Obstetric and Neonatal Care Practices for Infants 501 to 1500 g From 2000 to 2009

WHAT’S KNOWN ON THIS SUBJECT: Among infants with birth weights of 501 to 1500 g born between 2000 and 2009, mortality and major morbidities among survivors declined.

WHAT THIS STUDY ADDS: Obstetrical and neonatal care practices for infants 501 to 1500 g changed significantly from 2000 and 2009, particularly decreased conventional ventilation and use of steroids for chronic lung disease and increased nasal continuous positive airway pressure and surfactant treatment after delivery.

abstract

OBJECTIVE: To identify changes in clinical practices for infants with birth weights of 501 to 1500 g born from 2000 to 2009.

METHODS: We used prospectively collected registry data for 355,806 infants born from 2000 to 2009 and cared for at 669 North American hospitals in the Vermont Oxford Network. Main outcome measures included obstetric and neonatal practices, including cesarean delivery, antenatal steroids, delivery room interventions, respiratory practices, neuroimaging, retinal exams, and feeding at discharge.

RESULTS: Significant changes in many obstetric, delivery room, and neonatal practices occurred from 2000 to 2009. Use of surfactant treatment in the delivery room increased overall (adjusted difference [AD] 17.0%; 95% confidence interval [CI] 16.4% to 17.6%), as did less-invasive methods of respiratory support, such as nasal continuous positive airway pressure (AD 9.9%; 95% CI 9.1% to 10.6%). Use of any ventilation (AD –7.5%; 95% CI –8.0% to –6.9%) and steroids for chronic lung disease (AD –15.3%; 95% CI –15.8% to –14.8%) decreased significantly overall. Most of the changes in respiratory care were observed within each of 4 birth weight strata (501–750 g, 751–1000 g, 1001–1250 g, 1251–1500 g).

CONCLUSIONS: Many obstetric and neonatal care practices used in the management of infants 501 to 1500 g changed between 2000 and 2009. In particular, less-invasive approaches to respiratory support increased. Pediatrics 2013;132:222–228

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KEY WORDS
very low birth weight, NICU, interventions, practice, Vermont Oxford Network

ABBREVIATIONS
AD—adjusted difference
CI—confidence interval
CPAP—continuous positive airway pressure
VLBW—very low birth weight

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Very low birth weight (VLBW) infants, those weighing $\leq 1500$ g at birth, almost universally require intensive care and represent $\sim 15\%$ of all NICU admissions.1

Major neonatal networks reported significant declines in mortality among VLBW infants in the early 1990s: mortality decreased $15\%$ in the Vermont Oxford Network2 and $26\%$ in the National Institute of Child Health and Human Development Neonatal Research Network.3 However, mortality plateaued in the later part of the decade. The improvements in mortality and morbidity noted in the early 1990s were attributed to changes in practice, including increased use of antenatal steroids and the introduction of surfactant replacement therapy.4–8

From 2000 and 2009, mortality for infants weighing 501 to 1500 g and cared for at 669 North American hospitals in the Vermont Oxford Network declined from 14.3% to 12.4%, whereas major morbidities in survivors, including early bacterial infection, late bacterial or fungal infection, necrotizing enterocolitis, chronic lung disease, severe intraventricular hemorrhage, periventricular leukomalacia, and severe retinopathy of prematurity, declined from 46.4% to 41.4%.9 We undertook this study to identify changes in obstetric, delivery room, and neonatal practices for the same cohort of infants with birth weights of 501 to 1500 g born between 2000 and 2009.

METHODS

Vermont Oxford Network member hospitals submitted de-identified data for infants 401 to 1500 g born at their hospitals or transferred to them within 28 days of birth.10 This study was restricted to infants 501 to 1500 g cared for at 669 North American hospitals. Local staff collected data using uniform definitions and submitted the data electronically or on paper forms. All data, regardless of collection method, underwent the same automated data checks for quality and completeness at the time of submission. No protected health care information was collected. The Committee on Human Research at the University of Vermont approved the use of the database for research.

