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Effects of short term high frequency negative pressure ventilation on gas exchange using the Hayek oscillator in normal subjects

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Abstract

Background – **The Hayek oscillator is a negative pressure cuirass that can operate at a range of frequencies to provide ventilation, and is a technique which could potentially be used on a general ward. This study examined the effect of different frequencies and different ranges of inspiratory and expiratory pressures on gas exchange, respiratory rate, and blood pressure in normal subjects.**

Methods – **Eight normal subjects received five minute periods of ventilation using the Hayek oscillator at five different frequencies, and a combination of two spans of inspiratory and expiratory pressures and two mean chamber pressures. A "sham" or control period was also performed at each frequency. Measurements were made of changes in gas exchange, spontaneous respiratory rate, and blood pressure before and after ventilation.**

Results – **There was significant intersubject variation in all results, independent of their height and weight. "Sham" settings acted as true controls in terms of gas exchange, but produced a fall in respiratory rate at 30 oscillations/min. The lower oscillatory frequencies of 30 and 60 oscillations/min produced the greatest increase in oxygenation, decrease in end tidal carbon dioxide pressure, and decrease in spontaneous respiratory rate. These effects were most significant at higher spans of pressure and were different from "sham" settings. No adverse effects were observed on blood pressure.**

Conclusions – **The Hayek oscillator can provide assisted ventilation for short periods in normal conscious subjects with no adverse side effects on blood pressure. Maximal changes in gas exchange and a significant reduction in the spontaneous respiratory rate are seen when a combination of lower frequencies (30 and 60 oscillations/min) and higher spans of pressure are used.**

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Patients admitted to hospital with acute exacerbations of chronic obstructive airways disease may require further ventilatory assistance if they develop respiratory failure that fails to respond to standard treatment. The Hayek oscillator is a new method of assisted ventilation which uses a high frequency negative pressure cuirass and is potentially suitable for use on this group of patients on the general ward. The decision to institute conventional mechanical ventilation with endotracheal intubation currently requires admission to the intensive care unit and the possibility of associated complications of positive pressure ventilation.[1] Recent attention has focused on techniques of non-invasive ventilation using positive pressure delivered by a nasal mask or facemask. Some patients find this technique claustrophobic and difficult to tolerate either because of leakage from the mouth when using a nasal mask,[2] or because of excessive pressure and difficulty in managing secretions when using a facemask.[3] The technique can be costly in terms of nursing and supportive care.[4]

Initial work on the Hayek oscillator described it as a method of ventilation in cats, before and after saline lavage, as a model for patients with the adult respiratory distress syndrome.[5] It has also been used in two uncontrolled studies to provide ventilation in normal subjects during anaesthesia for microlaryngeal surgery,[6] and for short periods in stable hypercapnic patients with chronic obstructive lung disease using measurements of end tidal carbon dioxide pressure.[7]

In this controlled study the Hayek oscillator was used in normal subjects to define which aspects of this method of ventilation offer most improvement of gas exchange and reduce the spontaneous respiratory rate. In addition, we examined the effects on blood pressure which can be affected adversely by positive pressure ventilation.

Methods

The Hayek oscillator consists of a plastic cuirass (available in differing sizes) which connects via wide bore tubing to a power unit consisting of two pumps – a vacuum pump which creates a baseline negative pressure with a second pump superimposing oscillating pressures. There are four variables that can be altered during the use of the machine: frequency of oscillation, ratio of inspiratory to expiratory time, inspiratory and expiratory pressures. By altering these variables different mean negative chamber pressures and different spans of pressure can be created (where span is the difference between maximum inspiratory and maximum expiratory pressure).

