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Role of Hyperbaric Oxygen Therapy in the Treatment of Postoperative Organ/Space Sternal Surgical Site Infections

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Abstract
Background A prospective trial was designed to evaluate the effect of hyperbaric oxygen (HBO) therapy on organ/space sternal surgical site infections (SSIs) following cardiac surgery that requires sternotomy.
Methods A total of 32 patients who developed postoperative organ/space sternal SSI were enrolled in this study from 1999 through 2005. All patients were offered HBO therapy. Group 1 included the patients who accepted and were able to undergo HBO therapy ($n = 14$); group 2 included patients who refused HBO therapy or had contraindications to it ($n = 18$).
Results The two groups were well matched at baseline with comparable preoperative clinical characteristics and operative factors. *Staphylococcus* was the most common pathogen for both groups. The duration of infection was similar in groups 1 and 2 (31.8 7.6 vs. 29.3 5.7 days, respectively, $p = 0.357$). The infection relapse rate was significantly lower in group 1 (0% vs. 33.3%, $p = 0.024$). Moreover, the duration of intravenous antibiotic use (47.8 ± 7.4 vs. 67.6 ± 25.1 days, $p = 0.036$) and total hospital stay (52.6 ± 9.1 vs. 73.6 ± 24.5 days, $p = 0.026$) were both significantly shorter in group 1.
Conclusion Hyperbaric oxygen is a valuable addition to the armamentarium available to physicians for treating postoperative organ/space sternal SSI.

Although surgical site infection (SSI) occurs in only 1% to 4% of patients who undergo cardiac surgery via midline sternotomy, it represents a major problem, leading to increased morbidity, prolonged hospitalization with higher cost, and increased mortality [1]. The therapeutic approach to both incisional and organ/space sternal SSI consists of débriding infected avascular tissue, drainage, curettage, and irrigation with specific antibiotic medications [2].

Hyperbaric oxygen (HBO) therapy is the application of 100% oxygen under pressure that is adjusted two to three times higher than the atmospheric pressure at sea level. HBO therapy might be extremely valuable in the treatment of wound infections by several mechanisms. The sternal wound, by nature, is ischemic and hypoxic; and these local conditions can hinder the mounting healing cascade and the neutrophil-mediated killing of bacteria by free radicals. Therefore, when HBO is applied at the site of infection, it can reverse hypoxia, reduce local edema, salvage marginally perfused tissue, and improve host defenses [3, 4]. Moreover, it can decrease bacterial proliferation and inhibit growth of anaerobic bacteria [5].

Many researchers have examined the effect of hyperbaric oxygen therapy on various wound infections [6-10]. However, there is only a single report on the use of HBO therapy in patients with organ/space sternal SSI [2]. Therefore, we designed a prospective nonrandomized study at a single institution to investigate the safety, efficacy, and outcomes of HBO therapy in patients with organ/space sternal SSI.

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Materials and methods

Between January 1, 1999 and December 31, 2005, a total of 34 patients (mean age 66.6 ± 6.8 years) developed organ/space sternal SSI following cardiac surgery at Centro Cardiologico Monzino Hospital (0.006% of total sternotomies for cardiac operations during this interval). The presence of organ/space sternal SSI was determined using the Centers for Disease Control (CDC) criteria. Briefly, the criteria are any SSI that occurs within 30 days postoperatively and involves any part of the anatomy other than the incision site that was opened or manipulated during surgery. In addition, the diagnosis of organ/space sternal SSI requires the presence of at least one of the following criteria: (1) purulent drainage from the organ/space; (2) organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space; (3) an abscess or other evidence of infection involving the organ/space found on direct examination during reoperation or by histopathologic or radiologic examination; (4) diagnosis of organ/space sternal SSI by a surgeon or attending physician [11].

Management of organ/space sternal SSI in all patients started with initial empirical antimicrobial therapy. The subsequent therapy was dynamically guided by antibiotic susceptibility tests. Antibiotic therapy was managed by an infectious disease physician, together with the cardiac team. Sternal wound infections were approached aggressively by reopening the surgical suture, débriding all infected and avascular tissue, partial sternal wire removal, drainage, and curettage of the sternal edges and the cutaneous/subcutaneous tissues. Local débridement with antiseptic irrigation was performed daily until site sterility was reached. No vacuum suction or other specific devices were used for wound care in this population. The sternal wound was closed soon after sterilization. In the presence of sternal instability, sternal rewiring was performed; a secondary closure using omentum or a muscle flap was not performed in any case.

