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Hyperbaric oxygen therapy for thermal burns (Review)

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[Intervention Review]

Hyperbaric oxygen therapy for thermal burns

Elmer Villanueva[1], Michael H Bennett[2], Jason Wasiak[3], Jan P Lehm[4]

[1]Gippsland Medical School, Monash University, Churchill, Australia. [2]Department of Anaesthesia, Prince of Wales Hospital, Randwick, Australia. [3]Victorian Adult Burns Service, The Alfred Hospital, Melbourne, Australia. [4]Department of Diving and Hyperbaric Medicine, Prince of Wales Hospital, Randwick, Australia

Contact: Jason Wasiak, Victorian Adult Burns Service, The Alfred Hospital, Commercial Road, Prahran, Melbourne, Victoria, 3181, Australia. J.Wasiak@alfred.org.au, jwasiak1971@gmail.com.

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ABSTRACT

Background

Hyperbaric oxygen therapy (HBOT) consists of intermittently administering 100% oxygen at pressures greater than 1 atmosphere in a pressure vessel. This technology has been used to treat a variety of disease states and has been described as helping patients who have sustained burns.

Objectives

The aim of this review was to assess the evidence for the benefit of hyperbaric oxygen therapy (HBOT) for the treatment of thermal burns.

Search methods

We searched the Cochrane Injuries Group Specialised Register; CENTRAL (The Cochrane Library 2009, Issue 2); MEDLINE; PubMed; EMBASE; ISI Web of Science and Conference Proceedings Citation Index-Science (CPCI-S); DORCTHIM (Database of Randomised Controlled Trials in Hyperbaric Medicine: from inception to 2009); reference lists of relevant articles and Internet sources for published and unpublished trials. The latest search was carried out in June 2009.

Selection criteria

We included all randomised controlled trials that compared the effect of HBOT with no HBOT (no treatment or sham).

Data collection and analysis

Two authors independently extracted data using standardised forms. Each trial was assessed for internal validity with differences resolved by discussion. Data were extracted and entered into RevMan 4.2.3.

Main results

Five randomised controlled trials were identified, of which two satisfied the inclusion criteria. The trials were of poor methodological quality. As a result, it was difficult to have confidence in the individual results and it was not appropriate to pool the data.

One trial reported no difference in mortality, number of surgeries or length of stay between the control and HBOT groups once these variables were adjusted for the patients' condition. The second trial reported mean healing times that were shorter in patients exposed to HBOT (mean: 19.7 days versus 43.8 days). No further eligible trials were found when the search was updated in June 2009.

Authors' conclusions

This systematic review has not found sufficient evidence to support or refute the effectiveness of HBOT for the management of thermal burns. Evidence from the two randomised controlled trials is insufficient to provide clear guidelines for practice. Further research is needed to better define the role of HBOT in the treatment of thermal burns.

PLAIN LANGUAGE SUMMARY

Little evidence that burns patients benefit from hyperbaric oxygen therapy

Burns are very common, sometimes fatal, and have a high impact on the wellbeing of those affected. Recovery is often slow and complicated by infection and scarring. Hyperbaric oxygen therapy (HBOT) is a treatment designed to increase the supply of oxygen to the burnt area and improve healing. HBOT involves people breathing pure oxygen in a specially designed chamber (such as those used for deep sea divers suffering pressure problems after resurfacing). The review found only two randomised trials, with only a limited number of patients. There was no consistent benefit from HBOT, but one trial did suggest an improvement in healing time. Overall, there is little evidence to support or refute the use of HBOT for burns patients. More research is needed.

