

A retrospective study of diabetic foot ulcers treated with hyperbaric oxygen therapy

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ABSTRACT

A retrospective review of patient medical records was conducted to assess what factors influence the outcomes of diabetic foot ulcers treated with hyperbaric oxygen (HBO) therapy. Patients referred to the Diving Diseases Research Centre for HBO therapy for the treatment of diabetic foot ulcers during a 2-year period were included in this study. Data collected from 30 sets of patient records were entered into SPSS and statistical analysis was undertaken to investigate whether any underlying pathologies or confounding factors appeared to influence patient outcome. A 73.3% of patients achieved a successful outcome of partial healing, major amputation no longer required, amputation level lower than anticipated prior to HBO or healing at the end of HBO therapy and 70% remained successful 3 months later. A 13.3% of patients were lost to follow-up at 3 months and one patient (3.3%) had a major amputation. Steroid therapy, peripheral vascular disease, previous minor amputation, type of diabetes, previous HBO therapy, larvae therapy, the use of interactive dressings and haemoglobin A1c levels were all observed to have had a significant relationship with patient outcome ($P < 0.05$). These results were compared with data from other published research conducted in this area on similar patient groups. A larger scale study focussing on the factors found to be significant in this study is recommended. An improvement of patient documentation would allow patient outcomes to be more consistently monitored in the future.

Key words: Diabetic foot ulcers • Hyperbaric oxygen therapy

INTRODUCTION

Organisations such as the Undersea and Hyperbaric Medical Society now routinely review published prospective and retrospective studies and make recommendations for the use of hyperbaric oxygen (HBO) therapy for specific conditions (1,2). One of these recommendations is for HBO to be used in

the treatment of non healing diabetic foot ulcers. A Cochrane review (3) scrutinised four randomised controlled trials that investigated HBO for the treatment of diabetic foot ulcers and concluded that there is some limited evidence that HBO reduces the rate of major amputation in this patient group. However, the inclusion criteria, outcome measures and follow-up varied and the poor reporting in these studies led to the reduction in amputation rate being the only significant outcome detected.

Overall, there is a lack of any coherent policy in the UK and the provision of HBO is inconsistent with hospitals and medical centres relatively close to hyperbaric facilities having the most potential to use the treatment.

Key Points

- the provision of hyperbaric oxygen for diabetic patients with foot ulcers is inconsistent throughout the UK
- a retrospective review of diabetic foot ulcers treated with hyperbaric oxygen at one centre was conducted to assess outcomes and determine factors that influence those outcomes
- records from 30 patients with 51 wounds were reviewed

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In Plymouth, the Diving Diseases Research Centre (DDRC) has developed a protocol with the Joint Foot Clinic at the local hospital trust. This provides guidance on referrals to ensure that patients most appropriate for HBO are referred in a timely manner. HBO has become a relatively routine part of care provision by this multidisciplinary team. These patients provided a sample on which outcomes of such a treatment package could be reviewed.

A number of researchers have used retrospective study designs to investigate the efficacy of HBO for the treatment of diabetic wounds (4–11) and outcomes observed included improved healing rate and reduction of amputation rate.

The aim of this retrospective review was to assess what factors influence the outcome of diabetic foot ulcers treated with HBO. This was carried out by assessing the outcomes of diabetic foot ulcers treated with HBO at DDRC between January 2007 and December 2008, investigating the underlying pathology of patients and whether this or any other confounding factors influenced patient outcome.

The following questions were addressed:

- What were the outcomes of diabetic foot ulcers treated with HBO at DDRC between January 2007 and December 2008?
- Were there any underlying pathologies that appear to influence patient outcome?
- Were there any confounding factors that influence wound outcome?

The hypothesis was that patients with more complicated medical histories, major diabetic complications and with more risk factors for wound healing (such as smoking and age) experience poorer outcomes following HBO.

