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Inspiratory flow effects on mechanically ventilated patients: lung volume, inhomogeneity, and arterial oxygenation

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Abstract. Changes in the inspiratory flow rate of mechanically ventilated patients can affect arterial oxygenation. Although the mechanism producing this alteration is not certain, one possible mechanism is a change in ventilation inhomogeneity. This study was performed to determine if the inspiratory flow setting would affect ventilation inhomogeneity in patients who have minimal or no lung disease, but who require mechanical ventilation after cardiopulmonary bypass surgery. When inspiratory flows were doubled, PaO_2 increased and FRC fell. However, no associated change in ventilation inhomogeneity was detected. It is concluded that inspiratory flow rate can affect arterial oxygenation of subjects without severe obstructive pulmonary disease through mechanisms other than altering ventilation inhomogeneity, such as changes in cardiac output or in distribution of perfusion.

Key words: Ventilation inhomogeneity – Mechanical ventilation – Inspiratory flow rate – Gas exchange – Lung volume

Changing the inspiratory flow rate of mechanically ventilated patients can alter gas exchange. Increased inspiratory flow rates in mechanically ventilated dogs have been found to worsen gas exchange as evidenced by a fall in the partial pressure of arterial oxygen (PaO_2) or increase in the partial pressure of arterial carbon dioxide ($PaCO_2$) [4, 12]. In subjects with normal lungs undergoing anesthesia for surgery, increased inspiratory flow rates have also been found to result in an increase in physiologic dead space and/or an increase in the alveolar-arterial oxygen gradient [5, 10, 23, 24]. However, in patients with chronic obstructive pulmonary disease (COPD) who require mechanical ventilation, an increased inspiratory flow rate was found to increase PaO_2 [8].

How inspiratory flow rate influences gas exchange is not understood. One hypothesis is that the effect of inspiratory flow on gas exchange may be associated with a change in the distribution of ventilation. Using a mechanical ventilator to control the breathing pattern of non-intubated subjects with severe COPD, increases in inspiratory flow rate have been found to increase ventilation inhomogeneity as indicated by a multibreath N_2 washout [7]. Studies of subjects with normal lungs under voluntarily controlled breathing showed that increased inspiratory flow rate results in a more even distribution of ventilation as seen from Xe ventilation lung scans [1, 20]. These studies suggest that changing inspiratory flow rate may affect ventilation inhomogeneity in mechanically ventilated patients with or without obstructive lung disease. The purpose of this study was to determine if effects on gas exchange associated with increased inspiratory flow are related to ventilation inhomogeneity of subjects without severe COPD.

Methods

Eight patients admitted electively to undergo coronary artery bypass surgery were studied. Informed consent approved by the VA Medical Center Institutional Review Board For Human Studies was obtained from each patient. No patient had clinical or chest roentgenogram evidence of congestive heart failure. On the day prior to surgery, spirometry and arterial blood gas measurements were performed on each subject (Table 1).

The patients were studied between 1 and 3 h after coronary artery bypass surgery while still under the effects of anesthesia. All patients were in the recum-

Table 1. Pre-operative spirometry and arterial blood gas evaluation

Subject	Age (years)	FEV_1 (l)	FEV_1/FVC (%)	MMF (% predicted)	PO_2 (torr)	PCO_2 (torr)	pH
1	59	2.4	62	35	75	40	7.43
2	62	2.1	79	74	72	42	7.43
3	60	2.9	69	45	73	34	7.40
4	58	2.6	67	38	69	32	7.44
5	63	2.5	63	40	66	46	7.38
6	58	2.1	90	96	63	36	7.40
7	64	2.1	59	28	76	39	7.38
8	62	4.1	82	114	81	37	7.41

bent or semi-recumbent position and were ventilated with a volume ventilator (Bennett MA-1) through an oral endotracheal tube. No spontaneous inspirations were noted. Measurements were made at two flow settings (40 and 100 l/min), but without changing either the tidal volume (V_T) or respiratory rate.

A pneumotachometer (Fleish No. 2) was connected in series with the patient's endotracheal tube and the ventilator. Flow was measured continuously using a pneumotachometer, differential pressure transducer (Validyne MP-45), and signal processor (Validyne DC-19). Next to the pneumotachometer, a needle valve continuously sampled gas whose N_2 fraction was measured by an emission spectrometer (Hewlett-Packard 47302). Flow and N_2 signals were displayed on a strip-chart (Gould 2400) and recorded on FM tape (Hewlett-Packard 3963).