Eight normal subjects gave informed consent to participate in the study which was approved by the Central Oxford Research ethics committee. Subjects were non-smokers, aged from 25 to 45 years, with no history of respiratory disease. Each subject was fitted with a suitable cuirass covering the chest wall and abdomen whilst semi-recumbent or sitting on a bed. Each subject completed the protocol over the course of two separate days during which they received, in random order, a total of 25 periods of ventilation using a combination of five different frequencies (30, 60, 90, 120, and 180 oscillations/min), two spans (low and high) and two mean chamber pressures (-4 and -8 cm H_2O). As 25 different combinations were examined in each subject, short periods of ventilation lasting five minutes only were used in order to limit the total length of the protocol. Two spans were used according to each individual subject's weight because of the manufacturer's recommendation that heavier subjects would need wider spans than lighter subjects. For subjects weighing less than 70 kg spans of 20 cm H_2O (low) and 30 cm H_2O (high) were used, and for those heavier than 70 kg spans of 30 cm H_2O (low) and 40 cm H_2O (high) were used.

At each frequency there was a "sham" or control period of ventilation (span 10 cm H_2O, mean chamber pressure 0 cm H_2O). A ratio of inspiratory to expiratory time of 1:1 was used throughout the trial. Each period of ventilation lasted for five minutes and was separated by a five minute rest period, at the end of which resting oximetry and end tidal carbon dioxide measurements had returned to baseline. Subjects were given no specific instructions about how to breathe once the cuirass was attached. However, during the 5–10 minutes that the cuirass was being fitted subjects had an opportunity to adjust to the sensation of the cuirass when operating to ensure that there were minimum air leaks. During the study they were allowed to listen to music from headphones in order to distract from the noise of the pump. All signals were monitored continuously onto a digital recorder. Throughout the trial each subject inhaled nitrogen enriched air. Nitrogen at a high flow rate (15 l/min with total flow to the face in excess of 400 l/min) was connected to a large volume Venturi mask specially adapted so that no entrainment of room air could take place through the exhalation holes in the mask that would have raised the oxygen concentration. An entrainment ratio was selected for each subject to give a resultant inspired oxygen concentration of 18% and an arterial saturation of about 90%. A sampling catheter was positioned just inside the only opening port of the mask to measure oxygen concentration at a point where any entrainment of air from the surrounding environment would be detected; this was continuously monitored with an oxygen analyser (OA 272, Taylor Servomex) and no rise or fluctuations in oxygen concentration were seen either during or between periods of ventilation.

A pulse oximeter (Biox 3700, Ohmeda) was attached to the forefinger of either hand, and from these recordings steady state values at the time of onset of ventilation and at the end of each period of ventilation were taken. These reduced oxygen saturation readings, on a steeper part of the oxygen desaturation curve, enabled changes in oxygenation to be detected more easily. Oxygen saturation readings were then converted into theoretical oxygen tensions using a standard haemoglobin oxygen dissociation curve[8] and the change in oxygenation (ΔO_2) with each ventilatory setting was calculated.

A nasal catheter was positioned within the external nares in order to measure expired carbon dioxide (4721A Capnometer, Hewlett Packard), and a sample aspiration rate used that was low enough not to entrain air or nitrogen that might dilute expired carbon dioxide. Subjects were trained to perform a forced expiratory manoeuvre, from within the tidal volume range, before and after each period of ventilation. Readings were then taken from the end of each recorded end tidal alveolar plateau to give measurements of end tidal carbon dioxide pressure. The change in end tidal carbon dioxide measurements (ΔCO_2) for each ventilatory setting was calculated.

Respiratory rate was measured by two methods: (1) oronasal airflow using a thermistor attached above the upper lip, and (2) an inductance plethysmography belt worn around the upper chest so that it did not touch the sides of the cuirass. The thermistor had a slow response time and damped out the oscillations due to the high frequency cuirass, allowing spontaneous breaths to be easily recognised. The number of spontaneous respirations during the last three minutes of each period of ventilation were counted. Arterial beat to beat blood pressure was recorded from the third finger of each hand with the hand lying flat on the bed. An infrared plethysmographic clamp method was used (Finapres, Ohmeda). Systolic, diastolic, and mean arterial blood pressures were measured for the nine seconds before and prior to the end of each period of ventilation, and the change in blood pressure (ΔBP) was calculated. A transducer attached to the chamber of the cuirass allowed a continuous recording of chamber pressure to be made from which the frequency of oscillation, the span of pressures, and the mean chamber pressures could be measured. Such measurements were made over the last three minutes of each period of ventilation.

