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ORIGINAL ARTICLE

Reliability of Capnometry in Neonates on Patient Triggered Ventilation

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ABSTRACT

Introduction: Capnometry is not well studied in neonates on Patient Triggered Ventilation (PTV). We conducted this study to determine the reliability of Main Stream (MS) and Side Stream (SS) Capnometry in neonates on PTV.
Method: Neonates on PTV were enrolled in the study. Before each Arterial Blood Gas (ABG) assessment, MS and SS capnometer readings were recorded. Lung mechanics were recorded from the online graphics. ABG was collected from the arterial line. The EtCO2 – PaCO2 correlation was drawn for MS and SS capnometry under various disease conditions, ventilator settings and lung mechanics.
Results: A total of 74 ABGs were collected from 18 patients. The EtCO2 – PaCO2 correlation was better with MS capnometry than with SS capnometry ($r = 0.855$ vs.0.68, $p < 0.001$ for both methods). Both methods correlated well with PaCO2 in Flow cycled SIMV (MS: $r = 0.9$ & SS: $r = 0.82$). However, in Flow Cycled Assist Control mode, SS capnometry correlated poorly (SS: $r = 0.49$ vs. MS: $r = 0.76$). The EtCO2 - PaCO2 correlation by MS capnometry holds good for RDS, Apnea, Pneumonia and Congenital cyanotic heart disease ($r = 0.85$, 0.97, 0.84, 0.84 respectively, $p < 0.001$), but not for PPHN($r = 0.37$, $p = 0.35$). SS EtCO2 correlated well in RDS, Apnea, Pneumonia, ($r = 0.75$, 0.85, 0.94 respectively, $p < 0.001$), but not in PPHN (- 0.20, $p = 0.629$) and CCHD ($r = 0.73$, $p = 0.1$). At higher ventilator rates (> 60 /min), SS capnometry correlated poorly. The EtCO2 –PaCO2 correlation by both methods was better when lung compliance was $\geq$ 1 ml / cmH2O than when lung compliance was < 1 ml / cmH2O.
Conclusions: MS capnometry is superior to SS capnometry for neonates on patient triggered ventilation.

Key Words: End tidal capnometry (EtCO2), Patient triggered ventilation (PTV), lung mechanics

Key Messages:
Main stream capnometry is superior to side stream capnometry for neonates on patient triggered ventilation. In diseases with right to left shunt situation, capnometry may not be reliable. In ventilating diseases with poor lung compliance and high ventilator rates, capnometry correlates poorly to PaCO2.

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Introduction
End tidal capnometry ($EtCO_2$) allows exhaled carbon-dioxide (CO_2) to be measured non-invasively and continuously. $EtCO_2$ is a measure of the alveolar partial pressure of CO2 ($PACO_2$), which in turn is a measure of arterial PCO_2 ($PaCO_2$). Two types of capnometers which are in use are, Main stream (the CO_2 sensors are located directly in the patient's breathing circuit) and side stream (CO_2 sensor located in the machine base unit) [1],[2]. Till

recently, capnometry was not embraced by neonatologists as a means to measure ventilation and lung mechanics, as the neonatal lung volumes are small and the dead space of the capnometer adapters / sensors was higher [3],[4],[5] Low dead-space MS CO_2 analyzers for newborns have been available since the last decade and they have been found to be of clinical use [6],[7].

Patient Triggered Ventilation is characterized by complete respiratory synchrony between the patient and machine breaths, short inspiratory time (In flow cycled modes), better control over the delivered tidal volumes and ventilation at lower pressures. (8) SIMV allows spontaneous breaths between the machine breaths. PTV is rapidly replacing IMV as primary mode of ventilation in neonates. Because of lack of data, we evaluated the use of different capnometry methods in newborns on PTV.

Primary Objective

To determine the reliability of Main Stream (MS) and Side Stream (SS) capnometry in neonates on PTV

Secondary Outcome Measures:

1. To test the reliability of capnometry under various disease conditions, ventilator settings and lung mechanics.
2. Prediction of Pa CO_2 by MS and SS capnometry.

