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Pediatrics 2008;121;e1524-e1527; originally published online May 5, 2008;
DOI: 10.1542/peds.2007-2708

ARTICLE

Tidal Volume Threshold for Colorimetric Carbon Dioxide Detectors Available for Use in Neonates

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The authors have indicated they have no financial relationships relevant to this article to disclose.

What's Known on This Subject

Previous studies have demonstrated that colorimetric CO_2 detectors are helpful in confirming endotracheal intubation; however, the colorimetric CO_2 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 CO_2 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.

ABSTRACT

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 StatCO_2 [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 StatCO_2 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

www.pediatrics.org/cgi/doi/10.1542/peds.2007-2708

doi:10.1542/peds.2007-2708

Key Words
infant, intubation, capnography, resuscitation, colorimetric carbon dioxide detector

Abbreviations
CO_2—carbon dioxide
$ETCO_2$—end-tidal carbon dioxide
NRP—Neonatal Resuscitation Program
V_T—tidal volume

Accepted for publication Dec 14, 2007

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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[2]; 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 ($ETCO_2$) detection.[3–12] In the Fifth Edition revised Neonatal Resuscitation Program (NRP) guidelines, increasing heart rate and exhaled CO_2 detection including colorimetric CO_2 detectors are the primary methods recommended for confirmation of endotracheal intubation in infants[13]; however, current product labeling of colorimetric CO_2 detectors recommends use for infants and small children who weigh >1 kg and <15 kg.

Colorimetric CO_2 detectors are a semiquantitative, noninvasive method to evaluate $ETCO_2$ 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 CO_2 detector has a pH-sensitive chemical indicator that undergoes color change with each inspiration and expiration, thus reflecting the change in CO_2 concentration. These devices start at baseline color when minimal CO_2 is present and undergo gradual color change with increasing concentrations of CO_2 (Fig 1). $ETCO_2$ is a reflection of ventilation, cardiac output, pulmonary blood flow, and metabolism. In the setting of adequate perfusion, $ETCO_2$ represents partial pressure of CO_2 in circulating blood and thus changes with ventilation; however, during periods of inadequate pulmonary perfusion, such as during cardiorespiratory arrest, CO_2 is not delivered to the lungs and measured $ETCO_2$ is low. This is actually an indication of the inadequate cardiac output rather than the systemic CO_2 level. Conse-

Colorimetric CO_2 detector:		
	Pedi-Cap	**Mini-StatCO$_2$**
Color chart:	Purple to dark grey (color range A) = 0.03% to 0.5% CO_2 (<4 mm Hg) Light to dark tan (color range B) = 0.5% to <2% CO_2 (4 to <15 mm Hg) Mustard yellow to gold (color range C) = 2% to 5% CO_2 (15 to 38 mm Hg) Permanent yellow = damaged, discard device	Blue = No carbon dioxide present Green = 1.0 to 2.0 % CO_2 Yellow green = 2.0 to 5.0% CO_2 Yellow = 5.0% or more CO_2 Permanent yellow = Damaged, Discard Device
Internal volume (dead space):	3 mL	3 mL
Life span:	2 h	Up to 24 h
Resistance to flow:	2.5 cm H_20 ± 0.5 cm at 10 L/min flow	2.5 cm H_20 at 10 L/min flow
Current labeling:	1–15 kg	1–15 kg
Detector weight:	<5 g	5 g nominal

FIGURE 1
Pedi-Cap and Mini StatCO$_2$ directions for use and mechanical specifications.

quently, in the setting of significantly decreased cardiac output, there will be decreased pulmonary blood flow, and thus $ETCO_2$ will be negligible.

The colorimetric CO_2 detectors (Pedi-Cap [Nellcor, Pleasanton, CA] and Mini StatCO$_2$ [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 $ETCO_2$ detection, including colorimetric CO_2 detectors, decrease the time needed to recognize successful intubation.[3,10,11] In our clinical experience, colorimetric CO_2 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 (V_T) that causes a clinically recognizable cyclic color change on the 2 colorimetric CO_2 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 (Pechiney 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 (TSD 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% CO_2 and the dead space flushed with 2 to 4 mL of room air. Each colorimetric CO_2 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 StatCO$_2$ 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 V_T between 0.45 mL and 2.80 mL using a peak inspiratory pressure that ranged from 2 to 18 cm H_2O, a positive end expiratory pressure of 0 cm H_2O, 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 V_T between 0.28 mL and 2.00 mL by using a peak inspiratory pressure that ranged from 1 to 15 cm H_2O, a positive end expiratory pressure of 0 cm H_2O, 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 CO_2 detector recorded 20 seconds at each V_T, including the first breath. For each colorimetric CO_2 detector, we video recorded 12 to 14 different V_T 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 V_T, 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. V_T threshold was defined as the V_T 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 V_T 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 StatCO$_2$ V_T threshold was 0.85 mL (SD: ±0.22; range: 0.66–1.30 mL). There was no observed color change at a V_T <0.53 mL. With the use of the NeoPuff, the Mini StatCO$_2$ V_T threshold was 0.82 mL (SD: ±0.10; range:

