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Review Article

THE USE OF HYPERBARIC OXYGEN IN UROLOGY

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ABSTRACT

Purpose: We review the use of hyperbaric oxygen therapy in urology, and present the mechanisms of hyperoxia action in whole body hyperbaric chamber treatments, patient outcomes and patient selection criteria.

Materials and Methods: The literature on hyperbaric oxygen use in urology was reviewed.

Results: Hyperbaric oxygen is a treatment alternative for patients with an underlying ischemic process unresponsive to conventional therapy. Specific factors which may influence patient selection of hyperbaric oxygen include cancer and absolute contraindications of active viral disease, intercurrent pneumothorax and treatment with doxorubicin or cisplatin. This technique is particularly useful in the treatment of intractable hemorrhagic cystitis secondary to pelvic radiation therapy. Further investigation of the efficacy of hyperbaric oxygen is warranted for patients with necrotizing fasciitis (Fournier's gangrene), posttraumatic ischemic injury and/or impaired wound healing.

Conclusions: Hyperbaric oxygen is a therapeutic alternative which complements the surgical and medical options for select patients.

KEY WORDS: hyperbaric oxygenation, cystitis, ischemia

BACKGROUND

Definition of hyperbaric oxygen. Hyperbaric oxygen treatment of urology patients has gained greater clinical recognition during the last 10 years. Technically the delivery of hyperbaric oxygen occurs when the patient rests the whole body and breathes 100% oxygen in a treatment chamber which is pressurized to higher than sea level, for example greater than 1 atm. Pressurization between 1.4 and 3.0 atm. while the patient inhales oxygen meets the Undersea and Hyperbaric Medicine Society definition of hyperbaric oxygen treatment.[1] Treatment chambers are available at major medical centers and ambulatory care settings which include hyperbaric oxygen as wound care.

Mechanisms. It is helpful to think of hyperbaric oxygen mechanisms in terms of hyperbaria and hyperoxia. The first reports of studies on the physiological effects of hyperbaric oxygen were done at Harvard in the 1930s.[2] Historically hyperbaria has been the basis of hyperbaric oxygen interventions for gas bubble related diseases, for example cerebral air embolism and decompression sickness, leading to the earliest medical research on tolerance limits for treatment. In 1943 the procedure for delivering hyperbaric oxygen for decompression sickness was published by the United States Navy Department Bureau of Ships Directive and set the standard which became accepted worldwide in the 1960s.[3] As noted by Kindwall and others, the most familiar action of hyperbaric oxygen treatment is the mechanical compression to reduce gas bubbles that result from diving accidents and surgically or traumatically induced air embolism.[4–6] Gas bubbles obstruct the capillary circulation, creating an ischemic injury. Hyperbaria reduces the obstruction, relieving the ischemia, and the administration of oxygen simultaneously enhances re-oxygenation and improves gas elimination. At 5 atm. a bubble is reduced to 20% of the original volume and 60% of the original diameter.[7] The mechanical effect of hyperbaria may limit the inclusion of some patients from hyperbaric oxygen treatment. Patients with emphysema, a history of tympanic membrane spontaneous perforation or otological reconstruction may be at risk of spontaneous pnuemothorax, hemotympanum or disruption of reconstructed ear tissue.

In regard to hyperoxia, the biological effect of hyperbaric oxygen derives from hypersaturating circulating plasma with dissolved oxygen during and shortly after treatment, resulting in a transiently increased diffusion gradient between the circulation and surrounding tissues driving transport of oxygen into the interstitium and tissues. At 3 atm. with 100% oxygen, the highest oxygen partial pressure used in clinical practice, arterial oxygen partial pressure may reach 1,900 to 2,100 mm. Hg while dissolved oxygen content may achieve 6.8 volumes percent (6.8 ml. oxygen per 100 ml. blood).[8] Hyperoxia during treatment may result in side effects of oxygen toxicity seizures, loss of respiratory drive in hypercapnic patients and reflex vasoconstriction. Patients who are diabetic may have an exaggerated hypoglycemic response to hyperoxia, the mechanism of which is yet to be defined. To minimize these side effects the duration of hyperoxia during treatment is monitored.