For HBO therapy, patients breathed 100% oxygen at elevated pressures (two to three times the atmospheric absolute), leading to increased arterial oxygen partial pressure, approaching levels of 1500 mmHg. HBO therapy was administered in a multiplace chamber, which is a comfortable environment for the patient and where there is space to allow medical assistants to deal with acute problems, such as pneumothorax. Patients in the HBO group underwent one HBO therapy session a day, and each session lasted 90 minutes. HBO therapy was discontinued when the wound was sterilized.

All patients with organ/space sternal SSI were offered HBO therapy to improve wound healing. Data collection was prospective; and preoperative, perioperative, and postoperative data were obtained from our institutional database and reviewed using a standard data collection form. Two patients were excluded from the study group because they developed multiorgan failure and expired during the early postoperative period (at postoperative days 5 and 6, respectively). A total of 16 patients accepted HBO therapy and signed the consent forms. Of the 16 patients who consented, 2 were unable to undergo HBO treatment owing to the presence of a pneumothorax at the time of the evaluation visit prior to initiating therapy. Therefore, group 1 included the remaining 14 patients, who successfully underwent HBO therapy ($n = 14$). Group 2 consisted of the patients who did not consent plus the two patients who were unable to undergo HBO therapy ($n = 18$). The reasons for refusal were diverse among patients in group 2, but they can be classified into two categories: claustrophobia and the risks of hyperbaric therapy.

The two groups were compared with regard to their baseline characteristics, operative factors, and clinical outcomes. Baseline characteristics included age; sex; primary cardiac pathology; presence of hypertension, diabetes, chronic obstructive pulmonary disease (COPD), obesity, or previous cardiac operations. The operative factors examined were type of surgery, duration of operation, reexploration for bleeding, the amount of postoperative bleeding, incidence of postoperative intubation, and intraaortic balloon pump (IABP) insertion during or after surgery. The major clinical endpoints analyzed in this study were the duration of infection, infection relapse rate, hospital readmission rate, duration of antibiotic use, and total hospital length of stay.

Antibiotics were discontinued when no clinical signs or symptoms of infection persisted and when two cultures obtained from the wound were negative. Infection relapse was diagnosed by isolating organisms from an aseptically obtained culture and clinical data according to the CDC criteria.This study was approved by our Institutional Ethics Committee.

Statistical analysis

Data are represented as frequency distributions and simple percentages. Values of continuous variables are expressed as a mean ± SD. Continuous variables were compared using an independent *t*-test, and categorical variables were compared by χ^2 and Fisher's exact test, where appropriate. For all analyses, two-sided $p < 0.05$ was considered significant. Statistical analysis was performed using SPSS 9.0 software (SPSS, Chicago, IL, USA).

Results

Baseline characteristics of patients are represented in Table 1. The mean ages of the patients were comparable in

Table 1 Preoperative clinical characteristics

Characteristic	Group 1 (HBO)	Group 2 (non-HBO)	p
No. of patients	14 (43.7%)	18 (56.3%)	
Mean age (years)	68.0 ± 8.7	65.5 ± 6.6	0.467
Sex			
Male	12 (85.7%)	14 (77.8%)	
Female	2 (14.3%)	4 (22.2%)	
Cardiac pathology			
Coronary artery disease	14 (100%)	18 (100%)	
Other	0	0	
No. of diseased vessels	2.7 ± 0.5	2.8 ± 0.5	
Two-vessel disease	4 (28.6%)	4 (22.2%)	0.703
Three-vessel disease	10 (71.4%)	14 (77.3%)	
Hypertension	11 (78.6%)	12 (66.7%)	0.694
Diabetes	6 (42.8%)	11 (61.1%)	0.305
Non-insulin-dependent	3 (21.4%)	9 (50.0%)	
Insulin-dependent	3 (21.4%)	2 (11.1%)	
Body mass index	30.3 ± 6.3	32.4 ± 5.0	
COPD	8 (57.1%)	6 (33.3%)	0.178
Renal failure	2 (14.3%)	2 (11.1%)	0.597
Peripheral vascular disease	6 (42.9%)	2 (11.1%)	0.050
Previous stroke	0	0	
Congestive heart failure	3 (21.4%)	4 (22.2%)	0.649
Hypercholesterolemia	11 (78.6%)	11 (61.1%)	0.253
Smoking history	11 (78.6%)	14 (77.8%)	0.649
Previous cardiac surgery	0	0	
Length of hospital stay prior to surgery (days)	4.0 ± 3.0	3.6 ± 3.3	0.753
Inotropic drugs before surgery	2 (14.3%)	2 (11.1%)	0.597

