Hyperbaric oxygen as an adjuvant treatment for malignant otitis externa

Phillips JS, Jones SEM

This review should be cited as: Phillips JS, Jones SEM. Hyperbaric oxygen as an adjuvant treatment for malignant otitis externa (Cochrane Review). In: *The Cochrane Library,* Issue 1, 2006. Oxford: Update Software.

A substantive amendment to this systematic review was last made on 23 February 2005. Cochrane reviews are regularly checked and updated if necessary.

Abstract

Background: Malignant, or necrotising, otitis externa is a potentially fatal infection of the external ear canal and surrounding soft tissue and bone. It may be complicated by involvement of cranial nerves, principally the facial nerves and the contents of the jugular foramen. It is an uncommon condition mainly found in the elderly or in diabetics.

Objective: To assess the effectiveness of adjunctive hyperbaric oxygen treatment for malignant otitis externa.

Search strategy: We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 4, 2003), MEDLINE (January 1966 to April 2004) and EMBASE (January 1985 to April 2004) with pre-specified terms. The date of the last search was 5th April 2004.

Selection criteria: Randomised controlled trials, involving adults, undergoing hyperbaric oxygen therapy in malignant otitis externa.

Data collection and analysis: No identified articles described randomised controlled trials of hyperbaric oxygen therapy in the treatment of malignant otitis externa.

Main results: Due to the lack of data no results could be presented.

Reviewers' conclusions: No clear evidence exists to demonstrate the efficacy of hyperbaric oxygen therapy when compared to treatment with antibiotics and/or surgery. No data were found to compare rates of complication between the different treatment modalities. Further research is required.

Background

Malignant otitis externa is a potentially fatal infection of the external auditory canal. This condition was originally described by Chandler in 1968 (Chandler 1968) but is also known as necrotizing external otitis (Kraus 1988). Diagnosis is made upon clinical, microbiological and radiological grounds. For the purpose of this review, we shall define malignant otitis externa broadly as 'a necrotizing infection of the external ear canal including surrounding soft tissue and bone' (Hickham 1996).

Patients with this condition are typically elderly, diabetic men but other groups have been described (Giamarellou 1992). The precise aetiology of this condition is unknown, but theories

related to altered host immunity, local tissue microangiopathy (Doroghazi 1981) and even altered cerumen biochemistry (Driscoll 1993) have been proposed. The disease originates in the external auditory canal and spreads through the osteocartilaginous junction to involve the soft tissues beneath the temporal bone. Initially osteomyelitis of the skull base ensues, followed by involvement of the facial and other cranial nerves. Malignant otitis externa is also complicated by parotitis, mastoiditis, jugular vein thrombosis, meningitis and death (Giamarellou 1992). Diagnosis is made on clinical grounds and is suspected in any diabetic or immunocompromised patient with pseudomonal otitis externa, especially when pain is a prominent feature. Technicium bone scanning has been described as the single most useful diagnostic tool (Parisier 1982), but other forms of radiological imaging play a role in indicating disease progression (Hickham 1996). The mortality for this condition has been reported to be as high as one third (Chandler 1972), but when cranial nerves are affected it may be as high as 80% (Aldous 1973).

Traditionally the mainstay of treatment for malignant otitis externa has been prolonged antibiotic therapy (Strauss 1982), stringent diabetes control (Resouly 1982), repeated debridement of necrotic tissue, and sometimes aggressive surgical management (Reines 1980). Hyperbaric oxygen is gradually gaining acceptance as a beneficial adjunctive therapy and has been recommended whenever a therapeutic pressure chamber is available (Shupak 1989). There are 24 centres offering such facilities in the United Kingdom. Hyperbaric oxygen is available for and currently being used in the treatment of many other medical conditions. Hyperbaric oxygen treatment is the administration of 100% oxygen for respiration at pressures above 1 atmosphere absolute (ATA). Hyperbaric oxygen treatment involves placing the patient in a compression chamber, increasing the environmental pressure within the chamber, 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 2 and 3 atmospheres absolute (ATA) for periods between 60 and 120 minutes once or twice daily. A typical course might involve 15 to 30 such treatments (HMP 1994). In the United Kingdom, 30 sessions of hyperbaric oxygen would typically cost £3000.00, i.e. £100.00 per session or £50.00 per hour (Laden 2005). Complications and side effects of hyperbaric oxygen treatment include barotraumas to the ear, round window blowout, 'sinus squeeze', visual refractive changes, numb fingers, dental problems, claustrophobia, seizures and pulmonary oxygen toxicity (HMP 1994). In general these effects are either very rare or are only temporary. It is postulated that hyperbaric oxygen treatment works by elevating the oxygen partial pressure from hypoxia to normal or above normal levels, which amplifies the oxygen diffusion gradient into the avascular tissues (Mader 1980). This is a prerequisite for efficient leukocyte function (Hohn 1976) and has been shown to promote fibroblastic division, collagen production, and capillary angiogenesis, thus enhancing soft tissue and bone healing (Hunt 1972).

