

HYPERBARIC OXYGEN TECHNOLOGY: AN OVERVIEW OF ITS APPLICATIONS, EFFICACY, AND COST-EFFECTIVENESS

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Abstract

Objectives: To examine the growing evidence and the consensus in the medical community concerning the efficacy and cost-effectiveness of hyperbaric oxygen therapy (HBO2T) and to suggest future research areas to ensure the appropriate use of this technology.

Methods: A literature search of articles published between 1985 and 2000 was conducted using PubMed to describe the growth of HBO2T-related articles published over the past fifteen years. In addition, articles involving the qualitative synthesis of the efficacy and cost-effectiveness of HBO2T in thirteen major application areas were identified and compared with the changing view of the medical community toward the evidence of HBO2T.

Results: The total number of HBO2T-related articles published annually has steadily increased over the past fifteen years. This increase has gradually contributed to a consensus in the medical community concerning the evidence of efficacy in its major application areas. However, information regarding the cost-effectiveness of HBO2T is still extremely limited.

Conclusions: Although evidence concerning the efficacy of HBO2T has been growing in the past, more evidence is still needed for some of its major application areas. Moreover, there is an urgent need to shift part of the research focus on HBO2T to its cost-effectiveness to provide decision makers with relevant information to evaluate this technology objectively.

Keywords: Hyperbaric oxygen, Cost-effectiveness, Efficacy, Technology assessment

Hyperbaric oxygen technology (HBO2T) is a therapy that administers 100% oxygen intermittently to patients in an elevated-pressure chamber. This technology was initially used to treat patients with caisson disease and has been existed for more than three centuries (8). Due to increasing knowledge about HBO2T, its applications have been expanded to many medical conditions including carbon monoxide intoxication, radiation injuries, problem wounds, etc. As of today, the U.S. Food and Drug Administration (FDA) has approved thirteen application areas for HBO2T.

There has been a rapid growth in the use of this technology over the past several years. According to the U.S. Office of the Inspector General (OIG) (4), the number of HBO2T providers increased 122% from 232 facilities in 1995 to 514 in 1998. Medicare payment for HBO2T also rose 52% from \$50 million to \$76 million during the same period. Such growth in the use of HBO2T is mainly due to the innovative use of this technology in wound management. As of 1999, there were 219 wound care centers providing HBO2T to their

patients, according to Frost and Sullivan, Industry Report 6016-54 (unpublished data, 2000). Yet, although use of HBO2T has been expanding in the United States, the German health care system recently disapproved of reimbursement for all HBO2T applications due to a lack of sufficient evidence to support its efficacy, need, and cost-effectiveness (18). Although it is still questionable whether the decision made by the German health care system was based on a thorough assessment of HBO2T, this disapproval raises a controversy over the existing evidence of HBO2T and its appropriate use in those approved indications. In fact, similar controversies occurred several times over the long history of hyperbaric medicine (8;10). This makes us question how much and what types of evidence has been generated over the past to support the applications of HBO2T and what the consensus in the medical community is toward its applications.

In addition to the contrast between the expansion of reimbursement in the United States and the contraction of reimbursement in Germany, there are two additional reasons why closer attention needs to be paid to HBO2T. First, a recent investigation conducted by the OIG (4) indicates that there is a substantial variation in the utilization of HBO2T across the United States. Colorado and other states in the west-south central region (e.g., Texas and Louisiana) have the highest use rates per capita of HBO2T. If other states have the same utilization rate of HBO2T as those in Colorado or Texas, the expenditures on HBO2T would be expected to grow by at least 500%. However, if evidence actually supports its efficacy and cost-effectiveness, HBO2T should be widely promoted, despite the potential increase in health care spending.

Second, in addition to these 13 approved applications, there are still many potential new applications of HBO2T that may be approved in the near future. Studies have shown a promising therapeutic effect of HBO2T in new clinical applications, including acute ischemic stroke (13) and cerebral palsy (12). Once evidence regarding its efficacy is sufficient to support the use of HBO2T in these new areas, many patients will benefit from it. Its associated costs, though, will be expected to increase rapidly. Due to these factors, along with the growing concerns about the appropriate use of medical technologies, the evidence of HBO2T regarding its efficacy and cost-effectiveness in its approved application areas needs to be examined.