METHODS

A quantitative retrospective systematic review of patient records was selected as the most appropriate method to investigate the outcomes of diabetic foot ulcers treated with HBO at DDRC. A list of all data to be retrieved from the patient records was made following review of the published literature (4–11), review of national guidelines and international consensus documents (12–14) and using local professional knowledge. Findings in the studies by Cianci and Hunt (5), Faglia *et al.* (6),

Zgonis *et al.* (7), Fife *et al.* (8), Oubre *et al.* (9), Lyon (10) and Ong (11) were all considered with particular interest because they all investigated factors related to outcome of diabetic foot ulcers treated with HBO. The choice of which data to collect was influenced greatly by the review by Fife *et al.* (8) as this study also investigated which factors had influenced outcomes for patients who received HBO for diabetic ulcers.

A questionnaire/data collection proforma was developed to collect demographic, treatment, management and outcome data for patients who received HBO for diabetic foot ulcers over a 2-year period. Ethical approval was gained from the local ethics committee and data were collected from patient medical records from DDRC, Plymouth, and Derriford Hospital, Plymouth, UK. A pilot study of 10 patient records was conducted to test the validity of the data collection proforma.

Data collection and entry were performed by one individual only to remove inter-rater variability. A nurse independent of the study scrutinised 10 randomly selected sets of patients' records for reliability and quality control purposes. The two sets of completed forms for each of the 10 patients were then compared for any discrepancies to expose any bias that might result from one individual collecting data and to ensure standardised methods were used.

All patients with diabetic foot ulcers referred through the local hospital and treated with HBO at the DDRC Plymouth over the 2-year period investigated were included regardless of ulcer severity. A total of 30 patient records were scrutinised with 35 separate admissions and a total of 51 diabetic foot ulcers. Outcomes for all wounds were recorded as separate cases for those patients with more than one wound. As this was a retrospective study, consent from patients was not required. However, wound photographs for patients were only collected if the patient had selected the research box on the consent form that is routinely completed by DDRC patients. Data were treated to comply with the Data Protection Act (15).

Exclusion criteria included ulcers above the malleolus and patients who received less than 15 HBO treatments. Standard treatment regime at DDRC is a minimum of 20 treatments. HBO is terminated according to clinical decision by the medical team. HBO is often discontinued at

20 treatments if there is no sign of improvement to the wound bed.

Data were collected at commencement of HBO and at two further time points: (i) at completion of HBO and (ii) 3 months following completion of the course of HBO. Outcome was assessed and assigned to one of the following groups by comparing the data at each time point to that at the start of treatment:

- Major/minor amputation now necessary (*treatment failure*)
- No or minimal improvement (minimal improvement being no signs of a reduction of inflammation, less than 80% granulating tissue present to the wound bed or no signs of epithelialisation) (*treatment failure*)
- Partially healed; major amputation no longer required; amputation level lower than anticipated prior to HBO (*treatment success*)
- Healed (100% epithelialisation) (*treatment success*)

Patients were assigned to these groups using a combination of evaluation of the wound size (Visitrak[®], Smith and Nephew, UK or a disposable tape measure), Texas classification (16), review of photographs and final medical assessment as documented in the patient records. As there were some missing data, consultant comments at review greatly influenced the choice of final outcome allocation. The consultants were all employed by the National Health Service and so had no conflict of interest.

Patients with more than one diabetic foot ulcer were recorded as separate cases but it was noted that they had more than one wound present at the time of treatment. Patients who received more than one course of HBO were recorded as separate cases with a note made that they had received previous HBO and whether this was for the same or a different wound.

STATISTICS

Descriptive statistics were presented for each outcome. Each variable was compared with the two main outcome groups (treatment success or treatment failure) using Pearson's chi-square tests for categorical variables and the nonparametric Mann-Whitney test for quantitative variables. A significance level of $P < 0.05$ was used.

RESULTS

Nine patients had more than one diabetic foot ulcer present and 5 patients received more than one course of HBO, so data were collected for a total of 51 wounds in 30 different patients. In order that comparisons of underlying pathology and other potentially confounding variables with patient outcome could be made without data from patients with multiple wounds skewing the results, statistical analysis was performed per subject rather than per wound using the index wound for each patient. Each individual factor was analysed in relation to the strength of its association with the outcome at the end of the course of HBO and the outcome 3 months later to address the aims and objectives of this study. Patient characteristics are displayed in Table 1.

HBO treatment is generally administered on a once or twice daily basis Monday to Friday with weekends off. In this sample, only one patient (3.3%) received anything other than once daily HBO and they had some treatment once daily and some twice daily. The mean number of HBO treatments received for this sample was 40 (range = 19–60).

