J Neurosurg Spine 10:16–20, 2009

Role of hyperbaric oxygen therapy in the treatment of bacterial spinal osteomyelitis

Clinical article

Raheel Ahmed, M.D., Ph.D., Meryl A. Severson III, M.D., and Vincent C. Traynelis, M.D.

The University of Iowa, Department of Neurosurgery, Iowa City, Iowa

Object. Hyperbaric oxygen therapy (HBO) is used as primary and/or adjunctive therapy in the treatment of various clinical conditions complicated by local hypoxia. It may have therapeutic potential in the treatment of neurosurgical infections such as spinal osteomyelitis that are associated with significant morbidity rates. The purpose of this study was to evaluate the efficacy of HBO therapy in the treatment of spinal osteomyelitis.

Methods. The clinical records of patients diagnosed with spinal osteomyelitis who received HBO therapy during their treatment at the authors' institution over the past 10 years were retrospectively reviewed. Six adult patients were identified. Four patients had recently undergone spinal surgery and secondary spinal osteomyelitis had developed. These patients received adjunctive HBO therapy due to significant comorbidities and risk factors for poor healing.

Results. All patients remained symptom and infection free over the subsequent follow-up period. Two patients had primary spinal osteomyelitis that had recurred despite a full course of appropriate antimicrobial therapy. Infection control was achieved after HBO therapy in 1 patient. The mean follow-up period for the study group was 2.9 years (range 5 months to 5 years).

Conclusions. Hyperbaric oxygen therapy enabled infection cure in 5 of 6 patients with spinal osteomyelitis complicated by medical comorbidities or the failure of primary therapy. These results show that HBO may be a useful adjunctive therapeutic modality in the treatment of spinal osteomyelitis, particularly when there are medical comorbidities that increase the risk of poor healing. Hyperbaric oxygen therapy may also be beneficial in patients with relapsing primary spinal osteomyelitis after standard therapy has failed. *(DOI: 10.3171/2008.10.SPI08606)*

Key Words • **hyperbaric oxygen** • **spinal infection** • **spinal osteomyelitis**

Spinal osteomyelitis is associated with significant rates of morbidity and mortality.[15] Risk factors include both local (such as recent spine surgery or adjacent soft-tissue infection) and systemic factors (chronic systemic illness and infections, immunosuppression, and diabetes mellitus).[6] The incidence of spinal osteomyelitis has been rising because of an increase in the number of individuals with immunocompromised status, an increase in the prevalence of intravenous drug use, the emergence of drug-resistant microbes, and the resurgence of tuberculous infections.[4,16] The management of spinal osteomyelitis consists of aggressive antimicrobial therapy. Surgical intervention is indicated in patients with symptomatic neural compression and/or spinal instability.[15] Eradication of the infection is often hampered by local hypoxia and/or ischemia, which delays wound healing and impedes the oxidative bactericidal function of neutrophils.[5]

Initially used to treat decompression sickness, HBO therapy is now recommended as a primary and/or adjunctive treatment for a wide range of clinical disorders.[17] Hyperbaric oxygen therapy raises the absolute oxygen tension at the infection site, which improves neutrophilic oxidative activity and promotes wound healing and neovascularization.[8] There are numerous published reports on the use of HBO therapy in the treatment of soft tissue and musculoskeletal infections, but to date there have been no randomized controlled studies examining the treatment indications and efficacy of HBO therapy in the management of spinal osteomyelitis. We report our experience with HBO therapy in the treatment of primary and postoperative spinal osteomyelitis.

Abbreviation used in this paper: HBO = hyperbaric oxygen.