STATISTICAL ANALYSIS

Statistical analysis was performed on a personal computer using the SAS suite of computer programs (SAS Institute, Cary, North Carolina, USA). Each outcome measure (ΔO_2, ΔCO_2, respiratory rate, and ΔBP) was analysed separately for factors affecting it. To establish that "sham" settings were acting as true controls these results were initially explored in two ways. Firstly, analysis of variance (ANOVA) with Duncan's post hoc analysis was performed to look for differences between subjects and frequencies whilst receiving "sham" settings.

Secondly, Student's t tests were used to look for significant changes from zero in any of the outcome measures at each of the five frequencies, with Bonferroni's correction for multiple comparisons. Analysis of variance was then performed on all data (including "sham" results) using a general linear models procedure; the variance of each outcome measure (ΔO_2, ΔCO_2, respiratory rate, and ΔBP) was separately apportioned to differences between subjects, span, frequency, and chamber pressure. Duncan's post hoc analysis was used to explore which groups were significantly different from the others. In the results section all results are significant with $p<0{\cdot}05$ unless otherwise stated, and r^2 values only are quoted.

Results

VENTILATORY SETTINGS

All programmed frequencies were obtained and the actual mean chamber pressure achieved for "sham" settings was $-0{\cdot}87$ (0·08) cm H_2O, for a setting of -4 cm H_2O it was $-4{\cdot}76$ (0·25) cm H_2O, and for a setting of -8 cm H_2O it was $-8{\cdot}26$ (0·29) cm H_2O. Wider spans were

