Original articles

Changes in oxygenation in mechanically ventilated critically ill patients following hyperbaric treatment

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Key words
Hyperbaric oxygen therapy, ventilators, pulmonary function, physiology, right-to-left shunt, clinical audit

Abstract
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Background: Some ventilated intensive care unit (ICU) patients may experience reduced oxygenation following hyperbaric oxygen treatment (HBOT).
Methods: In a prospective, single-centre, observational study, we documented changes in oxygenation and the need for associated changes in ventilator settings in 25 consecutive, mechanically ventilated ICU patients immediately post-treatment and 1, 2, 3 and 6 hours following 61 HBOT sessions. The primary outcome measure of oxygenation was the ratio of arterial partial pressure of oxygen (P_aO_2) against the level of inspired oxygen (F_iO_2), P_aO_2/F_iO_2.
Results: Following HBOT, the P_aO_2/F_iO_2 ratio decreased by 27% on return to ICU ($P < 0.001$, 95% confidence intervals (CI) 20.6 to 34.2); 22% at 1 hour post-HBOT ($P < 0.001$, 95% CI 15.1 to 28.6); and 8% at 2 hours post ($P = 0.03$, 95% CI 0.8 to 14.4). The ratio showed no significant differences from pre-HBOT at 3 and 6 hours post-HBOT. P_aO_2/F_iO_2 ratio changes necessitated adjustments to ventilation parameters upon return to ICU following 30 of 61 HBOT sessions in 17 out of the 25 patients. The most common ventilation parameter altered was F_iO_2 ($n = 20$), increased by a mean of +0.17 (95% CI 0.11 to 0.23) above baseline for two hours following HBOT.
Conclusions: Following HBOT, oxygenation is reduced in a majority of mechanically ventilated ICU patients and requires temporary alterations to mechanical ventilation settings. Further study to identify predictive characteristics and to determine causation for those at risk of needing ventilation alterations is required.

Introduction

Hyperbaric oxygen therapy (HBOT) is recognised for the treatment of a variety of conditions for which recipients may require concurrent mechanical ventilation.[1] Subsequent to HBOT, oxygen requirements in some mechanically ventilated patients increase.[2] However, published data on this phenomenon remain limited.[2–4] Possible mechanisms for the transient reduction in arterial oxygenation, which in some patients may result in hypoxaemia following HBOT, are listed in Table 1.[2–6]

Our aim was to document the incidence and magnitude of changes in oxygenation following HBOT utilising the arterial partial pressure of oxygen against the fractional inspired oxygen ratio (P_aO_2/F_iO_2) as the primary outcome measure, and secondarily to look at changes in ventilator settings necessitated post-HBOT to maintain stable oxygenation.[7]

Methods

SUBJECTS

A prospective, single-centre, observational study of 25 consecutive, mechanically ventilated intensive care unit (ICU) patients referred to the Alfred Hospital hyperbaric unit for HBOT from November 2007 to November 2008 was undertaken. This observational study involved only analysis of information routinely collected for clinical care. The institutional ethics committee approval received did not, therefore, stipulate additional informed consent from either the patient or their family.

Although patients received multiple HBOT sessions, data

Table 1
Possible mechanisms for transient hypoxaemia following HBOT

- Increased pulmonary venous admixture (described in both healthy and critically ill patients)
- Blunting of the hypoxic pulmonary vaso-constrictive response
- Hyperoxia-induced atelectasis
- Worsening oxygen efficiency due to changes in patient position
- Changes to vasoactive drug therapies
- Inadequate mechanical ventilation
- Loss of positive end-expiratory pressure or pressure support during changeover of mechanical ventilators for transportation

were gathered from between two to three sessions per patient, typically HBOT session 1, 2 and/or 3. These sessions were chosen based on previous studies, and patient, researcher and recording equipment availability. Data were collected from 61 (36%) of a total of 171 HBOT sessions delivered to the 25 patients.

PROCEDURES

Patients were mechanically ventilated in the ICU by a Puritan Bennett 840 ventilator (Tyco Healthcare, Pleasanton, CA); during transport to and from the hyperbaric unit, either the PB840 ventilator or a Draeger Oxylog 3000 (Draeger Corp, Lübeck, Germany) matched to the ICU ventilator settings was used. Mechanical ventilation during HBOT was achieved with a Servo 900C ventilator (Siemens Corp, Lübeck, Germany). Mechanical ventilation data from the PB840 ventilator pre- and post-HBOT were collected electronically on a computer (IBM Thinkpad™ T30, Ormonk, NY), which queried the ventilator at one-minute intervals using a serial port data management programme (Advanced Serial Data Logger, Version 3.1.0 build 18, AGG Software).

