Original articles

Monitoring cardiac output during hyperbaric oxygen treatment of haemodynamically unstable patients

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Abstract

(Hansen MB, Treschow F, Skielboe M, Hyldegaard O, Jansen EC, Nielsen JB. Monitoring cardiac output during hyperbaric oxygen treatment of haemodynamically unstable patients. *Diving and Hyperbaric Medicine*. 2013 March;43(1):3-8.)

Introduction: Patients suffering from necrotizing fasciitis (NF) are often haemodynamically unstable and require extended monitoring of cardiovascular parameters; yet this is limited during hyperbaric oxygen treatment (HBOT). We aimed to evaluate the use and safety of transoesophageal Doppler (TED) monitoring of cardiac output (CO) under hyperbaric conditions in haemodynamically unstable patients diagnosed with NF and sepsis or septic shock.

Methods: Cardiac output was measured prior to, during and after HBOT with the use of TED in seven consecutive patients diagnosed with NF and sepsis or septic shock. The HBOT followed our standard protocol for NF patients, consisting of 90 minutes' exposure to 100% oxygen at 284 kPa. The difference between mean CO just prior to HBOT initiation and at near-maximum treatment duration was assessed using the Student's paired *t*-test.

Results: TED was feasible and easy to use under hyperbaric conditions. We experienced no problems with the measurement of CO or with equipment-related safety during HBOT. Five patients had an increase in CO from initiation of HBOT to near-maximum treatment duration, one patient had a stable CO, while one patient experienced a slight decrease in CO. Overall, there was an increase in mean CO of 1.7 L min^{-1} (95% CI 0.02 to 3.34 L min^{-1}, $P = 0.048$) from initiation of HBOT to near-maximum treatment duration.

Conclusion: This is, to the best of our knowledge, the first study to document that TED can provide a minimally-invasive estimate of CO in haemodynamically unstable patients with NF and sepsis or septic shock during HBOT.

Key words

Doppler, cardiovascular, patient monitoring, hyperbaric oxygen therapy, necrotising infections, physiology

Introduction

Hyperbaric oxygen treatment (HBOT) is used routinely as treatment for several clinical conditions including necrotizing fasciitis (NF).[1,2] In Denmark (population 5.6 million people), the incidence of NF has increased over the years from three new cases in 1997 to 64 cases in 2011. NF is a rapidly progressive, life-threatening soft tissue infection with a high morbidity and mortality.[3] The infections are usually polymicrobial, spread along the subdermal facial planes and are often complicated by sepsis or septic shock.[4,5] The treatment protocol in our centre is based on prompt and aggressive surgical debridement, intravenous antibiotics with broad-spectrum antibacterial coverage, intravenous immunoglobulin, supportive therapy in an intensive care unit and HBOT.[6]

Patients suffering from NF complicated by sepsis or septic shock are haemodynamically unstable and require extensive haemodynamic monitoring; yet this is limited during HBOT because of technical difficulties including fire safety issues and the physical confinement of the hyperbaric chamber. Standard haemodynamic parameters such as blood pressure, heart rate, diuresis, and peripheral oxygen saturation (SpO_2) are often insufficient and fail to reveal the true haemodynamic status during septic shock.[7,8] In these circumstances, additional monitoring parameters, such as cardiac output (CO), are needed to optimize treatment of these patients.[9]

Various technologies are available with which to measure CO in the intensive care and peri-operative settings. Transoesophageal Doppler (TED) is an established, validated, and minimally-invasive case method, which has been described in numerous studies as showing good agreement compared to more invasive procedures (e.g., a Swan-Ganz catheter and thermodilution technique) with respect to relative changes in CO.[10] Whether TED can be used to monitor CO in haemodynamically unstable patients during HBOT is unknown. In addition, previous studies have examined how HBOT affects the normal cardiovascular system, but existing theories regarding CO and the haemodynamic profiles during HBOT in NF patients with sepsis are few and contradictory.[9,11–14]

We aimed to evaluate the use and safety of TED monitoring of CO in haemodynamically unstable patients diagnosed with NF and sepsis or septic shock under hyperbaric conditions.

