Impact of Continuous Capnography in Ventilated Neonates: A Randomized, Multi-Center Study

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Conflict of Interest

- The study was funded by Covidien, Respiratory and Monitoring Solutions, Jerusalem, Israel.
- M.R is employed by Covidien in R&D Department.

Introduction

- Continuous noninvasive monitoring of CO_2 levels in NICUs is important because it may protect ventilated infants from the complications of
  - Hypocarbia (Garland JS, et al. Arch Pediatr Adolesc Med. 1995; Fujimoto S, et al. Arch Dis Child. 1994)
  - Hypercarbia (Wyatt JS, et al. Pediatr Res. 1991; Van de Bor M, et al. Am J Dis Child. 1986)
- Avoid extra blood sampling (Rowan CM, et al. J Clin Med Res. 2015)

9 מיליון שקל פיצוי לילד הסובל משיתוק מוחין

בית־המשפט קבע כי מצבו של הילד נגרם עקב התרשלות בטיפול בו ב־40 השעות הראשונות לחייו – ואישר סכום יוצא דופן

יורם ירקוני

פיצוי יוצא דופן בגובהו נפסק בחשבונץ לחדריה של ילד בן 13, שנולד סב ומוכל מאז לידתו משיתוק מוחין: בית־המשפט קיבל את עמדת פרקליטיו של הילד ושל הוריו כי יש לכבד את רצונם שהילד יגור בביתו עם משפחתו בעמדה, וקבע כי הם יקבלו 9 מיליון שקל פיצויים חלאומי ומהמדינה.

בכתב התביעה טענו הורים, באמצעות עוה"ד ישראל וינברג ושירי הסידוב, כי הילד סובל משיתוק מוחין עקב טיפול רשלני שניתן לו בבית־החולים [redacted] במהלך 40 השעות הראשונות לחייו, לאחר שנולד בשבוע [redacted]

הצוות הרפואי לא ניטר בתכיפות מספקת את רמת הפחמן הדו־חמצני בדמו וזרכר הקטין את אספקת הדם למוח – מה שהוביל לשיתוק המוחין.

עו"ד ישראל וינברג

בכ"דובים של כלי דם כדי להסת את כמות החמצן המגיעה אליו. במצב בזה, כשהוא נמשך לאורך זמן, נפגעת אספקת הדם למוח. "הצוות הרפואי בשל בשל כך שלא ניטר בתכיפות מספקת את רמת הפחמן הדו־חמצני", נאמר בפסק הדין, "ולא ניסה לשנות את שיטת הטיפול – דבר שהיה עשוי להעלות את רמת הפחמן הדו־חמצני בדמו ולטנוץ מגיעה מהיות". עם זאת קובע השופט כי "אין מחלוקת שבכלל, הטיפול בתינוק על ידי רופא [redacted]

מניטור של ניטור ורמות הפחמן הדו־חמצני בדמו ב־40 השעות הראשונות היתה התרשלות מצד הרופאים". לפי פסק הדין, אצל 75 אחוז מהתינוקות שלקו בשיתוק מוחין הסיבה לכך היא ערכי פחמן דו־חמצני נמוכים.

הילה בן 13 כיום, סובל מאי לידתו מנכות של 100% לצמיתות. הוא נזק שקד מבחינה קוגניטיבית ותפקודית, מורץ למצבו ומסוגל לקבל החלטות הנוגעות לחייו, אך סובל משיתוק בכל הלקי נופו ואין לו כמעט יכולת תנועה. השופט קבע כי מודעותו של הילה למצבו מגרילה את סבלו.

נקבע כי כתוך כך כל הפיצוי יש־לם הביטוח הלאומי 9 מיליון והמדינה 6 מיליון. בנוסף תשלם המדינה מיליון וחצי שקל שכר טרחת לעו"ד דכי הדין של הורי הילה את המדינה ייצגו עוה"ד רפאה רוזן־וינגר ושירי שאלתיאל.

ידיעות אחרונות 4.2.15

Introduction

- The use of end-tidal CO_2 ($EtCO_2$) for monitoring and as a tool for verifying ETT position is a common practice in the OR and in the PICU.

- Currently, capnography is not commonly used in NICUs because of
  - Technical problems (leakage around uncuffed ETTs)
  - Relative inaccuracy in conditions of ventilation-perfusion mismatch.

