Determinants of oxygenation during high frequency oscillation

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Abstract. Two studies are reported in which the aim was to assesses whether oxygenation on transfer to or during high frequency oscillation (HFO) was influenced by the mean airway pressure (MAP) level. Sixteen infants, median gestational age 28 weeks, were recruited into the first study and 14 with a median gestational age of 29 weeks into the second. In the initial study, blood gases were measured immediately before and 30 min after transfer to HFO and comparison made of those infants in whom oxygenation did or did not improve. In the second study the infants were studied at two MAP levels, 2 and 5 cmH$_2$O, above that used during conventional ventilation (baseline MAP) and at two frequencies (10 and 15 Hz), arterial blood gases were measured after 20 min on each setting. In the initial study, on transfer to HFO, oxygenation improved by a median of 21 mmHg in eight infants, but was either unchanged or deteriorated ($n = 7$) in the other eight infants, the median impairment in oxygenation was by 17 mmHg. The infants in whom oxygenation improved had required a significantly higher MAP during conventional ventilation than the rest of the study group. In the second study, increasing the MAP from 2 to 5 cmH$_2$O above baseline resulted in a significant increase in oxygenation, which was significantly greater at 10 rather than 15 Hz. Infants whose MAP remained below 13 cmH$_2$O had impaired oxygenation during HFO compared to that experienced during conventional ventilation. The results of these two studies demonstrate that the MAP level during HFO is an important determinant of oxygenation.

Key words: High frequency oscillation – Mean airway pressure – Oxygenation – Respiratory distress

Introduction

High frequency oscillation (HFO) was first introduced to support infants with severe respiratory failure unrespon-

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sive to conventional ventilation [5]. Amongst such infants HFO proved to be the superior form of respiratory support, in that its use was associated with acute improvements in blood gases. A recent randomized study has demonstrated that HFO compared to conventional ventilation significantly reduces bronchopulmonary dysplasia (BPD) [2]. Despite that result, optimum settings to use during HFO remain to be defined.

Our aim was to assess if oxygenation on transfer to or during HFO was influenced by the mean airway pressure (MAP) level or frequency employed. Such data would provide guidance to the most appropriate settings to be used on initiation or HFO and thus is of relevance to future randomized clinical trials.

Methods

Consecutive infants who required mechanical ventilation were recruited into the two studies according to the availability of the oscillator. The two studies were performed consecutively. All infants had initially been ventilated conventionally using the Sechrist IV ventilator via oro-endotracheal tubes. Once the infant was stable for at least 2 h with blood gases within the desired range (pH 7.25–7.45, PO_2 50–70 mmHg and P_aCO_2 35–45 mmHg) [7] they were transferred to HFO using the SensorMedics 3100 oscillator.

The SensorMedics oscillator has an adjustable frequency, fractional inspiratory time, oscillatory amplitude and MAP. On transfer to the oscillator the inspired oxygen concentration was kept constant and a fractional inspiratory time of 0.30 was used, this remained unchanged throughout the study periods. The oscillatory amplitude was increased by adjusting the "displacement" or "power" of the oscillator, until visible chest wall movement was observed, this then remained unchanged during the study.

In the first study a frequency of 15 Hz and a MAP 1–2 cm$_2$O greater than that used on conventional ventilation at the time of recruitment (baseline MAP) was employed. Arterial blood gases were measured immediately prior to and 30 min after commencing HFO. Sampels were taken from indwelling arterial catheters sited for clinical purposes. Arterial blood pressure was also continuously measured. The arterial cannula (umbilical or peripheral) was connected to a Horizon 2000 monitor via a Medex Accuflush transducer. The monitor gives a continuous display of the arterial waveform and minute by minute changes in the systolic and diastolic blood pressure. The arterial waveform was considered to be damped if there was absence of a dicrotic notch und less than a 5 mm Hg difference between the systolic and diastolic blood pressure [4]. Systolic blood pressure was recorded only from traces which were non-damped. In infants in whom the arterial waveform was damped, their systolic blood pressure was monitored non-invasively with an oscillometer (Horizon 2000).

In the second study a frequency of 10 or 15 Hz was used, the frequency a particular infant received first was chosen in random order. The infant was studied at that initial frequency at two MAP levels; 2 and 5 cmH₂O above the baseline MAP. The infant was then transferred to the alternative frequency and again studied at the two MAP levels. Each oscillatory setting was maintained for 20 min. Blood gases were checked from an indwelling arterial catheter sited for clinical purposes immediately prior to commencing HFO and at the end of each 20 min period.