Methods

STUDY SUBJECTS

The study was carried out in the Hyperbaric Medicine Unit at Copenhagen University Hospital, Rigshospitalet, a tertiary referral centre, where the HBOT treatment of NF has been centralised in Denmark. Patients diagnosed with NF and who received HBOT were offered participation if they fulfilled the study criteria. The inclusion criteria were:

- diagnosed NF and sepsis or septic shock defined as previously described;[15]
- HBOT was indicated and
- if the patient was intubated, receiving intravenous sedation and being mechanically ventilated prior to HBOT.

Exclusion criteria were:

- age < 18 years;
- mean arterial blood pressure (MAP) < 60 mmHg despite optimal intensive treatment and intravenous norepinephrine;
- known or suspected oesophageal cancer or other pathological conditions of the pharynx and oesophagus;
- pregnancy or
- in case of deviation from the standard HBOT protocol.

Each patient was only included once. The patients or, if they were already sedated at the time of arrival at the tertiary referral centre, their relatives gave written informed consent. The study protocol was approved by the institutional ethics committee (KF 01 300992).

HYPERBARIC OXYGEN TREATMENT

Patients were treated with HBOT according to a standard protocol for NF. During the first 48 hours after arrival at the tertiary referral centre, patients typically received three sessions of HBOT. Each treatment consisted of pressurization over 5 minutes to a pressure of 284 kPa. The pressure was applied for 90 min followed by 5 min decompression. The multiplace pressure chamber (Drass Galeazzi Underwater Technology, Italy) was pressurized with air, and the patients were mechanically ventilated with 100% oxygen via an endotracheal tube using a Siaretron 1000 IPER™ (Siare, Bologna, Italy) ventilator. During the study, there were no deviations from the standard HBOT protocol or existing safety procedures. Patients did not undergo myringotomy prior to compression

CARDIAC OUTPUT

Cardiac output was measured with transoesophageal Doppler (CardioQ™, Deltex Medical Inc., UK). As the CardioQ™ is currently not approved for usage in a pressure chamber, the monitor was placed outside the chamber. The connection between the monitor and the Doppler probe inside the chamber was established by a pressure-resistant power cable made specifically for the purpose (Deltex Medical Inc., UK).

Two trained persons performed the measurements; one inside the chamber handling the probe, while the other controlled the CardioQ™ monitor outside the chamber. They were able to communicate via intercom and visually through a porthole in the pressure chamber. Upon arrival at the hyperbaric unit, the TED probe was inserted via the oral or nasal route to the mid-thoracic level between the fifth and the sixth vertebrae where the aorta and oesophagus run parallel. After the initial placement, the probe was rotated for optimal flow signal. On two occasions, insertion of the TED probe was performed on patients with a gastric tube, which slightly prolonged the time to optimal probe positioning.

Since the oesophageal Doppler probe was not produced specifically to be operated under hyperbaric conditions, we performed a single safety test of a standard 6 mm probe prior to the study to ensure that it did not generate heat under pressure conditions. The probe was placed in a test tube (internal volume 200 ml) filled with water and the water temperature was measured. The probe was pressurized with air to a pressure of 284 kPa and followed the standard HBOT protocol for NF patients.

HAEMODYNAMIC MEASUREMENTS

To validate the use and safety of TED during HBOT, several measurements were performed. CO was measured:

- on arrival at the HBOT unit;
- prior to HBOT initiation and at least 10 minutes after any final ventilator changes were made, assuming a steady cardiopulmonary state;
- after 15 minutes at maximum depth;
- after 80 minutes at maximum depth and
- 15 minutes after the end HBOT.

Secondary observations were cardiac index (CI), heart rate (HR), mean arterial pressure (MAP), and estimated systemic vascular resistance (SVR = [MAP-CVP]/CO, assuming a central venous pressure = 0). To address a possible effect of HBOT on haemodynamic parameters including CO, we calculated mean differences of these parameters between baseline just prior to HBOT initiation (measurement no. 2) and at near-maximum treatment duration (measurement no. 4). Each measurement was taken as an average of five cycles to minimize the significance of any beat-to-beat variation. All measurements were repeated three times with search for optimal flow signal between each repetition, and the final result was expressed as mean and 95% confidence interval (95% CI).