Introduction

- Sampling breath close to the carina (distal CO_2 measurement, $dEtCO_2$) may be less susceptible to air leak and/or mixing of the measured CO_2 with inhaled air.

- We have demonstrated (Kugelman A, et al; Pediatrics 2008) that $dEtCO_2$ measured by the Microstream technology via a double-lumen ETT had better or as good as correlation and agreement with $PaCO_2$ when compared with $EtCO_2$ measured by the mainstream capnography (Rozycki HJ, et al. Pediatrics. 1998).

Introduction

- Previous studies on $EtCO_2$ were all observational, assessing the feasibility of capnography, and its agreement and correlation with $PaCO_2$ in intubated infants ventilated with conventional ventilation (CV).

- No previous study, to the best of our knowledge, has assessed the clinical implications of continuous monitoring of $EtCO_2$ in this group of infants.

Study Hypothesis

- Because
  - We have shown that continuous $dEtCO_2$ has good agreement and correlation with $PaCO_2$,
  - Hyper or hypocarbia may be harmful,

- We hypothesized that continuous $dEtCO_2$ could have clinical benefits in the care of ventilated infants.

Study Aim

- To compare the time spent within a pre-defined safe range of carbon-dioxide (30 mmHg< PCO_2 <60 mmHg) during conventional ventilation between infants who were monitored with $dETCO_2$ and those who were not.

Methods
Study design

- This was a randomized, controlled multicenter study conducted at 3 tertiary university affiliated NICUs.

- Ventilated infants with a double lumen ETT were randomized to:

1. Open monitored (study) group: Data derived from the capnograph were recorded, displayed to the medical team and allowed to be used for patient care.

2. Masked (control) group: Data derived from the capnograph were recorded; however, the measurements were masked and not available for patient care.

Methods
Study design

- The study was approved by the Israeli Ministry of Health review board.
- Parents of all infants signed an informed consent form.

Study Population

- Inclusion criteria:
  1. Intubated infants with a double-lumen ETT and on CV,
  2. Parents signed Informed Consent,
  3. Expected to provide at least 3 pairs of blood samples and $ETCO_2$ measurements.

- Exclusion criteria:
  1. Single-lumen ETTs,
  2. Ventilated with HFV.

Study Procedure

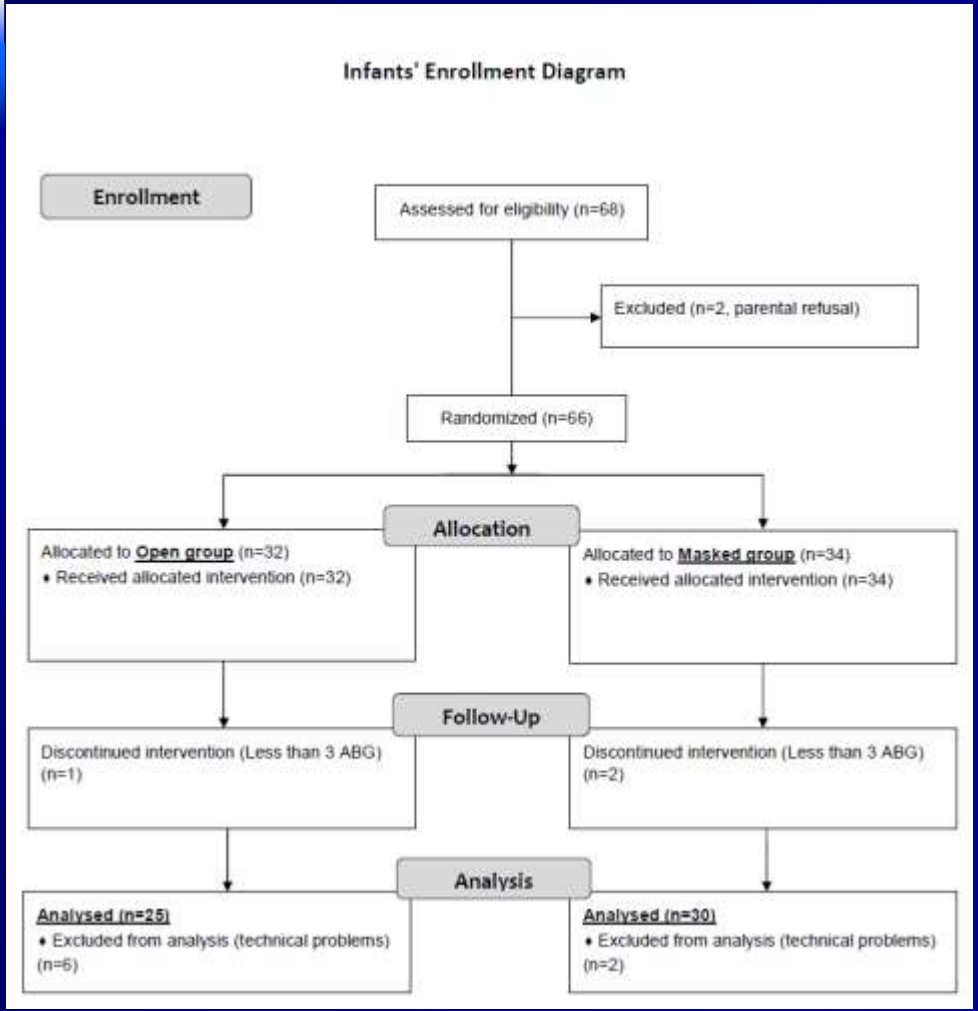
- All infants who needed MV were intubated in the DR or in the NICU with a double-lumen ETT (Uncuffed Tracheal Tube [Mallinckrodt Inc, Chih, Mexico]).
- This ETT has an extra small lumen designed originally for exogenous surfactant administration and we used it for measurements of $dEtCO_2$.
- $ETCO_2$ was measured by the Capnostream 20p (Covidien, Respiratory and Monitoring Solutions, Jerusalem, Israel).