Methods

We identified 103 patients with a clinical diagnosis of spinal osteomyelitis through a retrospective search of the hospital database at the University of Iowa Hospitals and Clinics, Iowa City, Iowa, over a 10-year period between January 1996 and December 2006. The diagnosis of spinal osteomyelitis in these patients was made on the basis of clinical, laboratory, and radiological evaluations, and patients with primary osteomyelitis (absence of preceding spinal surgery) and secondary (postoperative) osteomyelitis were included. We next identified a subset of 9 patients with spinal osteomyelitis who received HBO therapy. Of these, 2 patients died of significant medical comorbidities unrelated to their spinal infection during the course of treatment and were thus excluded from the study group. Another patient did not complete the recommended number of HBO sessions and was also ex-

cluded. Patient records of the remaining 6 patients with spinal osteomyelitis who had undergone HBO therapy were reviewed for: 1) patient demographic characteristics (age, sex, and comorbidities); 2) microbiological results (microbial isolates and antibiotic sensitivity patterns); 3) medical treatment received (duration and nature of antimicrobial therapy); 4) surgical intervention (wound care and instrumentation); 5) hyperbaric therapy received (primary indication, number, and duration of sessions); and 6) final clinical outcome based on laboratory, clinical, and radiological evaluations performed by the neurosurgical and infectious diseases services. To extend the total clinical follow-up period, telephone interviews were undertaken to assess any recurrence and/or persistence of symptomatic clinical infection. The University of Iowa Human Subjects Office Institutional Review Board approved this retrospective study.

Hyperbaric Oxygen Therapy

A typical HBO treatment protocol at our institution is conducted in a multiplace chamber (Perry Baromedicals) at a pressure of 2.0–2.4 atmospheres absolute over 3 periods of 30 minutes each during which patients breathe 100% oxygen via a hood. A 10-minute rest period (air break) occurs between the first and second oxygen exposure, as well as between the second and third. Patients undergo 1 session 5 days a week for a total of 30 sessions over a 6-week period. All patients who received HBO therapy underwent myringotomy tube insertion to reduce middle ear pressure changes and minimize the risk of barotrauma during therapy.

Results

We identified a total of 6 patients who underwent HBO therapy after spinal osteomyelitis over a 10-year period from July 1996 to December 2006 at our institution. These patients included 3 men and 3 women with an age range of 31–81 years (mean 53 years; Table 1).

Two patients had no prior history of spinal surgery and received a diagnosis of primary spinal osteomyelitis. Spinal osteomyelitis involving the L4–5 disc space and an L1–3 epidural abscess developed in 1 patient (Case 1) after recurrent episodes of *Staphylococcus aureus* septicemia. Despite appropriate intravenous antibiotic treatments, the patient continued to manifest the clinical signs of residual infection, and a tagged white blood cell scan indicated persistent infection in the lumbar spine at the L4–5 level. Hyperbaric oxygen therapy was therefore initiated because the spinal osteomyelitis was refractory to medical therapy. Following HBO therapy his infection resolved and there was no evidence of a new or recurrent infection at the 5-month follow-up examination. The patient in Case 2 had a history of methicillin-resistant *S. aureus* septicemia. He responded clinically (improvement in laboratory parameters and subjective complaints) to in-hospital treatment with a sensitivity-guided intravenous antibiotic regimen. Three weeks later back pain developed again and he was found to have spinal osteomyelitis at T4–5 involving the vertebral bodies and disc space. Hyperbaric oxygen therapy was instituted after primary antimicrobial therapy failed to cure the infection. His infection subsequently resolved with normalization of his laboratory parameters. One month later he suffered a clinical relapse, and there was radiological evidence of worsening osteomyelitis. In addition to resuming intravenous antibiotic treatment, the infectious diseases specialists started the patient on long-term oral antibiotic suppressive therapy. He subsequently remained asymptomatic over a 2-year follow-up period.

The remaining 4 patients in our series had a prior history of spinal surgery. The patient in Case 3 had undergone multiple spinal instrumentation procedures over a 5-year period due to a traumatic spinal injury. The patient in Case 4 had undergone multiple spinal procedures for chondrosarcoma resection and had received instrumented fusion. Two patients were treated with a lumbar arthrodesis for symptomatic lumbar spondylolisthesis and spondylosis, respectively. In each of these patients, HBO therapy was instituted as an adjunct to antibiotic therapy and surgical debridement because spinal osteomyelitis developed postoperatively. Hyperbaric oxygen therapy was typically initiated within 1 week after debridement and continued daily thereafter. All patients received a total of 30 sessions over a 6-week period. Surgical intervention involved removal and revision of spinal instrumentation in 3 patients (Cases 4–6) within this subgroup. A wound vacuum was applied in 4 patients (Cases 3–6) postoperatively.