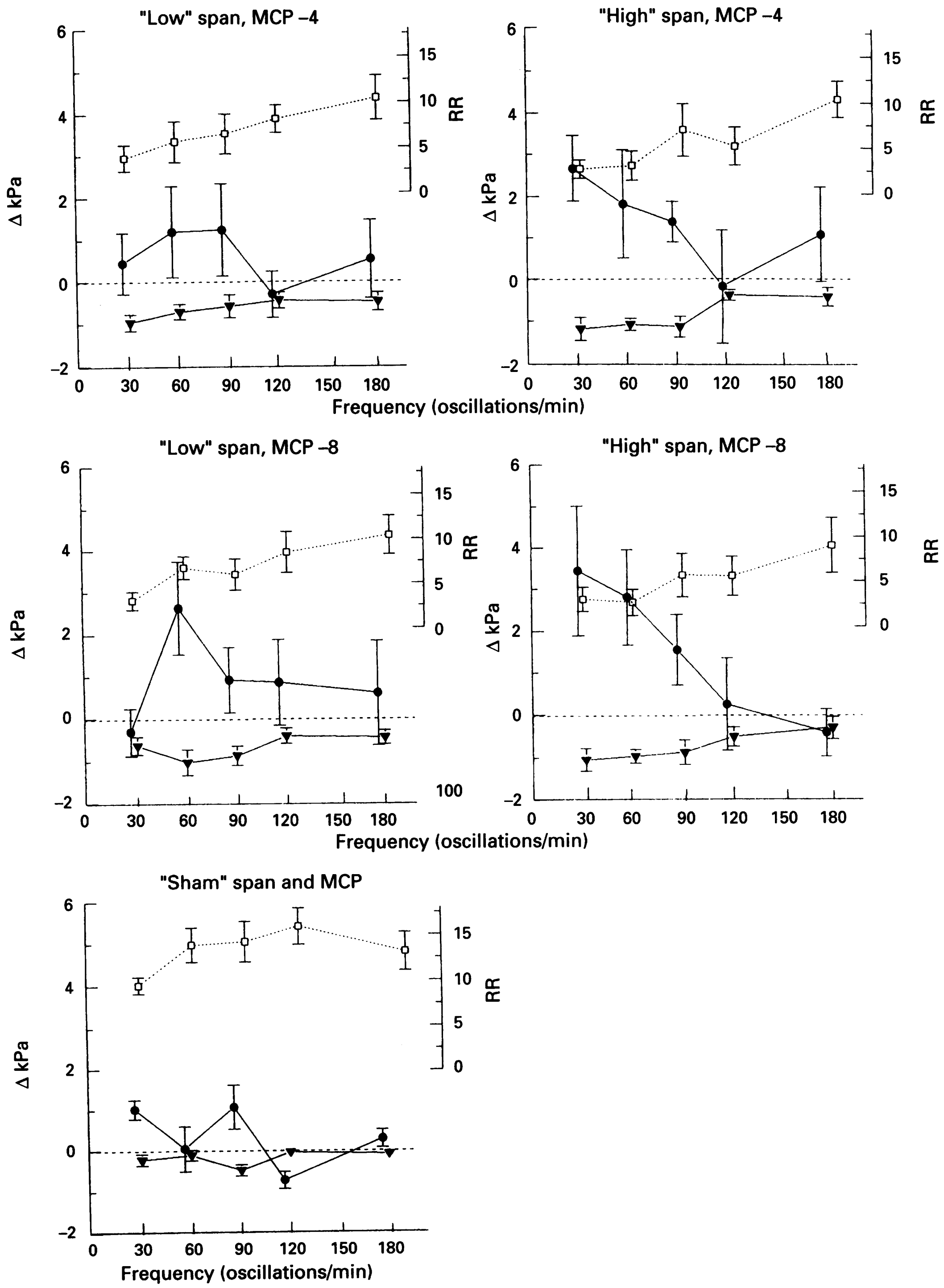

Figure 1 Mean (SE) changes (ΔkPa) in estimated oxygen tension (●), end tidal carbon dioxide concentration (▼), and the respiratory rate (□, RR, breaths/min) at different combinations of span (low and high), mean chamber pressure (MCP, cm H_2O), and frequency.

Table 1 Mean values for ΔO_2, ΔCO_2, and respiratory rate at five frequencies

Frequency (osc/min)	*ΔO_2 (kPa) (mean)*	*Duncan grouping*	*ΔCO_2 (kPa) (mean)*	*Duncan grouping*	*Respiratory rate (mean)*	*Duncan grouping*
30	1·46	A	−0·81	A	4·4	A
60	1·70	A	−0·78	A	6·4	B
90	1·23	A B	−0·79	A	8·3	C
120	−0·02	C	−0·36	B	8·7	C
180	0·40	B C	−0·35	B	10·7	D

Means with different letters are significantly different ($p<0·05$, ANOVA and Duncan's post hoc analysis).

more difficult to achieve at lower frequencies, especially in heavier subjects, and were sometimes less than 90% of the desired span.

GAS EXCHANGE

"Sham" settings

"Sham" ventilation had essentially no effect on gas exchange although ΔO_2, but not ΔCO_2, varied slightly with frequency, but in a non-ordered fashion, ($r^2 = 0·3$, fig 1). However, when ΔO_2 and ΔCO_2 were compared against baseline values there were no significant differences at any level. The "sham" settings were therefore acting as a true control for gas exchange at each individual frequency.

All ventilatory settings

When all data, including "sham" results, were analysed to look at the different effects caused by altering frequency, span, and chamber pressure, a significant variation between subjects was observed for ΔO_2 ($r^2 = 0·2$) and ΔCO_2 ($r^2 = 0·25$). This variation was not related to body weight. Alteration of the frequency of oscillation had a highly significant effect on both ΔO_2 ($r^2 = 0·11$) and ΔCO_2 ($r^2 = 0·15$). Lower frequencies of 30 and 60 oscillations/min gave greater changes than the three higher frequencies (table 1). Span had a small but just significant effect on ΔO_2 ($r^2 = 0·02$), and had similar effect on ΔCO_2 data which was just above the 5% significance level. A "high" span was shown to produce a significantly greater rise in ΔO_2 than "sham" (table 2). There was also a small but significant interaction between frequency and span ($r^2 = 0·07$), with use of a "high" span producing a greater effect at the lower frequencies (fig 1). Alteration of mean chamber pressures had no significant effect on either ΔO_2 or ΔCO_2.