Outcomes for the index wounds in the 30 patients at completion of HBO and 3 months post HBO are presented in Table 2. Data showed that most patients achieved a successful outcome at the end of HBO (73.3%) and 3 months later (70%). A smaller majority of the 51 wounds were in the successful groups at the end of HBO (64.7%) and 3 months later (62.7%) (Table 3).

The variables found to be statistically significant at the end of HBO and/or 3 months later were steroid therapy, peripheral vascular disease, previous minor amputation, type of diabetes, previous HBO, the application of larvae therapy, use of interactive dressings and glycated haemoglobin (Hb) A1c levels.

Steroid therapy was associated with a poorer outcome. Only two patients (6.7%) were taking steroids and they were both in the failed outcome group at completion of HBO (Pearson $\chi^2 = 5.89$, $df = 1$, $P = 0.015$). This was no longer significant 3 months later ($\chi^2 = 1.32$, $df = 1$, $P = 0.250$).

Patients without peripheral vascular disease had significantly better outcome 3 months after HBO (Pearson $\chi^2 = 5.63$, $df = 1$, $P = 0.018$). There was no statistically significant

Table 1 Patient characteristics*

Number of patients	30	
Mean age	63 years (36–80)	ns
Males/females	6/24	ns
Mean age of females	59.8 years (48–73)	ns
Mean age of males	63.9 (36–80)	ns
Type 1/type 2 diabetes	6 (20%)/23 (76.7%)	ns
Mean time since diagnosis	Data missing for one patient 17.3 years (4 months 47 years)	ns
Insulin/diet controlled	23 (76.7%)/1 (3.3%)	ns
Referring consultant		
Diabetologist	14 (46.7%)	ns
Vascular surgeon	14 (46.7%)	ns
Orthopaedic surgeon	1 (3.3%)	ns
Plastic surgeon	1 (3.3%)	ns
Reason for referral		
Non healing wound	20 (66.7%)	ns
Perioperative	10 (33.4%)	ns
Mean duration of wounds	19.8 weeks (0–104 weeks)	ns
Texas classification		
A1	8 (26.7%)	ns
A2	3 (10%)	ns
A3	4 (13.3%)	ns
B1	6 (20%)	ns
B3	2 (6.7%)	ns
C1	1 (3.3%)	ns
D1	3 (10%)	ns
D3	2 (6.7%)	ns
Mean number of hyperbaric oxygen treatments	40 (19–60)	ns

ns, not significant.

*Range and percentages are in brackets.

relationship immediately post HBO ($\chi^2 = 0.46$, $df = 1$, $P = 0.500$). However, three patients with a history of peripheral vascular disease were lost to follow-up compared with just one who had no history of peripheral vascular disease and this may have led to inaccurate and unreliable results.

At the end of HBO, four patients (33.3%) who had peripheral vascular disease were in the failed group and four (44.4%) remained in this outcome group 3 months later. A total of 12 patients (40% of the total sample) had a history of peripheral vascular disease compared with 18 (60% of the total sample) who did not. Four patients (22.2%) who did not have peripheral vascular disease were in the failed outcome group at the end of HBO while only one (5.9%) remained in this group 3 months later.

Previous minor amputation (defined as ankle level or lower) ($n = 8$) was found to be significantly related to negative outcome

both at the end of HBO ($\chi^2 = 7.16$, $df = 1$, $P = 0.007$) and 3 months later ($\chi^2 = 3.44$, $df = 1$, $P = 0.064$). The majority of patients (22 patients – 73.3%) had not received a previous minor amputation and of these 22 patients, 19 (86.4%) achieved a successful outcome at the end of HBO compared with only 3 of the 8 patients (37.5%) who had previous minor amputation. Three months later, three patients who had not had a previous minor amputation were lost to follow-up but 17 (89.5%) remained in the successful outcome group. In comparison, one patient who had received a minor amputation was lost to follow-up and four (57.1%) were in the successful group.