Follow-Up Examination

All patients were followed up by both the neurosurgery and the infectious diseases services. The mean duration of follow-up was 1.9 years (range 5 months to 5 years). To extend the total clinical follow-up period, telephone interviews were conducted to access any recurrence and/or persistence of symptomatic clinical infection. The overall patient response to medical/surgical and HBO therapy was monitored through the following: 1) laboratory evaluation with serial white blood cell counts, erythrocyte sedimentation rate, and C-reactive protein measurements; 2) clinical evaluation of pain, neurological function, and the wound site; and 3) interval radiological imaging. Infection cure was adequately achieved in 5 of 6 patients at the end of their respective follow-up periods. The patient in Case 2 experienced a relapse that necessitated long-term antibiotic therapy to suppress the infection.

Microbiology of Spinal Infections

Staphylococcus aureus was the most common organism identified in blood and wound site cultures, consistent with its role as the most common microbial cause of spinal osteomyelitis (Table 2).[15] Coagulase-negative *Staphylococcus* was identified in 1 instance. Of the 2 patients with recurrent primary spinal osteomyelitis, methicillin-resistant *S. aureus* was isolated from blood cultures in 1 patient. In all cases, an appropriate antimicrobial regimen was chosen based on microbial sensitivity results and the recommendations of infectious disease consultants.

TABLE 1: Summary of clinical characteristics of patients with primary and postoperative spinal osteomyelitis who underwent HBO therapy*

Case No.	Age (yrs), Sex	Prior Spinal Sx	Diagnosis	Comorbidities	Surgical Tx	Infection Site	Primary HBO Indication	Timing of HBO Therapy	Response to HBO & Final Outcome†	Duration of FU
1	54, M	—	primary OM	IHD; chronic back pain	none	L4–5 disc space & L1–3 epidural abscess	chronic, refractory OM	2 days post-admission & antibiotic therapy	OM resolved	5 mos
2	68, M	—	relapse of (primary) spinal OM	HTN, COPD, IHD, DM, melanoma	none	T4–5 VB & disc & epidural abscess at T-4	relapsing, refractory OM	3 days post-admission & antibiotic therapy	OM resolved initially w/ improvement in pain control; developed relapse 1 mo later	2 yrs
3	41, M	laminectomy & PS insertion	spinal OM & postop wound infection	HTN; post-traumatic paraplegia w/ T-5 level	incision & drainage; WVP	L1–2 VB w/ epidural spread & bilateral psoas abscesses	adjunct	1 wk postop	OM & wound infection resolved	6 mos
4	31, F	pst decompression; T-9 arthrodesis; T-6 & T-7 PS placement	postop deep wound infection	thoracic chondrosarcoma	incision & drainage; WVP	T12–L3 paraspinal abscess	chronic, refractory OM	1 wk postop	wound infection healed completely	3 yrs
5	81, F	L4–5 facetectomy & posterior fusion w/ allograft	spinal OM & postop wound infection	osteoporosis, PUD, hypothyroidism	irrigation & debridement; hardware removal; WVP	L3–4 disc space & epidural abscess; psoas abscess	adjunct	2 days postop	OM resolved; improvement in neurological deficit & local wound pain	2 yrs
6	44, F	L3–4 & L4–5 PLIF; L3–5 PS fixation	spinal OM & postop wound infection	DM, HTN, OA	incision & drainage; hardware revision; WVP	L3–5 disc space & epidural abscess	adjunct	1 wk postop	OM resolved & improved wound healing	2 yrs

* Abbreviations: COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; HTN = hypertension; IHD = ischemic heart disease; OA = osteoarthritis; OM = osteomyelitis; PLIF = posterior lumbar interbody fusion; PUD = peptic ulcer disease; PS = pedicle screw; VB = vertebral body; WVP = wound vacuum placement.

† Assessed based on erythrocyte sedimentation rate, C-reactive protein levels, white blood cell count, and interval imaging results.