Indications for hyperbaric oxygen. In clinical situations of impaired oxygen delivery or impaired oxygen metabolism hyperbaric oxygen is considered adjunctive treatment to medical and surgical care (see Appendix). For example, in post-ischemic muscle hyperbaric oxygen treatments have been shown to reduce edema and enhance aerobic metabolism.[9–11] Hyperbaric oxygen may also facilitate the transport of some antibiotic agents across the bacterial cell wall, thus improving their overall effectiveness.[12,13] In the treatment of infections and open wounds increased oxygen concentrations may lead to a direct toxic effect on some anaerobic bacteria by

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inducing free radical formation.[14] Although oxygen has no significant direct antibacterial effects on aerobic organisms and facultative anaerobes, neutrophils require oxygen to aid in phagocytosis of all microbials.[15] In infected or traumatized tissue white blood cells frequently function poorly because of inadequate tissue oxygen levels. These diminished oxygen tensions are secondary to a decrease in tissue perfusion due to bacterial overgrowth and from leukocyte phagocytosis, which results in a 15 to 20 times increase in oxygen consumption.[15,16] Hyperbaric oxygen leads to a net gain in oxygen concentration in infected wounds which enhances leukocyte function in part by increasing phagocytic killing, thereby aiding in the resolution of the infectious process.[14] In addition, hyperoxia improves collagen formation, fibroblast growth and angiogenesis,[17] which also enhance wound healing.[15] Finally, hyperbaric oxygen may improve the demarcation between viable and necrotic tissue, and may permit more accurate débridement and less extensive loss of healthy tissue.[12]

The therapeutic effects of hyperbaric oxygen for the treatment of long-term radiation effects were initially described by Marx and Ames for post-radiated head and neck cancer.[18] Marx redefined the sequence of the pathogenesis of radionecrosis as 1–radiation, 2–hypoxic-hypocellular-hypovascular tissue, 3–tissue breakdown and 4–chronic nonhealing wound.[19] Beneficial effects of hyperbaric oxygen on radiation damaged tissue are related to hyperoxia induced primary neovascularization and secondary growth of healthy granulation tissue.[20,21] Additional benefits include vasoconstriction, which may help control bleeding, and improvements in wound healing and immune function.[21–23]

HYPERBARIC OXYGEN IN UROLOGY

Urological conditions which have been suggested as benefiting from hyperbaric oxygen share an underlying impairment of tissue oxygenation. For certain diagnoses, such as priapism or testicular torsion, clinical experience and peer-reviewed reports are insufficient presently to allow an assessment of hyperbaric oxygen efficacy. As a preventive strategy to reduce postoperative complications, Pomeroy et al suggested further evaluation of hyperbaric oxygen as preoperative intervention for patients with previous pelvic irradiation and a history of radiation related complications.[24] Baert et al reported on a patient with severe radiation ulcers of the bladder wall who responded to hyperbaric oxygen treatment after failure of conventional therapy.[25] In addition to case reports, published data on hyperbaric oxygen treatment experience are more readily available for hemorrhagic cystitis as a long-term radiation effect and for life threatening infections, such as Fournier's gangrene. In general the shortcomings of published series include the lack of contemporary control groups,[24] short-term (less than 60 months) and varied followup durations, and differences in categorization of patient acuity[26,27] and outcomes. A consistent definition of successful hyperbaric oxygen intervention is absent from the literature, with studies generally relying on survival, symptomatic relief and avoidance of further surgery to describe positive results. Also, the contribution of patient treatment preference to the selection and acceptance of hyperbaric oxygen has received only limited attention. Finally, the signal transduction pathway and molecular mechanism of the effect of hyperbaric oxygen at the cellular level remain to be defined. For example, a number of adaptive responses to hypoxia are understood at the molecular level to involve transcriptional activation of gene expression by hypoxia inducible factor 1.[28] To address whether hyperbaric oxygen can "cure" a disease, such as radiation injury, new knowledge is needed regarding the role of periodic hyperoxia in modulating the expression of hypoxia inducible factor 1 in affected tissue.

