Research Article

Correlation of end tidal and arterial carbon dioxide levels in critically Ill neonates and children

Hiren Mehta[1,2], Rahul Kashyap[3], Sangita Trivedi[4,5]

Abstract

Aim of the Study: End tidal carbon dioxide ($EtCO_2$) monitoring is considered to reflect real-time estimation of partial pressure of carbon dioxide in arterial blood ($PaCO_2$) noninvasively. However, knowledge about its relationship with $PaCO_2$ in critically ill pediatric and neonatal patients is limited.The primary objective was to evaluate predictive capability of end tidal carbon dioxide monitoring and secondary objective was to determine the influence of severity of lung disease on $EtCO_2$ and $PaCO_2$ relationship. **Materials and Methods:** This was a prospective, nonrandomized, consecutive enrollment study carried out in neonatal and pediatric intensive care units of a tertiary care children hospital. It was conducted in 66 neonates and 35 children receiving mechanical ventilation. Severity of lung disease was estimated by ventilation index and PaO_2/FiO_2 (P/F) ratio. Simultaneous recording of $EtCO_2$ and $PaCO_2$ levels was done and data were analyzed for correlation and agreement. **Results:** In neonates, 150 $EtCO_2$ and $PaCO_2$ pairs were recorded. The mean weight ± SD of patients was 2.1 ± 0.63 kg. $PaCO_2$ had a positive correlation with $EtCO_2$ (r = 0.836, 95% CI = 0.78-0.88). P/F ratio <200 adversely affected relationship. In infants and children, 96 pairs were recorded. Mean age ± SD of patients was 4.20 ± 4.92 years and mean weight ± SD was 13.1 ± 9.49 kg. $PaCO_2$ had an excellent correlation with $EtCO_2$ (r = 0.914, 95% CI = 0.87 and 0.94). P/F ratio <200 adversely affected relationship. **Conclusion:** $EtCO_2$ monitoring displayed a good validity to predict $PaCO_2$. Correlation was affected by low P/F ratio (<200); hence, it is recommended that blood gases be measured in these patients until such time that a good relation can be established between end tidal and arterial CO_2 values.

Keywords: Capnography, carbon dioxide monitoring, end tidal carbon dioxide, $EtCO_2$, $EtCO_2$ and $PaCO_2$ correlation, $PaCO_2$

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Introduction

Ventilatory status monitoring of critically sick newborns and children admitted to the intensive care unit is done by invasive and noninvasive methods. There are several complications and limitations of invasive arterial blood gas (ABG) monitoring which can arise from percutaneous arterial punctures, presence of indwelling vascular catheters, or by blood loss due to repeated measurements.[1] Alternative methods to arterial sampling are capillary blood sampling that is painful and transcutaneous monitoring which may not be well tolerated by infants with fragile skin and is also affected by hypoxia and acidosis. Both have only a fair relationship with $PaCO_2$. Therefore, noninvasive monitoring by capnography to monitor carbon dioxide status of critically ill infants and children has become increasingly popular. In addition to avoiding complications related to invasive monitoring, it also helps in reducing the cost. The $PaCO_2$ and $EtCO_2$ relationship is influenced by alterations in lung mechanics. In critically ill patients, in the intensive care units, the ventilation-to-perfusion ratio is frequently

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abnormal; thus, limiting the ability to use $EtCO_2$ to estimate PaCO2. However, studies have reported a variable correlation between $EtCO_2$ and $PaCO_2$ in adults and infants in a variety of clinical settings including critically ill or injured patients.[2-8] Most of the studies evaluating the $EtCO_2$ and $PaCO_2$ relationship have been done in adults and only a few studies have reported good correlation in pediatric population. Moreover, knowledge about the relationship between $EtCO_2$ and $PaCO_2$ in pediatric and neonatal patients with severe lung disease is limited. Hence, we embarked on this study with the primary objective to evaluate predictive capability of end tidal CO_2 monitoring in neonates and children and secondarily to determine the influence of severity of lung disease on $EtCO_2$ and $PaCO_2$ relationship.