Setting

Tertiary care Neonatal Intensive care unit

Inclusion Criteria

Newborns on patient triggered ventilation, having online pulmonary graphic display and an indwelling functioning arterial line were included.

Exclusion Criteria

Situations where urgent arterial blood gas reports are clinically indicated.

Methodology

All patients who were ventilated in the unit during three consecutive months were enrolled in the study. All babies were ventilated on the Bear 750 PSV ventilator on different patient triggered modes with flow trigger sensor (Hot wire anemometer) having capabilities of online continuous graphics monitoring of waveforms, loops and lung mechanics. Distal Main stream Et CO_2 (MS Et CO_2) monitoring was done by using the respiratory monitor CO_2SMO+ (Novametrix Medical Systems,). The 'flow through' airway adapter had a dead space of 0.7 ml. Side stream Et CO_2 (SS Et CO_2) monitoring was done by inbuilt capnogram with the multichannel monitor, (Criticare Systems Inc.), with a sample aspiration rate of 50 ml/ min and an airway adapter with 0.6ml of dead space.

Method

ABG samples were collected as per the clinical condition of the baby and the unit policy. Before each investigation, in the MS capnograph, the CO_2 sensor was calibrated with two independent calibration cells provided by the manufacturer. The SS capnometer was calibrated to zero as per the manufacturer's instructions. Lung mechanics were recorded on the proforma. The SS capnograph reading was recorded for complete one minute and the mode value was taken as the "Side stream Et CO_2" value. Then, the patient was disconnected from the side-port airway adapter and was connected to the MS $EtCO_2$ adapter and the "Main stream $EtCO_2$" value was recorded in a similar manner after a period of equilibration of 30 seconds or till a stable EtCO2 reading was displayed, whichever occurred early. Arterial blood gas (ABG) samples were collected immediately after $EtCO_2$ measurement. ABG samples were transported on ice slush and were analyzed on an Instrumentation Laboratory Inc. (US) machine within 10 minutes of their collection. ABG, $EtCO_2$ values and lung mechanics were recorded on a pre-designed proforma.

The data was entered in a computer and was statistically analyzed by using the SPSS ver.11 for windows. A statistical correlation between EtCO2 and $PaCO_2$ was drawn for the MS and SS methods. The EtCO2-PaCO2 correlation was tested under different modes of PTV, various disease conditions (i.e., RDS, Apnea etc.), ventilator settings (viz. ventilator rate, mean airway pressure) and lung mechanics parameters (viz. lung compliance, tidal volume and minute ventilation.) The effect of categorical variables was assessed by drawing a correlation between EtCO2 and PaCO2 by paired t test, under different categories. The effect of continuous variables(eg. mean airway pressure) was assessed by calculating the $EtCO_2$ – $PaCO_2$ difference for the type of $EtCO_2$ monitoring by paired t test. Ninety five percent confidence intervals were taken as significant.

Results

During the three month study period, 74 ABG samples with corresponding MS and SS capnographic readings and lung mechanics were recorded from 18 patients. The patients were ventilated for various lung conditions like, RDS, pneumonia, Apnea, Meconium aspiration with PPHN and congenital cyanotic heart disease. The gestational ages of the babies ranged from 27 weeks to 40 weeks and the birth weights ranged from 920 to 2600 grams.

I) Correlation between Et CO_2 And Pa CO_2 [Table/Fig 1]

The average SS Et CO_2 reading [24.18 mmHg (SD = 6.06)] was significantly lower than the average MS Et CO_2 reading [30.68 mmHg (SD = 6.24), $p < 0.001$].