Multibreath N_2 washouts were performed on each subject with humified oxygen. The concentration of humidified inspired oxygen was increased by changing the fraction of inspired oxygen (F_IO_2) setting of the ventilator to 1.0. Because the immediate post operative period is inherently unstable, with the effects of recovery from cardioplegia and anesthesia, four washouts were performed on each subject. The first and third washouts were obtained with the ventilator flow set at 40 l/min; the second and fourth with the flow set at 100 l/min. Nitrogen was washed out until the end-tidal N_2 concentration was less than 2%. This required from 2 to 6 min. After the washout was complete, the O_2 level was returned to its initial value. The next washout was not performed until the end-tidal N_2 concentration was constant over 1 min. This protocol required 10 to 15 min. Examples of the flow signals from washouts at the two flow settings for one patient are shown in Figure 1. The associated N_2 washout signals for the same patient at the two flow settings are shown in Figure 2.

The signals recorded on FM tape were processed and analysed by computer (Digital Equipment, PDP 11/45). The analog data was digitized at a sampling rate of 50 Hz, filtered, compensated for delays, and corrected for viscosity and temperature changes [21].

Volume changes were calculated by integrating the digitized flow signals. Functional residual capacity (FRC) was estimated from a mass balance of inspired and expired N_2 after the start of the washout using integrated flow and N_2 concentration signals (see Appendix).

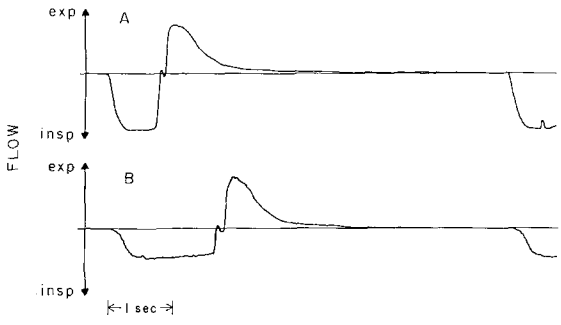

Fig. 1A and B. Flow patterns at the high (**A**) and the low (**B**) inspiratory flow settings of a patient being mechanically ventilated

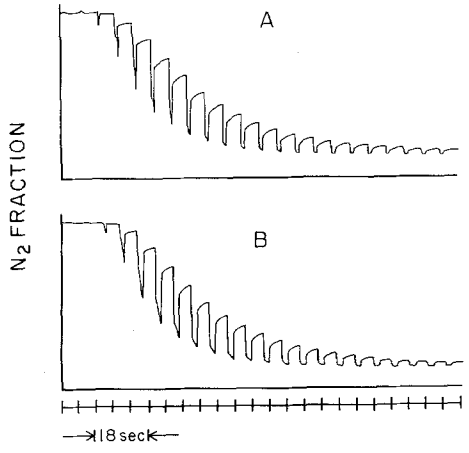

Fig. 2A and B. Nitrogen washout from patient being mechanically ventilated. High (**A**) and low (**B**) inspiratory flow settings

Mean dilution number (MDN) was used as the index of ventilation inhomogeneity [13]. The MDN is obtained from a moment analysis of the multibreath N_2 washout, which usually follows a step decrease in the inspired N_2 concentration. To compensate for the exponentially changing N_2 concentration delivered by the ventilator after the step change in the F_IO_2 setting as illustrated in Figure 2, the washout data had to be mathematically transformed for comparable analysis [11] (see Appendix).

When the four multibreath N_2 washouts were completed, arterial blood samples were obtained through indwelling arterial canulas in the radial artery. At each flow setting, PaO_2, $PaCO_2$, and pH were measured (Radiometer ABL3). At least 20 min elapsed between changes in flow or input O_2 fraction and blood gas measurements. The first measurements were made at 40 l/min for five subjects and at 100 l/min for the other subjects. The alveolar-arterial O_2 difference, $P(A\text{-}a)O_2$, was calculated using the standard alveolar air equation assuming the respiratory quotient R = 0.8.

Results

The consequences of more than doubling the average inspiratory flow without changing the tidal volume (V_T) or respiratory rate are given for each of the eight subjects in Table 2. The variables evaluated were the PaO_2, $PaCO_2$, $P(A\text{-}a)O_2$, MDN, FRC, and V_T. The difference of the means of each of these indices was tested for statistical significance using a paired t-test. The increase of inspiratory flow caused a significant increase in PaO_2 and a significant decrease in $P(A\text{-}a)O_2$ and FRC. The relative magnitude of these changes are shown in Figure 3. Although $PaCO_2$ increased, it was not statistically significant. The mean dilution number, MDN, an index of ventilation inhomogeneity, showed no significant change. Also, V_T showed no significant change.