Several qualitative studies have been conducted in different time periods to synthesize the evidence with respect to the efficacy of HBO2T over the past fifteen years. Thus to avoid repetition, this study will not review and summarize the results of existing clinical trials and retrospective case reports concerning HBO2T. Instead, it will first provide an overview of the growth of HBO2T-related articles of all types (e.g., clinical trial, case report, review, and editorial comment and letter) published from 1985 to 2000. Next, this study will identify those qualitative studies and compare their conclusions on the evidence regarding the efficacy of HBO2T in its thirteen major applications. Finally, the evidence regarding the economic evaluation of HBO2T in its thirteen approved application areas will also be examined to determine its cost-effectiveness. By doing so, we will be able to (i) see how much and what types of evidence has been generated in the field of hyperbaric medicine to support its major applications over the past 15 years, (ii) determine whether the conclusions of those qualitative studies has changed over time as evidence grows, (iii) summarize the consensus in the medical community concerning the evidence in terms of the efficacy and cost-effectiveness of HBO2T, and (iv) suggest future research areas that should be addressed to ensure the appropriate use of this technology.

METHODS

To achieve the objectives of this study, we started with a literature search of articles published between 1985 and 2000 by using PubMed from the National Library of Medicine.

The keyword *hyperbaric oxygen* was used to identify relevant published HBO2T-related articles of all types each year. The search included only human studies and was limited to only published, English-language articles. After identifying all of the relevant articles, we reviewed the abstracts of these articles and categorized them into each specific application areas. Based on the same search, articles involving the qualitative synthesis of study results from the applications of HBO2T in the thirteen major application areas were also identified and reviewed. Our intent was to compare the synthesized results regarding the efficacy of HBO2T across different studies, to determine whether the consensus toward the uses of HBO2T has changed over time in the medical community, and finally to summarize the overall consensus.

Another search was performed within the same time frame using the keyword *hyperbaric oxygen* combined with *cost*, *cost-effectiveness*, and *economic analysis*, respectively, to identify articles involving the economic evaluation of HBO2T in the treatment of the thirteen medical conditions. Articles published in languages other than English were excluded. All identified articles were evaluated by using the ten criteria for critical assessment of economic evaluation proposed by Drummond et al. (5) to determine the quality of evidence and to summarize the cost-effectiveness of HBO2T in these thirteen different illnesses.

RESULTS

A total of 1,014 HBO2T-related articles published during 1985 to 2000 were found based on the search. Articles relating to topical hyperbaric oxygen therapy were eliminated because it is a different treatment modality. Articles appearing twice or more were only counted as one article. Among these articles, approximately 10.5% of them were based on clinical trials, 11.7% were editorial comments and letters, and the rest of them (77.8%) were review and case report articles. Figure 1 exhibits the number of HBO2T-related articles of all types published each year between 1985 and 2000. As can be seen, the total number of HBO2T-related articles published annually has steadily increased over the past 15 years, particularly in the past several years. In contrast, the number of HBO2T-related articles based on a clinical trial has remained relatively stable, showing only a slight increase beginning in 1995. Among those articles based on clinical studies, randomized and nonrandomized, only fifteen articles were conducted in some of the thirteen approved indications, including problem wounds (5), carbon monoxide poisoning (4), radiation injuries (2), thermal burns (2), refractory osteomyelitis (1), and crush injuries (1). These data suggest that most existing HBO2T-related articles are retrospective case reports or review studies, which provides only lower level of evidence to support the current applications of HBO2T (15). Moreover, no evidence based on clinical trials has been generated in some of its approved application areas over the past 15 years.

