

Arterial oxygen tension increase 2–3 h after hyperbaric oxygen therapy: a prospective observational study

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Background: Inhalation of hyperbaric oxygen (HBO) has been reported to decrease arterial oxygen tension (PaO₂) in the early period after exposure. The current investigation aimed at evaluating whether and to what extent arterial blood gases were affected in mechanically ventilated intensive care patients within 6 h after HBO treatment.

Methods: Arterial blood gases were measured in 11 ventilated subjects [nine males, two females, synchronized intermittent mandatory ventilation (SIMV) mode] undergoing HBO therapy for necrotizing soft tissue infection (seven patients), burn injury (two patients), crush injury (one patient) and major abdominal surgery (one patient). Blood gases were obtained with the patients in the supine position under continuous analgesia and sedation before the hyperbaric session (baseline), during isopression, after decompression, after each transport, and 1, 2, 3 and 6 h after exposure. Heart rates and blood pressures were recorded. Intensive care unit (ICU) ventilator settings remained unchanged. Transport and chamber ventilator settings were adjusted to baseline with maintenance of tidal volumes and positive end-expiratory pressure (PEEP) levels. The hyperbaric protocol consisted of 222.9 kPa (2.2 absolute atmospheres) and a 50-min isopression phase. The paired Wilcoxon's test was used.

Results: Major findings (median values, 25%/75% quantiles) as per cent change of baseline: PaO₂ values decreased by 19.7% (7.0/31.7, $P < 0.01$) after 1 h and were elevated over baseline by 9.3% (1.5/13.7, $P < 0.05$) after 3 h. SaO₂, alveolar-arterial oxygen tension difference and PaO₂/FiO₂ ratio behaved concomitantly. Acid-base status and carbon dioxide tension were unaffected.

Conclusion: Arterial oxygen tension declines transiently after HBO and subsequently improves over baseline in intensive care patients on volume-controlled mechanical ventilation. The effectiveness of other ventilation modes or a standardized recruitment manoeuvre has yet to be evaluated.

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HYPERBARIC oxygen (HBO) is used in the treatment of various conditions (1).

Some patients have been reported to require increased inspiratory fractions of oxygen (FiO₂) shortly after exposure to HBO (2). Few data are available on the impact of HBO on mechanically ventilated patients. An increase in the pulmonary venous admixture and a decline in arterial oxygen tension with a trend towards baseline have been reported in the 2-h period after exposure (3). We prospectively measured arterial blood gases in mechanically ventilated intensive care patients before, during and over a 6-h observation period after the hyperbaric session.

Patients and methods

The study protocol was approved by the institutional Ethics Committee. Eleven mechanically ventilated patients (nine males, two females; age: 47–69 years) undergoing HBO therapy were enrolled (Table 1).

Exclusion criteria were: evidence of a condition contraindicating HBO therapy, signs of hypoventilation using blood gas analysis (an increase in PaCO₂ more than 25% from baseline or more than 45 mmHg) and a change in the patient's position during the study period.

All subjects received midazolam (0.03 mg/kg/h) and sufentanil (0.7 ± 0.2 µg/kg/min) continuously

Table 1

Patient diagnosis and ventilation parameters.								
Patient	Diagnosis	V _t (ml/kg)	VE (l/min)	p _{aw} mean	p _{aw} peak	PEEP (cmH ₂ O)	FiO ₂	HBO session
1	necrotizing soft tissue infection	8	9.76	14	27	6	0.50	2
2	oesophageal resection	8	7.54	10	20	5	0.40	2
3	necrotizing soft tissue infection	8	6.7	10	22	5	0.40	2
4	burn injury, 20% BSA	9	10.7	16	29	10	0.55	2
5	crush injury, necrotizing fasciitis	8	7.68	12	20	7	0.40	4
6	burn injury, 20% BSA	8	8.1	11	30	7	0.40	2
7	necrotizing soft tissue infection	8	7.44	15	31	8	0.39	3
8	necrotizing soft tissue infection	8	8.68	12	32	5	0.44	3
9	necrotizing soft tissue infection	8	8.04	19	34	3	0.47	2
10	necrotizing soft tissue infection	8	7.9	14	25	8	0.47	3
11	necrotizing soft tissue infection	8	6.3	9	26	5	0.34	2

V_t, tidal volume (ml/kg body weight); VE, minute ventilation (l/min); P_{aw}, airway pressure (cmH₂O); PEEP, positive end-expiratory pressure (cmH₂O); FiO₂, inspiratory fraction of oxygen (% 10⁻²); hyperbaric oxygen session, number of the investigated session. BSA, body surface area.

and were ventilated using the synchronized intermittent mandatory ventilation (SIMV) mode. Analgesedation was continued throughout the whole study period so that no event of additional spontaneous breathing occurred. Nursing activities entailing changes in the patient's position were postponed. Blood samples were obtained with the patient supine. During the study period, there were no interventions in addition to HBO therapy.

