COST-EFFECTIVENESS OF ADJUNCTIVE HYPERBARIC OXYGEN IN THE TREATMENT OF DIABETIC ULCERS

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Abstract

Objectives: This study estimates the cost-effectiveness (CE) of the adjunctive use of hyperbaric oxygen (HBO2) therapy in the treatment of diabetic ulcers based on the payer's and societal perspectives.
Methods: The study population was a hypothetical cohort of 1,000 patients sixty years of age with severe diabetic foot ulcers. A decision tree model was constructed to estimate the CE of HBO2 therapy in the treatment of diabetic ulcers at years 1, 5, and 12. Scenario and one-way sensitivity analyses were also undertaken to identify parameters that may significantly influence the estimates.
Results: The CE model estimated that the incremental cost per additional quality-adjusted life year (QALY) gained at years 1, 5, and 12, was $27,310, $5,166, and $2,255, respectively.
Conclusions: The study results indicate that HBO2 therapy in the treatment of diabetic ulcers is cost-effective, particularly based on a long-term perspective. However, the results are limited by the clinical studies that provide the basis of the CE estimation.

Keywords: Hyperbaric oxygen, Diabetic ulcers, Cost-effectiveness, Technology assessment

Foot ulcers are a common problem that has adversely affected a large number of diabetic patients (25). Due to a lack of effective treatment, diabetic foot ulcers have been reported to be associated with higher utilization of health care (6;18;23;24) and an elevated risk of lower extremity amputations (LEAs) (25). In addition, patients often experience high mortality and a diminished quality of life after major LEA due to lifelong disability (22). Hyperbaric oxygen (HBO2) therapy is one of the treatment modalities that have been recently found to be beneficial to patients with diabetic foot ulcers (27). Several clinical studies have indicated that the adjunctive use of HBO2 therapy significantly improves wound healing and reduces the risk of lower extremity amputation (8;11;15;17;29).

Although the role of HBO2 therapy in diabetic ulcers remains undefined (28), insurers such as Medicare in the U.S. have been recently considering extending coverage for HBO2 therapy in the treatment of diabetic foot ulcers. Such a coverage decision may benefit a large number of patients with diabetic ulcers, but at the same time, it may also have considerable economic consequences for the health-care system. Currently, little is known about the economic impact of the application of HBO2 therapy in diabetic ulcers. To provide more information for better decision making, this study seeks to estimate the cost-effectiveness (CE) of adjunctive use of HBO2 therapy in the treatment of diabetic ulcers.

METHODS AND RESEARCH DESIGN

The CE Model

The study population was a hypothetical cohort of 1,000 patients with severe diabetic foot ulcers (Wagner's classification III or above) (5). Patients were assumed to be sixty years

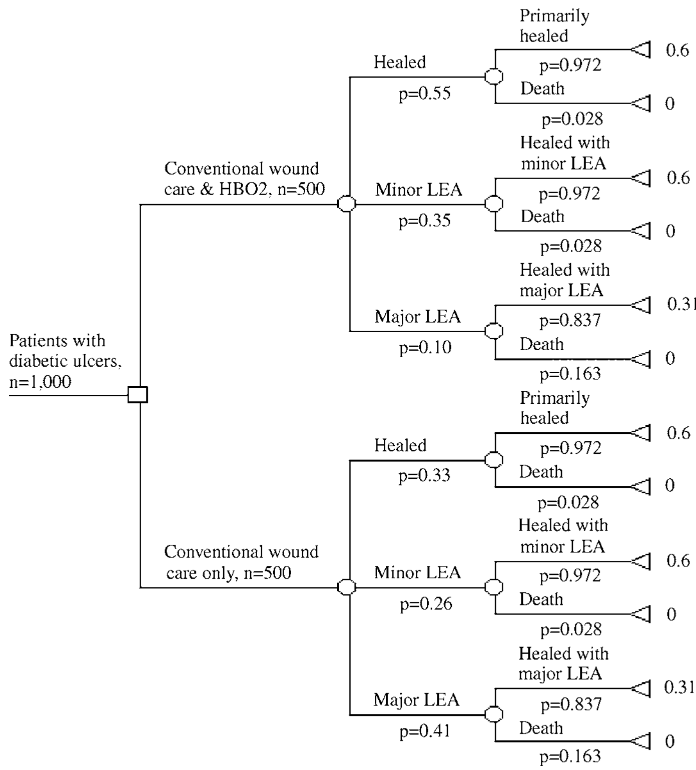

Figure 1. Decision tree diagram for cost-effectiveness analysis of hyperbaric oxygen (HBO2) therapy at year 1 in the treatment of diabetic foot ulcers. LEA, lower extremity amputations.