Throughout both studies, oxygenation was monitored continuously either by an indwelling arterial catheter (Searle) or a transcutaneous electrode (Draeger). If this monitoring indicated the P_aO_2 to have fallen below 40 mmHg, the inspired oxygen concentration was immediately increased and the infant returned to conventional ventilation.

Statistical analysis

In the first study comparison was made of infants in whom oxygenation improved on transfer to HFO with those in whom oxygenation deteriorated or remained unchanged. Differences between the two groups were assessed for statistical significance using the Wilcoxon rank sum test. The systolic blood pressure immediately before and 30 min after commencing HFO was compared and differences assessed using a paired Wilcoxon rank sum test. In the second study differences in oxygenation resulting from each change in oscillatory setting and in the change in oxygenation on increasing the MAP level from 2 to 5 cmH₂O above baseline at 10 compared to 15 Hz were assessed for statistical significance using the paired Wilcoxon rank sum test. Differences in MAP between infants in whom oxygenation was improved or impaired during HFO at the highest MAP level (baseline + 5 cmH₂O) compared to that during conventional ventilation were assessed for statistical significance using the Wilcoxon rank sum test.

Patients

In the first study 16 infants were included. Their median gestational age was 28 weeks (range 23–37), birth weight 678 g (range 544–2580) and postnatal age 4.5 days (range 1–26). All had initially suffered from respiratory distress. In addition one infant, the most mature of the study population, had a diaphragmatic hernia and was studied post-operatively. At the time of study 4 infants were

Table 1. Comparison of infants in whom oxygenation improved during HFO (group A) with the the remainder of the study population (group B)

Median (range)	Group A	Group B
n	8	8
Gestational age (weeks)	28	26
	(23–31)	(23–37)
Birth weight (kg)	0.626	0.859
	(0.590–1.678)	(0.544–2.580)
Postnatal age (days)	8	3
	(1–26)	(1–7)
Ventilatory settings during conventional ventilation:		
FiO₂	0.71	0.35
	(0.34–0.98)	(0.22–0.78)
MAP (cmH₂O)	11.6	7
	(8–23.2)	(4.8–11)

older than 7 days of age, they all had the chest radiograph appearance of Type I chronic lung disease (CLD) [6].

In the second study 14 patients were included. Their median gestational age was 29 weeks (range 23–37, birth weight 802 g (range 520–2800) and postnatal age 1.5 days (range 1–23). All the infants had initially suffered from respiratory distress syndrome. At the time of the study three infants were older than 4 days of age. During HFO, 8 infants were studied initially at a frequency of 10 Hz and 6 infants at a frequency of 15 Hz (Table 2).

The study was approved by the King's College Hospital Ethics Committee.

Results

During the study periods, continuous monitoring did not indicate any infant to require an increase in the inspired oxygen concentration.

First study

Oxygenation improved in eight infants after 30 min on HFO (group A), the median increase in oxygenation was 21 mmHg (range 5–49). Oxygenation deteriorated in seven infants and remained unchanged in the remaining infant (group B). The median change in oxygenation in group B overall was −16.5 mmHg (range 0 to −39 mmHg). Comparison of groups A and B revealed no significant difference in their gestational age, birth weight or postnatal age. Oxygenation improved in all four infants whose postnatal age was greater than 7 days. Group A, however, had required a significantly higher inspired oxygen concentration ($P < 0.02$) and mean airway pressure ($P < 0.01$) prior to commencing HFO than group B (Table 1) (Fig. 1). Improvement in oxygenation was associated with increased carbon dioxide elimination in four infants. The median overall decrease in P_aCO_2 in group A was 2 mmHg (range from a decrease of 21 mmHg to an increase of 7 mmHg). The median overall increase in P_aCO_2 in group B was 5 mmHg (range from a decrease of 26 mmHg to an increase of 38 mmHg). There was no significant change in blood pressure during the study period and no infant received blood pressure support. The median blood pressure prior to commencing HFO was 52 mmHg (range 32–80) and after 30 min of HFO was 50 mmHg (range 37–81).