Arterial blood gas measurements were obtained from the radial artery at the following time points: before therapy (baseline); in the intensive care unit; after transport to the chamber (Tr1); before compression with the patient ventilated by the chamber ventilator (A); during the hyperbaric session in the isopression phase (HBO); 1 min after decompression under normobaria (B); after transport to the intensive care unit (ICU) (Tr2); and 1, 2, 3 and 6 h after the session (Fig. 1).

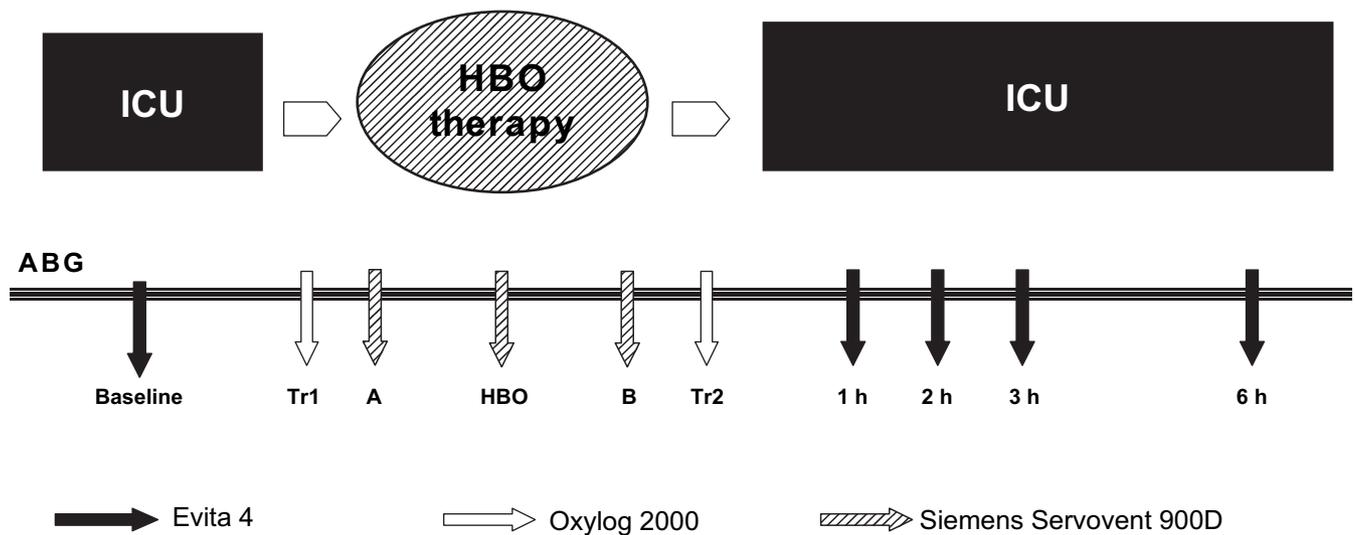


Fig. 1. Experimental setting. Blood gas sampling at the following measuring points. Tr1, after transport to the chamber; A, before decompression; hyperbaric oxygen (HBO), during isopression; B, 1 min after decompression; Tr2, after transport to the intensive care unit (ICU). At 1, 2, 3, 6 h after the hyperbaric session. The pattern of arrows indicates the type of ventilator used at the corresponding measuring point.

Standard sterile techniques were used for blood gas sampling. A heparinized 3-ml syringe (Arterial blood sampling kit, REF 4043E; Sims Portex Ltd, Kent, England) was filled with 2 ml of blood drawn from the radial artery with close attention to the removal of visible gas bubbles. After the sample had been drawn, the arterial catheter and line were flushed with saline. Each sample was immediately analysed using the same device (ABL 700; Radiometer, Copenhagen, Denmark) which had been checked by a technician. The blood gas analyser was automatically single-point calibrated every 4 h and two-point calibrated every 8 h.

Arterial blood pressure and heart rate were recorded at each measuring point.