Prior to commencing transport, the transport mechanical ventilation settings were adjusted to match ICU ventilation parameters or adjusted to achieve target end-tidal CO_2 or pulse oximetry (S_pO_2) values. During the brief changeover between ICU and transport ventilators, positive end-expiratory pressure (PEEP) was not maintained or any recruitment manoeuvre applied to the patient. F_iO_2 was increased to 1.0, as per the hospital transport ventilation protocol.[8] During transportation, monitoring of ventilation data was not possible. Therefore, the transportation phase of the treatment was observed by the principal researcher to detect and document any episodes of hypoxaemia and elucidate possible causes.

The same ventilator settings as in ICU were used on commencement of HBOT, then adjusted to compensate for the effect of raised ambient pressure upon the ventilator as described in the literature.[9–11] In most patients, this involved an increase in tidal volume of about 10% and, in some, a slight increase in ventilation rate (mean rate during HBOT 18 breaths per min, compared to 17 per min pre-HBOT). These settings were returned to the baseline ICU levels by the end of HBOT.

Arterial blood gas (ABG) samples were drawn from an in-dwelling arterial catheter using a standard aseptic procedure prior to and during HBOT, on return to ICU and at 1, 2, 3 and 6 hours post-HBOT (range of variation in sampling times was 5 minutes early to 6 minutes late). The F_iO_2 being delivered was recorded, along with other physiological and clinical parameters. The blood gas analyser (RapidLab 1265; Bayer HealthCare AG, Leverkusen, Germany) was automatically single-point calibrated every 4 hours and two-point calibrated every 8 hours as per the manufacturer's guidelines. Of the P_aO_2 values reported here, none were taken during HBOT, when the values were outside the range of the ABG analyser. From the 61 measured HBOT sessions, only one of 244 possible sampling times was missed.

To minimise the chance of alterations in oxygenation incurred as a consequence of patient position changes during transport (with associated changes of sedation, vasoactive drug infusion rates, or mechanical ventilation settings) patients remained on their normal ICU bed throughout. Any changes in ICU ventilator settings required after HBOT to achieve pre-HBOT targets for P_aO_2 and/or S_aO_2 were recorded.

HBOT commenced with an approximate pressurisation rate of 10 kPa min^{-1} and reached a maximum treatment pressure of 284 kPa, held for 60 minutes. A F_iO_2 of 1.0 was delivered throughout, interrupted by two, 5-minute 'air breaks' after 25 and 55 minutes, during which the F_iO_2 was reduced to 0.21. A stepped decompression was then conducted over 35 minutes with a F_iO_2 of 1.0. Three of the 61 HBOT sessions were given at 243 kPa for 99 minutes and one at 203 kPa for 105 minutes, both with a single 5-minute air break.

STATISTICAL ANALYSIS

Power analysis *a priori* determined that 25 patients would provide an 80% power to detect a difference between any two time points equivalent to 80% of one standard deviation (SD), equivalent to an approximate reduction in P_aO_2/F_iO_2 ratio of 19%, with a two-sided *P*-value of 0.05. Changes in the P_aO_2/F_iO_2 ratio from baseline approximated a normal distribution. Analyses were performed using statistical analysis software (SAS) version 9.1 (SAS Institute Inc., Cary, NC, USA). In order to assess the effect of time point on change in P_aO_2/F_iO_2 ratio, a mixed-effects analysis was performed using the PROC Mixed procedure in SAS.

Time was treated as a categorical variable to facilitate specific comparisons and data were analysed using a true intention-to-treat analysis for all patients. Results from the mixed-effects model are presented as percentage change from baseline (95% confidence intervals, CI). A two-sided *P*-value of 0.05 was considered to be statistically significant. Patient demographics were summarised descriptively. Continuous data were reported as mean and standard deviation, whereas categorical data were reported as count and proportions.

