Original Article

Effect of Stepwise Reduction in Minute Ventilation on $PaCO_2$ in Ventilated Newborns

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Objective: *To study the effect of step reduction of expired minute ventilation (MV) on $PaCO_2$ in ventilated newborns and to determine whether MV within a defined range can predict $PaCO_2$.* ***Design:*** *Prospective descriptive.* ***Setting****: Referral neonatal unit of a teaching hospital.* ***Methods****: Forty neonates stable on mechanical ventilation receiving minute ventilation in the range of 150-210 ml/kg/min. were studied. The spectrum of disorders for which the babies were ventilated included apnea of prematurity in 16, pneumonia in 14, meconium aspiration syndrome in 6 and hyaline membrane disease in 4. Median age at study was 6 days and median weight at study was 2.1 kgs. The MV was reduced from 210 to 150 mL/kg/min in three steps and concomitant $PaCO_2$ was measured. Reductions were not done if $PaCO_2$ was more than 50 mmHg. MVs were plotted against $PaCO_2$ and a regression equation to predict $PaCO_2$ from MV was calculated.* ***Results:*** *A stepwise increase was seen in CO_2 with reduction of MV over the range studied. The median MV and median $PaCO_2$ achieved in the three steps were 201 mL/kg/min and 36.7 mm of Hg, 180 mL/kg/min and 41.7 mm of Hg, 160 mL/kg/min., and 44.3 mm of Hg. The regression equation to predict $PaCO_2$ was $PaCO_2 = 70 - 0.17 x MV$ in mL/kg/min, $r = -0.45$, $r^2 = 0.20$, $p<0.001$, residual variance (s^2) = 39.37; 95% C.I. gave a predicted $PaCO_2$ within ± 12.5 mmHg. for a given MV.* ***Conclusion:*** *Reducing minute ventilation led to an increase in the levels of $PaCO_2$. Minute volumes of 160 ml/kg/min correlated with $PaCO_2$ value of 44.3 mm of Hg. MV as low as 160 mL/kg/min are well tolerated by newborns.*

Key words: *Mechanical ventilation, MInute ventilation, Neonate, $PaCO_2$.*

NORMAL values of minute ventilation in spontaneously breathing neonates have been determined using varying methodology and show wide variations(1-11). The focus in neonatal ventilation is now shifting from pressure controlled ventilation to volume controlled ventilation. This is due to recognition of the fact that hypocarbia and volutrauma and not barotrauma is the causative agent for lung damage and adverse neurodevelopmental outcome. Newer ventilators are being available that target specific volumes. There are few studies on evaluation of minute ventilation required to avoid unacceptable levels of $PaCO_2$ in mechanically ventilated neonates. This prompted us to undertake the present study with the objective of (*i*) evaluating $PaCO_2$ in neonates ventilated with minute ventilation of 200mL/kg. (*ii*) Evaluating the effect of step reduction of minute ventilation on $PaCO_2$.

Methods

The study was conducted in the referral neonatal unit of the Department of Pediatrics, Maulana Azad Medical College and Lok Nayak Hospital between March and December 2000. The institutional research committee approved the study. The referral neonatal unit is a tertiary care unit catering to neonates referred from hospitals in Delhi and surrounding states or brought directly from home.

Neonates stable on mechanical ventilation were eligible for the study if all the following criteria of stability were met: SaO_2 90-95%, Capillary Filling Time (CFT) <3 seconds, skin temperature 36.5–37.5ºC, pH 7.3–7.45, peak inspiratory pressure (PIP) <20 mbar, set respiratory frequency <60/min, fraction of inspired oxygen (FiO_2) <60%. A total of 40 neonates stable on mechanical ventilation fulfilling the inclusion criteria were enrolled for the study. All neonates received assisted ventilation with Babylog 8000 plus (Drager Inc.); a pressure limited time-cycled ventilator.