In the ICU, the patients were ventilated with an Evita 4 ventilator (Draeger Corp., Lübeck, Germany). ICU ventilator settings, minute ventilation and positive end-expiratory pressure (PEEP) level at baseline and after the treatment remained unchanged. Ventilation patterns of the Oxylog 2000 ventilator (Draeger Corp.) used during transportation were recorded and closely adjusted to the baseline settings with care to maintain the initial minute ventilation and PEEP level. Transport ventilator settings were the same for both transports. None of the subjects inhaled pure oxygen but a mixture of oxygen and air (air mix) at a FiO_2 of 0.6. Blood gases were obtained after both transports (Tr1, Tr2).

Patients were brought into the chamber in their original ICU bed. Ventilation under pressure was provided by the Siemens Servovent 900D (Siemens Corp., Lübeck, Germany) in the volume-controlled ventilation (VCV) mode at a FiO_2 of 1.0 and adjusted to maintain carbon dioxide tensions of 35–45 mmHg in the arterial blood with the PEEP level identical to baseline. Because the increased gas density in the hyperbaric environment causes a decrease in inspiratory flow and tidal volume which is overestimated and wrongly displayed by the ventilator (4, 5), the tidal volume and minute ventilation delivered in the isopression phase were continuously measured by a spirometer (Medishield RW 211) and adapted to baseline values necessitating an up-regulation of the minute volume by 3 l/min on average. Adequacy of ventilation was ensured by blood gas monitoring before compression (A), during isopression (HBO, after 15 min bottom time) and after decompression (B) with the patients breathing pure oxygen.

Prior to HBO therapy, a hyperbaric performance check consisted of the inspection of a chest radiograph to rule out bullous emphysema and myringot-

omy by an ENT specialist in pressure equilibration. The hyperbaric protocol was run at 222.9 kPa (2.2 absolute atmospheres) with an isopression phase of 50 min. Compression and decompression were performed at a rate of 0.2 atmospheres per minute with a 3-min safety stop at 1.3 absolute atmospheres during decompression. Usually, the second session was recorded. Patients were accompanied by an intensive care physician trained in hyperbaric medicine.

The $\text{PaO}_2/\text{FiO}_2$ ratio and alveolar arterial oxygen tension difference [P(A-a)O_2] were calculated from the measured values (Table 2). P(A-a)O_2 was calculated as follows: $\text{P(A-a)O}_2 = \text{FiO}_2 (\text{Pb}-47) - \text{PaO}_2 - \text{PaCO}_2/0.8$ (Pb, ambient pressure; PaCO_2 , arterial carbon dioxide tension; pressure unit, mmHg; 0.8, respiratory quotient). These calculations were not performed to measure points Tr1 and Tr2, because of varying oxygen concentrations of the inhaled gas ($\text{FiO}_2: 0.6 \pm 5\%$) during the transport phase.

Statistical analysis was performed using the SPSS program (Version 12.0, SPSS Inc., Chicago, IL). Differences between post-session values and baseline were compared using a paired Wilcoxon's test. P -values < 0.05 were considered statistically significant.

Results

Tables 2 and 3 show the results as median values and 25–75% quantiles.

Individual arterial oxygen tensions are shown in Fig. 2.

Arterial oxygen tension decreased by 19.7% ($P = 0.005$) and arterial oxygen saturation (SaO_2) by 1.9% ($P = 0.008$) at 1 h. Three hours after the session, PaO_2 increased by 9.3% ($P = 0.041$) over baseline. $\text{PaO}_2/\text{FiO}_2$ ratios and alveolar arterial oxygen tension differences are shown in Table 2.

The decrease of PaO_2 remained within a clinically acceptable range in all subjects but one: in patient 8, PaO_2 decreased from 10.5 kPa at baseline to 7.3 kPa at 1 h before increasing to 11.9 kPa at 3 h (Fig. 2). The largest decrease in PaO_2 was seen in patient 7, who was ventilated at a FiO_2 of 0.39, not in patient 4, who was ventilated at the highest FiO_2 (0.55) (Fig. 2).

Discussion

In the mechanically ventilated patients in our series, exposure to HBO was likely to promote a delayed decline in arterial oxygen tension, which was reversed within 2 h after treatment. A brief improvement in oxygenation above baseline was seen after

Table 2

Blood gases and haemodynamic parameters before, during and after hyperbaric oxygen (HBO) therapy.