Malignant otitis externa is an uncommon condition associated with significant rates of morbidity and mortality (Shupak 1989). It is important to construct a systematic review to fully define the role of hyperbaric oxygen in the treatment of this condition.

Objectives

To assess the effectiveness of adjunctive hyperbaric oxygen treatment for malignant otitis externa.

Criteria for considering studies for this review

Types of studies

Randomised controlled trials only.

Types of participants

Adults (over 16) with malignant otitis externa were included.

Types of intervention

Any treatment(s) where hyperbaric oxygen was an adjuvant therapy versus the same treatment(s) alone.

Types of outcome measures

The primary outcome measure was death.

- The secondary outcome measures were:
- 1. Time until clinical improvement. This was to be measured by resolution of pain and aural discharge.
- 2. Time until radiological improvement. A variety of radiological techniques exist to measure the course of malignant otitis externa. Our intention was to allow improvement to be measured by whichever technique was deemed appropriate by the authors of the study.
- 3. Recovery from cranial nerve palsies.

Search strategy for identification of studies

See: Cochrane Ear, Nose and Throat Disorders Group search strategy

We sought studies where patients were treated for malignant otitis externa by performing searches of the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 4, 2003), MEDLINE (January 1966 to April 2004) and EMBASE (January 1985 to April 2004) according to Cochrane guidelines. The search strategy developed by The Cochrane Collaboration for identifying randomised controlled trials (RCTs) was combined with the following search terms:

- CENTRAL
- (MeSH terms appear in uppercase and are exploded. Free text terms appear in lower case.)
- #1OTITIS EXTERNA
- #2(otitis near extern*)
- #3(auditory near extern*)
- #4(antrum next otitis)
- #5#1 or #2 or #3 or #4
- #6maligna*
- #7necroti*
- #8necrosis
- #9#6 or #6 or #7 or #8
- #10#5 and #9
- #11HYPERBARIC OXYGENATION
- #12oxygen*
- #13hbot
- #14hbo
- #15#11 or #12 or #13 or #14
- #16#10 and #15

- MEDLINE
- (The following strategies are suitable for OVID implementations of MEDLINE/EMBASE.)
- 1. exp otitis externa/
- 2. (otitis adj3 extern$).tw.

- 3. (auditory adj3 extern$).tw.
- 4. "antrum otitis".tw.
- 5. or/1-4
- 6. maligna$.tw.
- 7. necroti$.tw.
- 8. necrosis.tw.
- 9. or/6-8
- 10. 4 and 8
- 11. exp hyperbaric oxygenation/
- 12. oxygen$.tw.
- 13. HBOT.tw.
- 14. HBO.tw.
- 15. Or/11-14
- 16. 10 and 15

- EMBASE
- 1. exp external otitis/
- 2. (otitis adj3 extern$).tw.
- 3. (auditory adj3 extern$).tw.
- 4. "antrum otitis".tw.
- 5. or/1-4
- 6. maligna$.tw.
- 7. necroti$.tw.
- 8. necrosis.tw.
- 9. or/6-8
- 10. 5 and 9
- 11. exp hyperbaric oxygen/
- 12. oxygen$.tw.
- 13. HBOT.tw.
- 14. HBO.tw.
- 15. Or/11-14
- 16. 10 and 15

The date of the search was 5th April 2004. Randomised controlled trials only were reviewed. The bibliography of each paper and relevant case reports was checked for further references. No restriction on language of publication was used. No trial reports were found where data were unclear requiring clarification by the original authors. Unpublished articles and proceedings were not included. The lead clinicians of major worldwide centres offering hyperbaric oxygen treatment were contacted for their input. No authors of relevant RCTs were contacted.

Methods of the review

- Data extraction
- The articles found by the searches were reviewed independently by the two review authors to identify studies of the types outlined above. Disagreement was to be resolved by discussion. Should this have failed to resolve the disagreement then the final decision was to be made by JP. Data were to be extracted onto standardised, pre-piloted forms.

- Quality assessment
- We intended to assess the quality of trials in relation to the methodology and the conclusions reached using the method described by Schulz in 1995 (Schulz 1995), where the following characteristics are assessed:

- 1. Adequacy of randomisation process and allocation concealment
- 2. The inclusion of all randomised patients in the analysis (intention-to-treat)

- 3. Adequacy of blinding (although it is difficult to blind a patient receiving hyperbaric oxygen treatment)

Studies included would be awarded an overall A, B or C grade for quality where:

- A. All of the above criteria have been adequately met
- B. One or more of the criteria have been partly met
- C. One or more of the criteria have not been met

- Data analysis
- Statistical analysis would be performed using Review Manager 4.2.7 (RevMan 2004). For dichotomous outcomes a relative risk (RR) was to be calculated. We intended to use a weighted mean difference (WMD) or standardised mean difference (SMD) for continuous outcomes as appropriate. A fixed-effect model was to be used where non-significant heterogeneity was found between studies. A random-effects model was to be used where great heterogeneity in studies was found.