Hemorrhagic cystitis. Hemorrhagic cystitis is defined as gross hematuria associated with bladder inflammation. There are a large number of potential causes of hemorrhagic cystitis, including infection, medications and chemical toxins, but the most common etiology is pelvic irradiation for cancer.[29] A categorical system of grading hematuria in hemorrhagic cystitis cases has been suggested by DeVries and Frieha as mild—not producing an acute decrease in hematocrit, moderate—producing a decrease in hematocrit and requiring 6 units or less of transfused packed red cells to maintain hemodynamic stability, and severe—refractory to simple irrigations, instillations or aminocaproic acid and requiring more than 6 units transfused packed red blood cells.[26] For radiation therapy patients Levenback et al[27] used a modification of the Radiation Therapy Oncology Group criteria for radiation morbidity and categorized those with hematuria due to radiation cystitis as grade 1—mild symptoms, single event, outpatient treatment; grade 2—mild symptoms, multiple events, outpatient treatment; grade 3—hospitalization and medical management of symptoms; grade 4—major surgical intervention, and grade 5—death. Hemorrhagic cystitis as a long-term effect of radiation occurs most frequently following treatment for prostate or cervical cancer but may also be seen in patients with rectal or bladder malignancy.[26] Bladder complications may be seen in 5 to 12% of patients treated with pelvic irradiation[27,30–32] and hemorrhage sequelae may occur in up to 9% of those receiving full dose treatment.[33] As suggested by these grading schemes, symptom severity in patients with radiation cystitis may vary from mild hematuria to life threatening hemorrhage. Efforts to prevent radiation cystitis have included the prospective use of steroids and vitamins.[29]

The acute changes in the bladder due to pelvic irradiation include mucosal edema and inflammation.[26] Hemorrhagic cystitis generally occurs 6 months to 10 years or more following treatment.[34] Histologically the initial diffuse mucosal edema leads to telangiectasia, submucosal hemorrhage, interstitial fibrosis and eventual smooth muscle fibrosis.[26] Finally, acute and chronic ischemia of the bladder wall occurs as a result of obliterative endarteritis.[35] In addition to bleeding complications, other associated symptoms commonly include urinary frequency, urgency, incontinence and bladder pain.[36] Many patients also have a significant reduction in bladder capacity secondary to fibrosis of the bladder wall.[26]

Conventional therapies for radiation cystitis include oral or intravenous hydration for mild cases, which may be sufficient to prevent large blood clots which can impede bladder emptying.[26,29] Other simple measures include catheter placement with intermittent or continuous bladder irrigation and/or the use of oral aminocaproic acid. In patients with more significant hemorrhage intravesical instillation of alum,[37] silver nitrate[38] and prostaglandins[39] may be effective. If these measures are unsuccessful in controlling bleeding, formalin instillation may be used, although it requires regional or general anesthesia, and may lead to severe bladder inflammation and fibrosis.[40] Sodium pentosanpolysulfate has been shown to be effective in treating the damaged bladder.[41] This semisynthetic polyionic compound coats the bladder mucosa in a similar manner to naturally occurring glycosaminoglycans and has recently become available in the United States. Finally, temporary or permanent urinary diversion, selective embolization or ligation of the hypogastric arteries and/or cystectomy may be necessary in the most severe cases.[26,29] Before consideration of hyperbaric oxygen as a treatment alternative for hemorrhagic cystitis unrecognized and untreated malignancy should be excluded by cytoscopy and biopsy, as suggested by DeVries and Frieha.[26]

A number of investigators have studied the use of hyperbaric oxygen in patients with radiation cystitis.[20,21,35,42–45] An advantage of hyperbaric oxygen in these patients is the absence of significant adverse effects on bladder structure or

