Hyperbaric Oxygen Treatment of Postoperative Neurosurgical Infections

Agneta Larsson, M.D., Mats Engström, M.D.,
Johan Uusijärvi, M.D., Lars Kihlström, M.D.,
Folke Lind, M.D., Ph.D., Tiit Mathiesen, M.D., Ph.D.

Department of Anaesthesiology and Intensive Care (AL, JU, FL), Division of Hyperbaric Medicine, and Department of Neurosurgery (ME, LK, TM), Karolinska Hospital, Stockholm, Sweden

OBJECTIVE: To evaluate the clinical usefulness of hyperbaric oxygen (HBO) therapy for neurosurgical infections after craniotomy or laminectomy.

METHODS: The study involved review of medical records, office visits, and telephone contacts for 39 consecutive patients who were referred in 1996 to 2000. Infection control and healing without removal of bone flaps or foreign material, with a minimum of 6 months of follow-up monitoring, were considered to represent success.

RESULTS: Successful results were achieved for 27 of 36 patients, with a mean follow-up period of 27 months (range, 6–58 mo). One patient discontinued HBO therapy because of claustrophobia, and two could not be evaluated because of death resulting from tumor recurrence. In Group 1 (uncomplicated cranial wound infections), 12 of 15 patients achieved healing with retention of bone flaps. In Group 2 (complicated cranial wound infections, with risk factors such as malignancy, radiation injury, repeated surgery, or implants), all except one infection resolved; three of four bone flaps and three of six acrylic cranioplasties could be retained. In Group 3 (spinal wound infections), all infections resolved, five of seven without removal of fixation systems. There were no major side effects of HBO treatment.

CONCLUSION: HBO treatment is an alternative to standard surgical removal of infected bone flaps and is particularly useful in complex situations. It can improve outcomes, reduce the need for reoperations, and allow infection control without mandatory removal of foreign material. HBO therapy is a safe, powerful treatment for postoperative cranial and spinal wound infections, it seems cost-effective, and it should be included in the neurosurgical armamentarium. (Neurosurgery 50:287–296, 2002)

Key words: Artificial implant, Cranioplasty, Hyperbaric oxygenation, Osteomyelitis, Radiation injuries, Spinal infections

Infections remain a common complication of surgery. In neurosurgery, postoperative infections are particularly bothersome, sometimes virtually untreatable, and are associated with substantial morbidity and mortality rates (1). A 2.5% incidence of postoperative wound infections after craniotomies, including subdural empyemas and brain abscesses, was recently reported in a large, prospective, multicenter study (15). This rate of infection does not differ much from those observed in the 1950s and 1960s (3, 23), despite modern antibiotics and prophylactic regimens.

Conventional therapy involves the use of antibiotics, mandatory removal of the infected bone flap, and secondary reconstructive surgery with an acrylic implant (so-called delayed cranioplasty) (16). Such cranioplastic implants have hitherto required removal in cases of infection, leading to an even more complicated situation and often large cranial defects. Spinal infections represent another complex situation; the fixation material cannot be removed as easily, because of instability. The situation may be further complicated by factors such as malignant disease, radiation injury, chemotherapy, repeated surgery, tissue transplants, and foreign material. Such risk factors result in suboptimal conditions for healing, largely because of poor tissue quality and the presence of hypoperfused, hypoxic, infected wounds. Any treatment that could improve outcomes and reduce the need for reoperations would be of value.

Hyperbaric oxygen (HBO) therapy is used to treat a variety of infected, hypoperfused, and hypoxic wounds (11). Oxygen tensions play an important role in the outcomes of infections (21). The leukocyte bacteria-killing capacity is substantially impaired at the low oxygen tensions often observed in wounds (2, 13, 17). HBO therapy increases the oxygen tension in infected tissues, including bone (17), resulting in direct bactericidal effects on some anaerobic organisms. The therapeutic effect of HBO treatment on aerobic organisms is attributable to significant improvements in phagocytic killing of bacteria such as *Staphylococcus aureus*, which is the most common pathogen observed in infected incisional neurosurgical wounds (1, 15, 23). HBO therapy improves host defenses and has proved adjunctive, with antibiotics and surgery, for the treatment of infectious wound complications after surgery in the irradiated head and neck (20), gas gangrene and other necrotizing soft-tissue infections (11), infected ischemic diabetic foot ulcers (7), and chronic refractory osteomyelitis (5). It has also been successfully used to reduce complications after crush injuries of the extremities (4). In radiation-injured tissues, HBO therapy induces the formation of new capillaries, thus improving tissue oxygen tensions and host defenses (18, 19) and improving osseointegration and reducing implant failure rates (10). This article reports the clinical usefulness of HBO therapy in the treatment of postoperative neurosurgical infectious complications among 39 consecutive patients who were referred for HBO therapy for the treatment of neurosurgical infections.