BACKGROUND

Description of the condition

Thermal burns remain an important source of morbidity and mortality. Every year, approximately two million people are burned, 80,000 are hospitalised, and 6,500 die in the USA (Brigham 1996). Globally there were 238,000 fire-related deaths in 2000, with low and middle-income countries bearing 95% of the global burden. Mortality per 100,000 population is 1.3 in North America but 5.5 in Africa (WHO 2002). Burns are a complex and evolving injury, with both local and systemic consequences - the latter manifesting once the burn area is greater than about 20% of the body surface area (BSA) (Sheridan 2002). Locally, the burn wound tends to extend in the acute phase of the injury secondary to microvascular changes, profound activation of white cells and platelets, and the development of oedema. Many small vessels are directly coagulated by the application of heat, while others will thrombose late and develop tissue dehydration (Boykin 1980). The systemic response to burning is characterised by interstitial oedema in distant organs, secondary to a combination of wound-released mediators and hypoproteinaemia (Demling 1980; Youn 1992).

Burns are a difficult treatment challenge and ideally the province of specialised units with high-volume workloads. Such units do not exist in most parts of the world. Early treatment can positively influence mortality rate. It involves appropriate fluid resuscitation, usually involving attainment of resuscitation targets using consensus formulas for initial fluid administration (Sheridan 2002), together with topical agents to control pain, limit direct fluid losses and slow bacterial growth. Over the past two decades, early closure of full-thickness wounds has improved the outcome from extensive burns through the prevention of wound colonisation and infection (Sheridan 2002). Temporary skin substitutes are widely employed on a similar rationale when formal closure is not an option.

Description of the intervention

Hyperbaric oxygen therapy (HBOT) is an adjunctive therapy that has been proposed to improve outcome in thermal burns. HBOT is the therapeutic administration of 100% oxygen at environmental pressures greater than 1 atmosphere absolute (ATA). Administration involves placing the patient in an airtight vessel, increasing the pressure within that vessel, and administering 100% oxygen for respiration. In this way, it is possible to deliver a greatly increased partial pressure of oxygen to the tissues. Typically, treatments involve pressurisation to between 1.5 and 3.0 ATA, for periods between 60 and 120 minutes once or more daily.

How the intervention might work

Since 1965 it has been suggested that HBOT might improve the outcome following thermal burns (Wada 1965). HBOT has been shown to reduce oedema and preserve microcirculation in a number of injury models, including burns, through vasoconstriction with enhanced oxygen delivery, a direct osmotic effect and the inactivation of white cell adhesion (Hills 1999; Nylander 1985; Thom 1994). HBOT also exerts beneficial effects on infections in hypoxic tissues through a variety of mechanisms (Knighton 1984).

Despite nearly 40 years of interest in the delivery of HBOT in these patients, little clinical evidence of effectiveness exists. An experimental model of burn injury suggested some reduction in hyperaemia, exudate and wound size, but no overall improvement in healing (Niezgoda 1982), while small, non-random, comparative trials have reported lower mortality and shorter hospital stays following HBOT in significantly burnt individuals (Cianci 1988; Grossman 1978; Niu 1987). On the other hand, a comparative study of 72 matched patients suggested more renal failure and sepsis (although fewer grafts) in the HBOT group (Waisbren 1982).

HBOT is associated with some risk of adverse effects, including damage to the ears, sinuses and lungs from the effects of pressure, temporary worsening of short-sightedness, claustrophobia and oxygen poisoning. Although serious adverse events are rare, HBOT cannot be regarded as an entirely benign intervention.

OBJECTIVES

The aim of this review was to assess the evidence for the benefit of hyperbaric oxygen treatment (HBOT) for the treatment of thermal burns.

Specifically, we aimed to address whether HBOT;

- reduced mortality and morbidity following thermal burns
- reduced the time required to heal thermal burns
- reduced the degree of scarring following thermal burns
- reduced the requirement for debridements and/or grafts in the treatment of thermal burns
- reduced the requirement for fluid therapy in the acute treatment phase.

METHODS

Criteria for considering studies for this review

Types of studies

We included all randomised controlled trials (RCTs) that compared the effect of HBOT with no HBOT (no treatment or sham).

Types of participants

We focused on patients with thermal injuries to the epidermis, subcutaneous tissues, vessels, nerve, tendons, or bone. No restrictions on age or sex were made.