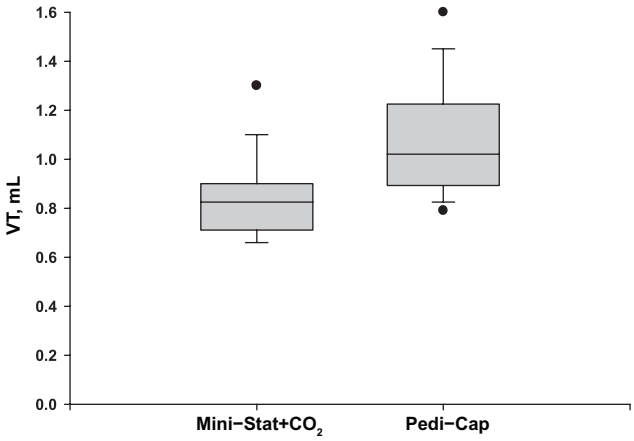

FIGURE 2
Box plot of V_T threshold for the Mini StatCO_2 and Pedi-Cap. The boundary of the box closest to 0 represents the 25th percentile, the line within the box marks the median, and the boundary of the box farthest from 0 indicates the 75th percentile. Whiskers (error bars) above and below the box represent the 90th and 10th percentiles. ●, Outliers.

0.71–0.90 mL. There was no color change at a V_T <0.28 mL. For the Mini StatCO_2, the V_T threshold during the live experiment was 0.66 mL by using the ventilator and 0.73 mL by using the T-piece resuscitator. With the use of the combined data for neonatal ventilator and the T-piece resuscitator, the V_T threshold for the Mini StatCO_2 was 0.83 mL (SD: ±0.16). Figure 2 is box plot showing the first and third quartiles, median, and outliers for the combined data of the Mini StatCO_2.

With the use of the Millennium ventilator, the Pedi-Cap V_T threshold was 1.06 mL (SD: ±0.29; range: 0.79–1.60 mL). There was no color change at a V_T <0.86 mL. With the use of the NeoPuff, the Pedi-Cap V_T threshold was 1.11 mL (SD: ±0.15; range: 0.87–1.3 mL). There was no color change at a V_T <0.72 mL. For the Pedi-Cap, the V_T threshold during the live experiment was 0.79 mL by using the ventilator and 0.87 mL by using the T-piece resuscitator. With the use of the combined data for neonatal ventilator and the T-piece resuscitator, the V_T threshold for the Pedi-Cap was 1.08 mL (SD: ±0.23). Figure 2 is box plot showing the first and third quartiles, median, and outliers for the combined data of the Pedi-Cap.

DISCUSSION

The current NRP guidelines state that "an increasing heart rate and CO_2 detection are the primary methods for confirming endotracheal tube placement."[13] This creates a dilemma because currently available colorimetric CO_2 detectors are labeled for use with infants and small children who weigh >1 kg and <15 kg. We have experience in the delivery room with video recording resuscitations for >8 years, during which we have not seen any infant with adequate perfusion, including extremely low birth weight infants, for which there was no detectable cyclic color change after successful intubation.[15,16] Our experimental results confirm our clinical observation by demonstrating that the V_T threshold for the colorimetric CO_2 detectors labeled for use with infants who weigh >1 kg and <15 kg is between 0.83 mL and 1.08 mL, which is less than the expected V_T (3 mL/kg) of a 400-g infant; therefore, the V_T of any viable infant is above the V_T threshold for these devices despite the current manufacturer labeling.