PATIENTS AND METHODS

The ethics committee at the Karolinska Hospital approved this retrospective study. Between January 1, 1996, and December 31, 2000, 39 consecutive patients were referred by the Department of Neurosurgery for adjuvant HBO treatment at the Division of Hyperbaric Medicine at the Karolinska Hospital. All patients had received a clinical diagnosis of a postoperative infection, on the basis of local signs, suppuration, sepsis, laboratory findings, and/or radiologically detectable pathological features. Only patients for whom the alternative treatment would have been repeated surgery with removal of the bone flap or foreign material and patients whose infections had a poor prognosis of healing, because of previous irradiation or other risk factors, were referred.

All patients received antibiotics appropriate to their bacterial culture results. The most common bacteria cultured were *Staphylococcus epidermidis* and *S. aureus*. Infectious disease specialists initiated and modified the antibiotic treatment of the pathogenic organism(s) for in-patients. Antibiotic treatment varied between 2 and 27 weeks. Eight patients underwent surgical procedures for wound drainage and removal of devitalized tissues or foreign materials, according to the judgment of the managing surgeon. For three patients, a plastic surgeon assisted in the repair of soft-tissue defects and the covering of acrylic implant areas.

One 17-year-old patient, who had undergone repeated surgery because of shunt infection, refused HBO therapy after the first session because of claustrophobia and was excluded from further analysis. The structure of our patient series suggested three subgroups, i.e., Group 1, with uncomplicated cranial wound infections; Group 2, with complicated cranial wound infections; and Group 3, with spinal wound infections.

Group 1

Group 1 included patients with osteomyelitis of a free cranial bone flap after craniotomy, without additional risk factors (n = 15). This group included 5 male and 10 female patients, with a median age of 55 years (range, 16–69 yr) (*Table 1*). Reasons for neurosurgery included meningiomas (n = 8), other benign tumors (n = 4), aneurysms (n = 2), and traumatic hemorrhage (n = 1). The mean interval between surgery and diagnosis of the wound infection was 9 weeks (range, 1–52 wk). The mean interval between surgery and initiation of HBO treatment was 15 weeks (range, 3–52 wk). The primary treatment goal was to avoid removal of the infected bone flap. *S. epidermidis* was cultured from seven patients and *S. aureus* from three patients. A variety of other microorganisms, such as *Propionibacterium* and *Streptococcus milleri*, were also observed.

Group 2

Group 2 included patients with osteomyelitis, with or without remaining bone/acrylic flap, after craniotomy with additional risk factors, such as repeated surgery, foreign material, malignant disease, or previous radiotherapy (n = 16). This group included 6 male and 10 female patients, with a median age of 53 years (range, 27–69 yr) (*Table 2*). Reasons for neurosurgery included malignant tumors (n = 6), recurrent meningiomas (n = 6), basal cell carcinoma and hydrocephalus (n = 1), and trauma (n = 3). The mean interval between surgery and diagnosis of the infection was 6 weeks (range, 0–26 wk). The mean interval between surgery and HBO treatment was 12 weeks (range, 0.5–48 wk). All patients were hospitalized and received intravenous antibiotic treatment. *S. epidermidis* was cultured from three patients and *S. aureus* from five patients. A variety of other agents, such as *Propionibacterium*, *Klebsiella*, and *Corynebacterium*, were also observed.

Patient 2.7 had undergone extensive transcochlear surgical treatment of a widely growing petrous meningioma and underwent initial wound closure with fat but developed a cerebrospinal fluid leak and a deep wound infection. Patient 2.14 had a subdural empyema after repeated burr-hole drainage of a chronic subdural hematoma. Patient 2.10 underwent a second series of HBO treatments 17 months after the end of his first series, and his outcome results have been reported as 2.10a and 2.10b. Patient 2.15 developed an infection after a highly contaminated, traumatic open fracture of the forehead and face. Patients 2.8 and 2.11 had undergone previous vascularized, microsurgical, tissue transplants to allow healing of atrophic radiation-injured tissues. The treatment goals were to achieve infection control and wound healing in complex situations and, if possible, to avoid removing the bone flaps/foreign material.

Group 3

Group 3 included patients with osteomyelitis and deep wound infections after spinal surgery with implantation of fixation material (n = 7). This group included four male and three female patients, with a median age of 37 years (range, 22–74 yr) (*Table 3*). Reasons for neurosurgery included cervi-

TABLE 1. Patients (Group 1) Treated with Hyperbaric Oxygen for Osteomyelitis of a Free Bone Flap after Craniotomy, without Additional Risk Factors[a]

