgar (mean)	6.2	6.3	0.82
5 min Apgar (mean)	7.7	7.8	0.76
10 min Apgar (mean)	7.2	7.2	0.99
SGA (%)	27.5	21.4	0.21
Chorioamnionitis (%)	10	7.7	0.49
Nosocomial Infection (%)	31	28	0.51
Antenatal Steroids (%)	57.1	64	0.24
Transports (%)	15	17	0.59
22 Calorie Formula (%)	43	51	0.83
Early Intervention (%)	62	64	0.92

and need to be monitored. Research regarding improved growth with the use of NCPAP is very limited. Geary et. al. found the introduction of surfactant at delivery followed by immediate extubation to CPAP, decreased oxygen exposure, and that giving early parenteral amino acids in extremely low birth weight infants was associated with improvements in growth and morbidity. Our NICU transitioned to NCPAP for the primary respiratory support system of premature newborns in January 2002. Within the first year, our observations suggested that our incidence of chronic lung disease had significantly declined. Over the next five years it was noted anecdotally that our babies seemed to achieve catch up in their growth and development faster than they had when managed by CV. We hypothesized that a retrospective review would show improved growth and improved BINS scores in our babies managed with NCPAP. At the same time we also opted to look at the incidence of ROP and CLD in our NICU during these two different treatment modes, expecting that they would decrease with NCPAP.

Patients and Methods

A retrospective chart review of two groups of NICU patients < 1500 grams was conducted. The first group was from January 1999 – December 2000 (n=140) and was managed by CV. The second group was from January 2003-December 2004 (n=168) and was managed primarily by NCPAP. As in other studies of NCPAP[10,13] each baby is managed individually and if clinical condition warrants, implementation of CV is executed. Our data showed our CV group had a mean of 17.4 days on the ventilator and no NCPAP days. The NCPAP group had a mean of 4.5 days on the ventilator and 19.2 days on NCPAP. So our NCPAP babies were exposed to a mean of 12.9 fewer ventilator days. Excluded from the study were babies who died or had Grade III or IV intraventricular hemorrhage. In order to evaluate the similarity of the two groups, demographic variables of gender, gestational age, birth weight, birth head circumference, birth length, APGAR scores, size for gestational age, maternal chorioamnionitis, nosocomial infections, antenatal steroid use, and transport status were compared between the two groups. Intervention variables compared included the use of high calorie formula and provision of early intervention services. Outcome variables measured included mean weight at two weeks, one month, 4-6 months, 9-12 months, 15-18 months, and two years. Mean head circumference and length were also evaluated at these intervals excluding two weeks and one month. Also evaluated were the percent having CLD and ROP. CLD was defined as an oxygen requirement at 36 weeks post menstrual age. Finally mean Bayley Infant Neurodevelopmental Screening (BINS) percentage scores at 4-6 months, 9-12 months, 15-18 months, and two years were calculated. Because there are a different number of BINS criteria at the various ages, a percentage of criteria met was used rather than a raw score. Categorical values were analyzed using Pearson Chi Square. Mean numerical values were analyzed with the student t-test. These parametric tests were selected because they have higher statistical power than non parametric tests and we assumed that our NICU population has a normal distribution.

Results

There was no statistically significant difference between the two groups in regard to any of the fifteen demographic and intervention variables. These variables, which were compared to assure similarity of the two groups, included gender, gestational age, birth weight, birth head circumference, birth length, Apgar scores, number of small for gestational age babies, maternal chorioamnionitis, nosocomial infections, antenatal steroid use, percentage of babies transported in, use of high calorie formula, and early intervention therapies. It should be noted that the % SGA was 27.5% in the CV group and only 21.4% in the CPAP group. While this did not achieve statistical significance, it may have had an impact on the outcomes studied. The

data and p values related to these variables are depicted in Table I.

Additional assurance of similarity between the two groups is derived from the fact that the same neonatologists were present during both time frames. No changes were made in feeding protocols, antibiotic usage, or parental interaction policies between the two time periods.

The NCPAP group demonstrated significantly improved growth and development. The mean one month weight in the NCPAP group was 1449 grams as compared to 1340 grams in the CV group ($p<0.05$). At the 9-12 month NICU follow up clinic visit mean weight was 9.0 kg in the NCPAP group and 8.3 kg in the CV group ($p<0.01$). Finally at the 15-18 month visit mean weight in the NCPAP group was 10.6 kg as compared to 9.6 kg in the CV group ($p<0.01$). While weight was also greater in the NCPAP group at 2 weeks, 4-6 months, and 2 years, these values were not statistically significant. Linear growth was significantly greater at all measured intervals. At 4-6 months, the NCPAP mean length was 64.4 centimeters as compared to 58.2 centimeters in the CV group ($p<0.05$). Similar differences were noted at 9-12 months (NCPAP = 73 centimeters, CV = 71.5 centimeters, $p<0.05$), 15-18 months (NCPAP = 81.3 centimeters, CV = 78.2 centimeters ($p<0.01$), and 2 years (NCPAP = 88.5 centimeters, CV = 85 centimeters, $p=.05$). Head circumference was also monitored and no difference was found between the two groups.