The study involved measuring the $PaCO_2$ in neonates receiving minute ventilation in the range of 150-210 mL/kg/min. PIP was set to provide tidal volumes between 5-8mL/kg and respiratory frequency was manipulated to get the desired expired minute ventilation. Concomitant $PaCO_2$ values were determined at minute ventilation of 200±10,180±10 and 160±10 mL/kg/min. The step reductions in minute volume were predominantly achieved by lowering the respiratory frequency. This was done by increasing the expiratory time for the breathing cycle. The inspiratory time was kept constant. Pancuronium was used only in neonates asynchronous with ventilator as a single dose and not used routinely. Endotracheal leak displayed as measured value by the ventilator was documented. It was ensured that there was no significant endotracheal leak while the observations were made (<10% difference between inspiratory and expiratory tidal volumes). The set ventilatory parameters were recorded. These included the Peak Inspiratory Pressure, Positive End Expiratory Pressure, inspiratory time, expiratory time, fraction of inspired oxygen and set frequency. Samples for $PaCO_2$ were drawn from an arterial line after the baby was on the targeted minute ventilation for a period of thirty minutes. If a PaCO2 value of more than 50 mm Hg were obtained further reduction in minute ventilation was not done. SaO_2 was continuously maintained in the desired range by manipulating the FiO_2. Expired minute ventilation was read from the displayed value measured by the flow sensor (hot wire anemometer) of the ventilator. It has low dead space (0.7 mL) and is lightweight. It has response characteristics that are suitable at high frequencies and avoids overshoot with sudden flow changes. It is little affected by the moisture content of the gas(12). It is attached to the *Y* piece to which the endotracheal tube is connected. The flow sensor was calibrated prior to each study.

The other recorded variables included compliance, resistance, mean airway pressure and C20/C (an index of over distension of lungs, it is the ratio of the compliance of the last 20% of the dynamic pressure volume curve to the overall compliance). These were measured and displayed by the ventilator.

Linear regression was performed with $PaCO_2$ as the dependent variable and MV as the independent variable to give a regression equation with 95% confidence interval. The R^2 (coefficient of determination), r (product moment correlation coefficient or Pearson correlation coefficient) and S^2 (residual variance) were calculated for the above two variables.

Results

The study population had 10 neonates less than 32 weeks gestation; 12 between 33 and 36 weeks and 18 between 37 and 42 weeks. The median and interquartile range for age at inclusion was 6 (3-12) days and for weight was 2.1 kg. (1.46 kg. - 2.58 kg). The indications for ventilation are shown in *Table I*.

The minute ventilation targeted in the first step was 200mL/kg/min.; the achieved median minute ventilation was 201 mL/kg/min. The median $PaCO_2$ at this minute ventilation was 36.7 mmHg. In the next step the achieved median minute ventilation was 180 mL/kg/min and the median $PaCO_2$ was 41.7 mmHg. In the last step the achieved median minute ventilation was 160 mL/kg/min., and the median $PaCO_2$ was 44.3 mmHg. (*Table II*). The ventilatory parameters are given in *Table III*.

TABLE I– *Indications of Ventilation in the Study Population*

Indication	Cases
Pneumonia	14
Hyaline membrane disease	4
Meconium aspiration syndrome	6
Apnea of prematurity	2
Apnea secondary to :	
Sepsis	9
Hypoxic ischemic encephalopathy	4
Milk Aspiration	1
Total	40

One hundred and rwenty measurements of MV and concomitant $PaCO_2$ were made from 40 neonates. The line of best fit and scatter plot is given in *Fig 1*. Regression equation for prediction of $PaCO_2$ (mm Hg) by MV (mL/kg/min) is: $PaCO_2 = 70 - 0.17 \times MV$. The correlation coefficient (r) was –0.45 and coefficient of determination (r^2) was 0.20. The regression coefficient was statistically significantly different from 0 ($p <0.001$). The residual variance (s^2) was 39.37 (s = 6.27), which gives 95% confidence intervals allowing the prediction of $PaCO_2$ to within ± 12.5 mm Hg for a given MV.

