



Hyperbaric oxygen as adjuvant therapy in the management of necrotizing fasciitis

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Abstract

Background: Necrotizing fasciitis (NF) is an uncommon but serious infection of fascia and skin associated with considerable morbidity and mortality. One modality proposed for improving the outcome of this condition is hyperbaric oxygen (HBO) therapy. This is a form of medical treatment that involves intermittent inhalation of 100% oxygen under pressures exceeding the atmosphere. The aim of this article is to review current practice and evidence for the use of HBO as adjunctive therapy in the management of NF.

Methods: A survey of published English literature through searches of Medline and PubMed was carried out using the following key words: “necrotizing fasciitis,” “Fournier’s gangrene,” “necrotizing soft tissue infections,” “hyperbaric oxygen therapy,” “and hyperbaric oxygen chambers.”

Results: The results of studies on the use of HBO therapy in NF are inconsistent. Some studies have demonstrated that HBO can improve patient survival and decrease the number of debridements required to achieve wound control, whereas others have failed to show any beneficial effect.

Conclusions: Encouraging results have been achieved with the addition of HBO therapy to standard treatment regimes, thus justifying further research in this field. More robust evidence by way of a prospective randomized trial is necessary before widespread and routine use of HBO in the management of NF can be recommended. © 2005 Excerpta Medica Inc. All rights reserved.

Keywords: Fasciitis; Hyperbaric; Infection; Necrotizing; Oxygen; Soft tissue

Necrotizing fasciitis (NF) is a life-threatening bacterial infection of the fascia that progresses rapidly to involve the skin primarily and subcutaneous tissue secondarily [1]. It is an uncommon condition that can affect patients of any age [2,3]; the perineum and extremities are preferred sites [4]. NF is associated with considerable morbidity, and patients ordinarily require multiple and extensive debridements [5]. The mortality rate of 20% to 40% [5,6] is perhaps even more significant and has been the catalyst for the use of a number of ancillary therapies to improve patient outcome [7,8]. A modality that has shown some promise is the use of hyperbaric oxygen (HBO) therapy. This is a form of medical treatment in which the patient is enclosed in a chamber and breathes 100% oxygen at a pressure >1 atmosphere absolute (ATA). Interest in HBO therapy started >40 years ago with Brummelkamp’s [9] seminal finding that hyper-

baric conditions inhibit anaerobic infections. Since then the indications for this modality have grown, and HBO has gained acceptance for the treatment of a variety of clinical conditions [10–12]. There is, however, considerable skepticism within the surgical community regarding the role of HBO in NF. The aim of this article is to review current practice and evidence for the use of HBO in the treatment of this devastating condition. It was prepared after surveying existing English literature with Medline and PubMed searches using the following keywords: “necrotizing fasciitis,” “Fournier’s gangrene,” “necrotizing soft tissue infections,” “hyperbaric oxygen therapy,” and “hyperbaric oxygen chambers.” A manual search of the reference list of all the articles was also carried out.

Physiologic Basis

Tissues at rest require 60 mL oxygen/L blood flow to maintain adequate cellular metabolism. At normal atmo-

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spheric pressure plasma oxygen concentration is only 3 mL/L [13], and oxygen is delivered to tissues mainly by hemoglobin. If the inspired oxygen concentration is increased to 100%, the amount dissolved in the plasma will increase to 20 mL/L. At a hyperbaric pressure of 3 atmosphere absolute (ATA) (304 kPa), the dissolved plasma oxygen increases to 70 mL/L, which exceeds the resting tissue oxygen requirements and does not require a contribution from hemoglobin [14].

Cellular, Tissue, and Systemic Effects

Oxygen is necessary for cellular metabolism, promotion of the hosts' defenses, and tissue repair [15]. When administered at pressures >1 ATA, oxygen assumes properties more akin to a drug [16]. White cells' ability to kill aerobic bacteria is enhanced [17]; collagen formation is stimulated [18]; and levels of superoxide dismutase (resulting in better tissue survival) are increased [19]. Macroscopically, HBO decreases tissue edema through vasoconstriction and thus improves local tissue swelling [20]. It also leads to increased tissue oxygen tension [21], which is critical for local defense mechanisms, particularly the efficacy of antibiotics [22]. Korhonen et al [23] measured the subcutaneous tissue P_{O_2} of patients with NF using an implanted Silastic tube tonometer. They demonstrated that after 60 minutes of HBO at 2.5 ATA, mean subcutaneous tissue P_{O_2} of 50 kPa (ie, 4 times normal) could be achieved in the vicinity of infected tissue. They proposed that the "superoxygenated" zone created by HBO forms a barrier against the spread of infection and may explain the observation by some investigators that HBO decreases the number of debridements required to achieve wound control.