STATISTICS

Differences between means were assessed using the Student's paired *t*-test. A *P*-value < 0.05 was considered

Table 1
Clinical characteristics of the patients prior to hyperbaric oxygen therapy (n = 7); data are mean (SD) unless otherwise indicated; * degree of sepsis according to Annane et al.[16]

Male/female (no.)	5/2	
Age, y (range)	51.3	(29–74)
Body mass index (kg m^{-2})	26.6	(7.3)
MAP (mmHg)	86	(10.6)
Heart rate (bpm)	88	(11.9)
Arterial blood gas values		
pO_2 (kPa)	27.2	(14.6)
pCO_2 (kPa)	4.9	(0.8)
HCO_3 (mmol L^{-1})	22.0	(1.6)
Base excess (mmol L^{-1})	-4.0	(2.5)
pH	7.36	(0.1)
K^+ (mmol L^{-1})	3.7	(0.3)
Na^+ (mmol L^{-1})	135.6	(5.1)
Ca^{2+} (mmol L^{-1})	1.1	(0.1)
Glucose (mmol L^{-1})	9.3	(2.9)
Haemoglobin (g L^{-1})	104.7	(9.6)
Haematocrit	0.32	(0.0)
Degree of sepsis*		
Severe sepsis, no.	1	
Septic shock, no.	6	
Norepinephrine infusion, no.	6	
Ventilator settings:		
IPPV/PRVC (no.)	6/1	
Minute volume (L min^{-1})	8.7	(1.2)
Peak insp pressure (kPa)	22.1	(6.0)
PEEP pressure (kPa)	6.1	(2.2)

MAP – mean arterial blood pressure
IPPV – intermittent positive pressure ventilation
PRVC – pressure regulated volume control
PEEP – positive end-expiratory pressure

statistically significant. We used the Stata 12.0 software package (StataCorp LP, Collage Station, Texas, USA) for the analysis.

Results

During the safety test of the oesophageal Doppler probe, there was no increase in temperature during the pressurization or during 90 minutes at 284 kPa.

The clinical characteristics of the seven patients studied are summarized in Table 1. An adequate probe position was achieved quickly in all seven cases and appropriate readings of CO were obtained within a few minutes of positioning the probe. We experienced no equipment-related safety problems during HBOT.

Five out of the seven patients had an increase in CO from initiation of HBOT (baseline) to near-maximum treatment length (80 minutes at maximum depth). CO in one patient remained stable during HBOT, while one patient experienced a slight decrease in CO (Figure 1). The mean increase in CO was 1.7 L min^{-1} (95% CI 0.02 to 3.34 L min^{-1}) for the seven patients from baseline to near-maximum HBOT duration (P = 0.048). CO continued to increase after the completion of HBOT, such that the mean increase in CO 15 minutes after HBOT was 2.3 L min^{-1} (95% CI 0.63 to 3.99 L min^{-1}, P = 0.015). During HBOT, we observed a decrease in mean MAP and a decrease in mean calculated SVR (Figure 1). Mean cardiac index increased from 2.5 L min^{-1} BSA m^{-2} (95% CI 1.5 to 3.5 L min^{-1} m^{-2}) at baseline to 3.3 L min^{-1} m^{-2} at near-maximum treatment duration (95% CI 1.7 to 4.9 L min^{-1} m^{-2}, P = 0.05). Mean heart rate did not change significantly: 84 bpm (95% CI 64 to 103 bpm) at baseline, 86 bpm at near-maximum treatment duration (95% CI 66 to 105 bpm, P = 0.227). Ventilator settings, intravenous medication and fluid administration were not modified from just prior to the initial measurement of haemodynamic parameters until after the last measurement. No patients deviated from the standard protocol for HBOT. All but one patient had their ventilator settings adjusted just prior to the initial measurement (arrival at the hyperbaric unit), increasing the minute volume by 10%.