old. By assumption, there are no patients with contraindications of HBO2 therapy, such as high fever, emphysema, or pneumothorax. Furthermore, it was assumed that both control and treatment groups had similar demographic and etiological characteristics.

A decision tree model (see Figure 1) was constructed to estimate the CE ratio of incremental cost per additional quality adjusted life year (QALY) gained (9) from the adjunctive use of HBO2 therapy. The incremental cost was estimated from the total cost of HBO2 therapy minus averted costs of major and minor LEAs saved. We excluded the costs of treating side effects of HBO2 therapy because major side effects that require medical attention rarely occur (21).

Because wound care is a standard treatment for both HBO2 and non-HBO2 groups, the cost of wound care treatment was excluded from the analysis, as it will not affect the incremental costs of HBO2 treatment. All costs identified for this analysis were inflated to 2001 dollars. QALYs for each patient were derived from assigning EuroQol weights (22) to four different treatment outcomes (see Figure 1). In addition, QALYs gained from the adjunctive use of HBO2 therapy were based on the difference of total QALYs in both treatment and control groups. A discount rate of 3% (13) was applied to adjust QALYs gained in the future years. The entire analysis was performed primarily based on societal and payers' perspectives (9).

Based on the model, we estimated the CE ratio at three time intervals – 1, 5, and 12 years after HBO2 treatments. The 5-year interval was chosen to represent the private payers' perspective, because 5 years later they will automatically become Medicare beneficiaries. The 12-year interval was selected to represent the societal perspective, because the expected life expectancy for people at age 60 is approximately 20 years (1) and the life expectancy for

Table 1. Summary of Clinical Studies of HBO2 Therapy in Diabetic Ulcers

Reference	Cases	Primarily healed (%)	Minor LEA (%)	Major LEA (%)	Number of treatments	Minutes/ treatment
Faglia et al., 1996 (11)						
HBO2	35	11 (31)	21 (60)	3 (9)	38	90
Non-HBO2	33	10 (30)	12 (37)	11 (33)		
Doctor et al., 1992 (8)						
HBO2	15	9 (60)	4 (27)	2 (13)	4	45
Non-HBO2	15	6 (40)	2 (13)	7 (47)		
Baroni et al., 1987 (2)						
HBO2	18	16 (89)	0 (0)	2 (11)	34	90
Non-HBO2	5[a]	1 (20)	0 (0)	4 (80)		
Zamboni et al., 1997 (29)						
HBO2	4[b]	4 (100)	0	0	30	120
Non-HBO2	1[b]	1 (100)	0	0		
Total						
HBO2	72	40 (55)	25 (35)	7 (10)	29[c]	81[c]
Non-HBO2	54	18 (33)	14 (26)	22 (41)		

Note: HBO2, hyperbaric oxygen; LEA, lower extremity amputation.
[a] Five subjects in the control group neither healed nor had any amputation during the study period and were excluded from the analysis.
[b] One subject in the HBO2 group and four subjects in the non-HBO2 group did not change condition during the study period and were excluded from the analysis.
[c] Weighted average based on all studies.

people with diabetes is approximately 8 years shorter than that of people without diabetes (14). Two assumptions were also made for this analysis: first, the mortality rate was assumed to be constant over the 12-year period; second, foot ulcers would not reoccur once they were healed.

The probabilities of treatment outcomes for both the treatment and control groups were based on the summarized results of four prospective, controlled, clinical studies (Table 1). These studies were selected through a complete MEDLINE search between 1985 and 2001 (February). Five studies (7;17;19;20;26) were excluded from the analysis because they failed to meet one of the inclusion criteria, including prospective controlled design, diabetic etiology and the measure of treatment outcomes as primary healing and healing with minor and major LEAs. Additional model parameters used in this analysis are described in Table 2.