function, which may be seen with other therapies, such as formalin or silver nitrate instillations.[39-41] However, with long-term followup Del Pizzo et al suggested recently that patients with recurrent hematuria may elect more definitive surgical intervention after undergoing a course of hyperbaric oxygen that abates the hemorrhagic condition in the short term.[46] An early study concerning the use of hyperbaric oxygen for the treatment of radiation cystitis in humans was performed by Schoenrock and Cianci.[35] A total of 19 treatments were given to patients with hemorrhagic radiation cystitis and a vesicocutaneous fistula, leading to spontaneous healing of the fistula and no voiding symptoms with followup of 18 months. Larger series treated with hyperbaric oxygen have also been reported, including a prospective study of 40 patients with radiation cystitis treated at a single center during an 8-year period (table 1).[21,42-44] All of these patients had recurrent symptoms despite 1 or more interventions for hematuria, including bladder fulguration, and the use of alum, silver nitrate and other agents. As an indication of the severity of hemorrhage in this group a mean of 8.2 units of blood had been transfused per patient before hyperbaric oxygen. No recurrent hematuria within 3 months following completion of hyperbaric oxygen was noted in 75% of patients (30 of 40). Recurrent bleeding requiring treatment was noted in 3 patients a mean of 13.3 months after hyperbaric oxygen but 2 of them had recurrent malignancy. Of the remaining 10 patients 7 had partial response with minimal hematuria within 3 months of hyperbaric oxygen and 3 had persistent hematuria with no apparent benefit after treatment. In addition to cancer recurrence, the severity of initial hematuria appeared to influence the likelihood of successful response to hyperbaric oxygen. Of the 40 patients 22 had mild to moderate initial bleeding and all of them had partial or complete hyperbaric oxygen response. Of the 18 patients with severe initial bleeding 83% (15) had a favorable treatment outcome.

In other series a positive response to treatment with hyperbaric oxygen has been reported in the majority of patients with radiation cystitis based on followup observations from 2 to 42 months (table 1).[21,42,44,45,47] Norkool et al noted that 3 of 4 patients with a poor outcome from hyperbaric oxygen had recurrent bladder or prostate cancer,[44] and others have similarly reported that cancer recurrence is the most important factor associated with persistent hemorrhage after treatment.[42] More recently Del Pizzo et al reported on 11 patients treated with hyperbaric oxygen for hemorrhagic cystitis requiring on average of 3.3 units blood transfusion, multiple hospitalizations and conventional therapies.[46] While on initial review (median duration 2.1 years) 8 of 11 patients were asymptomatic, at long-term followup (median duration 5.1 years) only 3 had complete and durable resolution of symptoms and 8 had been treated with definitive surgery to resolve recurrent symptoms.

Regarding hemorrhagic cystitis resulting from exposure to chemicals, the oxazaphosphorine chemotherapeutic drugs, that is cyclophosphamide and isophosphamide, are recognized etiological agents.[26,29] The active metabolite of these drugs is acrolein, which is excreted in the urine leading to urothelial sloughing and submucosal ulceration.[48,49] In addition to bleeding, patients with chemotherapeutic agent induced cystitis may have a variety of irritative voiding symptoms and pain. The use of 2-mercaptoethane sulfonate (mesna), which binds acrolein, thus limiting toxic effects on the urothelium, has reduced the incidence of hemorrhagic cystitis, which was previously noted in up to 40% of patients treated with cyclophosphamide.[50-53]

Although similar histological changes in the bladder are noted in patients irrespective of the primary cause of hemorrhagic cystitis, acrolein appears to damage smooth muscle and its microcirculation.[27,22] For this reason it has been suggested that hyperbaric oxygen is likely to be ineffective in treating acrolein induced hemorrhagic cystitis and should not be used in such cases.[22] However, experimental evidence in animal models indicates that hyperbaric oxygen may be of value for prophylaxis and treatment of hemorrhagic cystitis secondary to chemotherapy.[48] Hader et al treated rats with hyperbaric oxygen before and after exposure to acrolein, and noted a significant decrease in tissue damage and enhanced urothelial regeneration compared to control animals.[48] Given the availability of mesna as a prophylactic agent, it is not likely that hyperbaric oxygen would be cost-effective if used routinely before chemotherapy. However, there may be a role for hyperbaric oxygen in the treatment of certain patients with acrolein induced hemorrhagic cystitis. Hughes et al reported a case of hemorrhagic cystitis occurring after autologous peripheral stem cell transplantation for multiple myeloma.[54] The patient had received cyclophosphamide and busulfan, and the clinical course was complicated by BK virus and adenovirus infections. After antiviral therapy and conventional urological management for intractable hematuria and bladder spasms, the patient was referred for hyperbaric oxygen and completed 37 treatments with complete resolution of bleeding. At 14-month followup he was free of hematuria.