For one subject it was not possible to establish from their records whether they had type 1 or 2 diabetes. A statistically significant relationship was observed between the type of diabetes and outcome at the end of HBO ($\chi^2 = 5.78$,

Table 2 Patient outcomes following treatment and 3 months post HBO

Outcome	Outcome at completion of HBO		Outcome at 3 months post completion of HBO	
	Number of subjects	Percentage (%)	Number of subjects	Percentage (%)
Major/minor amputation now necessary	0	0	1	3.3
No/minimal improvement	8	26.7	4	13.3
Partially healed; major amputation no longer required; amputation level lower than anticipated prior to HBO	22	73.3	13	43.3
Healed	0	0	8	26.7
Missing data	0	0	4	13.3
Total	30	100	30	100

HBO, hyperbaric oxygen.

Table 3 Wound outcomes following HBO and 3 months post HBO

Outcome	Outcome at completion of HBO		Outcome at 3 months post completion of HBO	
	Number of subjects	Percentage (%)	Number of subjects	Percentage (%)
Major/minor amputation now necessary	0	0	2	3.9
No/minimal improvement	18	35.3	6	11.8
Partially healed; major amputation no longer required; amputation level lower than anticipated prior to HBO	31	60.8	17	33.3
Healed	2	3.9	15	29.4
Missing data	0	0	11	21.6
Total	51	100	51	100

HBO, hyperbaric oxygen.

df = 1, $P = 0.016$) with more patients with type 1 diabetes in the failed outcome group (4 patients – 66.7%) and more patients with type 2 diabetes in the successful outcome group (19 patients – 82.6%). This difference was no longer significant 3 months later ($\chi^2 = 0.88$, df = 1, $P = 0.349$) as four patients (66.7%) with type 1 diabetes were now in the successful outcome group and none of these subjects lost to follow-up. Sixteen patients (84.2%) with type 2 diabetes remained in the successful outcome group at 3 months after completion of HBO with four lost to follow-up. This missing data could have resulted in inaccurate results.

Three patients (75%) who had received previous courses of HBO were in the failed outcome group at the end of HBO and the relationship was statistically significant (Pearson $\chi^2 = 5.51$, df = 1, $P = 0.019$). Only five patients (19.2%) who had not had previous HBO were in the failed outcome group and this reduced to three (13.6%) 3 months later, although the four patients for whom outcomes were missing at this time point were all patients

who had not previously received HBO. Two of the patients (50%) who had received HBO previously had achieved a successful outcome 3 months after HBO and the relationship was no longer significant ($\chi^2 = 2.88$, df = 1, $P = 0.090$).

Those patients who received larvae therapy ($n = 4$) at some point during their HBO showed statistically significant worse outcomes when these were compared at the end of HBO (Pearson $\chi^2 = 5.51$, df = 1, $P = 0.019$) with three patients (75%) in the failed outcome group. This was compared with 5 of 26 (19.2%) of those who did not receive larvae therapy. There was no significant relationship between larvae therapy and outcome 3 months later when the number of patients who had received larvae and were in the failed group had reduced to two (50%) ($\chi^2 = 2.88$, df = 1, $P = 0.090$). Only 3 of 21 patients (13.6%) who did not receive larvae were in the failed group 3 months after HBO. However, four of those who did not receive larvae were lost to follow-up so these results need to be taken with caution.

As with larvae therapy, interactive dressings are often reserved for use on more indolent or severe wounds. Four of 6 patients (66.7%) who received interactive dressings (these included Promogran® and Urgo® Start although a breakdown of specific dressings for patients were not collected) were in the failed group at the end of HBO compared with 4 of the remaining 24 (16.7%) ($P = 0.013$). This outcome was also statistically significant 3 months after HBO with three of six patients (50%) who received interactive dressings in the failed group (Pearson $\chi^2 = 4.76$, $df = 1$, $P = 0.029$). Eighteen of 20 patients (90%) who did not have interactive dressings applied to their wounds were in the successful outcome group.