Types of interventions

We compared treatment regimens that included HBOT with similar regimens that excluded HBOT.

HBOT administered in a compression chamber between pressures of 1.5 ATA and 3.0 ATA and treatment times between 30 minutes and 120 minutes once or more daily were eligible for inclusion. We accepted any standard treatment regimen designed to promote burn healing as the comparator.

Types of outcome measures

Studies were eligible for inclusion if they reported any of the following outcome measures.

Primary outcomes

1. Mortality rate.
2. Major morbidity rate (wound infection, haemodynamic instability).

Secondary outcomes

1. Acute fluid requirement.
2. Time to healing.
3. Requirement for grafts and/or debridement.
4. Length of stay.
5. Scar quality (hypertrophic, retracted).
6. Pain scores.
7. Activities of daily living.
8. Adverse effects of HBOT: proportion of patients with visual disturbance (short and long-term), barotrauma (aural, sinus, pulmonary in the short and long-term) and oxygen toxicity (short-term) with respect to HBOT obtained from the included studies. Any other recorded adverse effects were reported and discussed.

Search methods for identification of studies

The searches were not restricted by date, language or publication status.

Electronic searches

We searched the following electronic databases;

- Cochrane Injuries Group Specialised Register (searched 1 June 2009);
- CENTRAL (*The Cochrane Library* 2009, Issue 2);
- MEDLINE (Ovid SP) 1950 to May (week 4) 2009;
- PubMed [www.ncbi.nlm.nih.gov/sites/entrez/] (searched June 1, 2009 (added to PubMed in the last 180 days);
- CINAHL (1982 to January 2007) (searches not re-run as previous searches yielded no useful results);
- EMBASE (Ovid SP) 1980 to (week 22) June 2009;
- National Research Register (to Issue 4, 2006);
- ISI Web of Science: Science Citation Index Expanded (SCI-EXPANDED) (1970 to June 2009);
- ISI Web of Science: Conference Proceedings Citation Index-Science (CPCI-S) (1990 to June 2009);
- DORCTHIM (Database of Randomised Controlled Trials in Hyperbaric Medicine) at www.hboevidence.com (Bennett 2002) from inception to June 2009

The search strategies are presented in Appendix 1.

Searching other resources

We also handsearched the following literature;

- textbooks (Kindwall, Jain, Marroni, Bakker, Bennett and Elliot),
- journals (Undersea and Hyperbaric Medicine, Hyperbaric Medicine Review, South Pacific Underwater Medicine Society (SPUMS) Journal, European Journal of Hyperbaric Medicine and Aviation, Space and Environmental Medicine Journal),
- conference proceedings (Undersea and Hyperbaric Medical Society, SPUMS, European Undersea and Baromedical Society, International Congress of Hyperbaric Medicine) published from 1980 to 2003.

In addition we checked the reference lists of the relevant trials and reviews. We contacted current researchers in the field for unpublished data and ongoing trials but were unable to contact the authors of the two included RCTs.

Data collection and analysis

Selection of studies

Two authors (JW and MB) independently reviewed titles and abstracts of articles retrieved using the aforementioned search strategy. Trials that clearly failed to meet the inclusion criteria were not reviewed. Those that could not be excluded were retrieved and reviewed in full-text by two authors. In all instances, differences of opinion were resolved by discussion. For the 2009 update, records were retrieved, scanned and reviewed in the same way.

Data extraction and management

Two authors independently extracted data from the trials using a paper data extraction form. The standardised form allowed for the extraction of specific data such as type of care setting, description of the intervention and the control, and key baseline variables of each group such as depth of burn wound, age, sex. Disagreements were resolved by discussion.

Assessment of risk of bias in included studies

Quality assessment

Assessment of study quality was based on the method outlined in Higgins 2008. The following characteristics were assessed.

Adequacy of the randomisation process:

- Yes: Adequate sequence generation is reported using random number tables, computer random number generator, coin tossing, or shuffling.
- Unclear: Did not specify one of the adequate reported methods in (A) but mentioned randomisation method.
- No: Other methods of allocation that may not be random.