Patient No.	Age (yr)/ Sex	Diagnosis	Infection	No. of HBO Sessions	Follow-up Period (mo)	Result	HBO Cost (SEK)
1.1	16/M	Epidural hematoma	Bone flap	40	27	Flap removed 2 mo after HBO	72,000
1.2	57/F	Aneurysm	Bone flap	40	57	Resolved	62,160
1.3	50/F	Aneurysm	Bone flap	40	24	Flap removed 2 mo after HBO	75,800
1.4	58/F	Arteriovenous malformation	Bone flap	16	28	Resolved	28,800
1.5	38/M	Foramen of Monro cyst	Bone flap	40	58	Resolved	62,160
1.6	66/M	Foramen of Monro cyst	Bone flap	40	31	Resolved	71,334
1.7	24/F	Cavernoma	Bone flap	40	13	Resolved	76,800
1.8	57/F	Meningioma	Bone flap	40	55	Resolved	62,160
1.9	40/F	Meningioma	Bone flap	47	27	Flap removed 9 mo after HBO	95,400
1.10	55/F	Meningioma	Bone flap	40	32	Resolved	103,770
1.11	43/F	Meningioma	Bone flap	40	28	Resolved	72,000
1.12	67/F	Meningioma	Bone flap	40	15	Resolved	72,000
1.13	51/M	Meningioma	Bone flap	40	12	Resolved	88,000
1.14	69/F	Meningioma	Bone flap	40	10	Resolved	88,000
1.15	59/M	Meningioma	Bone flap	15	7	Resolved	33,000

[a] HBO, hyperbaric oxygen therapy; SEK, Swedish kroner (1 American dollar equals approximately 10 kroner).

cal trauma (n = 2), thoracic spinal fractures (n = 1), lumbar spinal fractures (n = 2), cervical spinal stenosis (n = 1), and cervical intramedullary ependymoma (n = 1). The mean interval between surgery and diagnosis of the infection was 3 weeks (range, 1–12 wk). The mean interval between surgery and HBO treatment was 6 weeks (range, 3–16 wk). *S. epidermidis* was cultured from three patients and *S. aureus* from three patients. Other agents, such as *Propionibacterium* and enterococci, were also observed. The primary treatment goal was to achieve infection control and healing without removal of fixation material.

Follow-up monitoring

The patients were monitored through reviews of chart notes from clinic visits in the Department of Neurosurgery and the Division of Hyperbaric Medicine, as well as other clinics. Telephone interviews were conducted during February and March 2001, after examination of the Swedish National Register of deaths.

HBO treatment

The Karolinska Hospital Division of Hyperbaric Medicine is staffed by anesthesiology and intensive care physicians and nurses trained in the medical, mechanical, and physical aspects of hyperbaric medicine. Because of the long distance from the neurosurgical intensive care unit to the hyperbaric chamber, no intubated patients were treated with HBO therapy. All patients in this study were spontaneously breathing and were treated in either of our two acrylic monoplace chambers (model 2500B or 3200; Sechrist Industries, Inc., Anaheim, CA) pressurized with 100% oxygen, which allowed the patients to breathe without a mask or hood. Chamber passthroughs allowed continued intravenous therapy and monitoring.

Hyperbaric treatment was administered at a pressure of 2.5 to 2.8 bar (250–280 kPa), which is equivalent to a water depth of 15 to 18 m. The patients breathed pure oxygen for three 25-minute periods, which were interrupted by two 10-minute air breaks. The treatment protocol was chosen according to the clinical severity of the infection, as judged by the attending neurosurgeon and HBO specialist. Treatment was normally administered once daily for 5 days each week, with a schedule of up to 40 sessions. In cases of severe infections, threatened tissues, and/or life-threatening situations, initial treatments were administered at 2.8 bar, twice daily and on weekends.

RESULTS

Group 1

The infections resolved and the wounds healed for all patients with osteomyelitis after craniotomy (*Table 1*). For 12 of 15 patients, with a mean follow-up period of 29 months, healing occurred without removal of the bone flap.

TABLE 2. Patients (Group 2) Treated with Hyperbaric Oxygen for Osteomyelitis, with or without Remaining Bone/Acrylic Flaps, after Craniotomy, with Additional Risk Factors such as Repeated Surgery, Foreign Material, Malignant Disease, or Previous Radiotherapy[a]