Data

Analyses were adjusted for race and ethnicity (Hispanic, black non-Hispanic, white non-Hispanic, other), gender, gestational age, location of birth (in-born, out-born), multiple birth, small size for gestational age, any birth defect, and 1-minute Apgar score. Outborn infants were included if they transferred to a member center within 28 days of birth without having first gone home. Small for gestational age was defined within gender, race, and multiplicity as birth weight below the 10th percentile based on smoothed curves from the US Natality Dataset.11 Care practices included obstetric (use of antenatal steroids, cesarean delivery), delivery room (tracheal intubation, oxygen, epinephrine, cardiac compressions, face mask ventilation, surfactant), NICU (steroids for chronic lung disease, surfactant $\geq$ 2 hours after birth, surfactant any time after birth, conventional ventilation, high-frequency ventilation, any ventilation, high-flow nasal cannula, nasal ventilation, nasal continuous positive airway pressure [CPAP], CPAP before ventilation, ventilation after CPAP), and other (neuroimaging, feeding breast milk at discharge, retinal exam). Conventional ventilation was defined as positive pressure ventilation through an endotracheal tube with an intermittent mandatory ventilation rate of less than 240 per minute. High-frequency ventilation was defined as positive pressure ventilation through an endotracheal tube with an intermittent mandatory ventilation rate $\geq 240$ per minute. Nasal ventilation was defined as intermittent positive pressure ventilation (intermittent mandatory ventilation or synchronized intermittent mandatory ventilation) via nasal prongs or other nasal device. Neuroimaging was defined as at least 1 cranial ultrasound, computed tomography scan, or magnetic resonance imaging scan performed on or before day 28. Most outcomes were available for the entire study period (2000–2009). Exceptions were CPAP before ventilation, ventilation after CPAP, and feeding breast milk before discharge, which were introduced in 2002, and high-flow nasal cannula and nasal ventilation, which were introduced in 2006. Hospital characteristics came from an annual membership survey.

Statistical Analyses

The significance of changes over time was evaluated using logistic regression, with birth year represented as a categorical variable. To adjust for potential changes in infant characteristics, race and ethnicity, gender, gestational age, location of birth, multiple birth, small size for gestational age, any birth defect, and 1-minute Apgar score were included as covariates in the model. Standardized rates and the differences in these rates between the first year the item was available and 2009 were derived from the logistic regression model with characteristics of infants born in 2009 defining the reference population. A contrast was used to test for a linear trend in rates across years. Confidence intervals for the differences in standardized rates were computed based on standard errors using the δ method. The results of secondary analyses based on standardized rates computed using infants born in 2000 as the reference population were consistent with those using 2009 as the reference. All analyses accounted for clustering of infants within the hospital using generalized

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estimating equations. Additional analyses were performed within 250–g birth weight categories (501–750 g, 751–1000 g, 1001–1250 g, and 1251–1500 g). All analyses used SAS Statistical Software version 9.2 (SAS Institute, Cary, NC).

The primary analyses assessed the observed and adjusted rates of obstetric and NICU practices at 669 North American hospitals that were members of the Vermont Oxford Network from 2000 to 2009. To evaluate the potential effect of changes in participating hospitals over time, primary analyses were replicated for the 278 North American hospitals that participated for all 10 years. The results of these secondary analyses were consistent with the analyses of all 669 hospitals. Therefore, all reported results are derived from the sample of all 669 North American hospitals that participated in the Network from 2000 to 2009.

RESULTS

Hospitals and Infants

From 2000 to 2009, 669 North American hospitals contributed data to the Vermont Oxford Network VLBW database (Supplemental Appendix). Half of the 669 hospitals participated for ≥8 years, 75% participated for ≥4 years, and 42% participated for all 10 years. Of participants, 32% were located in the south, 28% in the west, 22% in the midwest, 16% in the northeast, and 2% in Canada or Puerto Rico. Seventeen percent of the hospitals performed ventilation without restriction and major surgery, including cardiac surgery; 49% performed ventilation without restriction and major surgery except cardiac surgery; and 34% had restrictions on ventilation or surgery. Seventy-six percent of the hospitals were not-for-profit, 10% were for-profit, and 10% were government-owned. Thirty-six percent reported having pediatric residents and neonatal fellows.

The median annual number of VLBW infants at the hospitals was 57 (interquartile range 30–103).