Parameter	Abs. values	Per cent change from baseline (baseline = 100%)				
	Baseline	HBO	1 h	2 h	3 h	6 h
pH	7.41 (7.3/7.4)	99.7 (99/100)	99.9 (99/100)	100.1 (99/100)	99.9 (99/100)	100 (99/100)
PaCO ₂ (kPa)	5.3 (4.8/6.1)	102.1 (82/129)	102.0 (90/112)	101.8 (89/106)	97.5 (91/107)	97.0 (92/122)
PaO ₂ (kPa)	13.1 (11/14)	815.8** (699/901)	80.3** (68/93)	92.2 (87/109)	109.3* (98/114)	98.2 (85/130)
PaO ₂ /FiO ₂	215.5 (179/285)	337.4** (298/397)	80.3** (68/95)	92.2 (88/112)	109.3* (99/114)	100.8 (85/130)
P(A-a)O ₂ (kPa)	20.0 (14/26)	605.6** (415/724)	112.5* (104/129)	102.7 (97/113)	93.3* (88/99)	95.3 (78/106)
HR (bpm)	88 (76/108)	93.4 (86/108)	105.7 (103/110)	98.7 (96/105)	100 (93/106)	100.5 (93/113)
ABP sys (mmHg)	105.0 (95/127)	98.4 (87/133)	104.7 (94/133)	101.1 (89/113)	110.5 (94/118)	112.0 (86/129)
ABP dia (mmHg)	54.0 (40/73)	97.2 (90/137)	103.6 (90/125)	102.0 (88/110)	107.1 (89/112)	112.7 (83/135)

Median values (25%–75% quantiles).

P* < 0.05, *P* < 0.01.

Paired Wilcoxon's test. *n* = 11. Baseline findings are presented as absolute values, the following ones as a per cent change from baseline. Baseline values correspond to 100%. Measuring points at conditions: baseline (before HBO therapy), during and 1, 2, 3, and 6 h after the hyperbaric session. HBO, isopression phase during HBO therapy; Parameters: PaCO₂, arterial carbon dioxide tension (kPa); PaO₂, arterial oxygen tension (kPa); PaO₂/FiO₂ ratio, oxygenation index. P(A-a)O₂, alveolar-arterial oxygen tension difference (kPa). For the calculation refer to the text. HR, heart rate (l/min); ABPsys, systolic arterial blood pressure (mmHg); ABPdia, diastolic arterial blood pressure (mmHg).

3 h. The aetiology of this phenomenon is not yet clear. Various non-respiratory conditions (e.g. right-to-left pulmonary shunt, hypobarica, cardiac failure) and respiratory conditions (e.g. right-to-left pulmonary shunt, ventilation-perfusion mismatch, oxygen diffusion defects, hypoventilation) can lower arterial oxygen tension.

None of the patients had a history or condition to suggest a non-respiratory cause for decreased arterial oxygen tension. As to the respiratory causes, with stable PaCO₂ profiles over the observation period, there was no evidence of hypoventilation in the patients in our series. The most common cause of

a low PaO₂ without elevated PaCO₂ is an imbalance of the ventilation/perfusion relationship (6, 7).

Inhalation of normobaric oxygen can induce atelectasis, decrease PaO₂ and change the venous admixture (8–12). This supports the hypothesis that an increased oxygen dosage administered under hyperbaric conditions can exert a similar or enhanced effect.

A previous study (3) reported an increase in pulmonary venous admixture with a concomitant decrease in arterial oxygen tension. Results of an animal experiment suggest that a hyperoxic stimulus may blunt the physiological pulmonary vasoconstrictive

Table 3

Blood gases and haemodynamics before and after hyperbaric oxygen (HBO) therapy.

Parameter	Per cent change from baseline (baseline = 100%)			
	A	B	Tr 1	Tr 2
pH	99.9 (99/100)	100.6 (99/101)	100.1 (99/100)	100.3 (99/100)
PaCO ₂ (kPa)	108.3 (91/122)	93.6 (79/121)	96.4 (86/105)	88.3 (77/112)
PaO ₂ (kPa)	231.1** (181/293)	248.0** (156/285)	163.1* (123/185)	149.2* (130/204)
PaO ₂ /FiO ₂	98.1 (84/117)	98.03 (63/154)		
P(A-a)O ₂ (kPa)	259 (195/336)	304.0 (166/342)		
HR (bpm)	97.4 (87/101)	98.2 (92/129)	99.7 (91/107)	106.8 (90/113)
ABP sys (mmHg)	83.8 (80/96)	87.0 (71/106)	88.6 (83/137)	95.0 (80/110)
ABP dia (mmHg)	89.5 (86/115)	90.0 (76/116)	97.3 (81/134)	89.6 (77/103)

Median values (25–75% quantiles).

P* < 0.05, *P* < 0.01.