Second study

In the group overall, on initially changing from conventional ventilation to HFO at a MAP level of baseline + 2 cmH₂O, there was no significant change in oxygenation. The median P_aO_2 was 56 mmHg (range 38–84 mmHg) immediately prior to transfer to HFO and was 54 mmHg (38–109 mmHg) after 20 min at the first MAP setting. During HFO increasing MAP from 2 to 5 cmH₂O above baseline brought about a significant increase in oxygenation to a median P_aO_2 of 63 mmHg (range 37–108 mmHg), $P < 0.01$. Increasing the MAP from 2 to 5 cmH₂O above baseline resulted in a significant increase in oxygenation in infants studied initially at 10 Hz but not at 15 Hz (Table 2) ($P < 0.05$). In the study group overall, the change in oxygenation on increasing the MAP level from 2 to 5
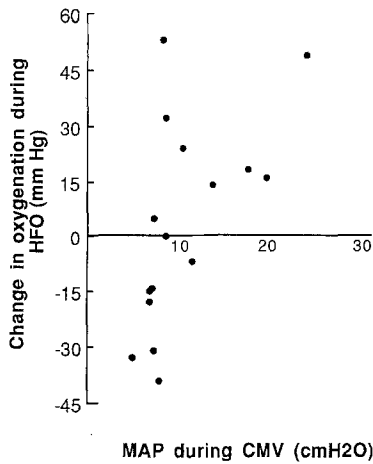
Fig. 1. Change in oxygenation resulting from transfer from conventional ventilation (CMV) to HFO (individual data demonstrated)
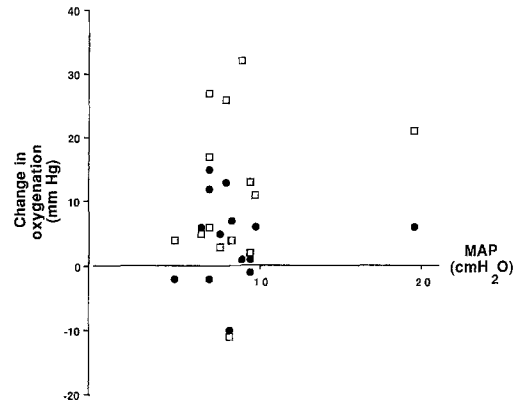

Fig. 2. The change in oxygenation during HFO on increasing the MAP level from 2 to 5 cmH$_2$O above the baseline MAP related to the baseline MAP (individual data demonstrated). ■ 10 Hz; ● 15 Hz

Table 2. Oxygenation and MAP at the initial randomized frequency

Baseline MAP (cmH$_2$O)	Level of oxygenation (mmHg)		
	A	B	C
I 10 Hz			
5	84	50	54
7	53	42	48
7.6	54	46	49
8.3	69	70	73
7.0	66	46	63
19.0	64	77	108
9.7	54	81	92
8.9	50	75	107
Median	64	70	73
(range)	(50–84)	(42–81)	(48–108)
II 15 Hz			
7.0	67	49	61
6.5	56	41	47
8.2	77	109	99
8.0	38	80	93
9.4	51	51	77
11.0	53	54	55
Median	54	52	58
(range)	(38–77)	(38–109)	(37–79)

Level of MAP: A – baseline i.e. during conventional ventilation
B – 2 cmH$_2$O above baseline
C – 5 cmH$_2$O above baseline

cmH$_2$O above baseline was greater when the 14 infants were studied at 10 rather than 15 Hz, $P < 0.05$, (Fig. 2).

Six infants had impaired oxygenation during HFO, even at MAP level of baseline + 5 cmH$_2$O, compared to that experienced during conventional ventilation. These six infants had a significantly lower baseline MAP than the rest of the study population, a median of 7 cmH$_2$O (range 5–7.6 cmH$_2$O) compared to a median of 9.2 cmH$_2$o (range 8–19 cmH$_2$O), $P < 0.01$. In the six infants with impaired oxygenation, even increasing their MAP 5 cmH$_2$O above baseline, still meant that their MAP was

below 13 cmH$_2$O. All eight infants in whom oxygenation improved during HFO, had a MAP level, when increased by 5 cmH$_2$O above their baseline, greater than or equal to 13 cmH$_2$O ($P < 0.005$, Fisher's exact test).

Discussion

In our first study, transfer to HFO had a variable effect on blood gases. In 50% of the infants, however, transfer to HFO resulted in an improvement in oxygenation which was not associated with significant carbon dioxide retention. HFO has been previously demonstrated to improve gas exchange in the acutely injured lung [9]. We, however, found no relationship between the acute success of HFO and postnatal age. Indeed, oxygenation improved on transfer to HFO in all the infants we studied who were older than 1 week of age. The latter group all suffered from Type I CLD, the characteristic feature of the chest radiograph appearance of that form of CLD is hazy lung fields [6]. In such infants, the higher MAP used during HFO would be likely to produce more uniform inflation, hence improving gas exchange.

