Tidal Volume Threshold for Colorimetric Carbon Dioxide Detectors Available for Use in Neonates
Donna M. Garey, Raymond Ward, Wade Rich, Gregory Heldt, Tina Leone and Neil N. Finer

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OBJECTIVE. Colorimetric carbon dioxide detectors are used for confirmation of endotracheal intubation. The colorimetric carbon dioxide detectors that are used for neonates are labeled for use with infants and small children >1 and <15 kg. The objective of this study was to determine the minimal tidal volume that causes a breath-to-breath color change on 2 colorimetric carbon dioxide detectors.

METHODS. Using an artificial-lung model, we determined the tidal volume threshold of 2 colorimetric carbon dioxide detectors (Pedi-Cap [Nellcor, Pleasanton, CA] or Mini StatCO2 [Mercury Medical, Clearwater, FL]) during ventilation with a T-piece resuscitator or neonatal ventilator. Digital video recordings of the colorimetric carbon dioxide detectors were made during 20 seconds of ventilation at each tidal volume. Seven clinicians who were blinded to the tidal volume reviewed the videos in random order and graded the color change to determine adequacy for clinical application.

RESULTS. The Mini StatCO2 tidal volume threshold was 0.83 mL, and the Pedi-Cap tidal volume threshold was 1.08 mL.

CONCLUSIONS. The lung model revealed that the tidal volume threshold for the tested colorimetric carbon dioxide detectors is less than the expected tidal volume of a 400-g infant and suggests that these devices are appropriate for use with any neonate to confirm intubation. Pediatrics 2008;121:e1524–e1527

In the United States, 4 million infants are born each year, and ~13% are preterm, including 1.5% who weigh <1.5 kg.1 A majority of intubations during neonatal resuscitation and in the NICU occur in preterm infants. In a recent large multicenter review, ~89% of extremely low birth weight (501–1000 g) infants were treated with intubation and mechanical ventilation; therefore, methods to improve confirmation of intubation for this preterm infant population are of great interest. Current methods for confirming intubation include direct visualization of the endotracheal tube passing through the vocal cords, inspection of chest wall movement, auscultation of breath sounds, condensation on the endotracheal tube during expiration, and more recently end-tidal carbon dioxide (ETCO2) detection.1–12 In the Fifth Edition revised Neonatal Resuscitation Program (NRP) guidelines, increasing heart rate and exhaled CO2 detection including colorimetric CO2 detectors are the primary methods recommended for confirmation of endotracheal intubation in infants13; however, current product labeling of colorimetric CO2 detectors recommends use for infants and small children who weigh >1 kg and <15 kg.

Colorimetric CO2 detectors are a semiquantitative, noninvasive method to evaluate ETCO2 and demonstrate breath-to-breath color change after successful intubation. In addition, we have shown that these devices are useful in determining whether the airway is patent during bag and mask ventilation.14 Each colorimetric CO2 detector has a pH-sensitive chemical indicator that undergoes color change with each inspiration and expiration, thus reflecting the change in CO2 concentration. These devices start at baseline color when minimal CO2 is present and undergo gradual color change with increasing concentrations of CO2 (Fig 1). ETCO2 is a reflection of ventilation, cardiac output, pulmonary blood flow, and metabolism. In the setting of adequate perfusion, ETCO2 represents partial pressure of CO2 in circulating blood and thus changes with ventilation; however, during periods of inadequate pulmonary perfusion, such as during cardiorespiratory arrest, CO2 is not delivered to the lungs and measured ETCO2 is low. This is actually an indication of the inadequate cardiac output rather than the systemic CO2 level. Conse-

What’s Known on This Subject

Previous studies have demonstrated that colorimetric CO2 detectors are helpful in confirming endotracheal intubation; however, the colorimetric CO2 detectors that are used for neonates are labeled for use with infants who weigh >1 kg.