Adequacy of the allocation concealment process:

Trials were awarded the following grades for allocation concealment:

- Yes: a randomisation method described that would not allow an investigator/participant to know or influence an intervention group before an eligible participant entered the study, such as central randomisation; serially numbered, opaque, sealed envelopes.
- Unclear: trial states that it is 'randomised', but no information on the method used is reported or a method is reported that was not clearly adequate.
- No: inadequate method of randomisation used, such as alternate medical record numbers or unsealed envelopes; or any information in the study that indicated that investigators or participants could influence the intervention group.

Potential for selection bias after allocation:

- Yes: specifically reported by study authors that intention-to-treat (ITT) was undertaken and this was confirmed on study assessment, or not stated but evident from study assessment that ITT was undertaken.
- Unclear: reported, but unable to confirm on study assessment, or not reported and unable to confirm by study assessment.
- No: lack of ITT confirmed on study assessment (Patients who were randomised were not included in the analysis because they did not receive the study intervention, they withdrew from the study or were not included because of protocol violation) regardless of whether ITT was reported or not.

Completeness of follow-up:

Percentage of participants for whom data were complete at defined study end-point.

Level of blinding (treatment provider, patient, outcome assessor):

It is unlikely due to the nature of the intervention that trials are able to blind the patient or treatment provider, therefore the level of masking for trials was rated as follows:

- Yes: trials which report any blinding of either outcome assessor (most likely) or treatment provider or patient (less likely).
- No: blinding not undertaken.
- Unclear: unclear whether any blinding was undertaken.

Data synthesis

There were no outcome measures in common with the two included trials so pooling of data was impossible. We had planned to perform a subgroup analyses with respect to participant age, i.e. adults versus children, oxygen received (pressure < 2.0 ATA versus >/= 2.0 ATA), time (< 60 mins versus >/= 60 mins) and length of treatment course < 5 sessions versus >/= 5 sessions), nature of the comparative treatment modalities and severity of injury, but the paucity of eligible trials did not permit this approach.

RESULTS

Description of studies

Results of the search

A total of 180 references were identified. Independent scrutiny of the titles and abstracts identified 22 potentially relevant articles. Of the 22 articles assessed in full text form, 18 were excluded because they failed to meet the pre-defined methodological criteria. Two further trials were excluded as they did not report on clinical outcomes, nor could they contribute data to the review. The remaining two trials formed the basis of the review.

Included studies

In Brannen 1997, 125 acutely burned patients (range of body surface area burnt not given), with or without inhalation injury and admitted within 24 hours of injury were randomised to either routine burn management or routine burn management with the addition of HBOT. The routine burn management employed was not specified. HBOT consisted of 100% oxygen at 2 ATA for 90 minutes twice a day for at least ten treatments and a maximum of one treatment per percent total body surface area. The primary outcome variable was length of stay. Mortality, acute fluid requirements and the number of operations required was also reported.

In Hart 1974, 16 patients with thermal burns to between ten and 50% of the total body surface area and admitted within 24 hours of injury were randomised to either routine burn management and HBOT or routine burn management with sham HBOT. Routine management included administration of Ringer's lactate solution titrated against central venous pressure and urine output (colloids after 24 hours as indicated), daily dressing with silver sulphadiazine cream, vitamin-B complex, vitamin C, alpha-tocopherol and antibiotics (unspecified). HBOT in the intervention arm consisted of 100% oxygen at 2 ATA for 90 minutes every eight hours for 24 hours, then every 12 hours until healed. The controls were placed in the same chamber at equivalent times and compressed rapidly to a trivial pressure breathing air to simulate HBOT. This trial reported mortality, mean time to healing, acute fluid requirements and the number of grafts required.