HBO: hyperbaric oxygen; COPD: chronic obstructive pulmonary disease

Table 2 Operative and perioperative details

Parameter	Group 1 (HBO)	Group 2 (non-HBO)	p
Type of surgery			
CABG	14 (100.0%)	18 (100.0%)	
Off pump	4 (28.6%)	1 (5.6%)	0.142
On pump	10 (71.4%)	10 (94.4%)	
No. of ITA grafts used			1.000
One	13 (92.9%)	16 (88.9%)	
Two	1 (7.1%)	2 (11.1%)	
No. of distal anastomoses	2.8 ± 0.6	2.9 ± 0.5	0.430
Duration of operation (min)	227.9 ± 65.5	264.1 ± 94.1	0.388
Reexploration for bleeding	0	2 (11.1%)	0.492
Postoperative bleeding (ml)	696.7 ± 184.0	727.8 ± 336.7	0.841
Transfused patients	3 (21.4%)	5 (27.8%)	1.000
Postoperative intubation (days)	0.5 ± 0.1	0.6 ± 0.2	0.322
IABP inserted during or after surgery	1 (7.1%)	1 (5.6%)	1.000
ICU stay (days)	2.4 ± 0.9	6.6 ± 13.4	0.500

CABG: coronary artery bypass grafting; ITA: internal thoracic artery (graft); IABP: intraaortic balloon pump; ICU: intensive care unit

the two groups (68.0 ± 8.7 vs. 65.5 ± 6.6 years for groups 1 and 2, respectively; $p = 0.467$). There were no significant differences in sex, cardiac pathology, number of diseased vessels, or the presence of co-morbidities between groups.

Operative data are shown in Table 2. All patients in this study underwent coronary artery bypass grafting (CABG) as the primary cardiac procedure. The off-pump approach, number of internal thoracic artery (ITA) grafts used, duration of bypass, reexploration for bleeding, postoperative intubation, and IABP insertion during or after surgery were similar for the two groups. The mean and SD of the intensive care unit (ICU) stay in group 2 was increased by an outlier with a long ICU stay. However, the difference was not significant. Additionally, the median ICU lengths of stay were also comparable between groups (2 days vs. 2 days for groups 1 and 2, respectively; $p > 0.05$).

None of the patients in either group had infections related to other organs or surgical sites. Glycemia was strictly monitored and controlled in all patients during the preoperative, perioperative, and postoperative periods.

The wound bacteriology was also comparable for the two groups, in the order of *Staphylococcus epidermidis*, *Staphylococcus aureus*, and coagulase(-) *Staphylococcus* in decreasing frequency (Table 3). The development of infection from the time of surgery took 14.9 ± 6.8 and 9.9 ± 7.1 days for groups 1 and 2, respectively ($p = 0.130$). The mean number of HBO treatments applied in group 1 was 17.1 ± 5.8.

Outcome parameters are summarized in Table 4. Duration of the infection and the time from diagnosis to wound closure were not different between groups. However, relapse of infection was significantly lower in the HBO therapy group (0% vs. 33.3%, $p = 0.024$). Two patients in group 2 were readmitted to the hospital after discharge, whereas none of the patients in group 1 were readmitted. The duration of intravenous antibiotic use was significantly shorter in group 1 than in group 2 (47.8 ± 7.4 vs. 67.6 ± 25.1 days; $p = 0.036$). The total hospital stay was 52.6 ± 9.1 vs. 73.6 ± 24.5 days for groups 1 and 2, respectively ($p = 0.026$). In-hospital mortality was 0% for the study population, and no patients had adverse events during the administration of HBO therapy.