Discussion

In patients without severe COPD being mechanically ventilated after cardiopulmonary bypass surgery,

Table 2. Post-operative evaluation of arterial blood gas, ventilation inhomogeneity, and lung volume at high and low inspiratory flows

Subjects	Breaths min	Average inspiratory flow (l/min)	MDN (l)	FRC (ml)	VT (ml)	PaO_2 (torr)	$P(A\text{-}a)O_2$ (torr)	$PaCO_2$ (torr)
1	11.2	36	2.19	1.68	773	121	171	39
	11.2	71	2.21	1.44	753	135	160	36
				(−14)		(+12)		
2	15.3	32	1.60	1.27	764	175	139	22
	15.5	72	1.62	1.06	772	187	120	28
				(−17)		(+15)		
3	8.6	26	1.98	1.26	749	102	188	39
	8.4	60	2.03	1.12	741	101	181	44
				(−11)		(0)		
4	12.1	30	1.98	1.24	686	180	286	37
	12.3	65	1.91	1.20	692	233	229	41
				(−3)		(+29)		
5	7.6	31	1.74	1.61	851	124	249	46
	8.3	60	1.78	1.50	839	155	218	46
				(−3)		(+25)		
6	7.5	32	1.58	0.91	769	157	130	38
	7.7	70	1.57	0.87	795	156	132	37
				(−4)		(0)		
7	9.2	33	2.24	1.28	732	175	203	50
	8.7	70	2.20	1.25	741	192	185	51
				(−2)		(+10)		
8	7.6	39	1.73	0.81	773	74	349	39
	7.5	81	1.73	0.71	780	75	346	41
				(−12)		(0)		

Numbers in parenthesis indicate the magnitude and direction of percentage change consequent to increase in inspiratory flow rate

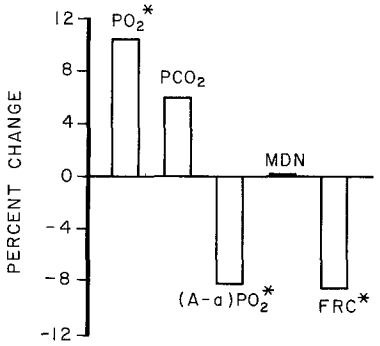

Fig. 3. Average difference between measurements of $PaCO_2$, PaO_2, $P(A\text{-}a)O_2$, MDN, and FRC at the low and high inspiratory flows. These are expressed as a percentage of the measurements at the low flow setting. The asterisk indicates a significant difference ($p < 0.05$)

higher inspiratory flow rates lead to no change in ventilation inhomogeneity as indicated by the MDN. Nonetheless, arterial blood gases were altered, with a significant increase in PaO_2. Assuming a constant CO_2 production, the fact that $PaCO_2$ did not fall helps rule out a decrease in physiologic dead space as the cause for the observed increase in PaO_2. The changes in PaO_2 associated with changes in inspiratory flow rate appears to be caused by mechanisms other than changes in distribution of ventilation or the rate of alveolar ventilation.

One previous study has found an increased PaO_2 resulting from an increased inspiratory flow rate in patients requiring mechanical ventilation because of severe COPD [8]. It was suggested higher inspiratory flow rate may affect arterial oxygenation in patients with severe COPD through changes of ventilation inhomogeneity [7, 8]. Our study of patients without severe COPD shows no change of ventilation inhomogeneity with increased inspiratory flow.

A higher inspiratory flow rate with a constant V_T results in a shortened inspiratory time (T_I) and lengthened expiratory time (T_E) as can be seen in Figure 1. Most previous studies have investigated the effects of changing inspiratory flow rate on gas exchange in terms of changing the T_E: T_I ratio. These studies used either dogs [2–4, 12, 20] or subjects undergoing anesthesia for surgery who had normal lungs and who did not require cardiopulmonary bypass [5, 10, 16, 24]. The results show an increased T_E caused either no change or a fall in PaO_2, and either no change or an increase in the $P(A\text{-}a)O_2$ gradient. The differences between the findings of our study and others may be due to underlying lung pathology. Cardiopulmonary bypass surgery has been shown to result in pulmonary edema and possibly micro-emboli [19], which would not be expected to be present after other types of surgery. The underlying lung pathology may influence how ventilation patterns affect gas distribution and mixing, cardiac output, and distribution of perfusion.

One previous study did examine the effects of T_E: T_I on gas exchange in patients who underwent cardiopulmonary bypass [23]. This study found no change in the PaO_2 or $P(A\text{-}a)O_2$. However, the mean tidal volume and respiratory rate used in that study were 385 ml and 20 breaths/min; in contrast, in our study the mean tidal volume and respiratory rate were 765 ml and 9 breaths/min, respectively. The smaller tidal volumes may not have produced a change in mean alveolar or pleural pressure great enough to affect PaO_2.