RESPIRATORY RATE

"Sham" settings

Respiratory rate (breaths/min) varied significantly between subjects ($r^2 = 0·51$) and with frequency ($r^2 = 0·15$, fig 1). All "sham" respiratory rates were below the resting respiratory rate of 18·3 (1·6) breaths/min measured with the cuirass attached, but non-operational. There were no periods of apnoea observed. At the lowest frequency of 30 oscillations/min, despite a significant fall in the respiratory rate to 9·5 (0·9) breaths/min, there was a non-significant increase in ΔO_2 of 1·02 (0·24) kPa and a decrease in ΔCO_2 of 0·22 (0·14) kPa. The sensation alone of the cuirass oscillating at that frequency therefore caused a reduction in respiratory rate, with gas exchange presumably being sustained by an increased tidal volume.

All ventilatory settings

Respiratory rates were found to vary significantly between subjects ($r^2 = 0·25$), with different frequencies ($r^2 = 0·02$, fig 1). All subjects had apnoeic periods of varying lengths at a variety of ventilatory settings, the longest lasting 90 seconds. Again, it was the lower frequencies and the highest spans which were associated with the greatest reduction in respiratory rate – the same ventilatory settings that had had the most significant effect on gas exchange. "High" and "low" spans were significantly different from "sham" and from each other (table 2). Alteration of mean chamber pressure again had no significant effect on respiratory rate.

BLOOD PRESSURE

For "sham" and all "active" ventilatory settings, analysis of variance of changes in systolic, diastolic, and mean arterial blood pressures from before and after ventilation showed significant intersubject variation only. No effect was exerted by frequency, span, or chamber pressure. During "active" settings mean arterial blood pressure fell in five subjects with the maximum mean fall of 6 mm Hg; the maximum mean blood pressure rise in the three remaining subjects was 11 mm Hg.

Discussion

Our results have shown that ventilation with the Hayek oscillator in normal subjects for five minute periods can produce favourable changes in gas exchange at frequencies of 30, 60, and 90 oscillations/min, in contrast to control or "sham" periods of ventilation. At these frequencies the wider the span used, the greater the increase in ΔO_2 and decrease in ΔCO_2, and the greater the corresponding decrease in respiratory rate. All subjects expressed a

Table 2 Effect of span at all frequencies and mean chamber pressures on ΔO_2, ΔCO_2, and respiratory rate in comparison with "sham" (control)

Span	*ΔO_2 (kPa) (mean)*	*ΔCO_2 (kPa) (mean)*	*Respiratory rate (mean)*
"Sham"	0·34	−0·19	13·4
"Low"	0·78	−0·75*	7·2*
"High"	1·44*	−0·75*	5·5*

* Significantly different from "sham" ($p = 0·05$, ANOVA and Duncan's post hoc analysis).