(Table/Fig 1) Correlation Between Et CO_2 And Pa CO_2

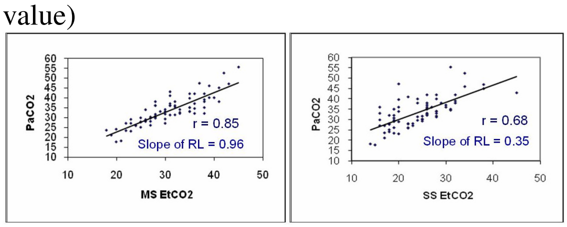
n = 74	MS capnometry	SS capnometry
p CO_2	33.40 (±14.62)	33.40 (±14.62)
Et CO_2	30.68 (± 12.48)	24.18 (± 12.12)
R	0.85	0.68
P	< 0.001	< 0.001

The arterial-end-tidal $PaCO_2$ difference for the MS method was 3.65 mmHg (CI +2.98 to +4.33), which was significantly less than the arterial – end tidal PCO_2 difference for the SS method- 9.22 mmHg. (CI + 7.97 to + 10.47),p< 0.001.

II) Linear Regression Equation for Pa CO_2 [Table/Fig 2]

MS Capnometry: $PaCO_2 = 4.01 + 0.96$ ($EtCO_2$ value)

SS Capnometry: $PaCO_2 = 24.94 + 0.35$ ($EtCO_2$ value)



(Table/Fig 2) Linear Regression Scatter For Main Stream (MS) And Side Stream (SS) Etco2. R= Regression Coefficient, RL = Regression Line.

III) Mode of Ventilation [Table/Fig 3]

(Table/Fig 3) Correlation Between $Etco_2$ And $Paco_2$ Under Different Modes Of PTV.

	Assist Control (Flow cycle) mode N = 39, $PaCO_2$= 33.07(±11.96)		SIMV (Flow cycle) mode N = 35, $PaCO_2$= 33.77 (± 17.28)	
	MS capnometry	SS capnometry	MS capnometry	SS capnometry
$EtCO_2$	30.33(±10.72)	22.28 (± 8.96)	31.06 (±14.28)	26.29 (±)
R	0.765	0.497	0.907	0.824
P	< 0.001	< 0.001	<0.001	<0.001

IV) Correlation between Pa CO_2 and Et CO_2 For Various Disease Conditions [Table/Fig 4]

(Table/Fig 4) Correlation Between Pa CO_2 And Et CO_2 For Various Disease Conditions

	Main Stream	Side Stream
RDS, (n =32) $PaCO_2$ = 35.28 (±16.24)	$EtCO_2$ = 31.28 (± 13.00) r =0.85, p =< 0.001	$EtCO_2$ = 23.97 (± 14.18) r = 0.75, p =< 0.001
Pneumonia (n= 9) $PaCO_2$ = 30.98 (±14.80)	$EtCO_2$ = 29.56 (± 14.34) R = 0.97, p = < 0.001	$EtCO_2$ = 25.22 (± 14.64) R = 0.945, p = < 0.001
Apnea (n= 19) $PaCO_2$ = 31.99 (± 8.02)	$EtCO_2$ = 30.58 (± 9.09) R = 0.84, p= < 0.001	$EtCO_2$ = 25.53 (± 7.27) R = 0.85, p= < 0.001
MAS with PPHN (n=8) $PaCO_2$ = 37.88 (± 12.2)	$EtCO_2$ = 35.63 (± 7.0) R = 0.37, p= 0.35	$EtCO_2$ = 25.10 (± 9.16) R = - 0.20, p= 0.62
CCHD (n=6) $PaCO_2$ = 25.52 (± 10.16)	$EtCO_2$ = 22.83 (± 6.62) R = 0.84, p= 0.036	$EtCO_2$ = 18.1(± 4.8) R = 0.73, p= 0.1

IV) Correlation between Arterial and End Tidal Pco_2 under Various Ventilator Settings

1. **Ventilator Breath Rate [Table/Fig 5]**
2. The effect of the **mean airway pressure** on the $EtCO_2$-$PaCO_2$ correlation was assessed by the correlation between the mean airway pressure and the Arterial-end-tidal pCO_2 difference. The mean reading for Mean airway pressure was 6.059 (± 2.98). Changes in the mean airway pressure had a weak linear correlation with the Arterial-end-tidal pCO_2 difference with the MS capnometry {3.65 (± 5.82), r = 0.27, p = 0.017}; however, changes in the mean airway pressure had a moderately positive linear correlation with the Arterial-end-tidal pCO_2 difference with SS capnometry, {9.22, (± 10.78), r = 0.46, p <

0.001}, thus indicating that as the mean airway pressure increased, SS capnometry gave significantly lower readings.