Increased inspiratory flow rates may have increased PaO_2 in our study through an increased cardiac output and/or improved distribution of perfusion. A greater T_E tends to decrease mean alveolar and pleural pressure, and some studies have found an associated increase is cardiac output [4, 9, 17, 18, 22]. While an increase in cardiac output in the presence of lung disease does not always result in an increased PaO_2 [6], a fall in intra-alveolar pressure may selectively increase blood flow in ventilated regions [14, 25] resulting in the observed increase in PaO_2. An increase in cardiac output as small as 5% could result in the increased PaO_2 found in this study if an increase in perfusion of ventilated alveoli occurred without change in absolute shunt flow.

In addition to a rise in PaO_2 and no change in ventilation inhomogeneity, a small but significant fall in FRC was observed when inspiratory flow rate was increased. This association of a fall in FRC with prolonged T_E is consistent with the prediction of others [8].

Although not statistically significant, $PaCO_2$ increased when T_E: T_I was increased, as observed by other investigators [4, 5, 10, 12, 23, 24]. This possibly could have been due to a difference in the distribution and mixing of inspired gas not detected by a change in MDN. However, it has been demonstrated theoretically, as well as in dogs, that increasing T_E: T_I alone may cause a rise in $PaCO_2$. When T_E is prolonged, the lung remains at a low volume longer during the respiratory cycle and the average $PaCO_2$ becomes greater (assuming the rate of CO_2 production and elimination remains the same). This higher average $PaCO_2$ during T_E is then reflected by a higher average $PaCO_2$. The same effect is associated with a lower FRC.

In conclusion, this study demonstrates increasing inspiratory flow rate in mechanically dependent patients can improve arterial oxygenation through mechanisms other than altering gas distribution and mixing. Further studies are necessary to determine

how breathing pattern and lung volume (operating point) may affect such determinants of gas exchange as cardiac output and shunt fraction, as well as ventilation inhomogeneity in patients with different types of lung pathology.

Appendix

Functional residual capacity and mean dilution number

In terms of the measured variables, the FRC can be estimated from a N_2 mass balance over n breaths:

$$\text{FRC} = \sum_{k=1}^{n} [V_E(k)\hat{F}_E(k) - V_I(k)\hat{F}_I(k)]/[F_0 - F_{\text{ET}}(k)]$$

where F_0 is the initial N_2 fraction in the lungs; $F_{\text{ET}}(k)$ is the end-tidal N_2 fraction of breath k; $\hat{F}_E(k)$, $\hat{F}_I(k)$ are the mixed-expired and mixed-inspired N_2 fractions of breath k; and $V_E(k)$ and the $V_T(k)$ are the expired and inspired volumes on breath k.

To quantify ventilation inhomogeneity from N_2 washout data, we must express these data in terms of appropriately scaled variables. The objective is to minimize the effects of variations in breathing patterns, lung volume (say, at the end of expiration), and inspired N_2 (or O_2) fraction during the washout. First, we define a scaled output for breath j:

$$X(j) = [F_{\text{ET}}(j) - F_I(\infty)]/[F_I^0(j) - F_I(\infty)]$$

and a scaled input for breath j:

$$U(j) = [\hat{F}_I(j) - F_I(\infty)]/[F^0(j) - F_I(\infty)]$$

where $F_I(\infty)$ is the asymptotically approached input value and $F^0(j)$ is the N_2 fraction in the lungs at the beginning at breath j.

The extent of dilution of gas on any breath j depends not only on $U(j)$, but also on the relative size of the tidal volume $V_T(j)$ with respect to the FRC:

$$\zeta(j) = V_T(j)/\text{FRC}.$$

For a washout over k breaths, we have derived [13] a modified dilution number, which represents the effective number of lung volume turnovers:

$$\text{DN}^*(k) = \sum_{j=1}^{k} \zeta(j)[1 - U(j)]/[1 + \zeta(j)U(j)].$$

Thus, a multibreath washout can be represented by a plot of $X(k)$ versus $\text{DN}^*(k)$.

To characterize multibreath washout data, we evaluate the zeroth and first moments (M_0 and M_1) of $X(k)$ as a function of $\text{DN}^*(k)$, i.e., $X[\text{DN}^*(k)]$. These moments are computed by summing over each breath k according to:

$$M_r = \sum_{k=1}^{n} X(k)[\text{DN}^*(k)]^r[\text{DN}^*(k) - \text{DN}^*(k-1)]$$

where the nth breath is such that $\min[\text{DN}^*(n)] \geq 8$. As an index of ventilation inhomogeneity, we use the mean dilution member:

$$\text{MDN} = M_1/M_0.$$

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