The role of hyperbaric oxygen therapy in ischaemic diabetic lower extremity ulcers: a double-blind randomized-controlled trial


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of hyperbaric oxygen therapy to treat ischaemic diabetic lower-extremity ulcers. The treatment was given in a multi-place chamber via a hood, at a pressure of 2.4 atmospheres absolute for 90 minutes daily, 5 days per week, for a total of 30 sessions.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised diabetic patients with ischaemic, non-healing lower-extremity ulcers. Patients were eligible if they had an ulcer of more than 1 cm in diameter and less than 10 cm in maximum diameter, which had not shown any signs of healing despite optimum medical treatment for more than 6 weeks since presenting. Patients for whom vascular surgery, angioplasty or thrombolysis was planned were excluded.

Setting
The setting was secondary care. The economic study was carried out at Hull Royal Infirmary, Hull, UK.

Dates to which data relate
The effectiveness data were gathered from a randomised controlled trial that started in April 1999 and ended in April 2001. The cost estimates were obtained from NHS Executive 2000 costs for the UK.

Source of effectiveness data
The effectiveness data were gathered from a single prospective study.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same group of patients as that used in the effectiveness study.

Study sample
No power calculations to determine the sample size were reported. Of the 25 patients screened, 5 were excluded and 2 refused to take part in the study. A total of 18 patients were randomised into one of two groups. There were 9 patients in the treatment group and 9 in the control group.
Study design
The study was a double-blind, randomised controlled trial that was conducted in a single centre. The randomisation was performed using sealed envelopes. All patients, carers and assessors were blinded to the treatment. The duration of follow-up was one year. The patients were assessed at baseline, after 15 and 30 treatments, at 6 weeks, 6 months and 1 year. Two patients withdrew during the course of the study (one in each group).

Analysis of effectiveness
The basis of the analysis was treatment completers only. The primary health outcome was the ulcer surface area measurement (using a special software program, SigmaScan) at 6 weeks after the end of the intervention. The ulcer assessment also included a measurement of ulcer depth and a visual examination for clinical signs of infection. Quality of life was measured using the generic form SF-36 and the Hospital Anxiety and Depression Scale (HAD scale). The patients were comparable at inclusion.

Effectiveness results
At the 1-year follow-up, complete healing was achieved in 5 of the 8 ulcers in the treatment group and in none of the 8 ulcers in the control group, (p=0.026, Fisher's exact).

At the 6-week follow-up, the median decrease of the wound areas was 100% (range: 34 - 100) in the treatment group and 52% (range: -29 - 100) in the control group, (p=0.027, Mann-Whitney). However, at the 6-month follow-up, the values were 100% (range: -206 - 100) in the treatment group and 95% (range: 0 - 100) in the control group. This difference was not statistically significant.

Patients in both the treatment and control groups showed a significant improvement in the depression score on the HAD scale.

Only the control group had a significant reduction in their anxiety score, (p=0.042, Wilcoxon).

The SF-36 scores showed only a significant improvement in the general health (p=0.012, Wilcoxon) and vitality (p=0.018, Wilcoxon) domains in the treatment group. However, there was no significant difference between the groups in the other domains and for all the domains together.

Clinical conclusions
Hyperbaric oxygen has the potential to enhance the healing of ischaemic diabetic lower-extremity ulcers. The lack of a significant difference between the groups in terms of physical functioning was surprising, and suggests that the ulcers largely did not limit their physical functioning.

Measure of benefits used in the economic analysis
There was no summary measure of benefit. A cost-consequences analysis was therefore conducted.

Direct costs
The cost/resource boundary was that of the hospital. The direct costs were for the inpatient and outpatient hospital visits for ulcer dressing, hyperbaric oxygen treatment, and the treatment of any complications. The costs of an outpatient hospital visit for ulcer dressing were obtained from the NHS Executive 2000 costs for the UK. Discounting was unnecessary since all the costs were incurred in 12 months. The costs and the quantities were not reported separately. The cost of treatment was derived from the Hull Hyperbaric Unit.

Statistical analysis of costs
No statistical analysis of the costs was performed.
Indirect Costs
No indirect costs were stated.

Currency
UK pounds sterling (£).

Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The mean cost per patient for ulcer dressing visits was £1,972 in the treatment group and £7,946 in the control group.

The cost of the entire hyperbaric oxygen treatment course was £3,000 per patient.

There was a significant potential cost-saving associated with the use of adjunctive hyperbaric oxygen. This amounted to an average of £2,960 for each patient treated.

Synthesis of costs and benefits
Not relevant as a cost-consequences analysis was conducted.

Authors' conclusions
Hyperbaric oxygen enhanced the healing of ischaemic, non-healing diabetic leg ulcers and induced potential cost-savings in the total cost of treatment for each patient during the study. Hyperbaric oxygen may be used as a valuable adjunct to conventional therapy when reconstructive surgery is not possible.

CRD COMMENTARY - Selection of comparators
The authors did not justify their choice of the comparator. It may have been a placebo because earlier studies had lacked a placebo comparison. However, the comparator may not have represented best medical practice. You should therefore decide if it is an appropriate comparator for your setting.

Validity of estimate of measure of effectiveness
The estimates of effectiveness were derived from a double-blind randomised controlled trial. The double-blinding, appropriate randomisation, strict treatment protocols, and small and balanced withdrawals from each group all indicate a high level of internal validity for the study. However, as the authors acknowledged, the sample size was small and no power calculations were conducted. There was no evidence to suggest that the sample accurately represented the study population.

Validity of estimate of measure of benefit
The authors did not derive a single measure of health benefit. The analysis was therefore categorised as a cost-consequences study.

Validity of estimate of costs
The perspective adopted was not reported, but it was likely to have been that of the hospital. The major direct costs seem to have been included. Although the indirect costs were not included, it is unlikely that they would affect the authors' conclusions since they should be common to both alternatives. The price year was reported, which helps the generalisability of the results. However, the costs and the quantities were not reported separately. No statistical or sensitivity analyses of the costs or quantities were performed. Discounting was unnecessary since the costs were incurred in one year.

**Other issues**
The generalisability of the results was not specifically discussed. Adequate comparisons were made with studies dealing with the same topic. The study enrolled patients with ischaemic non-healing diabetic lower-extremity ulcers and this was reflected in the authors' conclusions. The authors reported limitations of their study, which have been highlighted already. The authors acknowledged that a disease-specific quality of life measure might have been more appropriate.

**Implications of the study**
The authors concluded that hyperbaric oxygen might be used as a valuable adjunct to conventional therapy when reconstructive surgery is not possible. The authors recommend the implementation of a large multi-centre trial to confirm the results.

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