Study Procedure

- Masking of the capnography results was achieved by using a designated cover for the monitor's screen, that allowed the operator to watch only the capnography tracing to assure adequate measurements, but not any numerical data.

Results

Infant's Enrollment



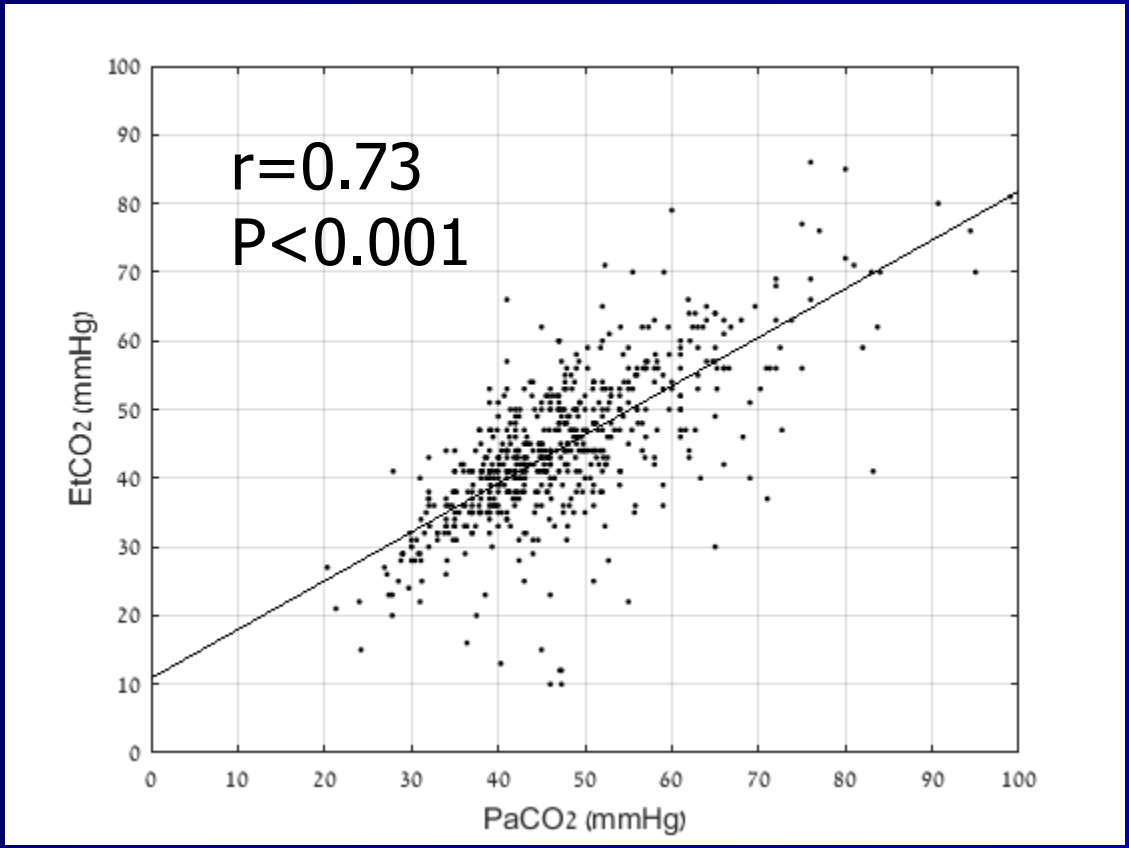
Analysis included:

