A Low-Sodium Solution for Airway Care: Results of a Multicenter Trial

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BACKGROUND: Normal saline is sometimes instilled into the endotracheal tube preparatory to airway suctioning, to assist in removing thick secretions. However, saline can damage the antimicrobial properties of airway secretions. We previously described a low-sodium physiologically based solution for airway care and reported a small (n = 60) randomized trial in neonates, which showed trends toward less ventilator-associated pneumonia (VAP) and less chronic lung disease with the new solution. We now report a multicenter trial of that solution. METHODS: We conducted a before-and-after study with a parallel control group, in 4 level-3 neonatal intensive care units (NICUs). During year 1, all 4 NICUs used saline for airway care. During year 2, one NICU used the test solution exclusively while the other NICUs used saline exclusively. The 2 study outcomes were VAP (cases/1,000 ventilator days) and chronic lung disease, defined 3 ways: supplemental oxygen at 28 days; supplemental oxygen at 36 weeks gestation; and supplemental oxygen on hospital discharge. RESULTS: During the study period 1,116 neonates had endotracheal intubation for respiratory management. Of those, 1,029 received the standard saline for airway suctioning, and the 87 in NICU 4 received the test solution. NICU 4 had a decrease in VAP rate, from 4.2 VAPs/1,000 ventilator days with saline, to 1.6 VAPs/1,000 ventilator days with the test solution (P = .04), and also had the lowest prevalence of chronic lung disease (P < .001 for each definition). CONCLUSIONS: The test solution significantly reduced the VAP and chronic lung disease rates. Key words: nosocomial infection; saline; airway care; endotracheal tube; ventilator-associated pneumonia; sepsis; chronic lung disease. [Respir Care 2010;55(12):1680–1685. © 2010 Daedalus Enterprises]
better than saline. We devised a prototype solution and conducted 2 previous studies\textsuperscript{19,20} that suggested that the test solution was feasible to administer with no more patient intolerance than saline. In a 60-patient 2-center randomized double-masked trial, the recipients of the test solution had trends toward less VAP and less chronic lung disease (CLD).\textsuperscript{20} The present study was intended to expand that work in a multicenter trial. We hypothesized that the test solution would lower the VAP and CLD rates.

**Methods**

**Study Design**

We selected a before-and-after study design with a parallel control group. All 4 intensive care units (NICUs) used standard saline for all airway care during a 12-month period (Period 1), then, during the subsequent 12 months (Period 2), one of the NICUs used the test solution exclusively, while the other 3 NICUs continued using saline. At the end of each month, a designated infection-control nurse at each NICU used a standardized VAP definition to determine the number of VAPs that month, and used a uniform reporting mechanism to report the VAP rate to the Intermountain Healthcare Women and Newborns Clinical Program.

**Standard Saline and Test Solution**

The standard liquid for airway care was normal saline (Cardinal Health, San Diego, California), which is dispensed in 5-mL plastic tubes. The test solution was produced in the hospital pharmacy of NICU 4. The composition of the test solution is: Na \(7.8 \text{ mEq/L}\), K \(24.5 \text{ mEq/L}\), Ca \(3.67 \text{ mEq/L}\), Mg \(1.2 \text{ mEq/L}\), Cl \(36.3 \text{ mEq/L}\), PO\(_4\) \(3 \text{ mEq/L}\), SO\(_4\) \(1.2 \text{ mEq/L}\), albumin \(1,940 \text{ mg/L}\). The test solution was steriley compounded with the hospital’s parenteral nutrition equipment, and was sent to NICU 4 in sterile, pyrogen-free syringes labeled “AIRWAY CARE STUDY SOLUTION.” When a NICU patient no longer required any liquid for airway care (because he or she was extubated, had no nasal cannula, and needed no liquid for nasal care), the pharmacist did not send any additional airway care study solution to the bedside.

During Period 1, only saline was used for airway care (i.e., suctioning of the ETT or nares). During Period 2, NICUs 1, 2, and 3 used only saline, whereas NICU 4 used only the test solution. No other liquids were used for airway care.

The Intermountain Healthcare Institutional Review Board approved the study. The informed-consent requirement was waived because the patient data was de-identified and the study was part of standard quality-assurance activities.

**Participating NICUs**

Intermountain Healthcare is a not-for-profit organization that owns and manages 20 hospitals with labor and delivery services. The 4 NICUs in this study are the 4 largest NICUs in the Intermountain Healthcare system. Three are in large perinatal centers: McKay-Dee Hospital Center, Ogden, Utah (32-bed NICU); Intermountain Medical Center, Murray, Utah (48-bed NICU); and Utah Valley Regional Medical Center, Provo, Utah (39-bed NICU). The other is in Primary Children’s Medical Center, Salt Lake City, Utah, which is the regional children’s hospital (50-bed NICU). The 4 NICUs are all located within a 40-mile radius of Salt Lake City. The 3 perinatal centers care for neonates with a similar range of conditions, whereas the NICU at Primary Children’s is the regional extracorporeal membrane oxygenation (ECMO) center and provides exclusive service for neonates requiring surgical and cardiac care.