Based on the review of the abstracts of the entire HBO2T-related articles, only 48% of them were reported to provide evidence for or comments on those thirteen approved indications. The remaining articles were published mostly to introduce the concepts and physiological effects of HBO2T or to demonstrate the therapeutic effects of HBO2T on other investigational indications, such as multiple sclerosis, acute ischemic stroke, brain injuries, and cerebral palsy. Among articles involving the thirteen approved indications, a large proportion of them were related to radiation injuries (25.4%), carbon monoxide poisoning (24.2%), problem wounds (13.2%), and gas gangrene (7.9%). Fewer articles were identified to report the evidence or information for decompression sicknesses, exceptional blood loss, intracranial abscess, compromised skin grafts and flaps, and thermal burns. It is important to note that the criteria used to assign articles into different groups were loosely defined. For example, articles assigned to the group of radiation injuries may include those involving HBO2T in the treatment and prevention of any type of radiation injuries such as

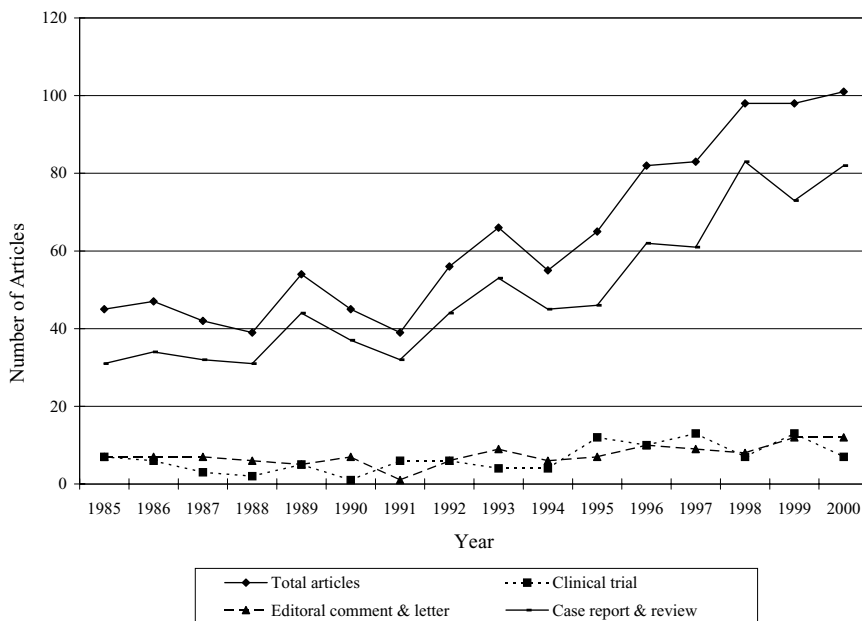


Figure 1. The number of published articles related to hyperbaric oxygen treatment between 1985 and 2000.

osteoradionecrosis and radiation cystitis. The presentation of all of the information above intends to provide a broad overview about how much and what types of evidence have been generated in each specific application areas over the past fifteen years. This overview will provide necessary background information to examine and discuss those qualitative studies.

Three review articles (6;11;17) involving the qualitative synthesis of clinical studies of HBO2T in thirteen application areas were identified in the search. They were compared in terms of the degree of evidence (e.g., sufficient evidence, some evidence, and no or little evidence) regarding the efficacy of HBO2T in 13 medical problems. The findings of the comparison are shown in Table 1.

The earliest qualitative study was conducted by Gabb and Robin (6). The authors concluded that there was no evidence to support the uses of HBO2T in these thirteen applications, except for decompression sickness. A decade later, Tibbles and Edelsberg (17) conducted a similar study and reported that there was increasing evidence to support the uses of HBO2T in all of its thirteen approved applications. Evidence was sufficient to demonstrate the benefits of HBO2T in decompression sickness, arterial gas embolism, CO intoxication, gas gangrene, radiation-induced tissue injury, and compromised skin flaps and grafts. Mitton and Hailey (11) conducted the most recent review article. Their conclusion was similar to that reported by Tibbles and Edelsberg, except that evidence was sufficient for problem wounds and insufficient for compromised skin grafts and flaps and exceptional blood loss.