The only statistically significant quantitative variable was HbA1c. Most diabetic patients are advised to aim for an HbA1c of below 7.5%. The mean HbA1c of the patients investigated in this study was 7.98% (median = 7.30%, range = 5.5–12.6%). HbA1c levels from the previous 3 months or within 1 week of commencing HBO were missing for six patients. It is generally anticipated that patients with poorer diabetic control, and hence higher HbA1c levels have problems with delayed wound healing (17,18). Using a Mann–Whitney test, it was found that the opposite of this was showed for this sample of patients receiving HBO. Patients who showed a statistically significant improvement at the end of HBO ($P = 0.039$) had a mean HbA1c of 8.47% (range = 5.5–12.6%) compared with 6.79% (range = 5.8–8.0%) in the failed group. Three months after HBO this was not statistically significant ($P = 0.052$) potentially due to missing data from the patients lost to follow-up. The mean HbA1c in the successful group was 8.55% (range = 5.5–12.6%) and in the failed group, mean HbA1c = 6.70% (range = 5.8–8.0%).

To test this result, the data were arranged into two categories – HbA1c < 7.5% and HbA1c > 7.6% – and were analysed using Pearson chi-square. The relationship between HbA1c and outcome at the end of HBO remained significant with patients who had a higher HbA1c level achieving a successful outcome (Pearson $\chi^2 = 3.96$, $df = 1$, $P = 0.047$). However, at 3 months after HBO the relationship was no longer significant (Pearson $\chi^2 = 2.76$, $df = 1$, $P = 0.097$).

Although not statistically significant, more previous or current smokers were observed to

be in the failed outcome groups. This variable was statistically significant in this study by Fife *et al.* (8) but Oubre *et al.* (9) also found no statistically significant link.

The majority of patients (24 patients – 80%) in the sample had no side effects from treatment. The side effects experienced by the remaining six patients were ear/sinus barotrauma, myopia and claustrophobia – two patients (6.7%) experienced each. These side effects are known to be common during HBO and are considered to be minor compared with the more severe side effect of oxygen toxicity. No patients in this study experienced oxygen toxicity, which is a relatively rare side effect.

DISCUSSION

Age and gender

No significant difference was observed in the distribution of patient age within gender. Neither age nor gender was found to be significantly related to outcome in this sample, although the majority of patients were male with only 6 of 30 patients being female. These data are consistent with other findings. A study in the UK investigating diabetic foot ulcers and outcome also observed no association between age, gender and outcome (19). It is a common understanding that males are more susceptible to diabetic foot ulcers (20–23), therefore, a greater number of male patients in the sample would be expected.

Other studies on HBO for the treatment of diabetic foot ulcers have found an association between age and outcome. Faglia *et al.* (6) observed that average age was significantly higher in the non HBO group than the HBO group ($P < 0.05$) in their retrospective study and there was a statistically significant higher number of major amputations in the non HBO group ($P = 0.012$). Oubre *et al.* (9) found that patients who achieved better outcomes were younger.

Diabetes

Twenty-three patients (76.7%) of the sample in this study had type 2 diabetes with the average time since diagnosis being 17.3 years. This history of diabetes would lead to an expectation of high numbers of patients with peripheral vascular disease and neuropathy within the sample. Indeed, 40% of subjects had a history of peripheral vascular disease

and 63.3% had severe peripheral neuropathy (insensate). Fife *et al.* (8) observed no statistically significant difference in neuropathy status and patient outcome following HBO although the 'insensate' category experienced twice the amputation rate of the 'normal' and 'decreased sensation' categories. The results of this study are consistent with those in the study of Fife *et al.* (8) as they also observed no significant link between neuropathy status and outcome, although all patients with normal sensation were in the successful outcome group 3 months after HBO compared with only 80% of the patients who had either decreased sensation or were insensate. Larger patient numbers would allow this finding to be investigated further and observe whether this outcome was coincidental or is consistent within a larger population in the UK.

Wound classification

The DDRC uses the Texas classification (16) system to assess diabetic foot ulcers, as do many specialist clinicians throughout the UK. Just over a quarter (26.7%) of the 30 patients in this study had wounds assessed as penetrating to bone or joint and 16.7% of patients had signs of infection and ischaemia. Only 6.7% of patients who had wounds penetrating to bone or joint also had signs of both infection and ischaemia. Faglia *et al.* (24) observed that HBO is effective in reducing the need for major amputation in patients with severe diabetic foot ulcers as patients with Wagner grade 4 ulcers (indicating severe gangrene) were the most common in their sample. Wagner grade 4 ulcers were also the most common in the retrospective study by Cianci and Hunt (5). However, Fife *et al.* (8) observed a poorer overall outcome in patients with ulcers classified as Wagner grade 3 or above. Because of the small patient numbers in this study presented here, it was not possible to investigate the relationship between ulcer classification and patient outcome.