Previous studies have already demonstrated the utility of $ETCO_2$ detection for the confirmation of endotracheal tube placement in infants and children in various settings, including operating rooms, ICUs, and emergency departments.[3–8,10–12] In a neonatal population that included infants who weighed <1000 g, Aziz et al[3] compared the colorimetric CO_2 detector with clinical evaluation to confirm endotracheal intubation in the delivery room and the NICU. They found that the CO_2 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 CO_2 detector may have several causes. Multiple studies have shown that no color change occurs in the setting of cardiopulmonary arrest.[7,10,11] NRP guidelines indicate that the CO_2 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 CO_2 monitor should not be used as an indicator of placement. Another potential false-negative result would be that the V_T 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 CO_2 in the stomach. An animal study by Garnett et al[9] demonstrated that after instillation of carbonated beverages in the stomach, there is a detectable level of CO_2, but it rapidly decreases with continued ventilation with a negligible amount remaining after 6 breaths. In addition, animal experiments with colorimetric CO_2 detectors by Bhende et al[17] 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 CO_2 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.[6]

CONCLUSIONS

Previous clinical studies have demonstrated the utility of colorimetric CO_2 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 CO_2 detectors to confirm intubation in any newborn infant and encourage the manufacturers to reevaluate current product labeling.

ACKNOWLEDGMENT

This work was supported by the Division of Neonatology, Department of Pediatrics, University of California, San Diego.

REFERENCES

1. Hamilton BE, Minino AM, Martin JA, Kochanek KD, Strobino DM, Guyer B. Annual summary of vital statistics: 2005. *Pediatrics.* 2007;119(2):345–360
2. Walsh MC, Morris BH, Wrage LA, et al. Extremely low birthweight neonates with protracted ventilation: mortality and 18-month neurodevelopmental outcomes. *J Pediatr.* 2005; 146(6):798–804
3. Aziz HF, Martin JB, Moore JJ. The pediatric disposable end-tidal carbon dioxide detector role in endotracheal intubation in newborns. *J Perinatol.* 1999;19(2):110–113
4. Bhende MS. End-tidal carbon dioxide detectors: are they useful in children? *J Postgrad Med.* 1994;40(2):78–82
5. Bhende MS. End-tidal carbon dioxide monitoring in pediatrics: clinical applications. *J Postgrad Med.* 2001;47(3):215–218
6. Bhende MS. End-tidal carbon dioxide monitoring in pediatrics: concepts and technology. *J Postgrad Med.* 2001;47(2):153–156
7. Bhende MS, Thompson AE. Evaluation of an end-tidal CO2 detector during pediatric cardiopulmonary resuscitation. *Pediatrics.* 1995;95(3):395–399
8. Bhende MS, Thompson AE, Cook DR, Saville AL. Validity of a disposable end-tidal CO2 detector in verifying endotracheal tube placement in infants and children. *Ann Emerg Med.* 1992; 21(2):142–145
9. Garnett AR, Gervin CA, Gervin AS. Capnographic waveforms in esophageal intubation: effect of carbonated beverages. *Ann Emerg Med.* 1989;18(4):387–390
10. Repetto JE, Donohue P-CP, Baker SF, Kelly L, Nogee LM. Use of capnography in the delivery room for assessment of endotracheal tube placement. *J Perinatol.* 2001;21(5):284–287
11. Roberts WA, Maniscalco WM, Cohen AR, Litman RS, Chibber A. The use of capnography for recognition of esophageal intubation in the neonatal intensive care unit. *Pediatr Pulmonol.* 1995;19(5):262–268
12. Salthe J, Kristiansen SM, Sollid S, Oglaend B, Soreide E. Capnography rapidly confirmed correct endotracheal tube placement during resuscitation of extremely low birthweight babies (<1000 g). *Acta Anaesthesiol Scand.* 2006;50(8):1033–1036
13. Kattwinkel J, ed. *Textbook of Neonatal Resuscitation*. 5th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006
14. Leone TA, Lange A, Rich W, Finer NN. Disposable colorimetric carbon dioxide detector use as an indicator of a patent airway during noninvasive mask ventilation. *Pediatrics.* 2006;118(1). Available at: www.pediatrics.org/cgi/content/full/118/1/e202
15. Carbine DN, Finer NN, Knodel E, Rich W. Video recording as a means of evaluating neonatal resuscitation performance. *Pediatrics.* 2000;106(4):654–658
16. Finer NN, Rich W. Neonatal resuscitation: toward improved performance. *Resuscitation.* 2002;53(1):47–51
17. Bhende MS, Thompson AE, Howland DF. Validity of a disposable end-tidal carbon dioxide detector in verifying endotracheal tube position in piglets. *Crit Care Med.* 1991;19(4): 566–568

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