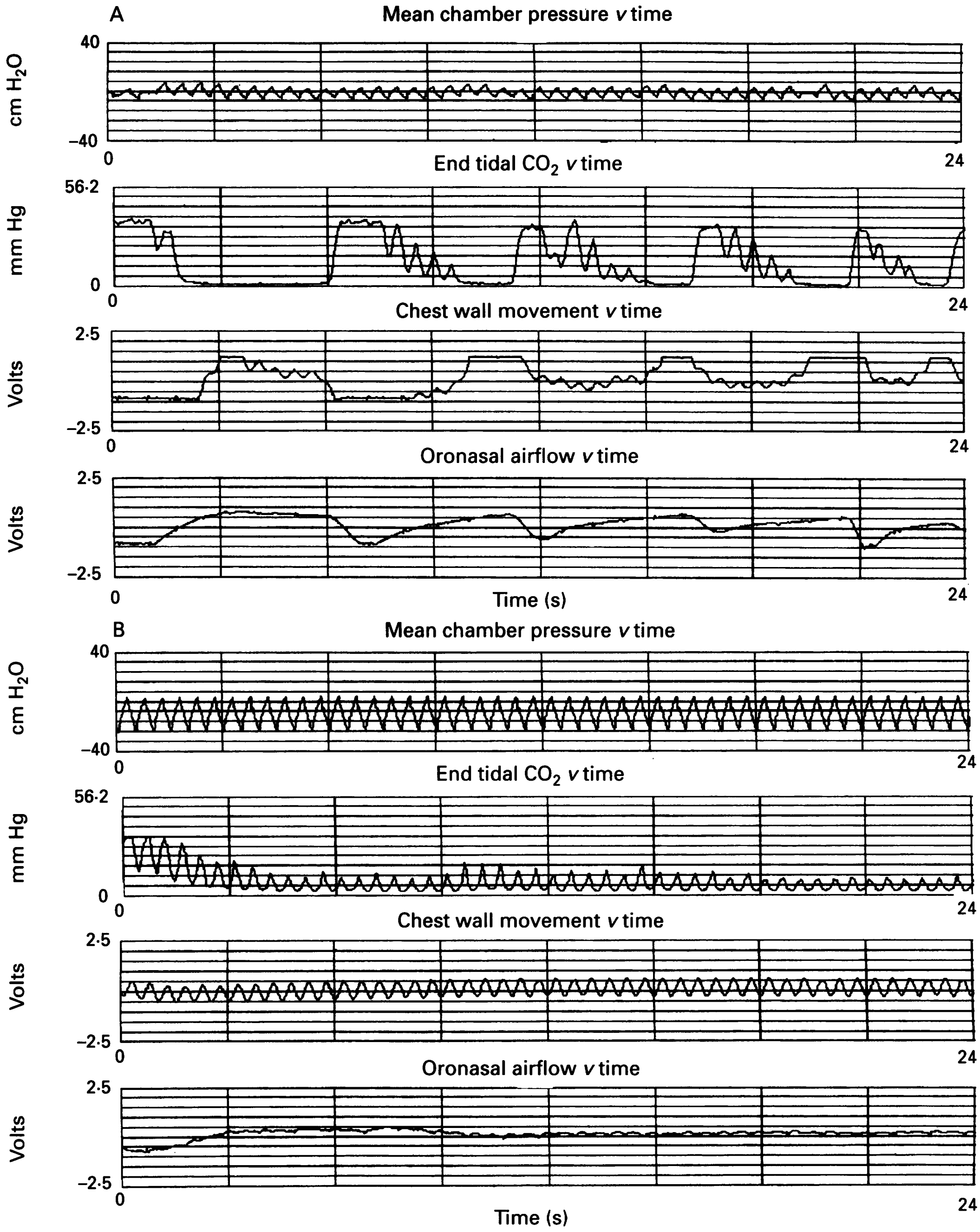

Figure 2 Different pattern of respiration seen with (A) "sham" ventilation at 120 oscillations/min (span 10 cm H_2O, mean chamber pressure 0 cm H_2O) and (B) the occurrence of an apnoeic period with "active" ventilation at 120 oscillations/min (span 30 cm H_2O, mean chamber pressure −8 cm H_2O) at the same frequency. Tracings of recorded mean chamber pressure, end tidal carbon dioxide concentration, chest wall movement measured by inductance plethysmography and oronasal airflow are shown.