Of the 355,806 infants with birth weight 501 to 1500 g, 51.1% of the infants were boys, 27.8% were multiple births, and 19.0% were small for gestational age. Mean birth weight was 1069 g in 2000 and 1071 g in 2009. The mean gestational age was 28.3 weeks in both years. From 2000 to 2009, the percentage of black infants (27.3%–29.3%, \( P = .046\)), Hispanic infants (15.5%–18.4%, \( P < .001\)), and infants of other races (5.0%–6.4%, \( P < .001\)) increased, whereas the percentage of white infants decreased (52.2%–45.9%, \( P < .001\)). The percentage of infants with birth defects increased (4.3%–5.1%, \( P = .004\)). There were no significant changes in the other infant characteristics (gender, birth weight, gestational age, birth location, multiple births, small size for gestational age, and 1-minute Apgar score). Additional details about the cohort were reported previously.

Clinical Practices

The observed annual rates in obstetric and delivery room, NICU respiratory, and other NICU practices are reported in Table 1. The differences in the standardized rates between 2009 and the first year the item was available are reported in Fig 1.

Obstetric and Delivery Room Practices

Treatment with antenatal steroids and cesarean delivery increased from 2000 to 2009. In the delivery room, face mask ventilation (adjusted difference [AD] 8.7%, 95% confidence interval [CI] 8.0% to 9.3%) and surfactant use (AD 17.0%, 95% CI 16.4% to 17.6%) increased significantly, whereas tracheal intubation (AD –3.7%, 95% CI –4.2% to –3.3%) and use of supplemental oxygen (AD –3.7%, 95% CI –4.4% to –3.1%) decreased significantly.

NICU Respiratory Practices

In the NICU, use of nasal CPAP increased from 2000 to 2009 (AD 9.9%, 95% CI 9.1% to 10.6%). Use of nasal ventilation (AD 6.0%, 95% CI 5.5% to 6.4%) and high-flow nasal cannula (AD 13.1%, 95% CI 12.5% to 13.8%) increased from 2006, the year data collection began, to 2009. The use of any ventilator support decreased significantly from 2000 and 2009 (AD –7.4%, 95% CI –8.0% to –6.9%). Use of conventional ventilation decreased significantly (AD –7.5%, 95% CI –8.0% to –6.7%), whereas use of high-frequency ventilation did not (AD = –1.0%; 95% CI –1.5% to –0.5%). The percentage of infants receiving a trial of nasal CPAP before assisted ventilation increased from 2002, the year data collection began, to 2009 (AD 8.3%, 95% CI 7.6% to 9.1%) and fewer infants required assisted ventilation after nasal CPAP (AD –6.6%; 95% CI –8.1% to –5.1%).

The percentage of infants receiving the first dose of surfactant more than 2 hours after birth declined significantly from 2000 to 2009 (AD –9.3%, 95% CI –10.0% to –8.5%), as did the use of steroids for the treatment or prevention of chronic lung disease (AD –15.3%; 95% CI –15.8% to –14.8%).

Other NICU Practices

Although the percentage of infants who had neuroimaging did not change from 2000 to 2009, the percentage of infants who had a retinal examination before discharge did increase significantly. The percentage of infants on any breast milk at discharge increased significantly from 2002, the year data collection began, to 2009.

Results by Birth Weight Strata

Many of the observed changes in respiratory care that were reported for the entire population of infants 501 to 1500 g were observed within each of the 4 birth weight strata (501–750 g,
decreased in infants weighing the lowest birth weight category and high-frequency ventilation increased in weight category. Additionally, use of delivery room intubation, supplemental oxygen, conventional ventilation, and ventilation after CPAP in infants in the lowest birth weight category were that no significant increases were observed in use of delivery room intubation, supplemental oxygen, conventional ventilation, and ventilation after CPAP in infants in the lowest birth weight category. Additionally, use of high-frequency ventilation increased in the lowest birth weight category and decreased in infants weighing >751 g.

DISCUSSION

For infants 501 to 1500 g, we observed significant increases in the use of antenatal steroids, cesarean delivery, and less-invasive strategies for respiratory support, such as nasal CPAP, nasal ventilation, and high-flow nasal cannula. Additionally, we observed increases in use of face mask ventilation and surfactant in the delivery room, and decreases in steroids for chronic lung disease, use of surfactant more than 2 hours after birth, and assisted ventilation using an endotracheal tube.

The use of antenatal steroids has a strong basis in evidence from randomized controlled trials and is strongly endorsed in a statement from the National Institutes of Health. Rates of antenatal steroid use increased since that statement and have continued to increase in the current decade. However, rates in Europe, Canada, and Australia still exceed rates reported by Vermont Oxford Network centers in 2009.