- ✓ 768 simultaneous measurements of $dETCO_2$ and $PaCO_2$,
- ✓ 13 [3-35] measurements per/patient,
- ✓ During 37.1 [5.3-132.0] hours per/patient.

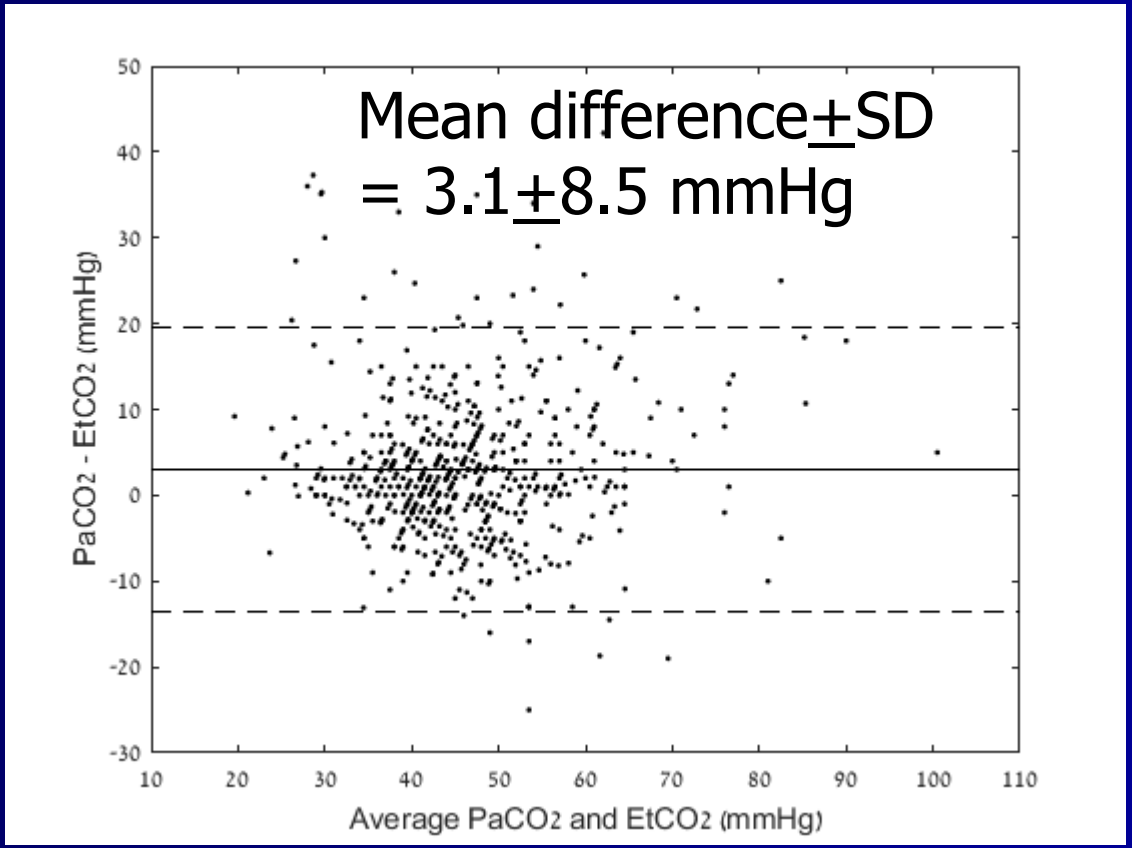
Table 1: Patient Characteristics and Respiratory Status at Study Enrollment