Risk of bias in included studies

Details of the quality assessment based on the method outlined in Higgins 2008 are given in the table 'Characteristics of included studies'. Additionally, a brief descriptive analysis of the studies is provided below. In general, study quality was assessed as poor to very poor. The trials included serious methodological and/or reporting shortcomings. Hart 1974 used the expression 'the envelope method' to describe randomisation, while Brannen 1997 did not elaborate on the method used. Neither study commented on allocation concealment, while double blinding was reported by Hart 1974 but not by Brannen 1997. Neither trial reported any losses to follow-up or withdrawals from treatment.

Effects of interventions

Data from the two studies (Brannen 1997; Hart 1974) comparing routine burn management versus HBOT or sham HBOT could not be pooled, and thus, are described individually.

Brannen 1997 reported no difference in length of stay (reported as a regression against age, %BSA, presence of inhalational injury and number of operations - actual length of stay in each group not reported), mortality (seven patients (11%) in each group), or number of surgeries (again only reported after regression) between the control and HBOT groups, once these outcomes were adjusted for the patient's condition.

Hart 1974 reported that mean healing times were significantly shorter in patients exposed to HBOT (mean: 19.7 days versus 43.8 days, P < 0.001) and that fluid requirements were also smaller in the HBOT group (mean: 2.2 ml/kg versus 3.4 ml/kg, no statistical analysis reported). No standard deviations or errors were recorded. One of two grafts required in the sham group did not succeed, while three of three required in the HBOT group succeeded: relative risk (RR) for failed graft without HBOT 2.0, 95% confidence interval (CI) 0.5 to 8.0.

Adverse events reported by Hart 1974 indicated three patients in the HBOT group experienced sinus barotrauma and one patient in the control group had transient viraemia during the course of therapy. No information was provided by Brannen 1997.

Other outcome measures such as mortality and morbidity rate, scar quality (hypertrophic, retracted), pain scores and activities of daily living were not recorded by either study.

DISCUSSION

This systematic review did not find evidence to support or refute the effectiveness of HBOT for the management of thermal burns. Important methodological problems existed with both studies and there were also potentially important methodological differences between the studies. In addition, the two trials were published 23 years apart and we presume the comparator therapy to be significantly different. As a result, it was difficult to ascribe sufficient validity to either the individual results or any attempt to pool results across the studies.

The two trials involved a modest total of only 141 patients, of which 125 were in the Brannen 1997 trial. The Hart 1974 trial was particularly constrained by a lack of power to detect useful clinical differences, and the finding that HBOT was no more effective than placebo in regards to length of stay, mortality or number of surgeries may have been erroneous for this reason alone. Furthermore, the sample sizes of these studies may have precluded any definitive statement on safety or frequency of adverse events.

Allocation concealment was not described in either study, while neither the method of randomisation or blinding was described by Brannen 1997. As a result, the potential for selection bias was considered high, and particularly so considering entry into one trial was dependent on the availability of HBOT facilities at the time of presentation (Brannen 1997).

Mean healing times were reported by Hart 1974 and showed promising results, with times being shorter in patients exposed to HBOT. However, no definition of 'healing' was given, nor was a description given as to the extent of wound size and depth at presentation. Acute fluid requirements and other outcomes such as successful skin-grafting were reported 'better' in those receiving HBOT, but no formal analysis was made. Neither trial measured long-term outcomes. In an accompanying analysis of a series of 191 patients treated at their facility (138 with HBOT), Hart 1974 reported that the overall death rate for those treated with HBOT was 9% (less than predicted on the basis of a national series rate), and that 92/138 patients also survived to undergo autografting, with an average of 1.35 grafts per patient.

We had planned to perform subgroup analyses with respect to age, oxygen dose (treatment profile and number of treatments) and comparator therapy. However, the paucity of eligible trials did not permit this approach. Patient inclusion criteria were not standard (Hart 1974 did not report burn size or depth), nor was the dose of oxygen administered.

There are a few major adverse effects of HBOT (pulmonary barotrauma, drug reactions, injuries or death related to chamber fire), and while these are all rare enough not to expect to see them in the trials included in this review, they should be included in consideration of any benefit of this therapy.