Fournier's gangrene. Necrotizing fasciitis involving the perineum and/or genitalia (Fournier's gangrene) was originally described in the 18th and 19th centuries.[55,56] While this process was originally noted in young, healthy men without apparent cause, most patients in contemporary series have had an identifiable urological or colorectal etiology.[55,57] In many patients with Fournier's gangrene a history of perianal disease, urethral stricture or diabetes, or recent rectal or urinary tract instrumentation has been noted.[55] The infectious processes usually begin as local cellulitis involving the perineum, scrotum and/or perianal region.[58] Rapid progression with pain, fever and sepsis may occur leading to gangrenous changes, crepitus and advancement of infection along fascial planes to involve the anterior abdominal wall.[55,58] Multiple aerobic and anaerobic organisms are usually noted on wound cultures.[55] Early recognition of Fournier's gangrene is critical in achieving a successful outcome. Mortality rates of 20% have been noted in most series.[55,59,60]

The mainstays of treatment in patients with Fournier's gangrene are fluid resuscitation, broad-spectrum antibiotic coverage, and prompt drainage and débridement of necrotic tissue. It is often difficult to define the extent of tissue damage initially and many patients benefit from repeat surgical débridement 1 to 2 days after the first procedure.[55] When available hyperbaric oxygen is most commonly initiated as soon as patients are stabilized following initial débridement. Treatment is often continued until wounds are healed, at which time reconstruction may be performed using primary

TABLE 1. *Hyperbaric oxygen therapy in patients with radiation cystitis*

References	No. Pts.	No. Treatments/Pt.	Duration (mins.)	% Success (No. Pts./Total No.)	Mos. Followup
Rijkmans et al[42]	10	20	90	60 (6/10)	2–24
Bevers et al[43]	40	20	90	92 (37/40)	23 (mean)
Weiss et al[21]	13	60	120	92 (12/13)	30 (mean)
Norkool et al[44]	14	9–58 (mean 28)	90	71 (10/14)	10–42
Del Pizzo et al[46]	11	40	90	27 (3/11)	71 (mean)

closure, or skin grafts or tissue flaps depending on the extent of tissue loss.[58]

Many investigators have explored the use of hyperbaric oxygen to enhance infection control and wound healing in Fournier's gangrene.[57,61-68] However, there have been no reported randomized studies of the efficacy of adjuvant hyperbaric oxygen in patients with necrotizing fasciitis. While there are many theoretical reasons to suggest that hyperbaric oxygen may be useful in treating these patients, clear demonstration that this treatment is beneficial and cost-effective is yet to be established, leaving room for controversy.[68,69] The Undersea and Hyperbaric Medicine Society Committee Report on treatment of soft tissue infections (tissue, muscle and fascia) notes that the principal treatment of necrotizing infections is surgical débridement and systemic antibiotics, with hyperbaric oxygen recommended as an adjunct to therapy only when morbidity and mortality are expected to be high.[70] In the 1996 Committee Report on Hyperbaric Oxygen therapy mortality outcomes of patients with gas gangrene and nonclostridial fasciitis, including and excluding hyperbaric oxygen treatment alternatives, are summarized in separate tables, suggesting that the trend in mortality is improved when hyperbaric oxygen is given for these conditions.[70] The value of retrospective studies is limited by patient selection biases, extended duration (years), and lack of controlled and blinded intervention strategies (table 2).

Riegels-Nielsen et al reported on 5 patients with no mortality in the 4 receiving hyperbaric oxygen.[64] Interestingly, Eltorai et al recommended hyperbaric oxygen as adjunctive treatment of Fournier's gangrene based on their review of 9 cases with no mortality.[71] Hollabaugh et al reviewed the outcomes of 26 men with Fournier's gangrene treated at the University of Tennessee where, based on chamber availability, 14 patients (56%) did and 12 (44%) did not receive adjuvant hyperbaric oxygen.[57] While the study was retrospective, the 2 groups appeared well matched by age, co-morbid disease, extent of initial surgical débridement and incidence of delay in treatment. There was no difference in the number of surgical débridements per patient or the mean length of hospitalization in these 2 groups. The mortality rate was 7% with (1 of 14 patients) compared to 42% (5 of 12) without hyperbaric oxygen ($p = 0.05$).