The benefits of HBO may be also mediated through damping of the systemic inflammatory response. Zymosan is a cell wall component of yeast that produces a generalized systemic inflammation consistent with consensus definition of the host inflammatory response. In a Zymosan-induced rodent shock model [24], morbidity was attenuated, and no mortality was observed by treatment with HBO. These beneficial effects were mediated through a significant decrease in the plasma levels of the proinflammatory cytokine, tumor necrosis factor- α . Although encouraging, these findings must be interpreted cautiously because the model is not similar to any clinically observed physiologic insult, and extrapolation to humans is precarious.

Methods of Administration

HBO therapy can be accomplished by way of commercially constructed monoplace (Vickers, USA; Oxycom, Finland) or multiplace chambers (Rauma Oceanics, Finland; Hytech, Netherlands). The former accommodates a single patient, and the chamber is pressurized with 100% oxygen,

thus negating the need for a mask or a hood. Portability and relatively low cost have made monoplace chambers the most common type of chamber worldwide [25]. Multiplace chambers are large tanks that permit medical staff to accompany and treat critically ill patients. The chamber is pressurized with air, and the patient breathes 100% oxygen through a mask or by way of an endotracheal tube (the mode of administration depends on the patient's respiratory function, level of consciousness, and cooperation). The advantages of multiplace chambers are that >1 patient can be treated at a time, and they are much less claustrophobic than their monoplace counterparts. In the treatment of NF, both types of chambers have been used [26,27]. Most therapy is administered at 2 to 3 ATA, and the average duration of sessions is between 60 and 120 minutes. However, the ideal duration and frequency of treatment in NF has yet to be established, and standard regimes do not exist.

Clinical Evidence

There is general consensus that resuscitation, radical debridement, and broad-spectrum antibiotics form the corner stones of management of NF [1]. HBO must complement and not substitute these interventions. However, few hospitals possess hyperbaric facilities [16], and the critical status of patients often precludes lengthy transport to these specialized units. These factors are probably responsible for the relative scarcity of reported studies in the literature (Table 1). The bona fide impact of adjuvant HBO therapy in NF is difficult to evaluate because of a number of limitations with these publications. First, robust evidence by way of prospective randomized trials does not exist, and investigators have used different treatment protocols making assessment of outcome problematic. Second, the small number of subjects in each study does not allow vigorous statistical comparisons of morbidity and mortality rates. Third, the outcome results may be biased because HBO therapy has often been reserved for critically ill patients [28,29] and also because differences exist in surgical teams; experience in managing NF.

In support of HBO therapy, several case reports have demonstrated enhanced patient survival [30,31], but they are only of anecdotal value. In a series consisting of 9 patients, Eltorai et al [32] reported no deaths when HBO therapy was combined with surgical debridement in treating Fournier's gangrene. The investigators, however, failed to state the duration of their study or the temporal relationship between debridements and HBO therapy. Gozal et al [33] achieved a mortality rate of 12.5% by administering HBO after radical debridement and broad-spectrum antibiotics. It is notable that there was only a short delay (≤ 7 hours) between surgery and HBO therapy, which may account for this favorable result. There were, however, no controls in this study, making the genuine impact of HBO treatment on patient outcome difficult to gauge. In a larger series, where

Table 1
Published clinical trials on the use of HBO therapy in NF

| Author | Year | Design | HBO group (n) | Control group (n) | Main outcome |
|---------------------|------|---------------|---------------|-------------------|--|
| Tehrani et al [34] | 1977 | Retrospective | 14 | 0 | Conservative surgery combined with HBO therapy was associated with high mortality (88%) |
| Eltorai et al [32] | 1986 | Retrospective | 9 | 0 | 100% survival |
| Gozal et al [33] | 1986 | Retrospective | 16 | 0 | Mortality rate of 12.5% |
| Riseman et al [27] | 1990 | Retrospective | 17 | 12 | Significant decrease in mortality and the number of debridements in the HBO-treated group |
| Brown et al [29] | 1994 | Retrospective | 30 | 24 | A nonsignificant decrease in mortality with HBO therapy; no difference in length of hospitalization or no. of debridements |
| Shupak et al [33] | 1995 | Retrospective | 25 | 12 | No significant difference in mortality or no. of debridements |
| Korhonen et al [26] | 1998 | Retrospective | 33 | 0 | Mortality rate of 9% in patients with Fournier's gangrene |

HBO = hyperbaric oxygen; NF = necrotizing fasciitis.

the treatment and control groups were well matched with regards to age, sex, and bacterial flora, the addition of HBO therapy to standard surgical management significantly decreased mortality from 66% to 23% [27]. This beneficial effect is particularly noteworthy considering that the patients receiving HBO were more seriously ill (using presence of shock as a criteria). Korhonen et al [26] also demonstrated an improvement in patient survival with the use of HBO. They achieved a mortality rate of 9% in patients with Fournier's gangrene, which is the lowest recorded rate in the literature for a relatively large series. This auspicious mortality rate is probably even better than the figure quoted by the investigators because 2 of the 3 patients who died were moribund on arrival. The study's other chief finding was that the period from onset of symptoms to the first surgical debridement and HBO treatment was significantly longer among those that died compared with those who survived (80 vs. 32 hours, respectively), thus highlighting the importance of prompt intervention. Although it is difficult to decipher the effects of early surgical input from HBO therapy, this study supports the view that swift and frequent HBO treatment is necessary to attain improvements in mortality.