Discussion

Hyperbaric oxygen therapy has been recommended for a wide variety of medical conditions [9, 12]. For wound

Table 3 Details of organ/space sternal SSI

Parameter	Group 1 (HBO)	Group 2 (non-HBO)	*p*
Organ/space sternal SSI pathogens			0.973
Staphylococcus aureus	5 (35.7%)	7 (38.9%)	
Staphylococcus epidermidis	6 (42.9%)	7 (38.9%)	
Staphylococcus coagulase(-)	3 (21.4%)	4 (22.2%)	
Time from surgery to recognized infection (days)	14.9 ± 6.8	9.9 ± 7.1	0.130

SSI: surgical site infection

Table 4 Clinical outcomes

Parameter	Group 1 (HBO)	Group 2 (non-HBO)	*p*
Duration of infection until sterilization (days)	31.8 ± 7.6	29.3 ± 5.8	0.357
Duration of infection until wound closure (days)	34.7 ± 7.7	31.1 ± 6.0	0.199
Infection relapse rate	0	6 (33.3%)	0.024
Interval between first and second infections (days)	—	7.67 ± 1.4	—
Duration of intravenous antibiotic use (days)	47.8 ± 7.4	67.6 ± 25.1	0.036
Total hospital length of stay (days)	52.6 ± 9.1	73.6 ± 24.5	0.026

healing, HBO therapy is mostly used for problematic wounds, especially diabetic foot infections and leg ulcers caused by arterial insufficiency [7, 13-18]. It is not yet clear if the results obtained with leg ulcers [19] can be generalized to patients with wound healing problems. Therefore, we conducted this prospective study to evaluate the possible role of HBO therapy in the management of organ/space sternal SSI.

One of the results of our study is the absence of significant differences in the duration of infection and the time from diagnosis to wound closure. This finding does not correlate well with the previous reports on other types of infected wound [20, 21]. HBO therapy combined with antibiotic therapy has been recommended for soft tissue infections, as this approach can shorten the treatment [20]; experimental studies have confirmed this finding [22, 23].

The lower rate of infection relapse in patients who were treated with HBO therapy represents an important clinical endpoint. This difference could be attributed to the positive effects of the higher concentration of oxygen on the healing tissue. Sternal wounds after cardiac surgery are hypoxic and ischemic, especially in patients who undergo CABG with harvesting of the left internal thoracic artery (ITA). The harvest of a pedicle left ITA causes temporary sternal ischemia in the ipsilateral hemisternum [24] that resolves over time but also can predispose to the development of a sternal wound infection during the perioperative period. Hyperbaric oxygen has been shown to reverse the local hypoxia. At 3 atmospheres, the dissolved-oxygen content is approximately 6 ml/dl, which is more than enough to meet the resting cellular requirements without any contribution from oxygen that is bound to hemoglobin [25]. Increased tissue oxygenation by HBO accelerates collagen synthesis by fibroblasts in the wound, promotes angiogenesis, reduces edema, and restores host defenses against infections acting on leukocytes [3, 20, 26, 27].

Another possible explanation for the high rate of infection relapse in the group not treated with HBO could be that it is difficult to determine when an infection is really annihilated. It can be hypothesized that in some patients the infection was not completely eradicated despite negative cultures. The microbiology for the first and second infections was exactly the same in patients with infection relapse, which further supports this hypothesis. The absence of relapses in the HBO therapy group suggests a role for HBO in eradication of the infection. Hyperoxia not only reverses ischemia, it has bacteriostatic and bactericidal properties [3] by inducing free-radical production, which is toxic to both anaerobic and aerobic bacteria [28]. HBO alone was demonstrated to be as effective as an antibiotic in the treatment of experimental osteomyelitis due to *Staphylococcus aureus* in rabbits [22]. Moreover, HBO can enhance the effect of antibiotic therapy by altering the microorganism's susceptibility to antimicrobial agents [20].

Limitations of the study

This study was prospective in nature, but patients were not randomized. We pointed out a possible role of HBO in the treatment of organ/space sternal SSI and found results similar to those from previous studies in which HBO was used for other types of wound infection. However, the outcomes of this study must be confirmed by randomized controlled trials to better understand the efficacy of HBO in organ/space sternal SSI and to define clinical indications for HBO therapy. Moreover, we focused only on clinical parameters and did not perform any evaluation of the local effects of HBO, such as measuring tissue oxygenation or angiogenesis.

Conclusions

Hyperbaric oxygen, a potentially remarkable modality, is a valuable addition to the armamentarium available to physicians treating postoperative organ/space sternal SSI. HBO therapy therefore may become an adjunctive treatment modality in such situations as part of a comprehensive program of wound care based on surgical and medical principles. The discovery of beneficial cellular and biochemical effects has strengthened the rationale for administering HBO for organ/space sternal SSI; however, additional studies are required to define the indications of HBO therapy.

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