**Standardization of Respiratory Care Across the 4 NICUs**

Guidelines for NICU respiratory care were developed to standardize and improve consistency of respiratory care across the Intermountain Healthcare NICUs. The respiratory therapy managers and medical directors of each NICU participated in developing these guidelines, and then instructed each NICU’s staff on implementation. Guidelines were developed for: use of airway-care solutions in the trachea, nose, or mouth; closed suctioning of ETTs; obtaining tracheal aspirate for Gram stain and culture; reducing nosocomial infections; ventilator weaning and extubation; and diagnosing VAP. The 4 NICUs developed: a consistent approach to reducing line-associated infections; intubation/extubation guidelines; and oxygen saturation ranges. A consistent definition of VAP was in place in the 4 participating NICUs.

**Calculation and Reporting of VAP and CLD**

A designated infection-control nurse at each NICU used the standardized VAP definition to determine the number of VAPs each month. Based on the number of VAP cases and ventilator days for the month, the Women and Newborns Clinical Program staff calculated and archived each center’s VAP rate each month. The CLD rate was calculated for each CLD definition: supplemental oxygen at 28 days; supplemental oxygen at 36 weeks gestation; and supplemental oxygen on hospital discharge. The individuals who collected the data and provided the monthly reports were not otherwise involved in the study.
A LOW-SODIUM SOLUTION FOR AIRWAY CARE

Table 1. Admissions, Birth Weight, Gestational Age, and Sex of the Patients

<table>
<thead>
<tr>
<th>NICU</th>
<th>Period 1</th>
<th>Period 2</th>
<th>Birth Weight (mean g)</th>
<th>Gestational Age (mean wk)</th>
<th>Male (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Period 1</td>
<td>Period 2</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>460</td>
<td>506</td>
<td>2,536</td>
<td>2,436</td>
<td>.09</td>
</tr>
<tr>
<td>2</td>
<td>493</td>
<td>533</td>
<td>2,566</td>
<td>2,545</td>
<td>.73</td>
</tr>
<tr>
<td>3</td>
<td>659</td>
<td>624</td>
<td>2,390</td>
<td>2,440</td>
<td>.36</td>
</tr>
<tr>
<td>4</td>
<td>621</td>
<td>646</td>
<td>2,194</td>
<td>2,295</td>
<td>.06</td>
</tr>
</tbody>
</table>

* Admissions to the 4 Intermountain Healthcare neonatal intensive care units (NICUs).

Table 2. Overall VAP Rates

<table>
<thead>
<tr>
<th>NICU</th>
<th>Period 1</th>
<th>Period 2</th>
<th>VAP Rate* (mean and 95% CI)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>VAP Rate* (mean and 95% CI)</td>
<td></td>
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<td></td>
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<td></td>
<td>Period 1</td>
<td>Period 2</td>
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<td>1</td>
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<td>2</td>
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<td>3</td>
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<tr>
<td>4</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>2.6 (1.48–3.85)</td>
<td>2.4 (1.35–3.65)</td>
<td>.93</td>
</tr>
</tbody>
</table>

* Cases per 1,000 ventilator days.
VAP = ventilator-associated pneumonia
NICU = neonatal intensive care unit

Fig. 1. Ventilator-associated pneumonia (VAP) cases per 1,000 ventilator days each month in neonatal intensive care unit 4, February 1, 2007, through January 31, 2009.

Table 3 shows the VAP rates according to birth weight and study group.

Tables 4, 5, and 6 show the proportions of NICU patients who developed CLD, under the 3 CLD definitions. The patients who received saline for airway care had a

Results

There were no significant differences in birth weight, gestational age at birth, sex, or number of patients admitted to the NICUs between Period 1 (February 1, 2007, through January 31, 2008) and Period 2 (February 1, 2008, through January 31, 2009) (Table 1). The mean ± SD numbers of patients admitted per month were: 42 ± 8 in NICU 1, 42 ± 8 in NICU 2, 53 ± 12 in NICU 3, and 53 ± 10 NICU 4. There were no significant differences between the 2 periods in the percent of patients who received antenatal steroids, duration of hospital stay, or mortality rate. In Period 1, 2,233 neonates were admitted to the 4 NICUs, and of those 598 received endotracheal intubation and airway suctioning with saline. In Period 2, 2,309 neonates were admitted to the 4 NICUs, and of those 518 received endotracheal intubation and airway suctioning, 431 with saline and 87 with the test solution.