Treatment regime

Only one patient in this study received anything other than once daily treatment. That patient received some treatment twice daily and some once daily and was in the successful outcome group with a partially healed wound at the end of HBO and 3 months later. Often, when a wound is critical, initial treatment will

be given on a twice daily basis before reverting to once daily HBO. Fife *et al.* (8) observed that patients treated once daily achieved more positive outcomes than those treated twice daily. They suggested that this was due to patients with more compromised limbs being treated more intensively rather than the higher frequency of treatment being less effective.

The mean number of HBO treatments for this sample was 40. McMillan and Glover (25) suggested that 30–40 HBO treatments are common for diabetic foot ulcers in the UK. A randomised trial by Abidia *et al.* (26) conducted in the UK administered 30 treatments to patients. The Undersea and Hyperbaric Medical Society do not recommend a specific number of treatments, but do advise a review after 30 days of treatment and at least that interval thereafter (2).

The number of treatments received was not found to be significantly related to outcome. Other studies have found links between treatment number and outcome. Zgonis *et al.* (7) found that patients with a successful outcome from postoperative HBO had a mean number of 20 treatments while Fife *et al.* (8) observed that 73.8% of patients improved with a mean number of 34 HBO treatments and those patients who did not improve received a mean number of 24 HBO. They suggested that treatment was discontinued sooner for those patients who did not appear to be responding.

Some clinicians speculate that administering HBO in a monoplace chamber allows 100% oxygen to be applied topically as well as systemically. Only three patients in this study received any treatments in the monoplace and no significant difference was found in outcome. Doctor *et al.* (27), Cianci and Hunt (5), Zamboni *et al.* (28), Kalani *et al.* (29) and Zgonis *et al.* (7) administered HBO in monoplace chambers. Because of the methodological differences between the studies, it is not possible to compare the outcomes of patients treated in monoplace chambers with those in studies where HBO was administered in multiplace chambers.

The treatment depth at DDRC was consistent with current practice elsewhere.

Patient outcomes

Twenty-two patients (73.3%) had achieved an outcome of 'partially healed, major amputation no longer required or amputation level lower

than anticipated prior to HBO' at the end of HBO and eight patients (26.7%) had healed 3 months later. Four patients (13.3%) were lost to follow-up. Some of these patients may have achieved 100% epithelialisation as when patients had healed they were discharged from DDRRC and the Joint Foot Clinic resulting in missing data. Of all 51 wounds treated within the 2-year period investigated, 60.8% had achieved an outcome of partially healed, major amputation no longer required or amputation level lower than anticipated and 3.9% were healed at the end of HBO. Three months later, 29.4% of wounds were healed.

Fife *et al.* (8) suggested the aim of HBO treatment for patients with diabetic foot ulcers should not be to heal the wound, but it should be administered with the intention of improving healing, especially for wounds that have been indolent for some time. Considering that the mean duration of ulceration for the 30 patients was 19.8 weeks and 60% of patients were referred to encourage healing of a non healing ulcer and 6.7% to prevent major amputation, these results show that HBO treatment was of benefit to these patients.

The results also indicate that healing continues following HBO as was also observed in studies by Cianci and Hunt (5), Kalani *et al.* (29) and Abidia *et al.* (26). It has been suggested that patients who have experienced their first diabetic foot ulcer have less than a 50% chance of remaining free from ulceration within 1 year of the ulcer healing (30); therefore a reduction in the risk of reulceration would be greatly beneficial. Follow-up for a year did not continue in the study presented here but such information would be useful to determine the long-term outcome of patients treated with HBO.

The number of patients achieving a successful outcome at 3 months may have been underestimated as some patients were discharged from clinic when their wound healed and were subsequently lost to follow-up at 3 months. Only one patient needed a major amputation following HBO. These outcomes show HBO to be of some benefit in the treatment of diabetic foot ulcers and are consistent with findings in other studies.