What This Study Adds

This study reveals that the tidal volume threshold for these colorimetric CO2 detectors is less than the expected tidal volume in a 400-g infant. Thus, these devices are appropriate for use with any neonate to confirm intubation.
Colorimetric CO₂ detector: Pedi-Cap Mini StatCO₂

**Color Chart:**
- Purple to dark grey (color range A) = 0.03% to 0.5% CO₂ (<4 mm Hg)
- Light to dark tan (color range B) = 0.5% to <2% CO₂ (4 to <15 mm Hg)
- Mustard yellow to gold (color range C) = 2% to 5% CO₂ (15 to 38 mm Hg)
- Permanent yellow = Damaged, Discard Device

**Technical Specifications:**

<table>
<thead>
<tr>
<th>Detector</th>
<th>Pedi-Cap</th>
<th>Mini StatCO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal volume</td>
<td>3 mL</td>
<td>3 mL</td>
</tr>
<tr>
<td>(dead space)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life span</td>
<td>2 h</td>
<td>Up to 24 h</td>
</tr>
<tr>
<td>Resistance to flow</td>
<td>2.5 cm H₂O or 0.5 cm at 10 L/min flow</td>
<td>2.5 cm H₂O or 10 L/min flow</td>
</tr>
<tr>
<td>Current labeling</td>
<td>1–15 kg</td>
<td>1–15 kg</td>
</tr>
<tr>
<td>Detector weight</td>
<td>&lt;5 g</td>
<td>5 g nominal</td>
</tr>
</tbody>
</table>

**FIGURE 1**
Pedi-Cap and Mini StatCO₂ directions for use and mechanical specifications.

Consequently, in the setting of significantly decreased cardiac output, there will be decreased pulmonary blood flow, and thus ETCO₂ will be negligible.

The colorimetric CO₂ detectors (Pedi-Cap [Nellcor, Pleasanton, CA] and Mini StatCO₂ [Mercury Medical, Clearwater, FL]) currently available in the United States for use with infants and small children, are labeled for use with infants who weigh >1 kg and children who weigh <15 kg. Previous studies have shown that ETCO₂ detection, including colorimetric CO₂ detectors, decrease the time needed to recognize successful intubation.1,10,11 In our clinical experience, colorimetric CO₂ detectors have always demonstrated easily detectable cyclic color change after intubation in any viable infant with adequate perfusion. Our objective for this study was to determine the minimum tidal volume (VT) that causes a clinically recognizable cyclic color change on the 2 colorimetric CO₂ detectors currently available in the United States and labeled for use with neonates.

**METHODS**

We created an artificial lung with a Pyrex (Corning Life Sciences, Lowell, MA) 1000 Griffin Low-Form 150-mL beaker that was covered with a VWR (VWR Scientific, Chester, PA) black rubber stopper and sealed with Parafilm M (Pechinex Plastic Packaging, Minneapolis, MN). A hole was made in the rubber stopper and a 2.5-cm endotracheal tube was inserted and sealed with Parafilm M. With the use of a commercially available data acquisition system (MP 150 [Biopac Systems Inc, Goleta, CA]), pneumotachometer (Fleisch OO [OEM Medical, Richmond, VA]), and amplifier/transducer (TSI 160A [Biopac Systems Inc, Goleta, GA]) the flow was measured and integrated to determine the tidal volume (VT). The compliance of the artificial lung was determined, and the system was calibrated. Calibration was confirmed by instilling 1 mL of room air into the system and verifying that the appropriate volume was calculated. Before each trial, the apparatus was charged with 5% CO₂ and the dead space flushed with 2 to 4 mL of room air. Each colorimetric CO₂ detector was connected to a 2.5-mm endotracheal tube placed in the artificial lung and ventilated with a neonatal ventilator or a T-piece resuscitator. The Pedi-Cap response degrades over its 2-hour life span; therefore, it was changed every 30 minutes during the experiment. The Mini StatCO₂ was not changed during the course of the experiment, because it has a 24-hour life span. With the use of the Millennium ventilator (Sechrist, Anaheim, CA), the artificial lung was ventilated at a VT between 0.45 mL and 2.80 mL using a peak inspiratory pressure that ranged from 2 to 18 cm H₂O, a positive end expiratory pressure of 0 cm H₂O, a flow of 8 L/minute, an inspiratory time/expiratory time ratio of 1:4, and a rate of 30 breaths per minute. With the use of the T-piece resuscitator (Neopuff [Fisher and Paykel Healthcare, Auckland, New Zealand]), the artificial lung was ventilated at a VT between 0.28 mL and 2.00 mL by using a peak inspiratory pressure that ranged from 1 to 15 cm H₂O, a positive end expiratory pressure of 0 cm H₂O, a flow of 8 to 10 L/minute, and rate averaged at 30 breaths per minute with 2 seconds per breath. A Sony (Sony USA, New York, NY) DCR-TRV 950 Digital Video Recorder focused on the colorimetric CO₂ detector recorded 20 seconds at each VT, including the first breath. For each colorimetric CO₂ detector, we video recorded 12 to 14 different VT by using both the neonatal ventilator and the T-piece resuscitator.