(Table/Fig 5) Correlation Between Etco2 And Paco2 For Different Ventilator Rates (VR)

	VR < 60 / min, n= 34, $PaCO_2$ = 33.96 (+16.72)		VR > 60 / min, n= 40, $PaCO_2$ = 32.92 (+12.74)	
	MS capnometry	SS capnometry	MS capnometry	SS capnometry
$EtCO_2$	32.06(+13.92)	26.85(+ 12.52)	29.50 (+10.70)	21.90 (+ 9.82)
R	0.883	0.837	0.820	0.569
P	< 0.001	< 0.001	<0.001	<0.001

V) Correlation with Lung Mechanics Parameters

1. **Lung compliance: [Table/Fig 6]**
2. **Tidal Volume: [Table/Fig 7]**

(Table/Fig 6) Correlation Between $Etco_2$ And $Paco_2$ For Different Lung Compliance (LC)

	LC < 1 ml/ cm H_2O, N= 18, $PaCO_2$ = 34.63(+10.2)		LC >1ml/ cm H_2O, N= 56, $PaCO_2$ = 30.75 (6.75)	
	MS capnometry	SS capnometry	MS capnometry	SS capnometry
$EtCO_2$	30.44(+8.8)	23.28 (+ 13.6)	33.01 (7.89)	33.01 (7.89)
R	0.629	0.639	0.891	0.742
P	0.005	0.004	<0.001	<0.001

(Table/Fig 7) Correlation Between $Etco_2$ And $Paco_2$ For Different Tidal Volumes (TV)

	TV < 10ml, n= 35, $PaCO_2$ = 32.90(+14.92)		TV >10ml, n= 39, $PaCO_2$ = 33.85(+14.5)	
	MS capnometry	SS capnometry	MS capnometry	SS capnometry
$EtCO_2$	29.57(+ 13.46)	23.77(+ 13.9)	31.67(+11.2)	24.54(+10.44)
R	0.875	0.77	0.84	0.59
P	< 0.001	< 0.001	<0.001	<0.001

Discussion

This is the first attempt to systematically test the reliability of capnometers in neonates on PTV. This study shows that both the capnometry methods show good correlation with $PaCO_2$; however, the MS method had better correlation coefficients. In MS capnometry, CO2 is estimated by the sensor placed in the breathing circuit, while in the SS method, the exhaled air is aspirated through the sample aspirator into the machine base unit. This could be the reason why CO2 changes were rapidly and more accurately reflected by the MS capnogram. In a previous study on the comparison of side-stream and mainstream capnometers in neonates by McEvedy et. al., the slope of the least square regression line for the distal side-stream capnometer- 0.67, was significantly less than that for the mainstream capnometer- 0.78 [10] Some of the other studies confirm these findings. [11], [12], [13]

During the Flow cycled SIMV mode of ventilation, both the methods of Capnometry gave good correlation with $PaCO_2$ values (r= 0.8). However, under the Flow cycled Assist control mode, the correlation coefficient obtained by the SS method was much lower than that obtained by the MS method (0.76 vs. 0.497). Ventilation in the FCAC mode is characterized by the delivery of a set pressure limited flow cycled breath, with every breathing attempt, reaching the trigger sensitivity. There was no control over the maximum machine breath-rate delivery in this mode. The alveolar phase of expiration may not be complete when the breathing rates are high or when the patient exhales out of phase with the machine breath [12], [16] These rapidly changing volumes may not allow sufficient time for the aspiration of the representative sample in SS capnometry. This could be the possible explanation for poor correlation coefficients in SS capnometry under FCAC modes of ventilation. Similar data was not available for comparison.