Patient No.	Age (yr)/ Sex	Diagnosis	Therapy and Complications	Infection	No. of HBO Sessions	Follow-up Period (mo)	Result	HBO Cost (SEK)
2.1	29/M	Astrocytoma	Malignant tumor	Bone flap	40	21	Resolved	72,000
2.2	36/M	Ependymoma	Radiotherapy, wound breakdown	Bone flap	40	8	Bone flaps removed 6 mo after HBO, wound healed	88,000
2.3	55/F	Glioblastoma	Radiotherapy	Bone flap	4	<6	Tumor recurrence, dead 3 mo after HBO	16,800
2.4	40/F	Glioblastoma	Radiotherapy, repeated surgery for tumor recurrence	Bone flap	38	<6	Tumor recurrence, dead 2 mo after HBO	67,014
2.5	27/M	Medulloblastoma	Radiotherapy, flap infection, flap removed, wound breakdown, dura mater exposed, MRSA	Soft tissue and bone	38	39	Resolved (no vancomycin used)	68,400
2.6	57/F	Cranial metastasis	Malignant kidney tumor	Acrylic flap	40	26	Resolved, acrylic flap retained	71,262
2.7	59/F	Meningioma	Large tumor, complicated surgery, soft-tissue transfer	Bone flap	40	35	Resolved	124,800
2.8	40/F	Meningioma	Radiotherapy, repeated surgery for tumor recurrence, angioplasty and free tissue transfer	Acrylic flap	40	29	Resolved, acrylic flap retained	72,000
2.9	63/F	Meningioma	Repeated surgery for tumor recurrence, infected bone and acrylic flaps and sinus frontalis fistulae, hemophilia	Acrylic flap	38	27	Acrylic flap removed 6 mo after HBO, wound healed	68,400
2.10a	69/M	Meningioma	Radiotherapy, repeated surgery for tumor recurrence and infected bone and acrylic flaps	Soft tissue and bone	38	16	Resolved, continued below	68,400
2.10b		Meningioma, same patient as 2.10a	Chemotherapy 3 wk after 1st HBO series, tumor recurrence and reoperation with angioplasty, 2nd HBO series 17 mo after 1st	Acrylic flap	37	7	Acrylic flap removed after HBO Session 14, meningitis, cardiac infarction, wound healed after HBO Session 37, tumor recurrence, dead 7 mo after HBO	67,000
2.11	53/F	Meningioma	Repeated radiotherapy, repeated surgery	Acrylic flap	36	12	Resolved, acrylic flap retained, tumor recurrence, dead 12 mo after HBO	64,800
2.12	60/F	Meningioma	Repeated radiotherapy, repeated surgery, bone flap removed, wound breakdown, cranium exposed	Soft tissue and bone	30	15	Resolved	88,242
2.13	66/F	Basal cell carcinoma	Radiotherapy, 40 yr repeated surgery for tumor recurrence, reconstructive surgery, postinfectious aqueduct stenosis with hydrocephalus, shunt infections, shunt exposed and removed, CSF drainage	Soft tissue and bone	46	18	Ventriculocisternotomy after HBO Session 6, persistent wound	82,800
2.14	48/M	Subdural hematoma	Repeated surgery, subdural empyema	Empyema, bone flap	7	41	Resolved	37,218
2.15	42/F	Cranial and facial fractures	Contaminated traumatic wound, fixation material	Soft tissue and bone	13	27	Resolved, fixation material left	69,600
2.16	53/M	Cranial fracture, epidural hematoma	Hemicranectomy	Acrylic flap	40	6	Wound healed, epidural abscess, acrylic flap removed 5 mo after HBO	88,000

[a] HBO, hyperbaric oxygen therapy; SEK, Swedish kroner; MRSA, methicillin-resistant *Staphylococcus aureus*; CSF, cerebrospinal fluid.

TABLE 3. Patients (Group 3) Treated with Hyperbaric Oxygen for Osteomyelitis and Deep Wound Infections after Spinal Surgery, with Implantation of Fixation Material[a]

Patient No.	Age (yr)/ Sex	Diagnosis	Surgery	Complications	Infection	No. of HBO Sessions	Additional Therapy	Follow-up Period (mo)	Result	HBO Cost (SEK)
3.1	74/F	Fracture at C6–C7, quadraplegia, cervical spine luxation, central cord syndrome	Frontal discectomies and fusions at C5–C7 and corpectomy at C6	Failure to close esophageal fistula, infection, removal of loose fixation material, posterior fusion with Apofix	Soft tissue and bone mediastinitis (life-threatening)	59	Repeated surgery, including closure of ruptured esophagus and bone transplantation	46	Resolved, fixation material left, survived	188,160
3.2	61/M	Fracture at C6–C7, epidural hematoma at C2–T6	Anterior and posterior fusion	Abscess, CSF leakage	Soft tissue and bone	40		36	Resolved, fixation material left	135,792
3.3	37/M	Fractures at T12, paraplegia	Laminectomy at T12, posterior fusion, bone transplantation	Abscess, fistula, necrotizing fasciitis, myositis, revision	Soft tissue and bone	40		17	Resolved, fixation material left	72,000
3.4	29/M	Fracture at L1, paraplegia	Laminectomy, posterolateral fusion	Reoperation, removal of bone fragment, discectomy, fusion, bone transplantation, CSF leakage	Soft tissue and bone	18	Fixation material removed 4 mo after HBO because of dislocation threatening to penetrate the skin	38	Resolved, fixation material removed	105,000
3.5	22/F	Fractures at L2 and calcaneus, paraplegia	Posterolateral fusion	Abscess, fistula	Soft tissue and bone	24	Fixation material removed 4 days after HBO, reoperation for fistula 6 mo later	21	Resolved, fixation material removed	43,200
3.6	60/M	Cervical spinal stenosis	Corpectomy at C5, bone transplantation, fusion	Intraspinal abscess at C2–C4	Soft tissue and bone	18	Two metal screws in danger of penetrating the esophagus removed surgically	32	Resolved, fixation material left	71,400
3.7	34/F	Ependymoma at C2–T3	Laminectomy at C2–T2, extirpation of tumor, fixation	Abscess, fistulae, radiotherapy postponed because of infection	Soft tissue and bone	40	One screw aborted	23	Resolved, fixation material left	71,604