Results

The demographic characteristics and indications for HBOT of the 25 patients (15 male, 10 female; mean age 56 (SD 13) years) enrolled in the study are shown in Table 2. On admission to ICU, the mean APACHE II severity of illness score was 16 (6). The median (interquartile range) values for

Table 2
Patient demographics, ICU and HBOT characteristics

Sex	Age (y)	APACHE II score	Length of MV (h)	Length of ICU stay (days)	Total HBOT sessions	ICU mortality	Presenting condition
M	42	10	148	9	11	No	Necrotising infection
F	53	10	271	13	11	No	Anaerobic septicaemia
M	47	8	19	3	2	No	Necrotising infection
F	56	14	390	14	10	No	Necrotising infection
M	78	28	162	7	7	No	Necrotising infection
M	58	10	166	8	3	No	Necrotising infection
M	47	21	127	11	6	No	Necrotising infection
M	76	16	475	8	9	Yes	Clostridial myonecrosis
F	65	12	116	2	11	No	Wound healing
M	65	14	200	7	7	No	Necrotising infection
F	69	17	219	11	7	No	Necrotising infection
F	39	24	741	3	9	No	Acute ischaemia/oedema
M	76	21	130	7	6	No	Necrotising infection
M	66	19	142	11	4	No	Fournier's gangrene
M	37	14	141	6	6	No	Anaerobic septicaemia
M	39	8	13	3	2	No	Necrotising infection
M	38	14	88	4	3	No	Necrotising infection
F	66	10	434	18	8	No	Fournier's gangrene
M	56	14	320	14	9	No	Acute ischaemia/oedema
M	51	28	230	14	10	Yes	Anaerobic septicaemia
M	49	17	268	7	7	No	Necrotising infection
F	40	16	233	11	9	No	Clostridial myonecrosis
F	76	21	119	5	2	No	Arterial gas embolism
F	64	14	200	10	5	No	Clostridial cellulitis
F	56	17	185	11	7	No	Anaerobic septicaemia

Table 3
Characteristics of oxygenation and related mechanical ventilation parameters; data are mean (standard deviation)

Respiratory parameter	Pre-HBOT	Return to ICU	+1 h	+2 h	+3 h	+6 h
F_iO_2	0.47 (0.1)	0.49 (0.2)	0.47 (0.1)	0.46 (0.1)	0.44 (0.1)	0.43 (0.2)
P_aO_2 (mmHg)	141 (85)	101 (54)	104 (28)	118 (35)	115 (32)	116 (43)
P_aO_2/F_iO_2 ratio	301 (99)	221 (87)	234 (75)	274 (86)	274 (16)	278 (78)
S_aO_2 (%)	98 (2)	95 (5)	96 (5)	97 (24)	97 (1)	97 (2)
P_aCO_2 (mmHg)	43 (7)	48 (9)	45 (10)	43 (8)	43 (7)	43 (6)
Respiratory rate min^{-1}	17 (4)	16 (4)	17 (4)	17 (4)	16 (4)	17 (4)
Tidal volume (mL)	551 (170)	553 (170)	549 (130)	540 (150)	558 (130)	549 (150)
PEEP (cmH_20)*	7.0 (3.0)	7.1 (3.2)	7.1 (3.3)	7.1 (3.3)	6.9 (3.1)	6.9 (3.1)
I:E Ratio (1:)	2.4 (0.7)	2.4 (0.6)	2.4 (0.6)	2.4 (0.7)	2.5 (0.7)	2.4 (0.7)
Pressure support (cmH_20)	11 (3)	11 (3)	11 (3)	11 (3)	12 (3)	11.0 (3)

* Positive end expiratory pressure

duration of mechanical ventilation and length of ICU stay were 168 hours (129–263 hours) and 8 days (5.5–11 days) respectively. The presenting indications for HBOT are also shown in Table 2. The modes of ventilation used for the 61 HBOT sessions were synchronized intermittent mandatory ventilation (SIMV)-volume control ($n = 32$), SIMV-pressure control ($n = 25$) and spontaneous-pressure support and PEEP ($n = 3$). Two patients died in ICU during the study.

Table 3 presents the mean (SD) oxygenation values for each time point. Following HBOT, the mean P_aO_2/F_iO_2 ratio decreased compared to the pre-HBOT ratio by 27% on return to ICU ($P < 0.001$, 95% CI 21 to 34), by 22% at 1 hour post-HBOT ($P < 0.001$, 95% CI 15 to, 29) and by 8% at 2 hours ($P = 0.03$, 95% CI 0.8 to 14). At 3 and 6 hours there were no significant differences from baseline.