Seven clinicians, including neonatologists, respiratory therapists, and neonatal fellows who were blinded to the actual tested VT, independently reviewed the video recordings in random order and graded the cyclic color changes. Reviewers were instructed to rate each color change from 0 (no color change) to 5 (full color change). When color change was present, each reviewer then determined whether it was clinically applicable and would be interpreted as successful intubation. VT threshold was defined as the VT at which all reviewers identified a clinically significant color change. To evaluate the effect of viewing the video recording on color change assessment, the researchers rated the color change during the live experiment by using the same evaluation system. These results were not used for any statistical calculations, and they were consistent with the VT threshold determined by the blinded reviewers. The results were analyzed by using simple descriptive statistics in Sigma Stat 2.03, and box plots were generated by using Sigma Plot 10.0 (Systat Software, Inc, Point Richmond, CA).

**RESULTS**

With the use of the Millennium ventilator, the Mini StatCO₂ VT threshold was 0.85 mL (SD: ±0.22; range: 0.66–1.30 mL). There was no observed color change at a VT <0.53 mL. With the use of the NeoPuff, the Mini StatCO₂ VT threshold was 0.82 mL (SD: ±0.10; range:...
With the use of the NeoPuff, the Pedi-Cap VT threshold for children who weigh 15 kg is between 0.83 mL and 1.08 mL, which is less than the expected VT (3 mL/kg) of a 400-g infant; therefore, the VT of any viable infant is above the VT threshold for these devices despite the current manufacturer labeling.

Previous studies have already demonstrated the utility of ETCO2 detection for the confirmation of endotracheal tube placement in infants and children in various settings, including operating rooms, ICUs, and emergency departments. In a neonatal population that included infants who weighed <1000 g, Aziz et al compared the colorimetric CO2 detector with clinical evaluation to confirm endotracheal intubation in the delivery room and the NICU. They found that the CO2 detector decreased the time needed to determine endotracheal tube position from a mean of 39.7 seconds (SD: ±15.3 seconds) to a mean of 8.1 second (SD: ±2.9 seconds). In this study 42% (19 of 45) of the patients weighed <1 kg. There were 3 false-negative results, including 1 infant who weighed <1 kg, all with cardiorespiratory compromise.

The failure to detect a cyclic color change with a colorimetric CO2 detector may have several causes. Multiple studies have shown that no color change occurs in the setting of cardiopulmonary arrest. NRP guidelines indicate that the CO2 monitor “may not change color if the cardiac output is very low or absent” and go on to indicate that if there is no detectible heartbeat, then a CO2 monitor should not be used as an indicator of placement. Another potential false-negative result would be that the VT is below the device threshold. Our study has revealed that this is rarely a factor in the newborn infant, consistent with our previous clinical observations.

In addition, false-positive results may occur with esophageal intubation as a result of CO2 in the stomach. An animal study by Garnett et al demonstrated that after instillation of carbonated beverages in the stomach, there is a detectable level of CO2, but it rapidly decreases with continued ventilation with a negligible amount remaining after 6 breaths. In addition, animal experiments with colorimetric CO2 detectors by Bhende et al of piglets showed that sensitivity and specificity were 100% with a P < .001 for all tracheal and esophageal intubations after instillation of carbonated beverages. Currently, the manufacturers recommend interpreting color change only after giving 6 breaths; therefore, esophageal intubation may produce an initial color change, but this effect quickly disappears.

Other limitations of the colorimetric CO2 detectors are that they demonstrate color change when the endotracheal tube is in any portion of the respiratory tree, such as the oropharynx or right main stem bronchus. Also, irreversible color change is caused by exposure to epinephrine or gastric juices and prolonged exposure to high humidity.

**CONCLUSIONS**

Previous clinical studies have demonstrated the utility of colorimetric CO2 detectors in confirming intubation, and our results establish that they are appropriate for use in
any viable infant with adequate perfusion; therefore, consistent with current NRP guidelines, we recommend the use of colorimetric CO2 detectors to confirm intubation in any newborn infant and encourage the manufacturers to reevaluate current product labeling.

ACKNOWLEDGMENT
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REFERENCES
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