Scenario and Sensitivity Analyses

Scenario analyses (9) were conducted to measure the range of the CE ratios between the least (11) and most (2) efficacious outcomes of HBO2 therapy in the treatment of diabetic ulcers shown in Table 2, holding the remaining parameters constant in the model. In addition, one-way sensitivity analyses (9) were also undertaken to evaluate the impact of each parameter on the CE ratios of the base case estimation in different time periods.

RESULTS

CE Ratios

In the base case estimation, 155 cases of major LEAs are averted (205 LEAs in control group versus 50 LEAs in HBO2 group) and approximately 50.2, 265.3, and 608.7 QALYs are gained at years 1, 5, and 12, respectively, due to the use of HBO2 therapy in the hypothetical cohort. The base model also estimates an increase of forty-five cases of minor

Table 2. Model Parameters Used to Estimate Incremental Cost per QALYs Gained and Additional Major LEA Saved from the Use of HBO2 Therapy in the Treatment of Diabetic Ulcers

Parameters	Worst case estimation	Base case estimation	Best case[a] estimation	Reference
Rate of Healing (%)				
HBO2	31	55	89	
Non-HBO2	30	33	20	
Rate of LEAs(%)				
Major LEA				
HBO2	9	10	11	
Non-HBO2	33	41	80	
Minor LEA				
HBO2	60	35	0	
Non-HBO2	37	26	0	
Mortality (%)				
Primarily healed	—	2.8	—	(3)
Minor LEA	—	2.8	—	(3)
Major LEA	—	16.3	—	(4)
EQ-5D weight				
Primarily healed	—	0.6	—	(22)
Minor LEA	—	0.6	—	(22)
Major LEA	—	0.31	—	(22)
Death	—	0	—	(22)
No. of HBO2 treatments/case	—	29[b]	—	
Treatment costs ($)				
HBO2/treatment	—	407[c]	—	(16)
Major LEA/case	—	39,404[d]	—	(10)
Minor LEA/case	—	40,673[d]	—	(10)

Note: QALYs, quality of life-years; LEA, lower extremity amputation; HBO2, hyperbaric oxygen.
[a] Five subjects in the non-HBO2 group neither healed nor had any amputation during the study period; thus, they were excluded from the analysis.
[b] The number was derived from Table 1.
[c] The costs of HBO2 treatment consisted of the technical and physician fees.
[d] The costs included surgery, inpatient care, rehabilitation, first-year outpatient visits, and physician fees.

LEAs in the HBO2 group (130 LEAs in control group versus 175 LEAs in HBO2 group). As a result, the incremental cost of the adjunctive use of HBO2 therapy is $1,370,965, calculated from ($5,901,500 of HBO2 treatments) + ($1,773,780 due to increased number of minor LEAs) – ($6,304,315 due to major LEAs averted). This calculation results in an incremental cost per additional QALY gained of approximately $27,310, $5,166, and $2,255 at the 1, 5, and 12-year periods, respectively (Table 3), indicating HBO2 therapy is more cost-effective based on a long-term perspective.

Scenario and Sensitivity Analyses

In the scenario analyses, the CE ratios vary substantially across different scenarios. For example, the CE ratio at year 1 is $142,923, $27,310, and $−72,799 in the worst, base, and best case scenarios, respectively (Table 3). In addition, the broad variation of the CE ratios indicates that the results are very sensitive to the efficaciousness probabilities drawn from the existing clinical studies. Table 3 also shows the results of one-way sensitivity analyses. Based on the analyses, the CE ratios are most sensitive to the quality weights, especially for major LEA. Other parameters such as the number of HBO2 treatments per case, the HBO2 cost per treatment, and the treatment costs of major and minor LEA per case also

Table 3. Estimated Cost-effectiveness of HBO2 Therapy in Different Scenarios and Results of Sensitivity Analyses