[a] **HBO, hyperbaric oxygen therapy; SEK, Swedish kroner; CSF, cerebrospinal fluid.**

Group 2

Three of six acrylic cranioplasties and three of four free bone flaps could be retained (*Table 2*). The infections resolved and the wounds healed for 13 of 16 patients. Treatment was discontinued for Patient 2.3 after only four HBO sessions, because of rapid tumor progression and transfer to a hospice for terminal care. Patient 2.4 received a full course of HBO treatments, with good results. Both patients exhibited improvement of their wound infections but were classified as failures because wound healing could not be satisfactorily evaluated. The patients were treated for terminal disease in other institutions and died as a result of recurrent glioblastomas within 3 months. Patient 2.13 exhibited a persistent wound in follow-up examinations.

One patient (Patient 2.10) underwent two series of HBO treatments. The first series (denoted 2.10a) was to achieve infection control in an area that had been subjected to repeated surgery and radiotherapy, in which both bone and acrylic flaps had been removed before HBO treatment. Infection control made chemotherapy possible, and the patient underwent replacement of an acrylic flap 3 months after HBO treatment. The second HBO series (denoted 2.10b) was administered 17 months after the first series, because of a renewed postoperative infection after surgery to treat a recurrence. At that time, the acrylic flap needed to be removed to ensure wound healing. The patient died 7 months after the second HBO series, as a result of yet another tumor recurrence.

Group 3

All infections resolved, and spinal fixation materials were retained for all except two patients (*Table 3*). Patient 3.5 exhibited a rapid favorable response, with infection control and wound contraction. The HBO series and medical and surgical therapies were discontinued after 24 HBO sessions by the patient, who left the hospital against medical advice. The fixation material was subsequently removed at another hospital. The remaining fistulae of the patient were surgically resolved 6 months later, with complete healing at the 21-month follow-up examination. Patient 3.4 received 18 HBO treatments, following our aggressive HBO treatment protocols, which led to rapid infection control and healing. The fixation material migrated 4 months after HBO treatment, threatened skin penetration, and was removed; the spine had become stable. Four months later, a recurrent wound infection was diagnosed and successfully treated with 6 months of antibiotic therapy based on bacteriological culture results.

Treatments were discontinued prematurely because of favorable responses and rapid healing for two patients (Patients 3.4 and 3.6). One elderly patient (Patient 3.1) had an epidural abscess, an esophageal fistula, and severe, life-threatening mediastinitis after surgery to treat a traumatic cervical dislocation. The patient recovered, despite a grim initial prognosis.

Compliance and side effects

The rate of compliance with HBO treatments was high. Only one patient refused additional HBO treatments after her first session, because of claustrophobia. Patient 1.15 discontinued therapy after 15 sessions because of alcohol abuse. Patient 3.5, with a history of heavy drug abuse, discontinued her HBO series and medical and surgical therapies after 24 HBO sessions when she left the hospital to return to her previous lifestyle. Treatment was discontinued prematurely, after only 16 HBO sessions, for Patient 1.4 because of transient myopia. Treatment series were prolonged for three patients with complicated infections. The number of treatments for each patient ranged from 7 to 57.

The side effects of HBO treatment were minimal. Some minor problems with pressure equalization and serous otitis occurred. In our series, only Patient 1.9 experienced a significant change in refraction, resulting in myopia. Her original refractive state returned within 6 weeks after the discontinuation of therapy.

DISCUSSION

Our previous clinical experience with neurosurgical infections indicates that the results achieved with HBO therapy are remarkable. HBO treatment allowed infection control and healing for 27 of 36 patients and became an alternative to standard treatment involving surgical removal of infected bone flaps, acrylic flaps, or foreign fixation material.

It is considered difficult to draw scientific conclusions from retrospective data for a series of selected patients. However, the selection used in our series would seem to have been biased against HBO therapy. Generally, patients with complications that were expected to be difficult to treat were referred for HBO therapy. Furthermore, conducting a randomized trial was not feasible, because the alternative treatment was removal of the bone flap or foreign material.

Clinical results

Among patients with uncomplicated cranial wound infections (Group 1), successful resolution with a retained bone flap was achieved for 12 of 15 patients. Attempts have been made to retain the flap via continuous suction with topical antibiotic irrigation (6), but the usual treatment involves removal of the bone flap and extensive debridement, followed by primary closure and antibiotic treatment (1). This is followed by secondary cranioplasty 3 to 6 months later. This approach involves the risks and expense of two operations, additional hospital stays, repeated failure, spread of infection to the brain, and large cranial defects and disfigurement if ablative surgery becomes necessary. In our hospital setting, the cost of these two surgical procedures alone, during the study period of 1996 to 2000, was 130,000 to 210,000 Swedish kroner, whereas the actual cost of HBO therapy in our series averaged 71,000 kroner.