	Masked group (n=30)	Open group (n=25)	p val.
Gestational age, weeks	28.2 (23.5-37.9)	29.1 (24.5-39.0)	0.16
Birth weight, g	1113 (525-3320)	1530 (744-2943)	0.14
Infants (%) <1500 g	20 (66)	11 (44)	0.85
BW in infants <1500 g, g	880 (525-1431)	912 (744-1290)	0.92
FiO_2 at enrollment	0.30 (0.21-0.76)	0.25 (0.21-0.85)	0.97
OI	4.5 (1.9-38.2)	3.8 (1.4-15.6)	0.20
PaO_2/PAO_2	0.31 (0.06-0.79)	0.34 (0.20-0.88)	0.20
$PaCO_2$	44.3 (34.7-72.0)	42.3 (24.0-55.7)	0.55
pH	7.33 (7.04-7.49)	7.34 (7.14-7.48)	0.44
Primary diagnosis			
RDS	27	19	0.27
TTN	3	5	0.44
Pneumonia	0	1	0.45
Pulmonary hypertension	3	2	1.00

$dETCO_2$ was in Good Correlation with $PaCO_2$

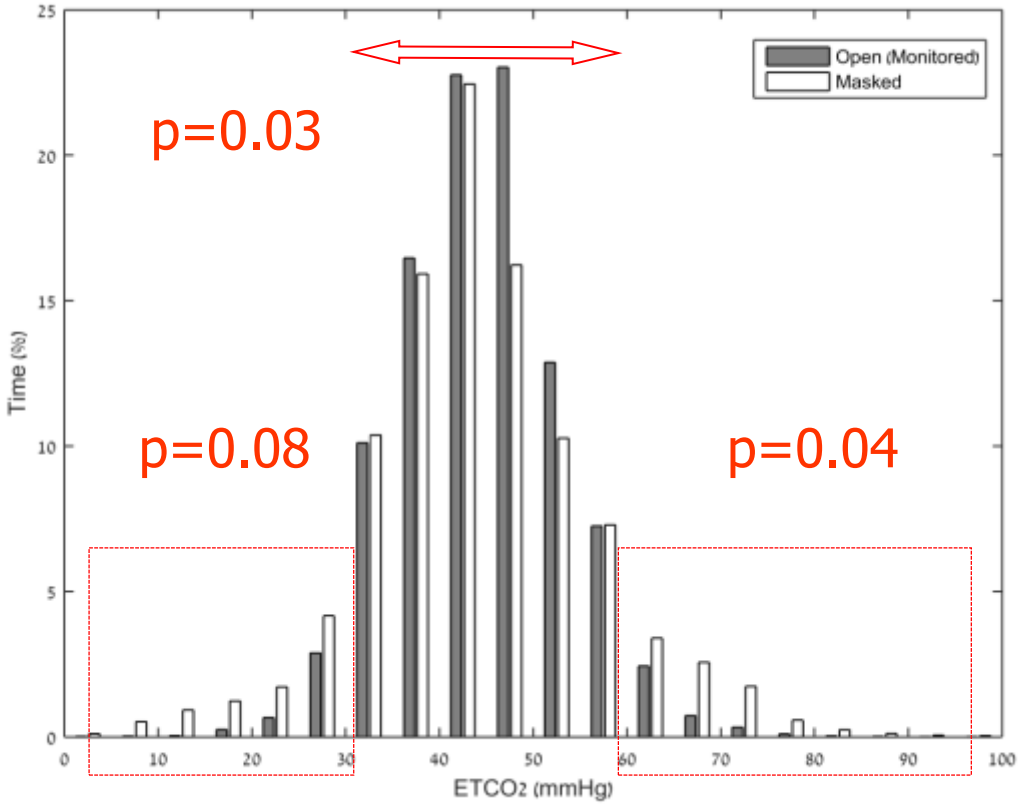


$dETCO_2$ was in Adequate Agreement with $PaCO_2$



% of Time Spent at Different $ETCO_2$ Levels

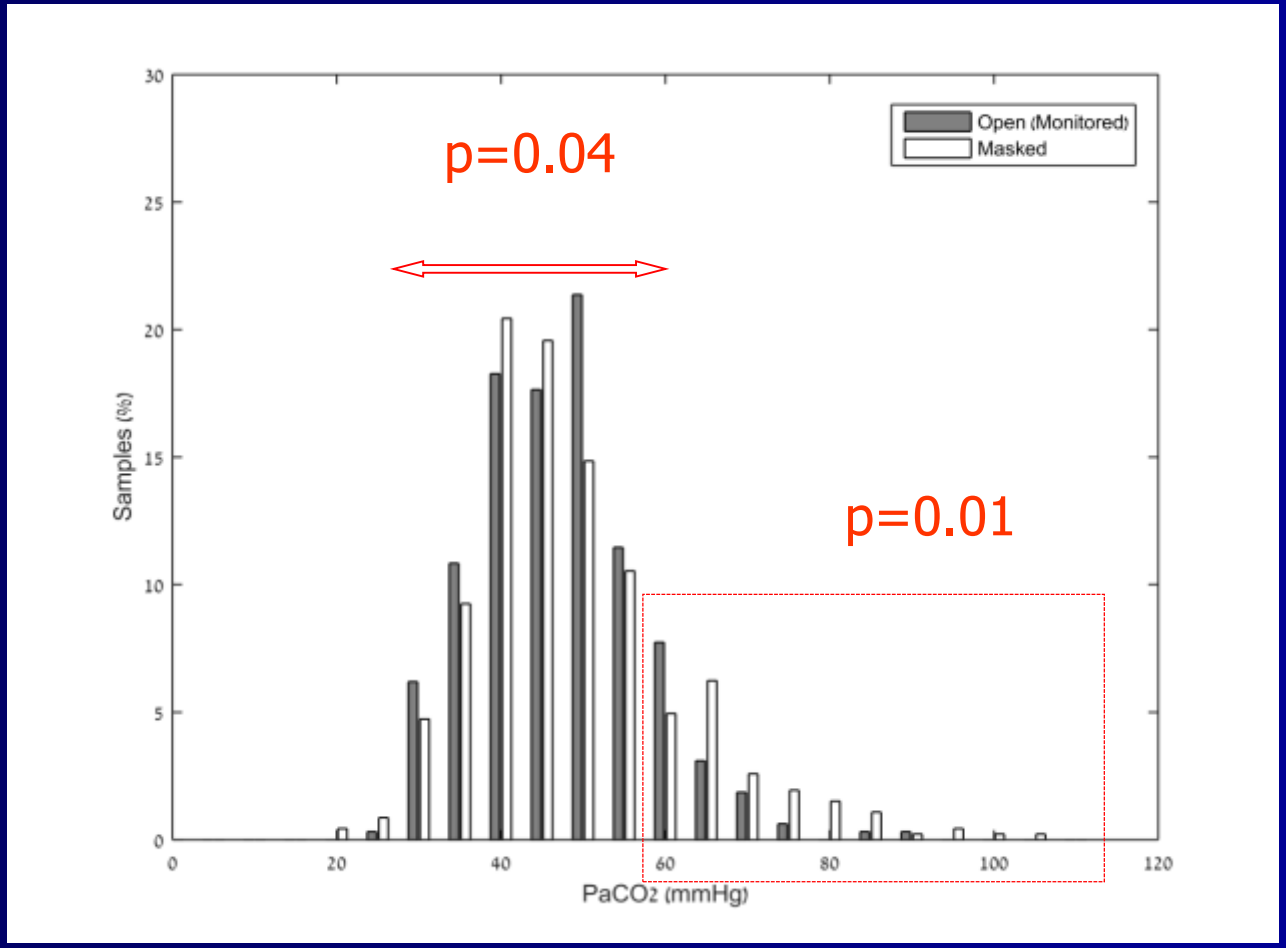
% time
<30 mmHg
3.8 vs. 8.9%



% time
>60 mmHg
3.8 vs. 8.8%

% of ABG Samples at Different Levels of $PaCO_2$

% ABGs
<30 mmHg
2.8 vs. 2.6%



% of ABGs
>60 mmHg
9.9 vs. 17.2%

Table 2: Clinical outcomes

	Masked group (n=30)	Open group (n=25)	p val.
No. of ABG samples	0.23 (0.13-0.39)	0.22 (0.09-0.72)	0.43
Transfusion during ventilation	0 (0-0.06)	0 (0-0.02)	0.02
Transfusions during hospitalization	1 (0-28)	1 (0-11)	0.32
HCT at discharge	33.9 (24.8-48.0)	34.5 (29.9-57.0)	0.11
No. of X-Rays	0.01 (0-0.14)	0.008 (0-0.19)	0.99
Sepsis	4	3	1.00
Necrotizing enterocolitis	1	3	0.31
PDA	14	8	0.41
Length of stay (d)	58 (5-213)	51 (8-166)	0.87

	Masked group (n=30)	Open group (n=25)	p val.
Average pH	7.26 (6.80-7.56)	7.33 (6.98-7.50)	<0.001