Discussion

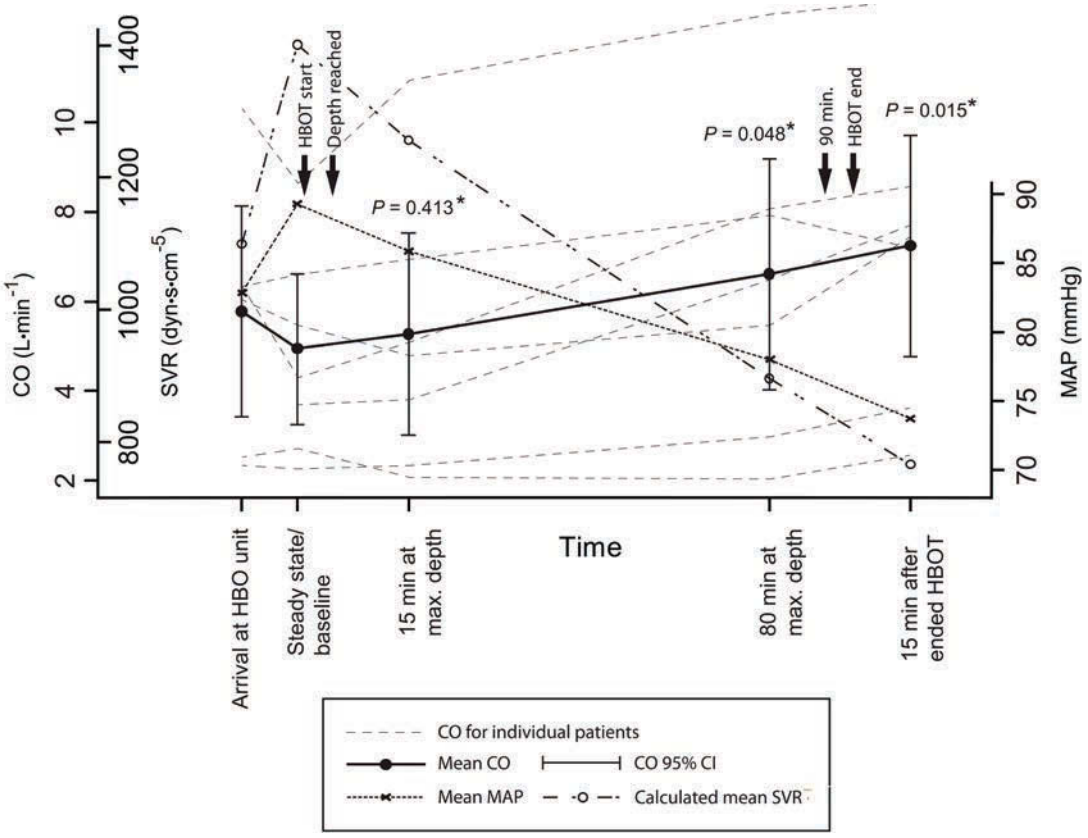
To the best of our knowledge, this is the first evaluation of TED monitoring of CO in haemodynamically unstable patients during HBOT.

METHODOLOGICAL AND EXPERIMENTAL CONSIDERATIONS

TED has previously been validated as compared to more invasive methods for measurement of CO such as the thermodilution method based on pulmonary artery catheterization (Swan-Ganz technique). The two methods have been found to agree with regard to relative changes in CO (trend monitoring) but less so for absolute values.[10] Accordingly, TED is well suited for estimation of changes in CO and thus the guidance of intravascular volume therapy and inotropic drugs, but not for precise estimation of an exact CO.[10] Neither TED nor the thermodilution method has previously been introduced for routine use in a HBOT setting of haemodynamically unstable patients, partly because it places heavy demands on such a procedure. First, the method should be simple and easy to handle during HBOT. Second, it has to provide valid and reproducible results. Third, it should pose a minimal risk to the patients. Fourth, the method must meet strict safety requirements with respect to electricity and fire precautions. Previous animal experimental studies and clinical trials have used other types of CO measurement during HBOT, with the thermodilution method as the most referenced.[10–13,16]

In addition to being easy and safe, the use of TED requires only a minimum of technical skills. It has been estimated

Figure 1
Haemodynamic parameters during HBOT (n = 7); CO – cardiac output with 95% confidence interval, measured with transoesophageal Doppler; MAP – mean arterial blood pressure; SVR – systemic vascular resistance (calculated from SVR = (MAP - CVP)/CO (assuming central venous pressure = 0);
* difference from 'steady state/baseline' just prior to HBOT



that training in about 10 to 12 patients is needed to achieve adequate positioning of the probe and to obtain reliable CO measurements.[17] In addition, TED has been shown to have a low inter- and intra-observer variability and the risk related to probe positioning is considered as low compared to the risk related to more invasive procedures such as pulmonary artery catheterization.[10,18] We experienced no problems related to the insertion procedure of the TED probes. However, the time to optimal signal might be slightly prolonged in patients with a gastric tube. During the experiment, we readjusted the probe before each measurement to optimize flow signal. However, the readjustment is probably not necessary under routine clinical settings, which makes the method useful in situations where only limited staff may be available or in situations where pressurization is performed without chamber attendants. The simple technique also minimizes the pressure exposure time of personnel compared to transthoracic echocardiography, where a technician has to be inside the chamber during every measurement.[16]