Discussion

Infection cure was achieved in 5 of 6 of our patients with spinal osteomyelitis who underwent HBO therapy, which suggests a role for HBO therapy as an adjunctive approach in the management of complicated spinal osteomyelitis. Our results demonstrate the efficacy of HBO therapy in patients with spinal osteomyelitis complicated by primary therapy failure or by medical comorbidities that may impede the eradication of microbial infection and delay wound healing. A direct comparison of final outcomes in patients with spinal osteomyelitis who undergo HBO therapy versus those who undergo treatment with the standard approach involving antibiotic therapy and aggressive wound care is complicated by several factors. First, patients with spinal osteomyelitis who are evaluated for adjunctive HBO therapy may inherently reflect a subgroup of patients with complicated infections caused by medical comorbidities and other risk factors for poor healing that have hindered infection cure through standard antimicrobial and/or surgical treatment. Secondly, even in patients with similar comorbidities, the local and systemic factors that hinder infection cure and wound healing vary greatly between individuals. Finally, the small sample size of this case series makes it difficult to stratify the risk factors in the patients, which would be useful for evaluating the efficacy of HBO therapy.

Although antibiotic prophylaxis has reduced the incidence of postoperative infections in neurosurgical patients who undergo spinal surgery involving instrumentation, wound infections still complicate 0.2–4.7% of spinal surgeries.[2] The standard approach to treating spinal osteomyelitis involves aggressive irrigation and debridement

TABLE 2: Summary of microbiology and pharmacological treatment of primary and postoperative spinal infections*

Case No.	Microbe	Site for Microbial Isolate	Antimicrobial Therapy & Duration
1	*S. aureus*	blood	IV vancomycin for 6 wks; rifampicin & sulfamethoxazole/trimethoprim prophylaxis for 4 wks
2	MRSA	blood	IV vancomycin for 6 wks; oral doxycycline prophylaxis for lifetime
3	*S. aureus*	blood & wound	IV nafcillin for 6 wks
4	*S. aureus*	wound	IV nafcillin for 6 wks; oral dicloxacillin prophylaxis for 6 mos
5	coagulase-negative *S. aureus*	wound	IV vancomycin for 6 wks; oral doxycycline prophylaxis for lifetime
6	*S. aureus*	wound	IV nafcillin for 6 wks

* IV = intravenous; MRSA = methicillin-resistant *S. aureus*.

of the infection along with administration of microbial sensitivity guided intravenous antibiotics for 4–6 weeks.[15] However, resolution of infection is often impeded by comorbid conditions such as diabetes mellitus, peripheral vascular disease, obesity, and concomitant degenerative bone disease. Each of these conditions may affect blood supply, drug penetration through soft tissue and infected bone, and healing of the involved bone and adjacent soft tissues.[1,5,7] Patients commonly have > 1 of these comorbid conditions.

Hyperbaric oxygen therapy is often used as an adjunctive modality in the treatment of various musculoskeletal and soft-tissue injuries/conditions. Currently, the Undersea and Hyperbaric Medical Society recommends the use of HBO therapy for 13 conditions ranging from soft-tissue infections and poor or delayed wound healing, to gas embolism and carbon monoxide poisoning.[8] Common to all of these conditions is impaired tissue oxygenation.

Hyperbaric oxygen therapy increases local soft-tissue oxygenation, which improves host defense mechanisms against infection.[8] The oxidative bactericidal activity of neutrophils through superoxide oxygen radicals is significantly enhanced with increased tissue oxygen tension. High oxygen levels also have a direct bactericidal and bacteriostatic effect and improve the efficacy of antimicrobial agents. Hyperbaric oxygen therapy also elevates the partial pressure of oxygen in bone, which enhances healing by promoting osteogenesis, neovascularization, and collagen production.[3,12]