Materials and Methods

This was a prospective, consecutive enrollment study. Each patient received standard critical care monitoring including $EtCO_2$ monitoring using commercially available mainstream 'Datex-Ohmeda S/5™ Light Monitor'. This device measures changes in CO_2 concentration in the gas passing between self-contained infrared emitter and detector in the range from 0-15% or 0-100 mm Hg and it is self-calibrating.[9] Single use mainstream CO_2 adapters which had a dead space of 6 ml and a maximum flow rate of 120 l/min were placed between end of endotracheal tube and Y-connector of breathing circuit. Patients admitted in neonatal and pediatric intensive care units of a tertiary care teaching hospital for women and children, in Gujarat, India, from August 2008 to January 2009 were eligible for study. The study was approved by scientific committee of the hospital and was waived consent requirements. All patients who were intubated, mechanically ventilated and had an indwelling arterial catheter, neonates (>32 weeks GA at birth, and 1-28 days old), and infants and children (between 1 month and 15 years) were included in the study. Exclusion criteria were patients with tracheostomy, ventilator circuit leak of more than 15% as detected by difference in inspiratory and expiratory tidal volumes, presence of air leak syndromes such as pneumothorax, pneumomediastinum, pulmonary interstitial emphysema, cyanotic congenital heart disease or with significant right to left intracardiac shunt, severe pulmonary hypertension based on echocardiography findings, and patients receiving high frequency oscillatory ventilation or extra-corporeal membrane oxygenation. Prior to data collection confirmation of endotracheal tube position by chest radiograph and its patency by suctioning was done. Simultaneous $EtCO_2$ and ABG measurements were recorded on a bedside data sheet. On an average, no more than two to three pairs per patient were drawn and a minimum interval of 8 h or more was maintained between two successive measurements on same patient. ABG analysis was performed in hospital clinical laboratory. Additional demographic and clinical data including patients' age, sex, vital signs, diagnosis, indication, and day of ventilation, endotracheal tube size, nebulization therapy, were abstracted and recorded on proforma. At the time of collection of samples data were collected on mode of ventilation, FiO_2 (Fractional Inspired oxygen concentration), inspiratory and expiratory tidal volumes, peak inspiratory pressure (PIP), positive end expiratory pressure (PEEP), respiratory rate (RR), and oxygen saturation. Calculated data as measures of severity of lung disease included were ventilation index (VI) and PaO_2 (partial pressure of arterial oxygen tension)/FiO_2 (P/F) ratio. VI = ($PaCO_2$ × PIP × RR)/1000 was considered high if >20. VI uses respiratory rate of mechanical ventilator and does not include spontaneous breaths. P/F ratio, if <200, was considered abnormal. Baseline characteristics were described using frequencies and proportions for categorical variables. Analysis of $EtCO_2$ and $PaCO_2$ pairs were done separately for neonates and children by computing Spearman test; and correlation coefficient (r), 95% confidence intervals (CI), and coefficient of determination (R^2) were calculated. A linear regression analysis was done to find the equation between $PaCO_2$ and $ETCO_2$ and Bland–Altman Plot was created to evaluate agreement. Data were analyzed using the SAS statistical software version 9.2. Statistical significance was considered as $P < 0.05$.

Results

From August 1, 2008 to Jan 30, 2009, a total of 130 patients were mechanically ventilated in neonatal and pediatric intensive care units [Figure 1]. Twenty-nine patients were subsequently excluded and 101 patients were included in the study: 66 neonates and 35 infants and children. Two hundred and sixty-eight $EtCO_2$ and $PaCO_2$ pairs were drawn, 22 were excluded, and 246 were included in analysis: 150 for neonates and 96 for infants and children. Demographic and diagnostic characteristics for neonates are shown in Table 1 and for infants and children in Table 2. Neonate population had a mean weight of 2.1 kg (SD ± 0.63), 57% were premature and 59% had pulmonary disease. The mean weight in infants and children was 13 kg (SD ± 9.49), mean age 4.20 years (SD ± 4.92), and 55% had pulmonary disease. Ventilator variables and derived data for all