TABLE II–*Correlation of Mean Ventilator Settings and Arterial Blood Gases with the Three Step Changes in Minute Ventilation.*

	Step1: Targeted MV = 200 ml/kg Median (95% CI)	Step2: Targeted MV = 180ml/kg Median (95% CI)	Step3: Targeted MV = 160 ml/kg Median (95% CI)
Actual MV	201(200-205)	180 (177-182)	160 (156-162)
$PaCO_2$	36.7 (34.6 -39.7)	41.7 (38.1-43.6)	44.3 (42.1-46.4)
Frequency	38 (36-40)	35 (33-38)	31 (30-32)
FIO_2	40 (40-50)	40 (35-50)	40 (35-50)
pH	7.38 (7.348-7.39)	7.35 (7.347-7.36)	7.32 (7.30 -7.36)
PaO_2	81.8 (72.8-86.5)	74.7 (69.0-77.4)	71.3 (67.7-76.0)
Bicarbonate	19.8 (18.8-20.3)	19.1(18.6-19.7)	20.2(19.0-21.0)

TABLE III–*Ventilatory Parameters (Median and Inter Quartile Range) in Relation to the Three Step Reductions of Minute Ventilation.*

	Step 1	Step 2	Step 3
MAP, (cm H_2O)	6.9(6.03-7.99)	6.3(5.59-7.28)	6.4(5.41-7.5)
Compliance (ml/mbar)	1.0(0.89-1.26)	1.0(0.86-1.2)	1.1(0.93-1.2)
Resistance (mbar/l/s)	77.0(68.5-87)	77.0(65.75-86.75)	76.0(65.25-89)
C20/C	2.1(1.51-2.3)	2.1(1.53-2.3)	2.0(1.46-2.32)

The regression equation to predict $PaCO_2$ from MV in neonates ventilated for pneumonia was:

$PaCO_2 = 69 – 0.16 \times MV$ (n = 42) $R^2 = 0.12$, r = – 0.35, *s* = 7.49

Regression equation to predict $PaCO_2$ from MV in neonates ventilated for HMD was:

$PaCO_2 = 70 -0.16 \times MV$ (n = 12) $R^2 = 0.17$, r = – 0.41, s = 4.92

Regression equation to predict $PaCO_2$ from MV in neonates ventilated for MAS was:

$PaCO_2 = 79 – 0.22 \times MV$ $R^2 = 0.42$, r = –0.65, s= 4.32

Regression equation to predict $PaCO_2$ from MV in neonates ventilated for apnea group was:

$PaCO_2 = 70 – 0.17 \times MV$ (n = 48) $R^2 = 0.23$, r = –0.48, s = 5.67

Discussion

Minute ventilation is a continuously displayed parameter that can be used to optimise ventilator settings. It can be used in conjunction with the intermittently available

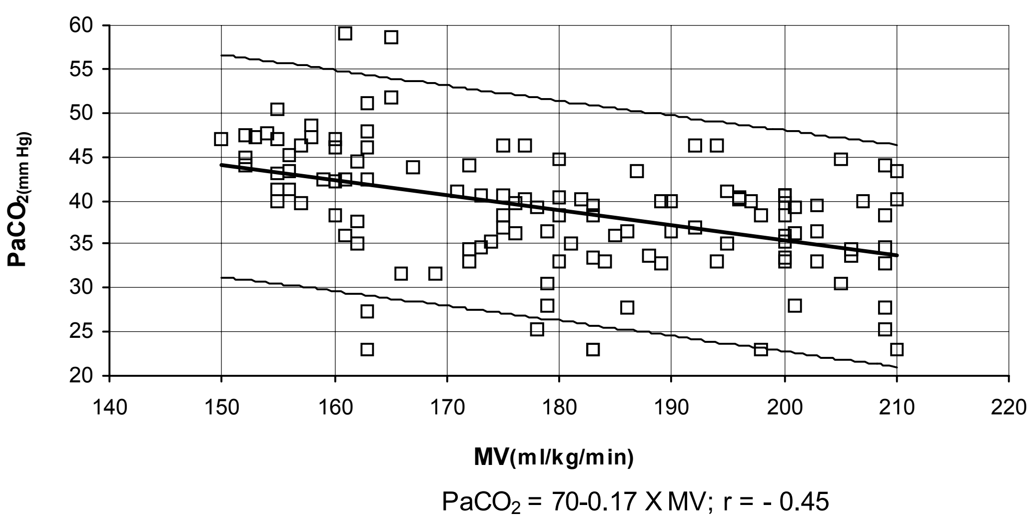

Fig. 1. MV vs. $PaCO_2$ for the study group (120 data points from 40 subjects)