Table 2 shows the overall VAP rates. In the 4 NICUs combined, the VAP rate did not change between Period 1 (2.6 VAPs/1,000 ventilator days) and Period 2 (2.4 VAPs/1,000 ventilator days). However, the VAP rate in NICU 4 (which used the test solution in Period 2) changed significantly, falling from the highest rate in the system in Period 1 (4.2 VAPs/1,000 ventilator days) to the lowest in the system in Period 2 (1.6 VAPs/1,000 ventilator days, \(P = .04\)). Figure 1 shows the monthly VAP rates at NICU 4. Table 3 shows the VAP rates according to birth weight and study group.

Tables 4, 5, and 6 show the proportions of NICU patients who developed CLD, under the 3 CLD definitions. The patients who received saline for airway care had a
higher prevalence of CLD than did those who received the test solution. The patients who weighed $>1,500$ g at birth had the greatest test-solution-associated improvement in CLD prevalence.

The number of days mechanical ventilation did not significantly differ between the saline and test-solution groups. The patients who weighed $1,000$ g at birth and were treated with saline had a median of 22 days (range 1–127 d) of mechanical ventilation, versus 12 days (range 2–65 d) in those treated with the test solution ($P=.31$). The patients who weighed $1,500$ g at birth and were treated with saline received mechanical ventilation for a median of 3 days (range 1–105 d), versus 3 days (range 1–10 d) in those treated with the test solution ($P=.46$).

**Discussion**

Consistent with our previous findings in a small ($n = 60$), 2-center, randomized trial, the recipients of the test solution appeared to benefit, with lower rates of VAP and CLD than those treated with the standard normal saline. More investigation is needed to determine the benefits and the risks of instilling this or other solutions into the airways of NICU patients, as a means of facilitating airway suctioning. Many NICU nosocomial infections are with organisms considered to be of low virulence in healthy adults, such as *Candida albicans* and coagulase-negative staphylococcus. Low concentrations of immunoglobulin A and immunoglobulin G, and other developmental immunodeficiencies probably predispose preterm neonates to such infections. Irritation of the airway endothelium by tubes in the trachea, nose, or mouth probably also contribute. In addition, instilled saline weakens the patient’s microbial defenses.

The type and quantity of liquid instilled before ETT suctioning are matters of ongoing discussion and study. Kinloch suggested not instilling any liquid, but the studies by Caruso et al in adult patients suggested that saline instillation is better than dry suctioning. It seems to us that most neonates intubated for several days will have at least occasional liquid instillation, and that liquid is always saline. Based on our present and previous trials, we speculate that a physiologically based low-sodium solution is better than saline.

**Limitations**

Our study design was less rigorous and less informative than a randomized, double-masked trial, but we selected this design for what we considered a sound reason. We learned from our previous randomized trial that all study subjects received saline for airway care during their first...
day following birth, because it required about one day to
give parents the study information, for them to make a
decision about study entry, and to bring the study solution
to the bed-side for use. We speculate that this confounding
aspect limited the value of the test solution, since it was
never used as the initial and sole treatment. The present
study design removed that confounder, in that all airway
care was always with only one solution or the other. An
additional design criticism is that the available grant fund-
ing to produce the test solution limited its use to only one
NICU; the study would have benefited from using the test
solution in more than one NICU.

Another limitation in our study is that changes in our
clinical practices, other than the airway solution, might
have affected respiratory outcomes in NICU 4 during
Period 2. Prior to Period 1, we attempted to minimize that
possibility by standardizing our respiratory care practices
to reduce nosocomial infections in all the NICUs (the lat-
ter effort was headed by RGF). But we realize that un-
known factors might be responsible for the improved res-
piratory outcomes in NICU 4, which we tentatively ascribe
to the test solution.

Another limitation is that the VAP data were de-
identified, which was required by privacy concerns. The
numbers of VAP cases and ventilator days were tabu-
lated by infection-control nurses who were not involved
as study investigators, and we collected the overall patient
demographics in each hospital each month but were un-
able to link each VAP case back to the clinical informa-
Consequently, we have meaningful data about the
VAP and CLD rates, but we could not engage in multivari-
ate analysis.

Another limitation is that we restricted our testing to
only the pre-suctioning liquid, but we recognize that other
approaches to VAP reduction might produce equal or
greater benefit. Other new VAP-reduction approaches in-
clude silver-coated ETTs and means of reducing aspira-
tion around the ETT.

Conclusions

Despite the deficiencies in our study, we interpret the
findings as an advance in knowledge over our previous
phase I and II studies, and encouraging toward our
overall efforts to reduce the prevalence of VAP and CLD
in neonatal patients.

ACKNOWLEDGMENTS

We thank Diane K Lambert RN, Daniel Woodhead RT, Scott Scoffield
PharmD, Tracy Karp MSc NNP-BC, Robert Muelleck RPh MBA, and
Karla Snow PharmD, all of Intermountain Healthcare, Salt Lake City,
Utah, for valuable assistance.

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