The increased rate of cesarean delivery, which suggests that for every 100 infants 501 to 1500 g, 10 more were delivered by cesarean delivery in 2009 compared with 2000, is based on less solid evidence. No randomized controlled trial has compared route of delivery in preterm infants, but observational studies support improved outcome with the use of cesarean delivery. In a review of US-linked birth and infant death certificates from 2000 to 2003, Malloy reports a significant reduction in neonatal mortality for infants delivered by cesarean at 22 to 25 weeks of gestation. We observed increases in the use of less-invasive modes of respiratory support, such as nasal CPAP, nasal cannula.
ventilation, and high-flow nasal cannula. We also observed increases in trial of CPAP before assisted ventilation and decreases in ventilation after CPAP. Surfactant treatment in the delivery room increased substantially, as did the administration of the first dose within 2 hours of birth. Currently there is uncertainty about whether to treat infants at risk for respiratory distress syndrome with CPAP or surfactant therapy immediately after birth.19–22

Our data suggest that both of these strategies are being used with increasing frequency. Fewer infants are being intubated in the delivery room, but if intubated, they are receiving surfactant shortly thereafter. Despite increased early use of noninvasive support, most infants did not require ventilation after stabilization; however, these changes did not occur uniformly across the birth weight strata. In particular, rates of tracheal intubation and supplemental oxygen use in the delivery room, conventional ventilation, and ventilation after a trial of CPAP did not change for infants weighing 501 to 750 g at birth.

Changes in the use of both invasive and noninvasive support have been reported in other neonatal networks. In southern Sweden between 1995 and 2004, Lundqvist et al23 reported an increased use of assisted ventilation in infants <25 weeks of gestation, but greater use of CPAP in infants 25 to 28 weeks of gestation. In New Zealand, Tingay et al24 reported increased use of high-frequency ventilation from 5.9% of ventilated infants in 1996 to 12.6% of infants in 2001, whereas the number of infants receiving conventional mechanical ventilation decreased by 20.8%. Tingay et al24 also reported increased use of nasal CPAP from 16% of infants receiving CPAP in 1996 to 43.2% of infants receiving CPAP in 2003. In Switzerland, Rüegger et al15 reported that the use of CPAP increased from 43.0% in 1996 to 73.2% in 2008. In our population, we found no change in use of assisted ventilation for infants 501 to 750 g, and increased use of CPAP, nasal ventilation, and high-flow nasal cannula for all infants. We also found increased trial

FIGURE 1
Adjusted differences for selected obstetric, delivery room, and NICU practices for infants 501 to 1500 g. Differences in rates standardized based on characteristics of infants born in 2009. *Data collected beginning in 2002. †Data collected beginning in 2006.
of CPAP before ventilation for all infants, and decreased use of ventilation after CPAP for all except infants weighing <751 g.

In a population identical to the population reported here, we observed an increase in survival and in survival without a major morbidity. The percentage of all infants who survived without a major morbidity increased by ~4.6% from 2000 to 2008, indicating that for every 22 infants weighing 501 to 1500 g treated in 2009, 1 additional infant would survive without major morbidity compared with 2000. Although we see marked changes in obstetric, delivery room, and neonatal practices over this same period, we cannot determine whether any of these changes in practice are responsible for the changes in outcomes.

We did observe a decrease in the rate of chronic lung disease between 2000 and 2009 of 1.4% (95% CI −2.1% to −0.8%) in this identical population. Although it is difficult to evaluate the impact of practice changes on this modest improvement, it is interesting to note that this decline was accomplished in a population that received significantly less exposure to postnatal corticosteroids. The decreased use of postnatal corticosteroids is well supported by the evidence and guideline statements from authoritative groups. Postnatal corticosteroid use reached its zenith in the late 1990s with >25% of all VLBW infants exposed. In 2008, only 8% of VLBW infants received steroid treatment of chronic lung disease.

There are several limitations to our study. Our study included infants if they had a birth weight of 501 to 1500 g. We did not include infants weighing <500 g because practices regarding care of infants of these weights vary greatly between centers. A previous report from the Vermont Oxford Network of infants 401 to 500 g born from 1996 to 2000 found that 17% of the infants survived to discharge with few surviving without major morbidity. Additional studies of infants at lowest ranges of birth weight and gestational age are warranted.