The percentage of items successfully achieved on the BINS was greater in the NCPAP group at all follow up visits and was statistically significant at the 9-12 month visit (NCPAP = .91, CV = .77, $p<0.01$) and the 15-18 month visit (NCPAP = .84, CV = .69, $p<0.01$). It should be noted that the number of babies in the study decreased at each subsequent visit. This occurred as some were lost to follow up and others were discharged from the clinic after achieving catch up in growth and development. See Table 2-4 for full data sets regarding growth and BINS scores. Incidence of CLD was 18.5% in the NCPAP group and 30% in the CV group ($p<0.05$). Incidence of ROP was 6% in the NCPAP group and 15% in the CV group ($p<0.01$).

Discussion

As advancements in the field of neonatology continue to lead to decreased mortality, it is imperative that the study of neurodevelopmental effects of various treatment modalities be ongoing. Just as practice changed regarding the use of postnatal steroids which have been linked to worsened neurodevelopmental outcomes, we must continue to strive toward better interventions, with improved outcomes. It has already been established that NCPAP decreases the incidence of CLD and this was confirmed in our NICU as well. As was reported in the Geary study[7] as well as ours, it appears NCPAP has additional benefits of improved growth. Perhaps these babies do not have to utilize as many calories for repair of lung damage related to CLD and for increased work of breathing, thereby enabling better growth.

What are possible explanations for the improvements in BINS scores? It could be directly related to their improved growth. Hack (1982) found that preterm infants who maintain good growth velocity and demonstrate catch up growth also do better neurodevelopmentally. Nutrition has been found to impact long term growth and development (Adamkin, 2008). Or perhaps it may be related to NCPAPs effect on CLD. Infants with CLD have poorer growth and disruption of normal brain

Tables II-IV. Comparisons of Weight, Length, and Bailey Infant Neurodevelopmental Screener scores.

Table 2. Weight

Age	CV	CPAP	p Value
2 wks (gm)	1170	1194	0.45
1 month (gm)	1340	1449	0.02
4 months (kg)	6.1 (n=87)	6.4 (n=92)	0.15
9 months (kg)	8.3 (n=66)	9.0 (n=59)	0.0009
15 months (kg)	9.6 (n=37)	10.6 (n=48)	0.002
2 years (kg)	11.2 (n=24)	12.1 (n=12)	0.16

Table 3. Length

Age	CV	CPAP	p Value
4 months (cm)	58.2 (n=87)	64.4 (n=92)	0.02
9 months (cm)	71.5 (n=66)	73 (n=59)	0.0009
15 months (cm)	78.2 (n=36)	81.3 (n=48)	0.002
2 years (cm)	85 (n=24)	88.5 (n=12)	0.05

Table IV. BINS

Age	CV	CPAP	p Value
4 months	0.87 (n=85)	0.89 (n=92)	0.29
9 months	0.77 (n=66)	0.91 (n=59)	0.000
15 months	0.69 (n=37)	0.84 (n=48)	0.006
2 years	0.66 (n=22)	0.74 (n=11)	0.42

development (Chiriboga, 2003). CLD has been found to increase the risk for later neurobehavioral impairment (Short, 2003). In infants less than 1500 gms 15% of those with CLD had CP compared with only 3-4% of those without CLD having CP (Skidmore, Rivers, and Hack, 1990). Anecdotally, our nurses report parents feel more comfortable holding and interacting with babies on NCPAP than those who are intubated. Therefore NCPAP babies may receive more positive stimulation because caregivers do not fear an accidental extubation.

A weakness of our study was the decreasing numbers we had at each follow up clinic visit. By the 2 year visit we only had 24 patients in the CV group and 12 in the NCPAP group. This of course lowered the power of our statistical analysis and contributed to the fact that the increased weight and increased BINS scores at this visit did not have statistical significance. However, a positive twist may be that part of the reason these numbers lowered is that we discharge babies prior to 2 years if they have achieved catch up. Even though we started out with more in the NCPAP group (168) than in the CV group (140), by the two year visit there were twice as many in the CV group. Some of the decreased numbers are the result of babies being lost to follow up but the majority is due to babies having achieved catch up in growth and development. Thus more babies in the NCPAP group no longer needed our services.

Weight was not consistently significantly higher at every interval. Perhaps at two weeks, enough time had not elapsed to yet show significance. Lack of significance at the 4-6 month visit is harder to explain as to why we would see significance before this at 1 month and afterward at 9-12 and 15-18 months. However linear growth difference was significant at every measurement (even with the small numbers at the 2 year visit) and this is generally considered to be a better indicator of appropriate nutrition.