Indication for HBO Therapy

Given the central role of tissue hypoxia in the development of complicated infections, HBO therapy may have therapeutic potential in the treatment of spinal osteomyelitis. There are published reports on improvement of chronic limb osteomyelitis with HBO therapy, with overall success rates of 60–85%.[8] There are limited published data to date that address the efficacy of HBO therapy as an adjunctive modality in the treatment of spinal osteomyelitis. In a subgroup of 7 patients with spinal osteomyelitis and wound infections after spine surgery with instrumentation, HBO therapy enabled infection control and healing without removal of fixation material in 5.[11] A single case report describes the use of HBO therapy to treat a primary spinal epidural abscess successfully without surgical intervention.[10]

The indications for HBO therapy in musculoskeletal infections such as foot ulcers in diabetic patients are based on standard wound classifications (dependent on the characteristics of the ulcer, depth of tissue involvement, presence of infection, and peripheral vascular disease).[9] In contrast, there are currently no classification systems in place for assessing the severity of spinal osteomyelitis that may guide the decision to include HBO therapy as an adjunctive treatment modality.

Titanium spinal instrumentation does not need to be removed simply because osteomyelitis is present.[14,19] However, the development of spinal osteomyelitis and deep wound infection may be associated with pseudarthrosis (failure of fusion), spinal instability, and adverse neurological outcomes.[15] In turn, this complication may necessitate repeated surgical procedures for wound management and revision of spinal instrumentation with associated risks of complications and death. Adjunctive HBO therapy may facilitate early and rapid infection control and wound healing, thereby decreasing the need to place or revise instrumentation. The clinical courses of patients with spinal osteomyelitis who had a history of previous spinal surgery were complicated by medical and surgical comorbidities (see *Results*). Institution of HBO therapy enabled infection control and promoted wound healing in all patients within this subset.

Adverse Effects of HBO Therapy

Hyperbaric oxygen therapy was well tolerated by all study patients, and no adverse effects were reported. All patients received myringotomy tubes, which may have alleviated the most commonly reported side effects of HBO therapy: middle ear discomfort and tympanic barotrauma.

Timing and Duration of HBO Therapy

The optimum timing and duration of HBO therapy is not well established. In our series, HBO therapy was instituted in patients with primary spinal osteomyelitis that persisted despite a course of antimicrobial treatment. In patients with postoperative spinal osteomyelitis and wound infections, HBO therapy was instituted within the first week of surgical intervention for wound irrigation and debridement.

The appropriate duration of HBO therapy for spinal osteomyelitis is unclear. Reported treatment regimens for various conditions typically vary from 20–40 HBO sessions in total.[17] All of our patients underwent 30 treatment sessions. It may be worthwhile to evaluate whether shorter HBO treatment regimens are effective in managing spinal osteomyelitis. This may improve overall treatment compliance and reduce the costs associated with HBO therapy, given that hyperbaric medicine facilities are not widely available.

We excluded a single patient from our analysis because he did not complete a full course of HBO treatment. This patient received only limited HBO therapy after failure of initial therapy for primary *S. aureus*, which included surgical debridement and intravenous antibiotics. He received only 9 sessions of HBO therapy with continued antibiotic treatment, and at 2-year follow-up period there was no recurrence of his primary infection.

Transcutaneous Oxygen Measurements

Transcutaneous oximetry has been recommended as an objective parameter to assess tissue hypoxia and perfusion when considering or using HBO therapy.[7] Measurements of oxygen tension at the infection site may aid in risk stratification of patients who are likely to experience poor wound healing and delayed infection control, and who may benefit from HBO therapy. Transcutaneous oximetry may objectively determine the efficacy of ongoing HBO therapy in improving oxygen tension within the infection zone, although this has not been studied for deep paraspinal and spinal infections.[13]

Conclusions

Despite the absence of randomized control studies, HBO therapy has consistently been reported as being beneficial in the treatment of a wide range of conditions.[17,18] The present study adds to a growing consensus on the efficacy of HBO therapy in the management of spinal osteomyelitis.[11] Our results also suggest that HBO therapy may be effective in patients with osteomyelitis following failure of primary therapy. Additional reported experience and the future use of risk scoring systems will be helpful for identifying subgroups of patients with spinal osteomyelitis that are particularly susceptible to complications or death from infection; it is these individuals who will benefit the most from adjunctive HBO therapy.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