Riseman et al reported a retrospective review of 29 patients with necrotizing fasciitis, including those with gangrene and nonperineal infections, treated at a single institution.[66] Patients who received hyperbaric oxygen were largely treated during the latter part of the 9-year study. While the hyperbaric oxygen treated and untreated groups appear to be well matched in terms of age, co-morbid health risk and extent of disease, the temporal difference in the use of hyperbaric oxygen suggests a bias in patient selection for treatment due to growing experience with disease management and ongoing improvements in critical care. Mortality was significantly lower in the group treated with hyperbaric oxygen (23%, 4 of 17) compared to the untreated group (67%, 8 of 12) ($p < 0.025$). In addition, only 1.2 débridements per patient were required to achieve wound control for those treated compared to 3.3 for those not treated with hyperbaric oxygen ($p < 0.03$). Elliott et al reviewed the results of 198 consecutive patients with necrotizing soft tissue infections treated at a single institution during an 8-year period.[67] Of the patients 71 (36%) had Fournier's gangrene and all study patients were treated with hyperbaric oxygen. Although no comparative data were reported, the authors concluded that hyperbaric oxygen offered the advantage of early wound closure. Pizzorno et al described their experience with the treatment of 11 patients with Fournier's gangrene.[62] Average patient age was 59.5 years and the most common predisposing condition was diabetes. Of the patients 6 underwent surgical débridement and 3 were treated with delayed reconstructive surgery. No mortality was observed.

In contrast Shupak et al describe a retrospective review of 25 of 37 patients (68%) who were treated with hyperbaric oxygen at a tertiary referral hospital in Israel.[65] The treated and untreated groups were similar with regard to age, gender and individual risk factors suggestive of a worse treatment outcome. However, selection criteria for the treated group and the etiology of the infectious process were not stated. The study included 12 women and many patients had nonperineal fasciitis. The average number of surgical débridements per patient was 3.3 in the treated compared to 1.5 in the untreated group ($p = 0.001$), and the mean length of hospitalization slightly favored the former, although the difference was not significant. The mortality rate was 36% for the treated compared to 25% for the untreated group ($p = 0.7$). The authors concluded that hyperbaric oxygen offered no advantage in reducing morbidity and mortality when used as adjuvant treatment for patients with necrotizing fasciitis.

PATIENT SELECTION

The appropriateness of hyperbaric oxygen as an adjunct to the medical and surgical treatment of urological patients rests on the determination of the role of hypoxia at clinical presentation. Hyperbaric oxygen is not indicated in all cases, and the selection of this therapeutic option depends on surgeon judgment of the viability of affected tissue, availability of the treatment chamber and clinical condition as well as patient willingness to spend time for the treatments, including when care is given in the ambulatory setting. Hyperbaric oxygen is usually well tolerated and adverse effects, including visual disturbances, eustachian tube dysfunction and claustrophobia, are uncommon.[21,42-44] Other possible hyperbaric oxygen complications, including pneumothorax or cerebral air embolism, oxygen toxicity seizures and hypoglycemia, are managed by recognition of risk factors, including a history of emphysema or spontaneous pneumothorax, seizure disorder, alcoholism or diabetes. An active viral infection, history of treatment with cisplatin or doxorubicin and the possibility of active neoplastic disease are usually considered contraindications to hyperbaric oxygen treatment. While active viral infection and history of treatment with cisplatin or doxorubicin are generally considered absolute contraindica-