Among patients with complicated cranial wound infections (Group 2), HBO therapy allowed healing despite risk factors such as malignant disease, radiation injury, chemotherapy, repeated surgery, or foreign material. Traditional therapy would have necessitated removal of bone or acrylic flaps (sometimes covering more than one-half of the calvarium) or entailed very protracted healing, if any, of irradiated tissues.

Several patients with a previous history of a "bad meningioma," with multiple recurrences, radiation treatment, and extensive complex cranioplasties, were cured of their open purulent infections without removal of foreign material. Because of tumor recurrence, two patients (Patients 2.3 and 2.4) were monitored for insufficient periods to reach the minimal 6-month evaluation. Their responses to treatment seemed to be acceptable, but the practice of subjecting patients with limited expected survival times to a prolonged HBO regimen, instead of rapidly removing the bone flap, may be questionable. The average cost of HBO therapy in Group 2 was 71,000 Swedish kroner.

Dramatic beneficial effects of HBO therapy were also observed for patients with spinal wound infections (Group 3). In particular, Patient 3.1 was considered to be in immediate danger of death as a result of a combination of old age, a spinal epidural infection, an esophageal fistula, and mediastinitis. We achieved infection control and healing in complex settings with deep postoperative spinal wound infections, without removal of fixation material, for five of seven patients. The failures were not primarily attributable to poor responses to HBO treatment. Discontinued treatment because of drug addiction may have caused one "failure" (Patient 3.5). The other patient (Patient 3.4) was classified as experiencing failure because the fixation material was removed 4 months after HBO treatment, after healing of the wound and fracture, because of migration of the screws. The costs of HBO therapy in Group 3 averaged 98,000 Swedish kroner.

Mechanism of action and rationale for HBO treatment

Most nonhealing infected wounds are hypoxic (13) because of ischemia. Ischemia not only hinders oxygen delivery to tissues but also compromises antibiotic delivery. These marginally viable tissues are vulnerable to infection and exhibit poor infection control and wound healing despite meticulous wound care and antibiotic treatment. For many years, surgeons have used revascularization procedures or flaps to counteract the deleterious effects of ischemia and hypoxia on wound healing. Animal experiments using microelectrodes to measure oxygen partial pressures in normal, healing, and infected tissues and in tissues containing foreign bodies demonstrated marked hypoxia, especially if the foreign body was infected (22). Infections, and concurrent inflammation, increase oxygen consumption dramatically, because phagocytes consume more oxygen. In parallel with this, oxygen delivery is reduced because of tissue edema and ischemia. Wound tissue oxygenation and resistance to infection are thus further compromised.

HBO therapy has been used to treat a variety of infections and postoperative complications in bone and soft tissues (11, 20). Osteomyelitic bone exhibits decreased blood flow and a markedly reduced partial pressure of oxygen (17). The mode of action of HBO treatment is chiefly via stimulation of the bactericidal action of white blood cells. The leukocyte bacteria-killing capacity is impaired in hypoxic surroundings, improves with normoxia, and is further enhanced with hyperoxia (2, 14). HBO therapy restores intramedullary bone oxygen tension and phagocytic killing to normal or above-normal levels (17). The greatly increased tissue oxygen levels in ischemic tissues during HBO therapy also stimulate neovascularization (18), fibroplasia (12), and bone remodeling (9), making the tissues less ischemic and improving long-term wound healing. Treatment with 100% oxygen under normobaric conditions has no such effect.

Irradiated tissues may not heal, despite aggressive procedures, because of progressive vascular damage leading to secondary microvascular ischemia and hypoxia. Infections involving atrophic irradiated tissues with reduced regional blood supply are feared but exhibited successful healing in this series. HBO treatment is the only therapy known to reverse this vascular compromise, and it has become a widely accepted adjuvant therapy for the treatment and prevention of osteoradionecrosis of the mandible (19). HBO therapy exhibits dose-dependent angiogenic effects, causing an eight- to ninefold increase in the vascular density of tissues (18). A good example of this is Patient 2.5, who had a continuously deteriorating wound after surgery, attributable to a medulloblastoma, irradiation, cranial flap removal, and chronic infection with methicillin-resistant staphylococci (*Fig. 1*). The wound healed well with 6 weeks of HBO therapy, and the methicillin-resistant staphylococcal infection was cured by the patient's own host defenses, without the use of antibiotics.