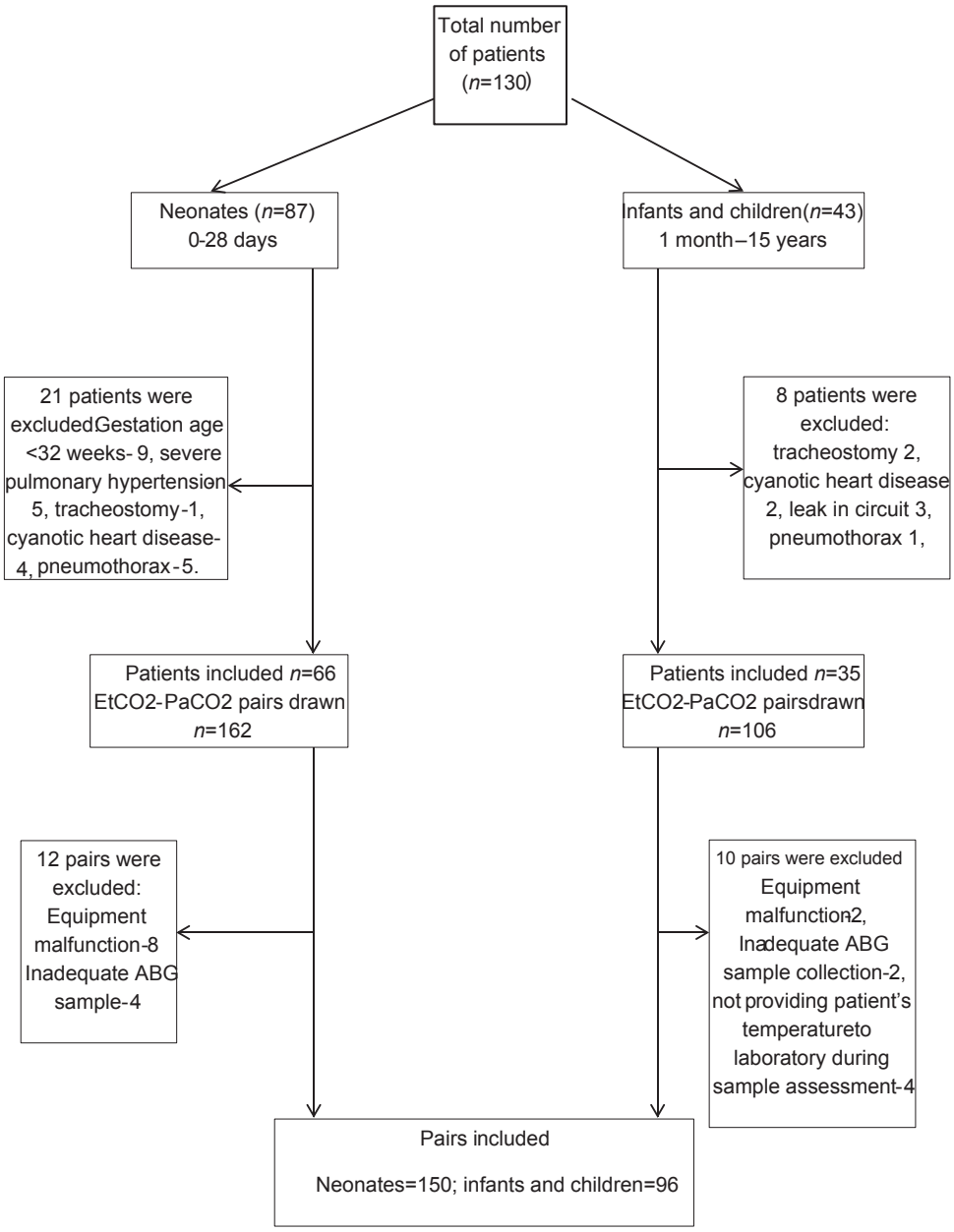

Figure 1: Enrollment of study pairs

patients are summarized in Table 3. Overall, a good correlation was found between the two variables in neonates [Table 4] with a narrow CI; $r = 0.836$, (95% CI 0.78–0.88) and $R^2 = 0.6,962$ ($P < 0.0001$). Bland–Altman Plot [Figure 2] shows an average difference of 0.66 (95% limits of agreement-15.54 to 16.86). The effect of severity of lung of disease as determined by VI and P/F ratio was analyzed on relationship between the two variables. It was observed that VI did not have any conclusive effect on correlation. R^2 was only 0.529 with a normal VI of <20 and 0.235 with VI >20. When considering P/F ratio >200 for mild to moderate lung disease, there was a strong correlation of $PaCO_2$ and $EtCO_2$ with $r = 0.89$ (95% CI = 0.84–0.92) and $R^2 = 0.765$ whereas P/F ratio <200 adversely affected the relationship showing a good correlation of $r = 0.80$, (95% CI = 0.67–0.88), but a relatively lower $R^2 = 0.64$. In general, an excellent correlation was found between $PaCO_2$ and $EtCO_2$ pairs in infants and children with $r = 0.914$, a narrow CI = 0.87–0.94, and $R^2 = 0.833$ [Table 5]. Bland–Altman Plot [Figure 3] shows an average difference-0.49 (95% limits of agreement-13.33 to 12.35). The effect of severity of lung of disease as determined by VI and P/F ratio was analyzed on relationship between the two variables in this age group too. It was observed that a normal VI of <20 had a strong correlation, $r = 0.803$; narrow 95% CI = 0.71–0.87, but $R^2 = 0.644$ underlined that only 64% of variation in $PaCO_2$ could

Table 1: Demographic and diagnostic characteristics of neonates (*n*=66)

Characteristics	Frequency *n* (%)
Sex	
Male	54 (82)
Gestational age (weeks):	
>37	28 (42)
32-37	38 (57)
Diagnosis	
Respiratory	39 (59)
Hyaline membrane disease	25
Meconium aspiration syndrome	8
Pneumonia	2
Apnea	3
Pulmonary hemorrhage	1
Cardiac disease (left to right shunt)	8 (12)
Post-operative (non-cardiac)	6 (9)
Central nervous system disorders	22 (33)
Hypoxic–ischemic encephalopathy	8
Seizure disorder	2
Intracranial hemorrhage	8
Metabolic disorder	4
Others	10 (16)
Treatment variables	
Surfactant therapy	18 (27)
Vasopressor therapy	45 (68)