Haemodynamic parameters such as MAP, SpO_2 and heart rate might be insufficient to detect a patient's true haemodynamic status.[19,20] Studies have shown that TED can improve early recognition of hypovolaemia and be a guide to intravascular volume replacement and drug-supportive therapy while avoiding the risk of hypervolaemia.[21,22] This could lead to shorter hospitalization and reduced mortality.[23] Besides providing a continuous estimate of CO during intensive and perioperative care, the fact that we report that TED can be applied under hyperbaric conditions suggests that TED might be used for continuous-trend monitoring of CO in patients with NF from arrival at the hospital until the patient is haemodynamically stable.

TRENDS IN CARDIAC OUTPUT

We observed an initial tendency toward a decrease in CO from arrival at the hyperbaric unit to initiation of HBOT. This decline may well be explained by the fact that the ventilator minute volume was increased by 10% for all but one patient after arrival at the unit, thus increasing positive alveolar pressure and thus decreasing cardiac preload and CO.

Current data suggest that patients with septic shock who experience adequately volume resuscitation are characterized by a hyperdynamic cardiac state with

pronounced vasodilatation and decreased SVR resulting in a compensatory increase in CO. This may partly mask concomitant underlying cardiac dysfunction.[24,25,] Prior reports on CO measurement in healthy subjects find that HBOT causes a reduction in heart rate leading to a decline in CO, but little is known about the effect of hyperbaric oxygen on CO in haemodynamically unstable patients.[11,26] Only one study in four critically ill patients has examined CO during their HBOT, but with the use of thermodilution in a monoplace chamber and with intermittent air breaks.[27] They observed an increase of CO in one patient, a stable CO in two patients, and a decrease in the fourth, whilst we observed a tendency towards an increasing CO during HBOT in five of seven patients, which may reflect the compensated physiologic response patterns seen in patients with sepsis and systemic vasodilation.

This is also supported by the decrease in SVR and MAP observed in this trial. Normally, peripheral vascular tone increases during HBOT due to the concomitant increased arterial oxygen content, but the effect is probably diminished by the infection itself and its vasodilator effect. In addition, HBOT has been reported to have inhibitory effects on inducible nitric oxide synthase (iNOS) expression during sepsis.[28] iNOS has been described as a myocardial depressant during sepsis and its down-regulation may contribute to a less pronounced myocardial depression.[29] The increase in CO may, therefore, be explained by a change in myocardial contractility due to a combination of sepsis and HBOT. However, it is not possible to draw any conclusion from this study regarding the causal effect of HBOT on CO.

LIMITATIONS

Patients with NF and sepsis or septic shock represent a complex study population where it can be difficult to isolate individual treatment factors that theoretically can affect the haemodynamic status. Potential confounders might be choice of anaesthesia, level of sedation, intravascular volume therapy, pressor agents, ventilator settings, degree of sepsis, and localization of NF. We tried to minimize these confounding effects by keeping the parameters constant during treatment. Additionally, this study was not designed specifically to elucidate the precise role and mechanisms of HBOT in CO.

Further studies with larger study populations and more standardized experimental conditions are needed. However, this study provides a template for future research on this area.

Conclusions

This is the first study to document that TED can be successfully adapted to hyperbaric conditions to provide a minimally-invasive estimate of CO in haemodynamically unstable patients with NF and sepsis during HBOT. In addition, we observed a rise in CO during HBOT in five of seven patients. Future studies with more individuals are feasible and needed in order to draw conclusions regarding the precise effects of HBOT on CO in NF patients.

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Conflict of interest: None

Acknowledgement

CardioQ™ monitor and probes were provided by Deltex Medical Inc. without expense.

Submitted: 11 August 2012
Accepted: 28 December 2012

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