In practice it is likely that a beneficial effect strong enough to be clearly identified in clinical trials would overwhelm the consideration of such rare events. There are, however, a number of more minor complications that may occur commonly and Hart 1974 reported three individuals as experiencing sinus barotrauma requiring symptomatic therapy. There is no indication that these individuals were withdrawn from treatment.

While HBOT is advocated as an adjunctive treatment for thermal burns in some centres, there are surprisingly few comparative reports that support its use. Given the substantial cost associated with these treatments, the routine use HBOT for thermal burns cannot be justified by the findings of this review.

AUTHORS' CONCLUSIONS

Implications for practice

Although there are some promising results from two small RCTs, there is insufficient evidence from this review to support the routine use of HBOT for patients with thermal burns.

Implications for research

Given the routine use in some centres, there is a case for further randomised trials of high methodological rigour in order to define the true extent of benefit from the administration of HBOT to patients with thermal burns. Specifically, more information is required on the subset of burn severity or size most likely to benefit from this therapy and the oxygen dose most appropriate. Any future trials would need to consider in particular;

- appropriate sample sizes with power to detect expected differences
- careful definition and selection of target patients
- appropriate oxygen dose per treatment session (pressure and time)
- appropriate comparator therapy
- use of an effective sham therapy
- appropriate outcome measures including all those listed in this review
- careful elucidation of any adverse effects
- the cost-utility of the therapy.

REFERENCES

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Hart 1974 *{published data only}*

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Brannen 1997

Methods	Randomised controlled trial comparing routine burn management or routine burn management with the addition of HBOT.
Participants	125 acutely burned patients (94 male, 31 female; age in years, range of body surface area burnt and dates of enrolment into study not given; location of study - USA) with or without inhalation injury admitted within 24 hours of injury.
Interventions	Routine burn management plus treatment in an unstated chamber HBO device using 100% oxygen at 2 ATA for 90 minutes twice a day for at least 10 treatments and a maximum of one treatment per percent total body surface area burn.
Outcomes	Length of stay, mortality, and number of surgeries.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Blinding? All outcomes	High risk	

Hart 1974

Methods	Randomised controlled trial comparing routine burn management and HBOT or routine burn management with sham HBOT.
Participants	16 patients (14 male, 2 female; age range 21.31 to 21.62 years and enrolment into a USA study between Nov 1972 and Jan 1974) with thermal burns amounting to between 10 and 50% of the total body surface area admitted within 24 hours of injury.
Interventions	Routine burn management and HBOT or sham HBOT in a monoplace HBO chamber with 100% oxygen at 2 ATA for 90 minutes every 8 hours for 24 hours, then every 12 hours until healed.
Outcomes	Mean healing time, requirements for grafts, adverse effects, acute fluid requirements.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Blinding? All outcomes	Low risk	

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Niezgoda 1997	Model burn in volunteers. Required little specific therapy - very minor burn.
Williamson 1993	No clinical outcomes reported. Abstract only available.
Xu 1999	No clinical outcomes reported. Abstract only available.

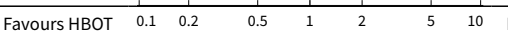
DATA AND ANALYSES

Comparison 1. Death

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality at last follow-up	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Analysis 1.1. Comparison 1 Death, Outcome 1 Mortality at last follow-up.

Study or subgroup	HBOT n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Brannen 1997	7/63	7/62		0%	0.98[0.37,2.64]

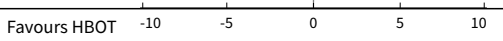


Comparison 2. Time to heal

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean time to healing (days)	1	16	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 2.1. Comparison 2 Time to heal, Outcome 1 Mean time to healing (days).

Study or subgroup	HBOT N	HBOT Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Hart 1974	8	43.8 (0)	8	19.7 (0)			Not estimable
Total ***	**8**		**8**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							



Comparison 3. Fluid requirement

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Intravenous fluid replacement (mls)	1	16	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 3.1. Comparison 3 Fluid requirement, Outcome 1 Intravenous fluid replacement (mls).