Peritoneal dialysis	2 (5)

Total are more than 66 because many patients had more than 1 indication

Table 2: Demographic and diagnostic characteristics of infants and children (*n*=35)

Characteristics	Frequency *n* (%)
Males	14 (40)
Diagnoses	
Respiratory	19 (55)
Bronchiolitis	6
Pneumonia	5
Acute respiratory distress syndrome	4
Asthma	1
Croup	1
Cardiac	6 (17)
Shock	4
CHF	2
Surgical	5 (14)
Intra-abdominal surgery	4
Elective repair cleft palate	1
Central nervous disorders	11 (22)
Guillain-Barre syndrome	2
Seizure disorder	4
Encephalitis	3
Others	2
Miscellaneous	8 (16)
Treatment variables	
Vasopressor therapy	20 (57)
Bronchodilator therapy	10 (28.5)
Peritoneal dialysis	2 (6)

Total are more than 35 because many patients had more than 1 diagnosis.
CHF: Congestive heart failure

be explained by variation in EtCO2. With an abnormal VI of >20 the correlation was excellent r = 0.897, but 95% CI was wide at 0.69–0.96 for this correlation. This may be due to small number of patients (n = 15) in this group. There was a strong correlation in patients with mild to moderate lung disease with P/F ratio of >200;

Table 3: Ventilator and clinical variables in neonates and children

Description	Neonates (*n*=150 pairs)		Infants and children (*n*=96 pairs)	
	Mean	SD	Mean	SD
FiO_2	0.528	0.241	0.534	0.259
PIP	15.76	5.068	14.99	4.45
PEEP	4.667	0.864	4.842	1.114
PSV	11.04	3.597	11.02	2.096
VR per min	40.07	12.91	33.51	11.07
Dynamic compliance	7.973	3.902	119.7	196.6
pH	7.3,529	0.1,435	7.397	0.1492
$PaCO_2$ mmHg	38.998	14.625	36.071	15.786
PaO_2 mmHg	105.85	53.842	126.84	74.94
SaO_2%	94.813	5.311	96.613	3.918
Ventilation Index	17.46	13.59	14.17	18.67
Oxygenation index	6.20	5.22	5.92	4.32
PaO_2/FiO_2 ratio	200.47	102.3	237.52	122.4

FiO_2: Fractional inspired oxygen concentration, PIP: Peak inspiratory pressure, PEEP: Positive end expiratory pressure, PSV: Pressure support ventilation, VR: Ventilator rate, $PaCO_2$: Partial pressure of carbon dioxide in arterial blood, PaO_2: Partial pressure of oxygen in arterial blood, SaO_2%: Percentage of arterial oxygen saturation

r = 0.94, (95% CI = 0.91–0.95) and R^2 = 0.88. In severe lung disease when P/F ratio was <200, the correlation was good r = 0.782, but there was a wide 95% CI = 0.71–0.92 and R^2 = 0.68.