Based on the search of articles involving economic evaluation of HBO2T, only one study (7) could be identified. However, this study fails to meet many of the criteria proposed by Drummond et al. (5). For example, it did not state stakeholders, perspectives (e.g., the society, payers, providers, or patients) on which the analysis was based. Other important and relevant costs such as the costs of treating side effects and the averted costs associated with HBO2T were not included in the analysis. Finally, there was no incremental analysis of both

Table 1. Comparison of Review Articles Concerning the Evidence of Hyperbaric Oxygen Therapy in Its Major Applications

Reference year published	Gabb & Robin 1987	Tibbles & Edelsberg 1996	Mitton & Hailey 1999
Decompression sickness/arterial gas embolism	+ ^a	+ ^a	+ ^a
Carbon monoxide poisoning	–	+	+
Gas gangrene	–	+	+
Osteoradionecrosis/soft tissue radiation injuries	–	+	+
Necrotizing soft tissue infections	NR	±	±
Skin flaps and grafts	NR	+	±
Chronic refractory osteomyelitis	–	±	–
Thermal burn	–	±	±
Traumatic peripheral ischemia	NR	±	±
Anemia due to blood loss	–	+ ^b	–
Problem wound	–	±	+

Note: +, sufficient evidence; ±, some evidence, but more studies required; –, no or little evidence; NR, not reported in the article.

^a There is no clinical trial available, but due to the extensive favorable treatment outcome, hyperbaric oxygen therapy was highly recommended.

^b The authors recommended hyperbaric oxygen therapy, but no clinical studies were available to support such an application.

costs and benefits in the study and no allowance made for uncertainty in the estimates of costs and consequences. Therefore, current information with regard to the cost-effectiveness of HBO2T is extremely limited.

DISCUSSION

The overview of HBO2T-related articles provides a general understanding of what types of research activities have occurred in the field of hyperbaric medicine and how much evidence has been provided to support the uses of HBO2T in its major application areas over the past fifteen years. Based on this overview, along with the review of those qualitative studies, three important findings emerge. First, the increasing number of HBO2T-related articles in the past few years reflects the recent growth in the use of HBO2T as reported by the OIG. It may also indicate an elevating research interest in the field of hyperbaric medicine. Such growing interest likely results from the potential benefits of HBO2T for medical problems increasingly recognized by health professionals, researchers, and policy officials and the rising demand for evidence relevant to medical technologies adopted in the health care system. However, the number of clinical studies published annually has not increased at the same rate. Furthermore, only a small proportion of the clinical trials identified in our search were conducted in those approved application areas. Most of them were conducted in other unapproved investigational application areas such as multiple sclerosis and acute ischemic stroke. This finding suggests that a large portion of the existing evidence supporting the uses of HBO2T in its approved indications is weak. This weakness is probably the major reason why the German health care system asserted that evidence was insufficient to support the uses of HBO2T in the 13 indications and declined to pay for this therapy. To further facilitate the acceptance of HBO2T by the policy makers and medical community, prospective studies and clinical trials in these approved application areas are needed because they usually provide much stronger evidence than other types of studies such as retrospective studies and case reports (9).

Second, the consensus regarding the efficacy of HBO2T in the medical community, particularly in the treatment of problem wounds, has been accumulating over the past fifteen years based on the comparison of three qualitative studies. HBO2T was once criticized as “a therapy in search of diseases,” (6) which suggests little or no evidence to support its uses in those thirteen approved indications, except decompression sicknesses. Currently, HBO2T has been widely accepted as a primary therapy for decompression sickness, gas embolism, and carbon monoxide poisoning. It has also been recommended as an adjunctive treatment for gas gangrene, osteoradionecrosis, and problem wounds. The acceptance of HBO2T in the treatment of these applications, except decompression sickness and air embolism, is due to the increasing evidence over the past fifteen years, as reported previously.

However, there is still not enough supportive evidence for the medical community to completely agree on the therapeutic effect of HBO2T in five of the thirteen approved indications, including refractory osteomyelitis, compromised skin flaps and grafts, thermal burns, necrotizing soft tissue infections, and exceptional blood loss. Such disagreement reflects on one of our findings that only a few clinical trials have been conducted in these application areas. Another finding indicates that evidence for compromised skin flaps and grafts was contradicted by two of the articles. Based on the review of all HBO2T-related articles, only two articles (2;16) addressed compromised skin grafts and flaps, but none of them had a clinical trial to provide stronger evidence. Thus, we agree with the results reported by Mitton and Hailey (11) that the existing evidence for compromised skin grafts and flaps is still insufficient. Despite the insufficient and contradicted evidence, these application areas still account for at least 30% of the total number of Medicare beneficiaries who received HBO2T (4). Thus more clinical studies of HBO2T in these application areas are needed to identify its appropriate uses.