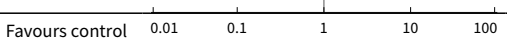
Study or subgroup	HBOT N	HBOT Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Hart 1974	8	2.2 (0)	8	3.4 (0)			Not estimable
Total ***	**8**		**8**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							

Comparison 4. Graft success

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Graft success at final follow-up	1	5	Risk Ratio (M-H, Fixed, 95% CI)	1.75 [0.53, 5.76]

Analysis 4.1. Comparison 4 Graft success, Outcome 1 Graft success at final follow-up.

Study or subgroup	HBOT n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Hart 1974	3/3	1/2		100%	1.75[0.53,5.76]
Total (95% CI)	**3**	**2**		**100%**	**1.75[0.53,5.76]**
Total events: 3 (HBOT), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.92(P=0.36)					



APPENDICES

Appendix 1. Search strategy

Cochrane Injuries Group Specialised Register (searched 1 June 2009)
(Hyperbaric and Oxygen*) and burn*

CENTRAL (The Cochrane Library 2009, Issue 2)
#1 MeSH descriptor Hyperbaric Oxygenation explode all trees
#2 high next pressure
#3 high next tension
#4 oxygen*
#5 (#2 OR #3)
#6 (#4 AND #5)
#7 HBO or HBOT
#8 (#1 OR #6 OR #7)
#9 multiplace near3 chamber*
#10 monoplace near3 chamber*
#11 (#8 OR #9 OR #10)
#12 MeSH descriptor Burns explode all trees
#13 Burn* or (thermal near3 injur*)
#14 (#12 OR #13)
#15 (#11 AND #14)

MEDLINE (Ovid SP) 1950 to May (week 4) 2009
1. exp Hyperbaric Oxygenation/
2. (high adj3 (pressure or tension) adj3 oxygen*).ab,ti.
3. oxygen*.ti.
4. (high adj3 (pressure or tension)).ab,ti.
5. 3 and 4
6. 2 or 5
7. (HBO or HBOT).ab,ti.
8. ((multiplace or monoplace) adj3 chamber*).ab,ti.
9. multiplace chamber*.ab,ti.
10. monoplace chamber*.ab,ti.
11. Hyperbaric Oxygen.ab,ti.
12. 1 or 6 or 7 or 8 or 9 or 10 or 11
13. exp Burns/
14. burn*.ab,ti.
15. (thermal adj3 injur*).ab,ti.
16. 13 or 14 or 15
17. 12 and 16
18. clinical trial.pt.
19. randomized.ti,ab.
20. placebo.ti,ab.
21. drug therapy.fs.
22. randomly.ti,ab.
23. trial.ti,ab.
24. groups.ti,ab.
25. 18 or 19 or 20 or 21 or 22 or 23 or 24
26. exp animals/
27. exp humans/
28. 26 not (26 and 27)
29. 25 not 28
30. 17 and 29

EMBASE (Ovid SP) 1980 to (week 22) June 2009
1.exp Hyperbaric Oxygen/
2.(high adj3 (pressure or tension) adj3 oxygen*).ab,ti.
3.oxygen*.ti.
4.(high adj3 (pressure or tension)).ab,ti.
5.3 and 4
6.2 or 5
7.(HBO or HBOT).ab,ti.
8.((multiplace or monoplace) adj3 chamber*).ab,ti.
9.multiplace chamber*.ab,ti.
10.monoplace chamber*.ab,ti.
11.Hyperbaric Oxygen.ab,ti.
12.1 or 6 or 7 or 8 or 9 or 10 or 11