preference for these lower rates of ventilation in terms of comfort. The two mean chamber pressures used in this study were not significantly different from each other in their effect on gas exchange or respiratory rate. There was significant intersubject variability in all parameters with use of the cuirass, and this was independent of their height or weight. The application of the cuirass using "sham" settings caused a reduction in respiratory rate, without altering gas exchange, in comparison with the resting respiratory rate when the cuirass was non-operational. This occurred at all frequencies and was most pronounced at 30 oscillations/min. As well as a further reduction in respiratory rate at all frequencies during "active" periods of ventilation, most subjects exhibited periods of apnoea of varying lengths, of which they were sometimes aware, when the cuirass was clearly taking over all ventilation (fig 2). This pattern has been observed in other techniques of high frequency ventilation[9] but the mechanisms whereby a reduction in respiratory rate or apnoea can occur are not clear; they may be due to hypocapnia causing a centrally mediated reduction in respiratory rate or to stimulation of pulmonary chest wall receptors.[10 11] The reduction in respiratory rate seen in these normal subjects whilst maintaining gas exchange at low frequencies of oscillation implies that gas exchange was taking place during respiratory muscle rest. If these findings can be reproduced in patients with acute respiratory failure in whom respiratory muscle fatigue contributes significantly to clinical deterioration, then any reduction in respiratory rate with consequent respiratory muscle rest should be of clinical benefit.

High frequency ventilation usually refers to artificial ventilation delivered at a rate of 2 Hz (120 oscillations/min) or above, either by means of an oscillating source of gas via an endotracheal tube or mouthpiece or by rapid thoracic or whole body surface compression. Work aimed at defining mechanisms of gas exchange has therefore been centred on these higher frequencies[12] where the small tidal volumes involved are often a fraction of the anatomical dead space. As with normal breathing, the two basic mechanisms of gas exchange in the lung are direct alveolar ventilation by bulk convection and molecular diffusion; other modes of gas transport involved are convection by high frequency "pendelluft", convection dispersion due to asymmetric inspiratory and expiratory velocity profiles, and longitudinal dispersion due to turbulent flow. In this study the Hayek oscillator functioned optimally at frequencies lower than 120 oscillations/min, and at 30 oscillations/min would seem to be inducing gas exchange conventionally (the only real difference from a conventional cuirass being that the expiratory phase is actively controlled and does not rely on passive lung recoil). At 60 and 90 oscillations/min it is possible that some of the additional modes of gas transport mentioned above are being recruited.

As a method of ventilation for patients with chronic obstructive airways disease the Hayek oscillator has potential advantages over nasal or facemask techniques; in particular, the oropharynx is easily accessible for the management of secretions. Clearance of mucus has also been shown to be enhanced by high frequency oscillation at higher frequencies of 3–17 Hz, possibly due to a reduction in sputum viscosity and enhancement of ciliary clearance.[13] Whether ventilation at lower frequencies has a similar effect is not known. Whilst the cuirass is attached, a pause in ventilation can easily be taken to allow patients to communicate with staff and to take oral fluids. In normal subjects, no harmful side effects were seen with the use of the cuirass and blood pressure was not adversely affected. The disadvantages were that the cuirass was sometimes difficult to fit, especially in larger subjects, when two operators were often needed to ensure a tight enough seal to minimise air leaks and thus achieve adequate pressures. The machine was also noisy, and while this would not be a problem when used in a sideroom, it could potentially cause disruption to other patients on a general ward.

The recommendations which can be made about the possible future use of the cuirass in patients with obstructive airways disease are that a combination of low frequency and high span should probably be used. However, the hyperinflation and increased lung compliance of these patients may mean that much higher spans and more negative mean chamber pressures than those used in this study will be needed. Our experience in normal subjects showed that these settings were the most difficult to achieve. We found significant variation between normal subjects, independent of their height or weight. It is therefore difficult to predict in which subjects the Hayek oscillator could be successfully used.

In conclusion, the Hayek oscillator can assist ventilation in normal conscious subjects for short periods of time, and exerts its maximal effect on gas exchange and reducing respiratory frequency at lower frequencies. It may offer a new method of assisted ventilation which could be used for patients with acute exacerbations of chronic obstructive airways disease in whom a controlled trial should be performed.

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