References

1. Allen DB, Maguire JJ, Mahdavian M, Wicke C, Marcocci L, Scheuenstuhl H, et al: Wound hypoxia and acidosis limit neutrophil bacterial killing mechanisms. **Arch Surg 132:**991–996, 1997
2. Bose B: Delayed infection after instrumented spine surgery: case reports and review of the literature. **Spine J 3:**394–399, 2003
3. Brismar K, Lind F, Kratz G: Dose-dependent hyperbaric oxygen stimulation of human fibroblast proliferation. **Wound Repair Regen 5:**147–150, 1997
4. Carragee EJ: Pyogenic vertebral osteomyelitis. **J Bone Joint Surg Am 79:**874–880, 1997
5. Gottrup F: Oxygen in wound healing and infection. **World J Surg 28:**312–315, 2004
6. Govender S: Spinal infections. **J Bone Joint Surg Br 87:**1454–1458, 2005
7. Hopf HW, Hunt TK, West JM, Blomquist P, Goodson WH, Jensen JA, et al: Wound tissue oxygen tension predicts the risk of wound infection in surgical patients. **Arch Surg 132:**997–1005, 1997
8. Jain KK: Hyberbaric oxygen therapy in infections, in Jain KK (ed): **Textbook of Hyperbaric Medicine, ed 4.** Cambridge, MA: Hogrefe & Huber, 2004, pp 133–146
9. Kessler L, Bilbault P, Ortéga F, Grasso C, Passemard R, Stephan D, et al: Hyperbaric oxygenation accelerates the healing rate of nonischemic chronic diabetic foot ulcers: a prospective randomized study. **Diabetes Care 26:**2378–2382, 2003
10. Kohshi K, Abe H, Mizoguchi Y, Shimokobe M: Successful treatment of cervical spinal epidural abscess by combined hyperbaric oxygenation. **Mt Sinai J Med 72:**381–384, 2005
11. Larsson A, Engström M, Uusijärvi J, Kihlström L, Lind F, Mathiesen T: Hyperbaric oxygen treatment of postoperative neurosurgical infections. **Neurosurgery 50:**287–296, 2002
12. Marx RE, Ehler WJ, Tayapongsak P, Pierce LW: Relationship of oxygen dose to angiogenesis induction in irradiated tissue. **Am J Surg 160:**519–524, 1990
13. Niinikoski JH: Clinical hyperbaric oxygen therapy, wound perfusion, and transcutaneous oximetry. **World J Surg 28:**307–311, 2004
14. Picada R, Winter RB, Lonstein JE, Denis F, Pinto MR, Smith MD, et al: Postoperative deep wound infection in adults after posterior lumbosacral spine fusion with instrumentation: incidence and management. **J Spinal Disord 13:**42–45, 2000
15. Quiñones-Hinojosa A, Jun P, Jacobs R, Rosenberg WS, Weinstein PR: General principles in the medical and surgical management of spinal infections: a multidisciplinary approach. **Neurosurg Focus 17(6):**E1, 2004
16. Rezai AR, Woo HH, Errico TJ, Cooper PR: Contemporary management of spinal osteomyelitis. **Neurosurgery 44:**1018–1026, 1999
17. Wang C, Schwaitzberg S, Berliner E, Zarin DA, Lau J: Hyperbaric oxygen for treating wounds: a systematic review of the literature. **Arch Surg 138:**272–280, 2003
18. Wang J, Li F, Calhoun JH, Mader JT: The role and effectiveness of adjunctive hyperbaric oxygen therapy in the management of musculoskeletal disorders. **J Postgrad Med 48:**226–231, 2002
19. Weinstein MA, McCabe JP, Cammisa FP Jr: Postoperative spinal wound infection: a review of 2,391 consecutive index procedures. **J Spinal Disord 13:**422–426, 2000

Manuscript submitted September 27, 2007.
Accepted October 9, 2008.

Address correspondence to: Vincent C. Traynelis, M.D., University of Iowa Hospitals & Clinics, Department of Neurosurgery, 200 Hawkins Drive, Iowa City, Iowa 52242. email: vincent-traynelis@uiowa.edu.