13.exp Burn/
14.burn*.ab,ti.
15.(thermal adj3 injur*).ab,ti.
16.13 or 14 or 15
17.12 and 16
18.exp Randomized Controlled Trial/
19.exp controlled clinical trial/
20.randomi?ed.ab,ti.
21.placebo.ab.
22.*Clinical Trial/
23.randomly.ab.
24.trial.ti.
25.18 or 19 or 20 or 21 or 22 or 23 or 24
26.exp animal/ not (exp human/ and exp animal/)
27.25 not 26
28.17 and 27

ISI Web of Science: Science Citation Index Expanded (SCI-EXPANDED) (1970 to June 2009)
ISI Web of Science: Conference Proceedings Citation Index-Science (CPCI-S) (1990 June 2009)
#1 topic=(hyperbaric same oxygen*)
#2 topic= (HBO or HBOT)
#3 topic=(high tension same oxygen*)
#4 topic=(high pressure same oxygen*)
#5 topic= (multiplace same chamber*)
#6 topic= (monoplace same chamber*)
#7 #1 or #2 or #3 or #4 or #5 or #6
#8 topic=(burn* or thermal injur*)
#9 #7 and #8

PubMed [www.ncbi.nlm.nih.gov/sites/entrez/] (searched June 1, 2009 (added to PubMed in the last 180 days)
#1Hyperbaric Oxygenation
#2(high and (pressure or tension) and oxygen*)
#3HBO or HBOT
#4(multiplace or monoplace) and chamber*
#5#1 or #2 or #3 or #4
#6(thermal and injur*) or burn*
#7#5 and #6

DORCTHIM (Database of Randomised Controlled Trials in Hyperbaric Medicine) at www.hboevidence.com (from ∽2002; searched June 1 2009)
[DORCTHIM was compiled from an unfocused search of PubMed using "hyperbaric oxygenation" as a MESH term, along with handsearching of primarily hyperbaric journals ((i.e.Undersea and Hyperbaric Medicine, Hyperbaric Medicine Review, South Pacific Underwater Medicine Society (SPUMS) Journal, European Journal of Hyperbaric Medicine and Aviation, Space and Environmental Medicine Journal) and checking references in identified RCTs.]

Burn or burns or thermal injury or thermal injuries

National Research Register Issue 4, 2006
Same strategy as for CENTRAL (no relevant records retrieved)

CINAHL to January 2007 (searches not re-run as previous searches yielded no useful results)
Search strategy adapted from the MEDLINE strategy

Zetoc January 2007 (searches not re-run as previous searches yielded no useful results)
(Hyperbaric, burn*)

WHAT'S NEW

Date	Event	Description
1 June 2009	New search has been performed	The search was updated to 1 June 2009. No new trials were identified. Risk of bias has been assessed according to Higgins 2008.

HISTORY

Protocol first published: Issue 1, 2004
Review first published: Issue 3, 2004

Date	Event	Description
11 June 2008	Amended	Converted to new review format.
3 January 2007	New search has been performed	January 2007 1. The search strategy was revised and updated by the Trials Search Co-ordinator. 2. An updated search for new trials using the revised search strategy was carried out in January 2007. No new trials for inclusions were identified. 3. A slight revision of the methodological quality section was undertaken to reflect the Schulz (1995) criteria. The narrative review detailing the methodological quality was maintained. Schulz (1995) criteria was included in 'Characteristics of included studies'.

CONTRIBUTIONS OF AUTHORS

Wasiak: Conception, search strategy and execution, critical appraisal, systematic review expert, author of study description and discussion sections.

Villanueva: Conception, protocol development, critical appraisal, lead author.

Bennett: Conception, background, critical appraisal, hyperbaric medicine content expert, statistical analysis, author of study description and discussion sectopms.

Lehm: Critical appraisal, hyperbaric content expert, text editor.

DECLARATIONS OF INTEREST

None known.
The authors of this article are responsible for its contents. Statements contained herein should be constructed as reflecting the views of the authors and not of the agencies or organisations involved in the work.

INDEX TERMS

Medical Subject Headings (MeSH)

*Hyperbaric Oxygenation; Burns [*therapy]; Randomized Controlled Trials as Topic

MeSH check words

Humans