Another widely touted potential benefit of HBO therapy is preservation of tissue. The necessity for debridements implies ongoing infective processes, and Riseman et al [27] demonstrated that the number of debridements required to achieve wound control was significantly less in patients who received HBO (3.3 vs. 1.2). Similarly, in another study that used subcutaneous tissue Po_2 monitoring to assess the adequacy of HBO therapy, surgeons achieved wound control with a single debridement [23]. The claim of some investigators that the addition of HBO therapy facilitates more limited surgical excision and thus maximizes tissue preservation are supported by these findings [33]. This effect alone could be an indication for the use of HBO, particularly when NF involves sites where tissue preservation is advan-

tageous, eg, the lower limb. However, more robust evidence is necessary to substantiate these claims.

Compared with the previously mentioned findings, a number of studies have cast doubt on the suggested advantages of HBO. Tehrani and Ledingham [34] reported their experience of treating 14 patients with HBO. The first 8 patients were managed with conservative surgery (ie, incision and drainage), and 7 of these died. In 6 subsequent patients, a 33% mortality rate was achieved by adopting a more aggressive surgical approach. These findings emphasize that HBO can not be regarded as a substitute for radical surgical debridement. In Brown et al's study [29], HBO treatment was not associated with any significant decrease in mortality (30% in HBO vs. 42% in controls); need for debridements (2.4 in HBO vs. 1.3 in controls); or length of hospital stay (31.6 days in HBO vs. 31.3 days in controls). There are, however, a number of serious concerns with this study. First, the adequacy of HBO therapy must be questioned because the majority of patients (66%) received <4 sessions. This is in marked contrast to Riseman et al's regime [27] of 3 HBO sessions in the first 24 hours, which was continued twice daily until the infection was controlled. Second, the patients in the HBO group had more advanced sepsis, which may have biased the mortality rate. Additionally, as highlighted by the investigators, the lack of a significant difference in survival may have been caused by a type II error because the size of sample in each group was small. Last, tissue samples taken for microbiologic purposes were considered a debridement, probably accounting for the increased number of operations in the HBO group as a result of improved survival. Shupak et al [35] retrospectively reviewed their experience of adjuvant HBO therapy in NF during a 10-year period. Their study also failed to show any sizeable contribution of HBO to improvements in the mortality rate (36% in HBO vs. 25% in controls) or the mean number of debridements (2.5 in HBO vs. 1.5 in controls). The average length of hospitalization for survivors was

shorter in the HBO-treated patients (15.9 vs. 20 days), although the difference did not reach statistical significance. A criticism of this series is that the majority of patients in the HBO group (16 of 25) were treated in the early period of the study (1984 to 1989), whereas most of control subjects (10 of 12) were treated in the latter part (1990 to 1993). Thus, there is a distinct possibility that the outcome was biased toward the control group by growing surgical experience and improvements in critical care. Additionally, compared with other reported series, treatments were administered less frequently on admission.

Complications of HBO Therapy

The potential risks and complications of HBO have often been overestimated. There are few absolute contraindications—such as untreated pneumothorax and chemotherapy with cis-platinum and adriamycin—because it has been shown that the cytotoxicity of these agents is potentiated by HBO therapy [36]. Relative contraindications include poorly controlled asthma, pregnancy, bone cysts, malignancy, and lung bullae. The possibility of active neoplastic processes is considered a contraindication caused by fears that HBO may promote cancer growth through enhancement of angiogenesis [37]. If pressures do not exceed 3 ATA (300 kPa) and the length of treatment remains <120 minutes, HBO is generally safe [14]. Many patients have minor alterations in respiratory function, but this is rarely clinically evident. The most common side effects are aural pain (as a result of inability to equalize middle-ear pressure) and sinus discomfort [38]. Oxygen toxicity may affect the brain and the lungs and lead to convulsions and pulmonary edema, respectively. However, the risk of oxygen toxicity is <1% [39] and can be decreased further by limiting therapy to 30 minutes and using 5 minutes of air between each session. Diabetic patients are particularly at risk of developing seizures because HBO enhances dextrose metabolism and results in hypoglycaemia [27,40]. Fire, a potentially fatal complication, principally occurs as a result of electrical ignition [41]. This risk is higher in monoplace chambers, but a recent 73-year analysis revealed no fatalities in the clinical hyperbaric chambers of North America [41].

Comments

There is physiologic rationale for the use of HBO in the treatment of NF. However, the results of clinical studies have been inconsistent. The main advantages of addition of HBO to standard regimes appear to be tissue preservation and decreased mortality. Thus, the ongoing use of adjuvant HBO therapy in institutions with such facilities can be justified. Despite the paucity of serious complications, more robust evidence, preferably by way of randomized con-

trolled trials, is necessary before routine and widespread use of HBO can be recommended.[6]

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