$PaCO_2$ values. Carbon dioxide elimination is inversely proportional to minute ventilation. In our study we have shown a correlation between MV and $PaCO_2$. Although alveolar ventilation correlates better with $PaCO_2$, determining it requires cumbersome technique, which is not feasible routinely. MV may be taken as a surrogate marker for alveolar ventilation. To the best of our knowledge this aspect has been studied in only one study(11). The predicted $PaCO_2$ level at a MV of 200 mL/kg/min in our study is 35 mm of Hg as compared to 43 mm of Hg observed by Davies, *et al.* in preterm neonates with Hyaline membrane disease(11). This difference could be attributed to the difference in the population studied. Davies, *et al.* took multiple measurements (up to 5) from the same patient, thereby making the observations not strictly independent(11). Although it is possible to determine a directional trend in $PaCO_2$ with a change in MV (*Fig. 1*) MV may not calculate $PaCO_2$ in an individual neonate due to variations because of other factors.

The median minimum minute ventilation in our study was 160 mL/kg/min, at which the $PaCO_2$ was 44.3 mmHg. This minute ventilation can be used as a goal in neonatal ventilation to optimise ventilator settings. The minute ventilation targeted and achieved in our study were comparably less than those earlier reported (*Table IV*). These high values probably reflected a tendency to aim for $PaCO_2$ levels between 35-45 mm Hg.

Optimal Carbon dioxide elimination is a

TABLE IV–*Studies on Minute Ventilation in Spontaneously Breathing Neonates.*

Author	N	MV (ml/kg/min)/ (ml/min)*	Group	Respiration	Technique used
Cross (1)	26	204 ± 19.3	Normal	Spontaneous	Body plethysmography
Cross (2)	30	396.3	Normal preterm	Spontaneous	Body plethysmography
Cook, *et al.* (3)	35	498*	Normal	Spontaneous	Body plethysmography
Nelson, *et al.* (4)	25	480*	Normal	Spontaneous	Body plethysmography
	14	632*	IDM		
Schulze, *et al.* (5)	40	286	Normal	Spontaneous	Bias flow pneumotachometry
Watts, *et al.* (6)	19	313.5± 18.8	Normal	Spontaneous	Pneumotachometer
	19	287.6 ± 18	Severe HMD		
	33	306.3 ± 17.5	BPD		
Chu, *et al.* (7)		270 ± 72	Normal	Spontaneous	Pneumotachometer
Mizuno, *et al.* (8)		450 ± 40	VLBW	Spontaneous	Pneumotachometer
		320 ± 20	Normal	Spontaneous	Pneumotachometer
Epstein, *et al.* (9)	15	295 ± 77		Ventilated	Spirometer
Greenspan, *et al.* (10)	36	1 week 476 ± 27 4 weeks 498 ± 21 8 weeks 467 ± 23	VLBW	Ventilated	Pneumotachometer
Davies, *et al.* (11)	14	252± 75	RDS	Ventilated	? Flow sensor

Key Messages

- Minute ventilation was found useful in optimising ventilator settings.
- Minute ventilation of 200, 180 and 160 mL/kg/minute correlated with $PaCO_2$ value of 36, 41 and 44 mm of Hg respectively.

crucial objective in mechanical ventilation. Traditional ventilator management in neonates aimed at achieving $PaCO_2$ values between 35-45 mm Hg even if high support was necessary. However, the need for ventilation strategies that reduce baro- and volutrauma has also led to tolerance of higher $PaCO_2$(13). Critical evaluation of present ventilator strategies focuses on what $PaCO_2$ levels are safe for newborn lungs and brain(15). Hypercapnia has physiologic effects on gas exchange that may provide important benefits(14-17).

Over ventilation, volutrauma and hypocapnia are associated with increased secondary lung damage, a higher incidence of chronic lung disease and adverse neurodevelopmental outcome(18-21).

To conclude, setting optimum minute ventilation can avoid abnormal $PaCO_2$ levels. Minute ventilation is a non-invasive continuously available parameter, which can be used to optimise ventilator settings.

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