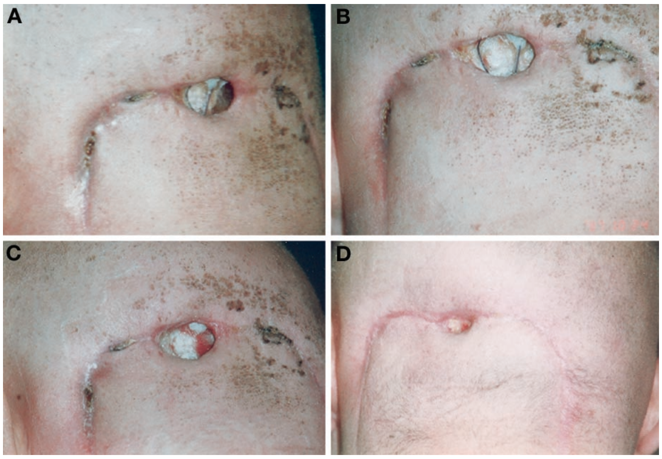

FIGURE 1. Photographs demonstrating HBO treatment results. Surgery to treat an occipital medulloblastoma (Patient 2.5) caused a suppurative wound infection that was treated by traditional methods, with removal of the osteomyelitic bone flap. The condition worsened after radiotherapy, with wound breakdown, exposed dura mater, and necrotic suppurative cavities. Methicillin-resistant *S. aureus* was cultured from the wound. Continuous deterioration was observed until HBO treatment, which allowed gradual healing, with granulation tissue in the necrotic cavities, disappearance of methicillin-resistant *S. aureus* without antibiotic treatment, and contraction of the wound within 38 HBO sessions. *A* and *B*, immediately before the initiation of HBO treatment; *C*, after 11 HBO sessions; *D*, after 29 HBO sessions.

Side effects

The side effects of HBO treatment were minimal, with only one patient experiencing reversible myopia. There were no episodes of central nervous system toxicity. Oxygen seizures may occur, especially when therapy is administered at very high pressures to patients with fever or when hypercapnia attributable to hypoventilation is present. An incidence of 1/10,000 treatments is often cited. Seizures are self-limiting, and sequelae are uncommon. Contraindications to HBO therapy are few but include concurrent administration of certain chemotherapeutic agents, e.g., doxorubicin, bleomycin, mitomycin C, and cisplatin, because of interference with oxygen radical-scavenging mechanisms. Pneumothorax is another condition that can be deleterious during decompression if not treated. Malignancy is not a contraindication. According to the literature (8), HBO therapy has no cancer-causing effects and does not stimulate growth of residual tumor.

Indications

The use of HBO therapy for the treatment of uncomplicated wound infections with osteomyelitis of a bone flap may be controversial. The standard treatment is not ineffective, and it does not require 40 sessions of HBO treatment. However, several of our patients preferred the prospect of HBO treatment in an attempt to avoid two additional operations. In addition, HBO therapy seems to be cost-effective (with a cost less than one-half that of surgery), with a moderate failure rate.

HBO therapy is particularly useful in complex settings. It has a good chance of helping to resolve complicated cranial and spinal wound infections for which no simple solution exists. Removal of foreign material is usually required even when potent parenteral antibiotics are administered.

On the basis of considerations similar to the rationale for the use of HBO therapy to treat gas gangrene and severe, necrotizing, soft-tissue infections, the treatment of intracranial abscesses with adjunctive HBO therapy has been approved by the Undersea and Hyperbaric Medical Society since 1996 (11). In our study, HBO therapy allowed discharge of a patient 4 days after surgical treatment of a subdural empyema. The beneficial effects of HBO therapy on complex infections, including the postoperative empyema, suggest that this treatment should be evaluated as an adjunctive treatment also for such primary, suppurative, central nervous system conditions.

Dose and duration

The issues of the dose and duration of HBO therapy remain unsettled. To achieve infection control in the acute phase, higher treatment pressures (2.8 bar) were initially used, with more than one treatment session per day and HBO therapy on weekends. After a positive clinical response had been obtained, pressures were decreased (2.5 bar) and treatments were administered once daily, 5 days each week. The general principle was to treat patients until we judged that their host responses could sustain infection control and healing. When surgical treatment was required, we continued HBO treatment postoperatively.

With our protocol of 40 HBO sessions at 2.5 bar, we may have overtreated some patients. Patients 1.9 and 1.15 were successfully treated with 16 and 15 sessions of HBO treatment, respectively. HBO treatment was discontinued early for Patients 2.14 and 2.15 because of rapidly resolving infection. One patient (Patient 2.14) with a subdural empyema after burr hole evacuation of a chronic subdural hematoma recovered rapidly and could be discharged, with orally administered antibiotics, after only seven HBO treatments. For other patients (e.g., Patient 3.4), a longer treatment period might have been beneficial. Some of the patients who experienced failure (e.g., Patients 1.1 and 2.9, with large open defects) might have experienced better outcomes with a more aggressive reconstructive surgical approach.

Our clinical experience regarding HBO treatment dose and duration indicates that infection control and establishment of the healing process can be quite rapid and that many patients continue to exhibit improvement after cessation of HBO therapy. However, the bone-remodeling phase and long-term infection control may require a longer treatment protocol with up to or more than 40 HBO sessions. Our initial treatment schedule has been successful, but future refinements could certainly improve individual responses to treatment.

CONCLUSION

We conclude that HBO therapy is a safe medical treatment for postoperative neurosurgical cranial and spinal infections. It is an alternative to standard surgical removal of infected bone flaps. It is also a powerful therapy for more complex infections involving multiple risk factors, such as radiotherapy and foreign material. Our results indicate that HBO therapy can reduce the need for reoperations and can probably improve outcomes and reduce overall costs. HBO therapy should be included in the neurosurgical armamentarium.