Parameter (base case – new valude)	Incremental cost/ QALY gained at year 1 ($), discount at 3% (%)	Incremental cost/ QALY gained at year 5 ($), discount at 3% (%)	Incremental cost/ QALY gained at year 12 ($), discount at 3% (%)
Base case estimation	27,310	5,166	2,255
Best case estimation	−72,799	−13,770	−6,011
Worst case estimation	142,923	27,033	11,801
Mortality (%)			
Primarily healed (2.8 – 3.25)	27,473 (0.6)	5,241 (1.5)	2,313 (2.6)
Minor LEA (2.8 – 3.25)	27,376 (0.2)	5,196 (0.6)	2,278 (1.0)
Major LEA (16.3 – 10.5)	28,916 (5.9)	5,751 (11.3)	2,551 (13.1)
EQ-5D weights[a]			
Quality weights-set 1 (0.8, 0.8, 0.31)	19,149 (−29.9)	3,798 (−26.5)	1,717 (−23.9)
Quality weights-set 2 (0.8, 0.6, 0.31)	17,063 (−37.5)	3,427 (−0.34)	1,565 (−30.6)
Quality weights-set 3 (0.6, 0.6, 0.51)	56,554 (107.1)	7,791 (50.8)	2,851 (26.4)
No. of HBO2 treatments/case (29 – 34)	47,588 (74.2)	9,001 (74.2)	3,929 (74.2)
Treatment/costs ($)			
HBO2/treatment (407 – 325)	3,614 (−86.8)	684 (−86.8)	298 (−86.8)
Minor LEA/case (39,404 – 47,284)	34,377 (25.9)	6,502 (25.9)	2,838 (25.9)
Major LEA/case (40,673 – 48,807)	2,184 (−92.0)	413 (−92.0)	180 (−92.0)

Note: HBO2, hyperbaric oxygen; QALY, quality of life-years; LEA, lower extremity amputation.
[a] Each set of quality weights represents the quality weight of primary healed, minor LEA, and major LEA, respectively.

have a significant impact on the CE ratios (see Table 3). The CE ratios are less sensitive to the mortality rate and discount rate (not shown).

DISCUSSION

CE analysis has been used frequently to improve the allocation of scarce health care resources. Treatment alternatives with lower CE ratios indicate a more effective use of resources than those with higher CE ratios. It has been suggested that medical interventions below the threshold of $50,000 per additional QALY gained are considered to be cost-effective (12). This study suggests that the adjunctive application of HBO2 therapy in diabetic ulcers, as compared with the threshold, is relatively cost-effective based on both the payers' and societal perspectives.

Results of the analysis also have several implications. First, HBO2 therapy is more cost-effective based on a long-term perspective. This finding suggests that HBO2 therapy may become less valuable to payers like HMOs if their enrollees, especially those with diabetes, frequently switch their medical plans in the short-term. Second, the negative CE ratio in the best case scenario suggests that HBO2 therapy not only improves the outcomes but also reduces the overall costs of treating diabetic ulcers. Third, the broad variations in the CE ratios across different scenarios and the significant impact of the number of HBO2 treatments on these ratios suggest that this therapy can be more cost-effective if proper clinical practice guidelines, such as criteria for selecting appropriate patients for HBO2 therapy and systematic evaluation to decide the number of HBO2 treatments needed for each patient, can be clearly established and strictly implemented. Fourth, the variation also suggests that more clinical trials of HBO2 therapy with randomized controlled designs, larger sample sizes, and especially long-term follow-up of patients are needed to improve the estimation.

There are three important limitations that need to be addressed. First, the CE estimation was based on a few, small, and methodologically weak studies (28). Thus, the CE of HBO2 therapy may not be so conclusive. Second, the assumption of no recurrence of foot ulcers in the analysis may have a significant influence on the CE ratios. It would considerably increase the CE ratios if foot ulcers reoccur frequently. Third, the improved speed of wound healing and reduction of the level of wound care utilization from the use of HBO2 therapy was not taken into account in the analysis due to the paucity of such information. If they were included in the analysis, the CE ratios could be much lower. Future research on this subject should make efforts to improve these limitations if information becomes available.

POLICY IMPLICATIONS AND CONCLUSIONS

Although the validity of this study may be seriously limited by the clinical studies that provide the basis of the analysis, we believe, given current inadequate information, this study still provides valuable information for better decision making and guidance for future research. To better estimate the CE of HBO2 therapy, economic evaluation should be incorporated into clinical trials of HBO2 therapy. If such direct measurement is not feasible, more clinical trials of HBO2 therapy with larger sample sizes, randomized controlled designs, and especially long-term follow-up of subjects will be needed to improve its CE estimation.

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