Influencing variables

Steroid therapy

Steroid therapy was observed to be significantly related to poorer patient outcome at the

end of HBO but one of the two patients taking steroids had moved to the successful outcome group at 3 months. These results are consistent with the knowledge that steroids are known to slow wound healing (31,32) since one of the patients' wounds had a delayed response to HBO. However, as the sample was small, the finding could be coincidental and would warrant further investigation in a larger study. Steroids were not mentioned as an influencing factor in any previous studies on HBO for diabetic foot ulcers. However, this finding is consistent with the knowledge that steroid therapy can impair wound healing.

Peripheral vascular disease

Peripheral vascular disease is known to be a contributory factor in the development of diabetic foot ulcers (21,33). It was observed to be significantly related to patient outcome at 3 months after HBO. Patients without peripheral vascular disease achieved better outcomes than those with the disease. This finding suggests that patients with peripheral vascular disease might not have the continuing benefit from HBO after it has completed, although three patients from this group were lost to follow-up, which could have led to inaccurate results. In a study assessing the impact of risk factors on the outcome of diabetic foot ulcers, Hokkam (23) identified peripheral vascular disease as significantly related to the development of ulceration in diabetics but not to the outcome of the wound. In a study on HBO for diabetic foot ulcers, Faglia *et al.* (6) observed that the severity of peripheral vascular disease was related to major amputation, although their univariate analysis was on all patients (control and HBO) so this result does not specifically relate to outcome from HBO. The influence of peripheral vascular disease on outcome following HBO warrants investigation in future research to clarify its significance.

Previous minor amputation

Fife *et al.* (8) found no significant difference between those patients who had a prior amputation and those who had not. These results are not comparable with the findings in this study presented here as Fife *et al.* (8) did not distinguish between minor and major amputation. In this study, patients who had

not received a previous minor amputation achieved significantly better outcomes at both time points. As this sample was relatively small, this finding should be interpreted with caution. However, patients who have had a minor amputation are reported to be at increased risk of reulceration (22,34). Sheahan *et al.* (35) found that limb salvage following initial minor amputation was 89.8% 1 year on and 82.3% 5 years later.

Type of diabetes

Hokkam (23) reported type 2 diabetes as a significant risk factor for the development of diabetic foot ulcers. However, in this study patients with type 2 diabetes achieved significantly better outcomes at the end of HBO than patients with type 1 diabetes, although this difference was no longer significant 3 months later. A study by Black *et al.* (36) observed that collagen deposition is decreased in patients with type 1 diabetes. This was not observed in patients with type 2 diabetes and could explain why patients with type 1 diabetes achieved poorer outcomes in this study. Data on diabetes type were missing for one patient. No previous studies on HBO for diabetic foot ulcers reported type of diabetes as an influencing factor.

Previous HBO

A significant relationship was observed between previous HBO and outcome at the end of HBO. Only five patients had received a course of HBO before but 75% of them were in the failure group at the end of HBO compared with just 19.2% of patients who had never received HBO in the past. This is not a factor that has been highlighted to affect outcome in any previous studies and further investigation with a larger sample would be indicated from this result.

Larvae therapy and interactive dressings

Patients who received larvae therapy or interactive dressings achieved significantly worse outcomes at the end of HBO and patients who had interactive dressings also showed significantly worse outcomes 3 months later. Larvae and interactive dressings are usually reserved for use on more severe wounds possibly explaining why these patients were more likely to be in the failure group.

Four of the patients who had larvae therapy were lost to follow-up, therefore these results at 3 months after HBO may be inaccurate. Hunt (37) reviewed evidence on the effect of different dressing types on wound healing rate in diabetics and found no results to show any one wound dressing to be more effective than another. Hunt (37) also found no evidence to suggest that using larvae to debride a wound increased the healing rate compared with the use of hydrogel. None of the studies on HBO and diabetic foot ulcers have reported any dressings to be linked with patient outcome.

Haemoglobin A1c

The mean HbA1c from the previous 3 months or within 1 week of commencing HBO of the group was 7.98%. This is higher than is generally recommended.