The elevation in the NCPAP BINS scores at the 4-6 month visit was not significant. This seems intuitive as not much is required developmentally at this age. As with all retrospective studies, association is not proof of causality. In order to truly compare the effects of NCPAP vs. CV on growth and development, a randomized, prospective study would be necessary.
A strength of our study is the strong similarity of the two groups. This is evident statistically, having found no difference in any of the demographic or intervention variables. Similarity of treatment protocols was also improved by the fact that the same neonatologists were practicing during both time periods. No changes were made in feeding protocols during the management of either cohort.

Conclusion

The use of NCPAP in premature infants has definitely been shown to decrease CLD. If it in fact also improves growth and development this could contribute to reduced morbidity in this vulnerable group. In our study NCPAP therapy in premature babies when compared with CV significantly:

- Increased weight at one month which was sustained at the 9-12 month and 15-18 month visits.
- Increased BINS scores at the 9-12 month and 15-18 month visits.
- Improved linear growth at all follow up visits.
- Decreased the occurrence of CLD and ROP.

We also noted that a greater percentage of the NCPAP babies were discharged earlier from the NICU follow up clinic due to complete catch up. Further study is needed to investigate the benefits of NCPAP use for smaller, sicker babies and those with high risk for neurodevelopmental abnormalities.

References

1. Fanaroff AA, Stoll BJ, Wright LL, et al. NICHD Neonatal Research Network: trends in neonatal morbidity and mortality for very low birthweight infants. *Am J Obstet Gynecol.* 2007;147.e1-147.e8
2. Costeloe K, Hennessy E, Gibson AT, Marlow N, Wilkinson, AR. The EPICure Study: outcomes to discharge from hospital for infants born at the threshold of viability. *Pediatrics.* 2000;106(4):659-671
3. Hack M, Fanaroff AA. Outcomes of children of extremely low birthweight and gestational age in the 1990s. *Semin Neonatol.* 2000;5:89-106
4. Vohr BR, Wright LL, Dusick AM. Neurodevelopmental and functional outcomes of extremely low birthweight infants in the National Institute of Child Health and Human Developmental Neonatal Research Network, 1993-1994. *Pediatrics.* 2000;105:1216-1226
5. Avery ME, Tooley WH, Keller JB. Is chronic lung disease in low birthweight infants preventable? A survey of eight centers. *Pediatrics.* 1987;79:26-30
6. Horbar JD, McAuliffe TL, Adler SM. Variability in 28 day outcomes for very low birthweight infants: an analysis of 11 neonatal intensive care units. *Pediatrics.* 1988;82:554-559
7. Bohlin K, Jonsson B, Gustafsson, AS, et al. Continuous positive airway pressure and surfactant. *Neonatology*. 2008, 93;309-315
8. Gordon PV, Gee RE. High Flow Nasal Cannula Use Correlates with Improved Outcomes in the Louisiana Neonatal Quality Improvement Collaborative (LNQIC). *e-Journal of Neonatology Research*. 2012;2:108-117
9. Buckmaster AG, Arnolda G, Wright IM, et al. Continuous positive airway pressure therapy for infants with respiratory distress in non tertiary care centers: a randomized, controlled trial. *Pediatrics.* 2007;120:509-518
10. Morley CJ, Davis PG, Doyle LW, et al. Nasal CPAP or intubation at birth for very preterm infants. *New England Journal of Medicine.* 2008;358:700-708
11. Roberts CL, Badgery-Parker T, Algert CS, et al. Trends in use of neonatal CPAP: a population-based study. *BMC Pediatrics.* 2011;11:89-96
12. SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Target ranges of oxygen saturation in extremely preterm infants. *New England Journal of Medicine.* 2010;362:1959-1969
13. Morly CJ. CPAP and Low Oxygen Saturation for Very Preterm Babies? *New England Journal of Medicine.* 2010;362:2024-2026
14. Geary CA, Fonseca RA, Casky MA, Mallory MH. Improved growth and decreased morbidities in < 1000 gram neonates after early management changes. *Journal of Perinatology.* 2008;28(5):347-353
15. Hack M, Merkatz IR, McGratin SK, Jones PK, Fanaroff AA. The prognostic significances of postnatal growth in VLBW infants. *Am J Obstet Gynecol.* 1982;143:693-699
16. Adamkin D. Nutrition impacts long term growth and development. *Pediatrics.* 2008;121(1):181-182
17. Chiriboga CA, Kuban KC, Durkin M, et al. Factors associated with microcephaly at school age in a very low birthweight population. *Dev Med Child Neurol.* 2003;45:796-801
18. Short EJ, Klein NK, Lewis BA, et al. Cognitive and academic consequences of bronchopulmonary dysplasia and very low birth weight: eight year old outcomes. *Pediatrics.* 2003;112:e359
19. Skidmore MD, Rivers A, Hack, M. Increased risk of CP among very low birthweight infants with chronic lung disease. *Dev Med Child Neurol* 1990;32:325-332.