Average FIO_2	0.30 (0.21-1.00)	0.29 (0.21-1.00)	<0.001
Average OI	4.6 (1.1-38.5)	3.7 (0.7-22.6)	<0.001
Average PaO_2/PAO_2 ratio	0.36 (0.04-1.14)	0.39 (0.03-2.48)	0.006
Length of ventilation (d)	6 (0.8-107)	5 (0.25-52)	0.62
BPD			
Mild	0	1	0.46
Mod	4	3	1.00
Severe	3	4	0.69
Brain US findings			
IVH	10	3	0.11
PVL	3	0	0.24
IVH or PVL	13	3	0.02

$dETCO_2$ Monitoring Safe Range of CO_2

- Our multicenter study demonstrates that continuous $dETCO_2$ monitoring improves the control of CO_2 levels within a safe range.
  - Continuous $dETCO_2$ recordings
  - Samples of ABGs drawn for patient care
- Being at a safer range was also shown in the VLBW infants.

$dETCO_2$- Monitoring Neurological Morbidity

- IVH or PVL rate was lower in infants who were on $dETCO_2$ monitoring.
- As expected, the rate of IVH/PVL was associated with GA or BW, but it was also independently associated with $dETCO_2$-monitoring.

$dETCO_2$- Monitoring Neurological Morbidity

- Pathophysiologic sense.
- We could not demonstrate causality.
- We should be cautious in concluding that monitoring reduced the rate of neurological morbidities.
  - Small number of VLBW infants
  - Small number of brain US findings

$dETCO_2$- Monitoring Respiratory Condition

- Despite comparable baseline characteristics and parameters of respiratory severity within 2 hours from study enrollment,
  - The infants in the monitored group showed significantly better respiratory condition during the study period
  - Better
    - Ventilatory [Lower $PaCO_2$ and higher pH]
    - Oxygenation [lower FIO_2 and OI and higher PaO_2/PAO_2 ratio).