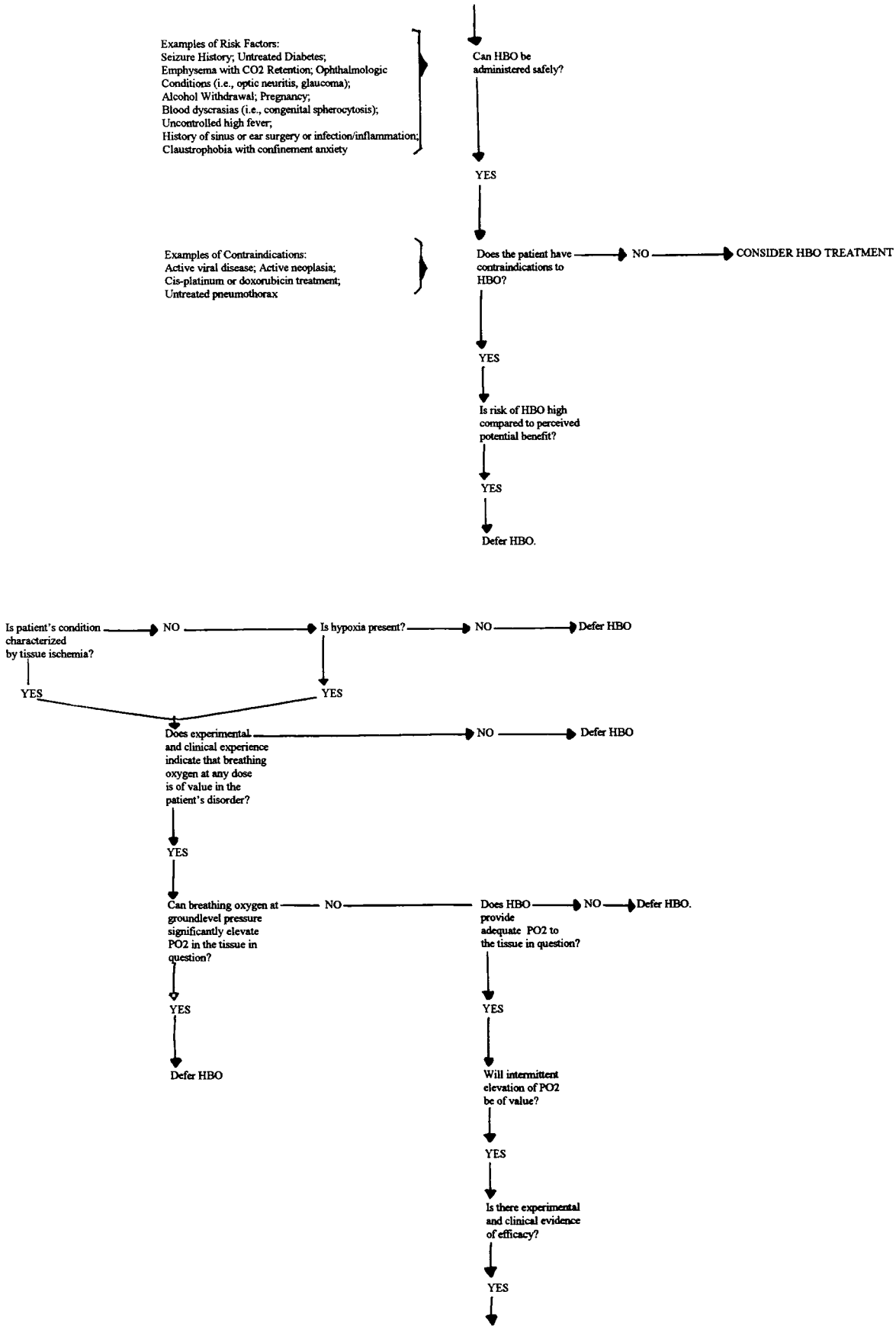
TABLE 2. *Select reports of hyperbaric oxygen in Fournier's gangrene and necrotizing fasciitis*

References	Total No. Pts. (No. hyperbaric oxygen group)	No. Treatments/Pt.	Duration (mins.)	% Hyperbaric Oxygen Treated Mortality	No. Hyperbaric Oxygen Group Surgeries/Pt.
Riegels-Nielsen et al[64]	5 (4)	2–7	70	20	*
Gozal et al[75]	16	5	90	12.5	1–3
Riseman et al[66]	29 (17)	7.4 (mean)	90	23	1.2
Elliott et al[67]	198 (198)	31.7 (mean)	90	25	†
Shupak et al[65]	37 (25)	2/Day‡	90	36	3.3
Pizzorno et al[62]	11 (11)	5–24	90	0	9/Group
Hollabaugh et al[57]	26 (14)	14	90	7	3.0

* Extensive débridement before first hyperbaric oxygen treatment followed by surgical revision when necessary.

† A mean of 3.8 débridements and a mean of 1.6 total reconstructions were done for all patients.

‡ Patients received hyperbaric oxygen twice daily during acute wound management and once daily after toxic signs resolved.