The hospitals participating in the Vermont Oxford Network changed over the study period. To determine if this influenced our findings, we conducted a secondary analysis restricted to the 278 hospitals that participated continuously for the entire study period. The results paralleled those obtained for all 669 hospitals. The demographic characteristics of the patients also changed over the study period. We accounted for these changes by including appropriate covariates in the risk adjustment models. However, it is possible that there were unmeasured differences for which we could not adjust.

### TABLE 2 Standardized Respiratory Care Practice Rates for Infants 501 to 1500 g by 250-g Birth Weight Categories

<table>
<thead>
<tr>
<th>Birth Weight, g</th>
<th>501 to 750</th>
<th>751 to 1000</th>
<th>1001 to 1250</th>
<th>1251 to 1500</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery room practices</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supplemental oxygen</td>
<td>89.6</td>
<td>89.5</td>
<td>96.3</td>
<td>94.6</td>
</tr>
<tr>
<td>Tracheal intubation</td>
<td>83.9</td>
<td>82.4</td>
<td>78.3</td>
<td>73.0</td>
</tr>
<tr>
<td>Face mask ventilation</td>
<td>62.8</td>
<td>73.4</td>
<td>63.3</td>
<td>75.2</td>
</tr>
<tr>
<td>Surfactant in delivery room</td>
<td>32.1</td>
<td>55.7</td>
<td>27.1</td>
<td>50.3</td>
</tr>
<tr>
<td>NICU practices</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steroids for chronic lung disease</td>
<td>51.3</td>
<td>23.7</td>
<td>36.1</td>
<td>11.3</td>
</tr>
<tr>
<td>Surfactant &gt; 2 h after birth</td>
<td>15.9</td>
<td>8.2</td>
<td>20.6</td>
<td>12.1</td>
</tr>
<tr>
<td>Surfactant any time after birth</td>
<td>82.1</td>
<td>84.5</td>
<td>80.5</td>
<td>82.5</td>
</tr>
<tr>
<td>Conventional ventilation</td>
<td>92.5</td>
<td>92.1</td>
<td>88.3</td>
<td>82.1</td>
</tr>
<tr>
<td>High-frequency ventilation</td>
<td>55.9</td>
<td>59.2</td>
<td>32.9</td>
<td>30.2</td>
</tr>
<tr>
<td>Any ventilation</td>
<td>97.3</td>
<td>96.5</td>
<td>90.9</td>
<td>84.6</td>
</tr>
<tr>
<td>Nasal CPAP</td>
<td>54.2</td>
<td>65.1</td>
<td>71.4</td>
<td>78.0</td>
</tr>
<tr>
<td>Ventilation after CPAP</td>
<td>78.3</td>
<td>81.7</td>
<td>63.0</td>
<td>58.2</td>
</tr>
<tr>
<td>CPAP before ventilation</td>
<td>10.3</td>
<td>15.0</td>
<td>17.8</td>
<td>26.7</td>
</tr>
<tr>
<td>High-flow nasal cannula</td>
<td>44.3</td>
<td>55.9</td>
<td>53.8</td>
<td>68.5</td>
</tr>
<tr>
<td>Nasal ventilation</td>
<td>15.1</td>
<td>26.0</td>
<td>14.8</td>
<td>23.7</td>
</tr>
</tbody>
</table>

a: Measures apply to infants (n = 355 806).
b: P < 0.05.
d: Measure applies to infants receiving surfactant (n = 337 677). Surfactant > 2 h after birth is missing 1.8% of the time.
e: Measure applies to infants receiving CPAP before initial ventilation (n = 67 123 2002–2008).
f: Data collected beginning in 2002.
g: Measure applies when infant receives CPAP (n = 191 885 2002–2009).
h: Data collected beginning in 2006.
Finally, our study sample is not population based. Therefore, our findings should be interpreted only to reflect practices and outcomes for infants receiving care at North American hospitals with NICUs, and not generalized to the population of all live-born VLBW infants.

CONCLUSIONS

There were significant changes in obstetrical, delivery room, and neonatal care practices in the management of infants 501 to 1500 g between 2000 and 2009. The most striking change was the trend toward increased use of noninvasive approaches to respiratory support, including nasal CPAP, nasal ventilation, and high-flow nasal cannula. How these changes in practice affected patient outcomes is uncertain.

REFERENCES


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