      - Better control of respiratory status or
      - Selection bias
      - Note- All other outcomes were comparable

Study Strength

- Methodology,
  - A multicenter, randomized prospective "real life" study,
  - Not unique to a single center experienced in $dETCO_2$-monitoring,
  - Including all ventilated infants in the NICU, term and preterm,
  - Including different modes of CV.

  - Thus,
    - The method could be generalized.

Study Limitations

- Limited in the number of VLBW infants.
- Despite randomization and the two groups being comparable in the demographic and respiratory parameters at study enrollment, there was a clinical, though not statistical, difference in BW between the groups.
  - Stratification for VLBW infants - being in a safe zone of CO_2
  - Regression analysis for the head US findings
    - The significance of our findings stands.

Conclusions

- Continuous $dETCO_2$ monitoring improves the control of carbon-dioxide levels within a safe range during conventional ventilation in the NICU.

- Our study confirms that $dETCO_2$ is in good correlation and adequate agreement with $PaCO_2$.

Conclusions

- There was a lower rate of IVH or PVL in the dETCO2-monitored infants though causality between dETCO$_2$ monitoring and less neurological US findings was not proven.
- We speculate that avoiding hypercabia or hypocarbia could decrease the rate of neurological and respiratory complications.
- Gaining trust and experience with dETCO$_2$ monitoring may also reduce the number blood tests and its possible sequellae.

Thank You