Table 4
Characteristics of alterations to F_iO_2 and pressure-assist levels following HBOT

Ventilation parameter altered	*n*	Pre-HBOT	Return to ICU	+1 h	+2 h	+3 h	+6 h
F_iO_2	20	0.41 (0.10)	0.58 (0.24)	0.58 (0.17)	0.53 (0.15)	0.50 (0.16)	0.47 (0.16)
PEEP* (cmH_20)	5	8.5 (3.3)	10.2 (4.2)	11.3 (3.5)	11.5 (3.7)	11.5 (3.7)	11.3 (3.5)
PS† (cmH_20)	5	9.4 (3.6)	12.0 (2.5)	12.4 (3.3)	12.4 (3.3)	13.4 (3.1)	13.4 (3.1)

* Positive end-expiratory pressure; † Pressure support; data are mean (standard deviation)

Changes in F_iO_2 or positive pressure settings to compensate for reduction in oxygenation such as lowered P_aO_2 or S_pO_2 were needed in 17 patients (68%) after at least one of their monitored HBOT sessions. These 17 patients required such changes to be made after 30 of the 61 sessions (Table 4). The most common change made (n = 20) was an increase in F_iO_2 above baseline values (mean change +0.17, 95% CI 0.11 to 0.23), followed by a return towards baseline values by 2–6 hours post-HBOT. A number of alterations in PEEP (n = 5) and pressure support (n = 5) too small for inferential statistical analysis also occurred (Table 4).

Discussion

This study confirms previous observations that post-HBOT oxygenation reductions of approximately 20–24% at 1 hour and 8–18% at 2 hours post-HBOT occur in many mechanically ventilated ICU patients.[3,4] This deterioration in oxygenation is sufficient to require compensatory alterations in ventilation settings, typically by raising the F_iO_2 or less frequently by increasing PEEP or pressure support. At the time of writing, the authors were unaware of other reports describing the incidence or magnitude of mechanical ventilation changes necessitated by impaired oxygenation in the post-HBOT period.

Because of the observational and non-invasive nature of this study, it is not possible to determine whether the reductions in oxygenation post-HBOT are related to blunting of the hypoxic pulmonary vasoconstrictive response, hyperoxia-induced atelectasis or other causes (Table 1). However, inadequate mechanical ventilation during HBOT compared to ICU ventilator settings is unlikely to have contributed, since ventilation was adjusted during HBOT to compensate for the hyperbaric environment. The placing of patients on F_iO_2 1.0 prior to transport may have resulted in absorption atelectasis leading to alterations in the P_aO_2/F_iO_2 ratio.[12] The deleterious effect on oxygenation of not maintaining PEEP during changeover to transportation ventilators is reported in the literature.[5] However, neither this nor the use of prophylactic recruitment manoeuvres were assessed in this study.

There are a number of limitations to this study. Firstly, although data were collected over one year from a consecutive set of patients, further, possibly larger studies will be required to characterise the differences between those subjects who require adjustments in ventilation versus those who do not. Secondly, this study gathered data at 1-hour intervals only, whereas more frequent observations within the first 2 hours post-HBOT would better characterise the time course of this phenomenon. Thirdly, indices of oxygenation such as the P_aO_2/F_iO_2 ratio have been reported to have varying reliability in describing the severity of alterations in oxygenation.[13–15] Fourthly, data were obtained from only about a third of the HBOT sessions these patients underwent, and no effort was made to look at whether these effects on oxygenation were progressive over time.

Conclusions

Significant reductions in oxygenation as measured by the P_aO_2/F_iO_2 ratio were observed among 25 mechanically ventilated ICU patients following HBOT. A majority of these reductions necessitated increases in F_iO_2 or pressure-assist levels. From the data gathered it is not possible to identify specific characteristics to predict those patients at risk, to determine causation or to infer any impact upon medium- and long-term outcomes. Prospective interventional studies could usefully investigate the impact of recruitment manoeuvres or maintenance of PEEP levels during changeover of transportation ventilators to minimise falls in oxygenation in mechanically ventilated patients post-HBOT.

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