Clinical studies to generate sufficient evidence regarding the efficacy of HBO2T in each of these application areas should be achieved strategically through a collaboration of research efforts among institutions and researchers. The reason for this suggestion is that many previous clinical studies concerning the efficacy of HBO2T were often criticized for having small sample sizes, flawed designs, and short-term follow-ups. Wunderlich, Peters, and Lavery (19) evaluating published clinical HBO2T studies in diabetic ulcers exemplifies these problems. Such problems likely result from the limited resources in terms of funding and human resources within a single research institution that carried out the entire clinical study. Pooling research resources and efforts among institutions with the same research interests will more easily resolve these problems. With respect to governmental funding support, further collaboration may be still required because it can facilitate recruitment of an adequate number of study subjects from different geographic areas within a timely manner, especially in some of application areas such as intracranial abscess and thermal burns. This strategy is more likely to provide valid and reliable evidence and allow the study results to be more generalizable. Yet, the proposed suggestion is difficult to accomplish without strong leadership in the field of hyperbaric medicine to coordinate various resources and efforts. The Undersea and Hyperbaric Medical Society (UHMS) may play a major role in such leadership.

Third, although the evidence concerning the efficacy of HBO2T has been growing over the past decade, the evidence concerning its cost-effectiveness has not been established. Given the increasing emphasis on economic evaluation of medical technologies (1;14), it is surprising that very few studies investigating the cost-effectiveness of HBO2T have been published. The one study (7) that attempted to estimate its cost-effectiveness did not meet the minimal standard for the economic evaluation of medical technologies. There are three possible explanations for this situation. First, economic evaluation of a medical technology is often conducted after its efficacy has been established (5). Consequently, very few economic analyses of HBO2T have been conducted in the past. Second, HBO2T

has attracted little attention from health service researchers. This finding is evident by the published articles concerning HBO2T that are conducted mostly by clinicians and focus on its efficacy. Third, decision makers in the past demanded only the evidence regarding the effectiveness of a medical technology when making their decisions of adopting that particular technology. However, as seen in Germany, policy makers have become unwilling to pay for medical technologies that do not demonstrate cost-effectiveness. Similarly, under the new Medicare coverage policy, if there are similar treatment modalities existing in the benefit categories, any new medical technology must demonstrate its added value, either medically or economically, to be financially covered (3). This issue is especially pertinent to HBO2T, because it is mostly considered as an adjunctive treatment in its applications. As a result, evidence with respect to the cost-effectiveness of HBO2T will become critical to its future adoption.

The best way to estimate the cost-effectiveness of HBO2T is to include cost-effective analysis in clinical trials so that all important and relevant information with respect to the costs and consequences can be more accurately measured. If such direct estimation is not feasible, the economic evaluation of HBO2T should be performed based on existing clinical studies to estimate its cost-effectiveness compared with other alternative treatments. When competing with other alternatives for resource allocation at the societal level, its aggregated benefits and costs among its various approved applications should be taken into consideration.

CONCLUSIONS

The growing number of HBO2T-related articles over the past fifteen years has provided greater evidence to support the use of HBO2T in its major applications. Such new evidence gradually affects the consensus in the medical community about its uses. However, there is still not enough evidence for some of its applications, despite the increasing research efforts devoted to HBO2T. The broad overview of the content of published HBO2T-related articles provides a possible explanation on this problem. The findings of this study also suggest that information concerning its cost-effectiveness is currently not available to aid decision-making in medical practices and resource allocation at the societal level. Given the health resource constraints and increasing demand for economic information about medical technologies by policy makers, the evidence with respect to the cost-effectiveness of HBO2T will become critical to its future adoption.

POLICY IMPLICATIONS

The potential benefits of HBO2T to patients and the overall health care system may be considerable. However, its potential benefits may become unrealizable if relevant information regarding HBO2T is not available when public or private policy makers are making coverage decisions or allocating resources for this technology. To assist decision making, more research efforts in the field of hyperbaric medicine should be shifted to the economic evaluation of HBO2T in the near future while continuously focusing on assessing the efficacy of HBO2T in those applications without sufficient evidence. This strategy will result in more relevant information regarding HBO2T being provided to policy makers who need to evaluate this technology objectively and make sound decisions.

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