A concern regarding HFO has been that its use may be associated with cardiovascular compromise. In the first study we thus monitored the infants' blood pressure to assess if any experienced such a side-effect. We found no significant difference in their blood pressure prior to and 30 min after commencing HFO. This suggestes that although we increased MAP on transfer to HFO, this had not resulted in hyperinflation of sufficient degree to interfere with venous return or cardiac output. The lack of cardiovascular side-effects may be explained by the type of oscillator used. The SensorMedics oscillator has an active inspiratory and an active expiratory phase, making hyperinflation less likely. In addition, it has an adjustable fractional inspiratory time and throughout the study an inspiratory time of 30% was used. The greater proportion of the cycle devoted to expiration also reduced the likelihood of hyperinflation [3].

On transfer to HFO in our initial study improvements in oxygenation occurred in those infants who, during conventional ventilation, had required the highest MAP

and inspired oxygen concentration. This would suggest that HFO was likely to be successful in infants with the most severe respiratory distress. We had followed the recommended policy [2] of increasing MAP by 1–2 cmH$_2$O on changing from conventional ventilation to HFO. Infants with severe respiratory distress are likely to have atelectatic alveoli. Thus our policy of increasing MAP in such patients would result in more uniform inflation and distribution of ventilation, with an improvement in ventilation-perfusion matching. In certain infants, however, transfer to HFO despite increasing MAP by 1–2 cmH$_2$O resulted in impairment of oxygenation; interestingly the infants so affected had required a MAP of less than 8 cmH$_2$O during conventional ventilation. There are two possible explanations for their poor outcome. Firstly, the low level of MAP required by the infants suggests they may have had mild respiratory distress and relatively normal lung function. Increasing MAP even only by a maximum of 2 cmH$_2$O could have resulted in lung overdistension with cardiorespiratory compromise and impairment of oxygenation. Conversely, although the infants apparently had relatively mild disease, this could have been associated with low lung volume, in which case although we had increased MAP on transfer to HFO, the level was still inadequate to recruit sufficient alveoli to improve oxygenation. The results of our second study suggest the latter hypothesis was the correct one.

The results of the second study demonstrate that, as has been found in animals [9], MAP is an important determinant of oxygenation during HFO of infants. In all but 1 of the 14 infants studied on HFO, increasing the MAP from 2 to 5 cmH$_2$O above baseline was associated with an improvement in oxygenation. This beneficial effect was also seen in infants who had been on a low MAP, less than 8 cmH$_2$O during conventional ventilation (Table 2). Thus, the likely explanation for the oxygenation impairment on transfer to HFO seen in our first study of the infants who had a low baseline MAP was that an increase in MAP of 2 cmH$_2$O had been insufficient to recruit adequate numbers of alveoli to improve gas exchange. Our results suggest it is essential to attain a critical MAP level if HFO is to be associated with superior oxygenation compared to that experienced during conventional ventilation. This hypothesis is supported by an earlier finding of a lack of improvement in oxygenation on transfer to HFO when a MAP level of approximately 8 cmH$_2$O was used [8]. The present data would suggest the critical level may be 13 cmH$_2$O.

Several authors [8, 10] have expressed concern that gas trapping or auto-positive end expiratory pressure may occur during HFO; this complication, however, seems unlikely to occur at the critical MAP level we demonstrated. Bryan and Slutsky [1] were unable to demonstrate trapping in normal or lung-lavaged rabbits studied at 15 or 25 Hz or in infants with respiratory distress syndrome studied at 15 Hz and they were only able to produce gas trapping by operating at unusually low, rather than high, MAP levels. Their explanation for this finding was that at the low pressures, lung volume is reduced and choke points develop limiting maximal expiratory flow.

We found the change in oxygenation on increasing MAP from 2 to 5 cmH$_2$O above baseline was significantly higher at 10 compared to that seen at 15 Hz. These two frequencies were chosen as they had both previously been used in clinical studies [2, 11]. The function of the oscillator we employed may explain the apparent relationship of oxygenation and frequency we demonstrated. The SensorMedics oscillator incorporates a variable fractional inspiratory time. Throughout the present study an inspiratory time of 0.30 was used, this meant that decreasing the frequency from 15 to 10 Hz allowed greater time for movement of the diaphragm. The likely consequence would be an increase in the delivered volume which may have influenced oxygenation.

We conclude that MAP is an important determinant of oxygenation during HFO in infants. Our results suggest that a critical level of MAP must be used during HFO if impairment of gas exchange is to be avoided. For infants with relatively mild disease, however, increasing MAP to the necessary level, might result in the very long-term respiratory morbidity one had hoped, by using HFO, to avoid [2].

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