Patients with a higher HbA1c level showed significantly better outcomes at the end of HBO, which was an unexpected result. This could be due to the missing results from six patients. However, it would be interesting to see whether glucose levels and diabetic control improved over the course of HBO for patients with higher HbA1c at the start. This might explain the improved outcome for these patients. When attending for HBO, patients spend more time with clinicians than they have performed previously. They see a nurse daily and a hyperbaric doctor at least weekly and these clinicians constantly remind the patients of the importance of diet and metabolic control. Patients attending for HBO may also be keen to participate in more positive health behaviour, especially those patients who are aware that should they achieve a poor outcome from HBO an amputation will be necessary. HbA1c levels were not collected at the end of treatment, but this would provide information on whether the levels reduced over the course of HBO or whether they remained high. These patients may have experienced better healing if their metabolic control had been lowered without HBO. A study with a control group would be necessary to investigate this factor more thoroughly.

It is known that HBO can lower the blood glucose level of a diabetic patient during treatment (38). However, Baroni *et al.* (39) and Faglia *et al.* (6) collected HbA1c levels at the start and at the end of treatment for both

the HBO group and the control group and observed that metabolic control improved for both over the course of the studies.

Hyperglycaemia inhibits normal polymorphonuclear leukocyte functioning (including neutrophils), leading to reduced polymorphonuclear leukocyte migration, adherence and phagocytosis and causes oxidative stress resulting in overproduction of reactive oxygen species (17,40). HBO reduces neutrophil adhesion and attenuates apoptosis leading to a reduction in pathological inflammation (41,42). This may provide another explanation for those patients with higher HbA1c levels achieving better outcomes. They may experience a greater reduction in pathological inflammation due to their hyperglycaemia causing increased oxidative stress. Gu *et al.* (43) observed that HBO reduced high blood glucose levels in rats with type 2 diabetes and improved oxidative capacity in their skeletal muscles. They also found that this effect was maintained following completion of HBO. Research focussing on these processes in human subjects is necessary to further investigate these theories.

Smoking

Although not significant, there was a difference in outcome between the 'never smoked' and 'previous/current smoker' groups in this study with less patients who had never smoked in the failure groups. This is consistent with the findings of Faglia *et al.* (6) who also observed no significant link between smoking and outcome of HBO.

However, other studies have showed a significant relationship. Fife *et al.* (8) found that patients who had a greater than 40 pack-year history of smoking had a significantly worse outcome than those with a less than 40 pack-year history or those who never smoked. It was not possible to collect data to calculate pack years in this study due to the lack of documented information on smoking history.

Otto *et al.* (44) investigated the effects of smoking on outcome following HBO and found statistically significant evidence that smoking is a risk factor for the healing of wounds in diabetic patients undergoing HBO. Oubre *et al.* (9) also observed a significant link between smoking and poorer outcome but this study included both diabetic and non diabetic patients.

This factor would be worthy of further investigation in a larger scale study.

CRITIQUE OF METHOD

As is common with retrospective studies, much of the information required for this review was difficult to locate and this led to missing data, particularly at 3-month follow-up. The missing data meant some factors could not be thoroughly investigated.

To reduce inconsistencies in the data, one observer scrutinised all the patient records and another reviewed 10 sets selected at random. Comparison of the data collection sheets for those 10 patients showed the reliability of data collection.

While providing interesting clinical data, the small sample size in this study means that statistically significant results may not be clinically significant. A larger sample could highlight other factors that significantly influenced patient outcome and allow more meaningful conclusions to be drawn. This was the entire population of patients with diabetic foot ulcers treated at DDRC within a 2-year period, therefore a review over a longer period or a multicentre study would allow a larger sample to be investigated.

Without a control group it is not possible to ascertain whether the findings here are due to HBO or the conditions unique to such a treatment, such as enforced rest for 2 hours and more intense contact with healthcare professionals.

CONCLUSION

Records of 30 patients with 51 wounds with a mean duration of 19.8 weeks were reviewed. At the end of HBO, 22 patients (73.3%) received a positive outcome on their index wound and at 3 months after completion of HBO, 21 patients (70%) remained in the positive outcome group with 8 of these patients (26.7%) being healed (4 patients were lost to follow-up).

A number of factors were found to have a significant relationship with outcome in this review. Steroid therapy, peripheral vascular disease, previous minor amputation, type of diabetes, previous HBO, larvae therapy and the use of interactive dressings were all observed to be significantly associated with poorer outcome while higher HbA1c levels were significantly associated with better patient outcome.

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