Discussion

We report our study evaluating the relationship between $PaCO_2$ and $EtCO_2$ in critically sick, mechanically ventilated newborns, infants, and children. Our data reveal that $EtCO_2$ shows an excellent validity and relationship with $PaCO_2$ providing clinically relevant and valid estimate of ventilation for neonates and children with mild to moderate lung disease to the extent that it can be substituted for $PaCO_2$ measurement. In patients with severe lung disease, it shows moderate to strong correlation, but R^2 is suggestive that only about 64-68% of variation in $PaCO_2$ can be explained by $EtCO_2$, understandably, more variability in dead space to tidal volume ratio (Vd/Vt) can be expected in these critically ill patients which actually drives the gradient between $EtCO_2$ and $PaCO_2$ underlining its importance only for monitoring trends in this subset of patients. Although, in neonates some studies evaluating this relationship have demonstrated poor correlation.[3,4,6,10] Findings of excellent correlation have been observed by other researchers irrespective of severity of lung disease.[7,11] Study by Rozycki *et al.* revealed that in premature, surfactant-treated newborns $EtCO_2$ monitoring was as accurate as in overall population of patients (r = 0.833 and 0.821, respectively).[7] Similar to our study, Bhat YR *et al.* found that patients with underlying lung pathology such as hyaline membrane disease and

Table 4: Association between $EtCO_2$ and $PaCO_2$ in neonates

Newborns	$PaCO_2$ mean (SD)	$EtCO_2$ mean (SD)	Correlation coefficient (*r*)	95% CI	Coefficient of determination R^2
Total pairs=150	38.99 (14.62)	38.33 (13.30)	0.836	0.78-0.88	0.698
Pairs with VI<20=106	34.00 (10.43)	34.56 (9.55)	0.728	0.62-0.81	0.529
Pairs with VI>20=44	51.07 (16.49)	47.04 (16.58)	0.485	0.22-0.68	0.235
Pairs with P/F ratio>200=52	37.8 (15.59)	38.7 (14.86)	0.89	0.84-0.92	0.79
Pairs with P/F ratio<200=98	39.6 (14.13)	38.13 (12.5)	0.80	0.67-0.88	0.64

$PaCO_2$: Partial pressure of carbondioxide in arterial blood, $EtCO_2$: Partial pressure of oxygen in arterial blood, VI: Ventilation index, P/F ratio: Ratio of partial pressure of arterial oxygen and fractional inspired oxygen concentration

Table 5: Association between $EtCO_2$ and $PaCO_2$ in infants and children

1 month to 15 years	$PaCO_2$ mean (SD)	$EtCO_2$ mean (SD)	Correlation coefficient (*r*)	95% CI	Coefficient of determination R^2
Total number of pairs=96	36.07 (15.7)	36.56 (14.2)	0.914	0.87-0.94	0.83
Pairs with VI<20=81	29.00 (11.9)	29.67 (10.9)	0.803	0.71-0.87	0.64
Pairs with VI>20=15	49.88 (20.4)	50.73 (15.4)	0.897	0.69-0.96	0.80
Pairs with P/F ratio>200=48	36.6 (19.2)	37.5 (17.4)	0.94	0.91-0.95	0.89
Pairs with P/F ratio<200=48	35.51 (11.5)	35.6 (10.3)	0.83	0.71-0.92	0.68

$PaCO_2$: Partial pressure of carbon dioxide in arterial blood, $EtCO_2$: Partial pressure of oxygen in arterial blood, VI: Ventilation index, P/F ratio: Ratio of partial pressure of arterial oxygen and fractional inspired oxygen concentration