Suggested decision schema regarding patient selection for hyperbaric oxygen (*HBO*) treatment.[3] *CO2*, carbon dioxide. *PO2*, oxygen partial pressure.

tions, clinical judgment may influence treatment decisions. For example, in the context of life threatening infection when hyperbaric oxygen is considered adjunctive treatment of last resort, the relative risk of significant contraindications is balanced against the potential perceived positive benefit of survival enhancement if hyperbaric oxygen is rendered. A suggested decision schema of patient evaluation is shown in the figure, which is based in part on the questions outlined by Davis.[3] The evaluation assumes the availability of a monoplace or multiplace hyperbaric oxygen treatment chamber that can be accessed by patient transportation. The schema is intended to help clinicians guide patients or others unfamiliar with hyperbaric oxygen technology through the logic of their decisions regarding hyperbaric oxygen as a therapeutic option.

Presence of cancer. For the treatment of cancer survivors with long-term radiation effects the role of hyperbaric oxygen in causing or promoting cancer has received considerable attention. There is published experience suggesting that hyperbaric oxygen does not promote cancer growth in the clinical literature.[43,72] However, new insights regarding the role of angiogenesis in the growth of tumors may influence how the risk of hyperbaric oxygen accelerating neoplastic growth is understood.[28,73] The efficacy of angio-statins as anti-cancer agents has drawn attention to the oxygen dependent behavior of certain tumors. Given the evolving basic knowledge of tumor biology and because it generally enhances angiogenesis, hyperbaric oxygen is not recommended when active primary or metastatic disease is suspected. In particular most clinicians recommend deferral of hyperbaric oxygen when the patient has untreated or untreatable cancer. Nevertheless, specific clinical scenarios may influence judgment about appropriateness of hyperbaric oxygen treatment. For example, hyperbaric oxygen might be elected as the treatment alternative for a patient with persistent radiation cystitis and active neoplasia who otherwise is not a candidate for definitive surgery due to the underlying medical condition. In this hypothetical situation of an "only option" risk of effects on tumor growth behavior from hyperbaric oxygen might be viewed by the surgeon and patient to be lesser than risk of dying.

Costs. Expenses related to hyperbaric oxygen include costs attributable to the chamber, staffing and monitoring, and vary depending on patient acuity and number of personnel involved in delivering the treatment. Norkool et al noted in 1993 that the average cost per patient (mean 28 treatments) for hyperbaric oxygen for radiation cystitis was $10,000 to $15,000.[44] While an economic comparison with other treatments was not performed, it was suggested that hyperbaric oxygen was cost-effective, especially in patients with severe symptoms who had not responded favorably to standard therapies. Marx et al noted an average 1-year cost of treating osteoradionecrosis without hyperbaric oxygen or surgery was $28,500 with an extended cost component of $62,000 for untreated disease effects, compared to an average total cost of approximately $30,000 for hyperbaric oxygen and surgery for definitive treatment (normalized to 1984 dollars).[74]

CONCLUSIONS

In the acute setting hyperbaric oxygen is an effective form of therapy for the majority of patients with radiation cystitis and may also offer significant benefit to those with hemorrhagic cystitis from chemical exposure. While further research is needed to determine the role of hyperbaric oxygen with time in patients with radiation tissue damage, short-term followup suggests that hyperbaric oxygen appears to lead to good outcomes, a high rate of bladder preservation and few serious side effects in radiation cystitis patients. Regarding hyperbaric oxygen for Fournier's gangrene and necrotizing fasciitis, further evaluation of the hypothesis that hyperbaric oxygen may help facilitate wound management in critically ill patients with life threatening infections is warranted.[75] Until such data are available, when hyperbaric oxygen can be administered safely to a critically ill patient whose clinical response is compromised by hypoxia and inadequate tissue oxygen delivery, consideration of hyperbaric oxygen treatment seems a reasonable strategy, particularly when surgical and medical options may be limited by patient acuity.

APPENDIX: UNDERSEA AND HYPERBARIC MEDICINE SOCIETY ACCEPTED TREATABLE CONDITIONS

Air embolism
Decompression sickness
Carbon monoxide poisoning complicated by cyanide poisoning
Necrotizing soft tissue infections, including clostridial myositis and myonecrosis (gas gangrene)
Problem wounds
Refractory osteomyelitis
Radiation tissue damage
Compromised skin grafts and flaps
Acute traumatic ischemia, as in crush injuries
Thermal burns
Exceptional blood loss anemia when transfusions are not possible

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