Paired Wilcoxon's test. *n* = 11. Findings are presented as per cent change from baseline. Baseline values correspond to 100%. Measuring points at the following conditions: A, before compression; B, after decompression; Tr1, after transport to the chamber; Tr2, after transport to the ICU. Parameters: PaCO₂, arterial carbon dioxide tension (kPa); PaO₂, arterial oxygen tension (kPa); PaO₂/FiO₂ ratio, oxygenation index; P(A-a)O₂, alveolar-arterial oxygen tension difference (kPa). For the calculation refer to the text. HR, heart rate (1/min); ABPsys, systolic arterial blood pressure (mmHg); ABPdia, diastolic arterial blood pressure (mmHg).

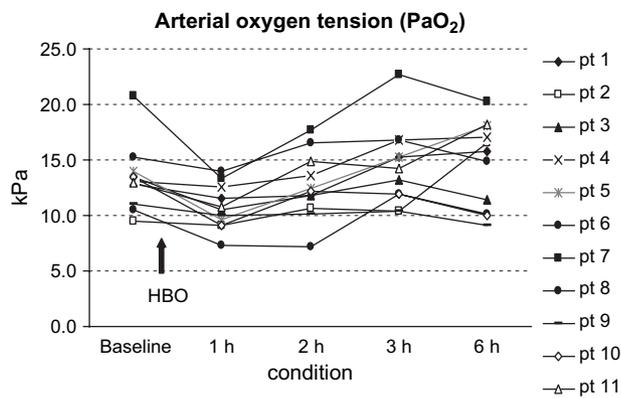


Fig. 2. Individual arterial oxygen tensions in the intensive care unit (ICU) at baseline and 1, 2, 3, 6 h after the session. During all conditions, the patients were ventilated using the same Evita 4 ventilator setting.

response to hypoxia and induce increased intrapulmonary shunting (13). No studies have looked at atelectasis formation as a result of inhalation of HBO.

Nevertheless, the observed phenomenon can be attributed to HBO only if the hyperbaric session had been the sole intervention. The question arises whether and to what extent altered ventilation modalities may exert an effect on the distribution of ventilation and perfusion within the lung although the PEEP level and minute ventilation were maintained and the ventilation pattern adjusted to the baseline setting. Our patients were sufficiently ventilated during transfer to and from the hyperbaric chamber and during the hyperbaric session. The impact of the elevated ambient pressure per se and the ensuing altered gas densities, humidification, temperature and gas kinetics has not yet been investigated in mechanically ventilated intensive care patients. There are no reports on how spontaneously breathing patients cope with the inhalation of hyperbaric oxygen.

The results of the current study have to be interpreted with caution with regard to constraints of possible limitations. Changes in cardiac output may influence respiratory parameters and oxygenation. We did not measure cardiac output but the unchanged heart rates of the patients suggest haemodynamic stability.

Generation of free radical intermediates and inflammatory responses to HBO may provoke signs of oxygen toxicity (14, 15). Pulmonary oxygen tolerance in man is extended by alternating hyperoxia and normoxia (16). Intermittent air breaks were not applied which might have modified the response to HBO exposure in the study participants.

The aetiology of the PaO₂ increase within the third hour and the subsequent decline towards baseline is not clear but strongly suggests a delayed drug effect.

Rare investigations deal with the early period after exposure. Delayed HBO-induced alterations have been reported with regard to expression of the murine intercellular adhesion molecule-1 (ICAM-1) (17), and to pulmonary vessel tone (13).

Hypothetically, renitrogenation of the alveoli may recruit more areas than have been ventilated at baseline thus inducing a reversal of ventilation/perfusion inhomogeneity. Inhalation of HBO may blunt the physiological vasoconstrictive response to hypoxia thus increasing the amount of pulmonary venous admixture when malventilated areas become well perfused. This effect may be reversed over time which results in an improvement of oxygenation.

The interference with nitric oxide metabolism in this context is not yet clear. On one hand, HBO is known to generate endogenous nitric oxide (18, 19) in the rat brain but, on the other hand, it inhibits nitric oxide biosynthesis in septic rats with lipopolysaccharide-induced lung injury (20).

However, with the hyperbaric protocol used in our collective, the extent of the decrease in arterial oxygen tension remained moderate, brief and reversible and the hyperbaric session was well tolerated. Further studies are required to define preventive therapeutic measures which might be a standardized recruitment manoeuvre or the application of another ventilation mode and to evaluate their effectiveness. The impact of dose dependency (pressure and duration) of the exposure to hyperbaric oxygen has to be determined.

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