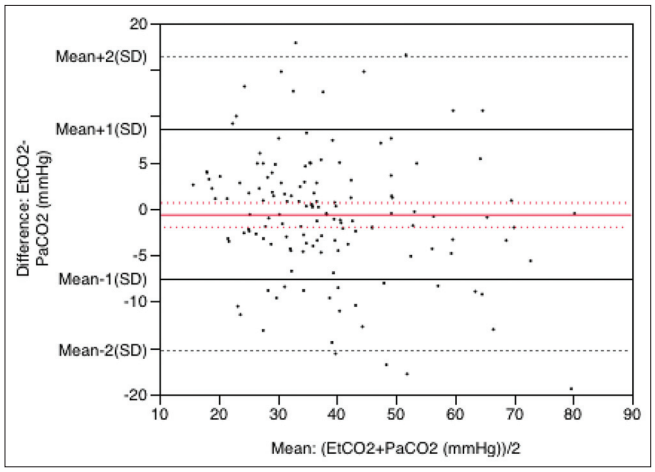

Figure 2: Bland-Altman plot in neonates ($EtCO_2$-$PaCO_2$ pairs=150)

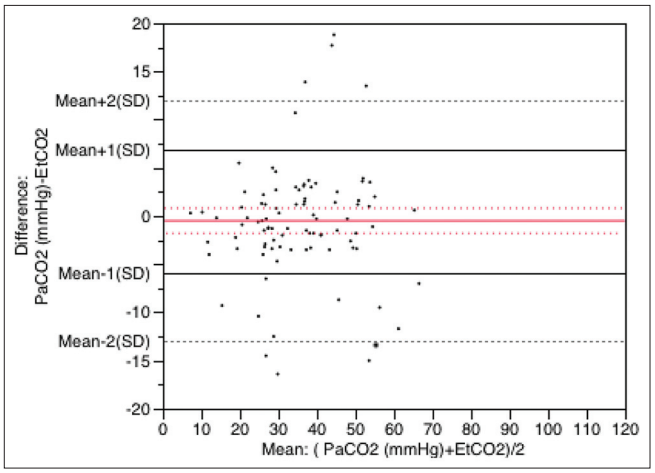

Figure 3: Bland-Altman plot in infants and children ($EtCO_2$$PaCO_2$ pairs=96)

meconium aspiration syndrome had lower correlation with R^2 = 44% and 47%, respectively. The $EtCO_2$ values were lower than $PaCO_2$ values with a mean bias of -6.65 ± 7.54 (95%CI-7.9–5.35).[14] Similarly, other studies conducted in very low birth weight infants (VLBWI) with severe lung disease by sidestream–microstream capnograph revealed less reliable correlation and mean bias 13.5 ± 8.4 (95% agreement levels 3-29.9 mmHg).[15,16] Among infants and children, our study found an excellent positive correlation between $EtCO_2$ and $PaCO_2$, but severe lung disease as defined by P/F ratio <200 had a negative impact on this relationship. Similar to this, Macdonald[12] *et al.* and Meredith *et al.*[6] also found a strong positive correlation (n = 1,708, r = 0.716), and (n = 132, r = 0.79) and a negative impact of severe lung disease, but both the studies had drawn an average of 17 and 8 pairs per patient, respectively, as compared to our study where we drew only two to three pairs per patient to maintain validity of coefficient of correlation and get an unbiased estimate of population parameter of interest. Previous studies reported an influence of both VI and P/F ratio on correlation of $PaCO_2$ and $EtCO_2$, but we found only P/F ratio to be useful in assessing the effect of severity of lung disease on this relationship.[12,13] There were several limitations that could have affected the result of this study. Probably, the sample size was not large enough to reveal the influence of VI on relationship; the role of dynamic compliance and oxygenation index as indicators of severe lung disease was not analyzed; effect of cointerventions such as surfactant therapy and time of suctioning the ET tube before the measurement was not taken into consideration; and co-existing conditions that could have adversely affected $PaCO_2$ and $EtCO_2$ relationship like shock/persistent hypotension were not excluded. There is also no evidence if certain pairs were obtained

during unstable clinical conditions. Further studies with a larger sample size are warranted to evaluate the impact of these situations.

Conclusion

Based on the study we recommend that $EtCO_2$ monitorhas an important place in the bedside monitoring of a patient in ICU as it provides excellent validity in both neonates and older children. Increased severity of lung disease as defined by P/F ratio <200 negatively affects $EtCO_2$ values in all the age groups; hence, it is recommended that blood gases be measured in such patients until such time that a good relation can be established between end tidal and CO_2 value.

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