EtCO2 monitoring was reliable with most of the disease conditions in neonates such as RDS, Apnea and Pneumonia. One previous study from India by Nangia et.al which was done on babies on conventional ventilation, showed a good correlation between EtCO2 and PaCO2, in babies with Recurrent Apnea and Meconium Aspiration syndrome (r = 0.96 & 0.94 respectively); however, the correlation coefficient was the lowest (0.55) for babies with RDS [15] In the present study, babies were ventilated on Patient Triggered modes of ventilation with a conscious effort to maintain the tidal volume between 5 to 8 ml/kg, which could have contributed to better correlation coefficients even in RDS.

$EtCO_2$ did not correlate with the $PaCO_2$ in Persistent Pulmonary Hypertension of the newborn (r = 0.37 & - 0.2, p =0.35 & 0.629, MS and SS respectively). In PPHN, due to the shunting of deoxygenated blood at the cardiac and extra-cardiac sites, there was ventilation perfusion mismatch; also, alkali therapy which is commonly used in PPHN may lead to the rapid rise in $PaCO_2$-which may not correlate with $EtCO_2$ [14],[15] The correlation coefficient was very low in patients with Congenital cyanotic heart disease. In a study by Lazzell VA et.al., the stability of the intraoperative arterial to end-tidal carbon dioxide partial pressure difference in children with congenital heart disease was assessed. It was seen that arterial end-tidal CO2 difference in children with acyanotic-shunting and cyanotic heart disease with intra-cardiac mixing (normal or increased pulmonary blood flow) was stable intra-operatively, although patients with cyanotic mixing congenital heart lesions (decreased or variable pulmonary blood flow) did demonstrate large individual variation. [14]. Therefore, $EtCO_2$ monitoring is not recommended in variable right to left shunt situations (PPHN) or in congenital cyanotic heart diseases with decreased or variable blood flow, as it is not very reliable [14]

Patients with higher ventilator rates (> 60 / min) had poor correlation of $EtCO_2$ and $PaCO_2$ by the SS method, (0.82 vs. 0.56). In a study by Pascucci RC et.al, side-stream and main-stream capnograms were compared in infants on rapid mechanical ventilation. The EtCO2-PaCO2 correlation was better with mainstream capnometers. The recordings obtained by the SS machine were grossly distorted, with flattening of the ascending limb (slope 37.3 vs.153.3 torr/sec, SS vs. MS, p less than 0.001) and absence of the alveolar plateau [17]. The alveolar phase of expiration may not be complete when the ventilator rates are high [16], [17]

As the tidal volume increased (> 10 ml), the correlation by MS capnometry remained good (r = 0.84). However, the side port $EtCO_2$ measurement decreased. (r = 0.59). Since, in case of SS capnometry, the exhaled air sample is aspirated in the machine base unit and the measurement of $EtCO_2$ is done during extremes of tidal volumes, exhaled PCO_2 may not equilibrate with the PCO_2 in the aspirated sample. $EtCO_2$ gave lower readings when the tidal volume was either too low or too high [17] .

As the lung compliance decreased below sub-physiological levels (< 1 ml/ cm H2O), the correlation of $EtCO_2$ with $PaCO_2$ decreased by both the methods of capnometry. This is because of the relative increased dead space ventilation with short time constants in diseases of decreased lung compliance [15].

Thus, When Used Properly, Etco2 Monitoring Along With Pulse-Ox Monitoring Has Great Potential To Reduce The Phlebotomy Losses In The Population Where It Matters Most!

Conclusions and Recommendations (Key Messages)

1. MS capnometry is superior to SS capnometry in neonates on patient triggered ventilation, especially if ventilated in Flow cycled assist control mode or with rapid ventilator rate.
2. For practical purposes, predicted Pa CO_2 by the MS method is $PaCO_2 = 4 + EtCO_2$ and by the SS method, it is $PaCO_2 = 25 +1/3\ EtCO_2$
3. Diseases with right to left shunt situation capnometry are less reliable.
4. We recommend using MS end tidal capnometry for neonates on the patient triggered mode of ventilation

Contributors

TBP was involved in concept, design, data collection and writing the primary draft. RNN was involved in design of the study and drafting the manuscript. RHU was involved in the overall supervision of the study.

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