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Reprint requests: Agneta Larsson, M.D., Department of Anesthesiology and Intensive Care, Karolinska Hospital, SE-171 76, Stockholm, Sweden.
Email: agneta.larsson@hbo.ks.se

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COMMENTS

The authors report their significant experience with hyperbaric oxygen (HBO) treatment of neurosurgical infections. The results obtained are commendable for this patient population. A search of the literature on neurosurgery and HBO treatment did not yield any other articles on this subject, and it is difficult to identify historical control subjects with whom to compare such patients. The traditional neurosurgical approach, as the authors discuss, is to remove the bone or prosthesis in the presence of infection. The use of HBO therapy to avoid such removal might be preferable, with the main limitation being the scarcity of such units in medical centers.

R. Loch Macdonald
Chicago, Illinois

In this retrospective study, Larsson et al. report their results of using HBO therapy to treat neurosurgical wounds. It seems most logical that HBO therapy would be effective in treating the Group 2 patients described by Larsson et al., for whom wound healing might be compromised by ischemia and poor wound oxygenation. HBO therapy has been routinely used to treat anaerobic wound infections and devascularized wounds throughout the body. In the presence of wound infections, HBO therapy can potentially have two positive effects, i.e., the killing of anaerobic bacteria and the potentiation of white blood cell function. It is not clear whether HBO treatment afforded superior results, compared with surgical therapy, for any other than Group 2 patients. Patients with spinal wound infections after instrumented fusion seem to respond to surgical therapy. A review of the literature indicates that spinal instrumentation can usually be left in place in infected spinal wounds treated with one or more surgical debridements (2, 3).

Similarly, the treatment of acute cranial infections, as observed for Group 1 in this study, seems to be evolving. I have had the opportunity to observe acute postoperative wound infections successfully treated with surgical debridement replacing the bone flap or with suction irrigation, as described by Erickson et al. (1). Unfortunately, I do not know of a series of patients reported in the literature for comparison with the patients treated with HBO therapy.

This study documents the effectiveness of HBO therapy in treating neurosurgical wounds. The relative effectiveness of HBO treatment and the indications defining when HBO treatment is superior to other modes of therapy will need to be defined in future reports.

Allan H. Friedman
Durham, North Carolina

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Larsson et al. retrospectively analyzed the effects of HBO therapy for patients with a variety of intracranial and intraspinal infections and/or foreign bodies. Although there is no comparison group and some of the follow-up periods are relatively short, the rate of successful treatment was generally better than might be expected. I disagree with the authors' contention that a randomized trial is not practical or ethical; if HBO therapy is to be considered an adjunctive treatment for neurosurgical infections, then it must be tested using valid scientific methods.

Marc R. Mayberg
Cleveland, Ohio

HBO therapy has been successfully used to treat carbon monoxide poisoning and decompression sickness. The use of HBO therapy to treat other disease processes, such as acute ischemic stroke and cerebral air embolism, is of unproved benefit. With respect to infected tissues, HBO therapy has been used to treat gas gangrene, diabetic foot ulcers, necrotizing soft-tissue infections, and chronic refractory osteomyelitis. In neurosurgery, HBO treatment has been used to assist in the healing of scalp infections among patients with malignant brain tumors that have been treated with radiotherapy. This study represents the first large series of cases in which HBO therapy was used to treat cranial osteomyelitis, complex cranial infections in the presence of implants, and spinal infections. As anticipated, the success rate for bone flap or implant preservation was highest for less complicated cases without cranioplasties. The excellent recovery results demonstrated in this report strongly suggest that HBO therapy is beneficial in the management of postoperative neurosurgical infections. However, it is not clear what the ideal treatment regimen for these patients should be and whether it is dependent on which microbes are responsible for the infection. The mechanism by which HBO treatment works probably involves a direct bactericidal effect on anaerobic organisms. *Propionibacterium acnes*, an anaerobic Gram-positive bacillus that is well known to cause focal intracranial infections after neurosurgery (1), was observed to be the causative infectious organism for several of the patients reported in this series. This fact makes it imperative for clinicians to identify the offending bacteria before initiating treatment. One concern associated with this form of therapy is that some patients (e.g., those with end-stage glioblastoma multiforme) may be too medically frail to tolerate a series of HBO treatments. Another unfortunate feature of this therapeutic modality is that it is not available to most neurosurgeons for the treatment of patients with severe postoperative infections.

Walter A. Hall
Minneapolis, Minnesota

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Call for Concepts and Innovations Contributions

The *Concepts and Innovations* section has been conceived to establish a new dimension in journalistic presentation. Because of individual variations in the creative mind and the ability to effectively carry ideas through to fruition, many concepts or novel ideas are left "on the shelf" or are unheard because, for one reason or another, individuals do not have the capability to see them through to absolute or practically developed completion.

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