Subgroup analysis of the following patient characteristics was to be performed:

- - Patients presenting with or without cranial nerve palsies
- - Patients presenting with or without diabetes

Study quality was intended for sensitivity analyses.

Description of studies

No randomised controlled trials were identified.

Methodological quality

Not applicable.

Results

Using our search strategy we identified some relevant articles. None fulfilled the requirements of our protocol. They were retrieved in order to search the bibliography for other articles which might fulfil our inclusion criteria. No further articles were identified using this method. No data could be entered for analysis.

Discussion

No randomised controlled trials were identified by our search strategy. The quality of the data identified was therefore not adequate to allow further discussion. We will, however, briefly describe the types of studies identified by our search strategy.

We found four case reports (Bath 1998; Lancaster 2000; Mader 1982; Shupak 1989) and five case series (Davis 1992; Lucente 1982; Lucente 1983; Robinson 1994; Tisch 2003) which included a total of 73 patients. These articles described the use of hyperbaric oxygen as adjuvant therapy with antibiotics in the majority of cases. In general, most regimens used 20 to 40 doses of hyperbaric oxygen treatment. Each treatment was of 90 minutes duration at 2.5 atmospheres absolute (ATA). Alternative regimens differed very little. There was no mention of any complications related to hyperbaric oxygen treatment.

Reviewers' conclusions

Implications for practice

The quality of the studies identified by our literature search was poor, lacking randomisation or other controls. In view of this the effectiveness of treatment with hyperbaric oxygen therapy compared with treatment with antibiotics and surgical debridement could not be statistically assessed in this review.

Implications for research

Our findings demonstrate the need for a well-designed, randomised controlled trial to compare hyperbaric oxygen therapy with standard therapy. Any future trials would need to consider in particular:

- 1. Appropriate sample size with the power to detect expected differences. Due to the infrequent diagnosis of malignant otitis externa it could be necessary to organise a multi-centre trial.
- 2. Careful definition and selection of target patients. It would be preferable to recruit patients who had not been previously treated for malignant otitis externa.
- 3. Appropriate oxygen dose per treatment session. Of the studies analysed, hyperbaric oxygen was instituted at a variety of disease stages with varying pressures, frequencies and durations. For this reason there would be need for standardised treatment protocols for any proposed hyperbaric oxygen regime.
- 4. Appropriate comparator therapy.
- 5. Use of an effective sham therapy
- 6. Appropriate outcome measures including all those listed in this review.
- 7. Careful elucidation of any adverse effects and their duration.
- 8. The cost-utility of the therapy.

Acknowledgements

With thanks to Jenny Bellorini, Carolyn Dorée and Annette Foley for their assistance with this review.

Also:

- Dr Michael Bennett MB BS, FANZCA, Dip DHM
- Department of Diving and Hyperbaric Medicine
- Prince of Wales Hospital
- Barker Street
- Randwick NSW 2031
- Australia

and

- Mr Gerard Laden
- Technical and Research Director
- Hull Hyperbaric Unit
- Hull and East Riding Hospital
- Lowfield Road
- Anlaby
- East Yorkshire
- UK

Potential conflict of interest

None known

References

Additional references

Aldous 1973

Aldous EW, Shin JB. Far advanced malignant external otitis: report of a survival. The Laryngoscope 1973;83:1810-5.

Bath 1998

Bath AP, Rowe JR, Innes AJ. Malignant otitis externa with optic neuritis. The Journal of Laryngology and Otology 1998;112(3):274-7.

Chandler 1968

Chandler JR. Malignant external otitis. The Laryngoscope 1968;78:1257-94.

Chandler 1972

Chandler JR. Pathogenesis and treatment of facial paralysis due to malignant otitis externa. The Annals of Otology, Rhinology and Laryngology 1972;81:648-58.

Davis 1992

Davis JC, Gates GA, Lerner C, David MG Jr, Mader JT, Dinesman A. Adjuvant hyperbaric oxygen in malignant external otitis. Archives of Otolaryngology - Head & Neck Surgery 1992;118(1):89-93.

Doroghazi 1981

Doroghazi RM, Nadol JB, Hyslop NE, et al. Invasive external otitis. Report of 21 cases and review of the literature. The American Journal of Medicine 1981;71:603-14.

Driscoll 1993

Driscoll PV, Ramachandrula A, Drezner DA, et al. Characteristics of cerumen in diabetic patients: a key to understanding malignant external otitis?. Otolaryngology - Head and Neck Surgery 1993;109:676-9.

Giamarellou 1992

Giamarellou H. Malignant otitis externa: the therapeutic evolution of a lethal infection. The Journal of Antimicrobial Chemotherapy 1992;30:745-51.

Hickham 1996

Hickham M, Amedee RG. Malignant Otitis Externa. The Journal of the Louisiana State Medical Society 1996;148:511-13.

HMP 1994

Kindwall EP (Ed). Hyperbaric Medicine Practice. Best Publishing Company, Flagstaff AZ, 1994.

Hohn 1976

Hohn DC, MacKay RD, Halliday B, Hunt TK. The effect of oxygen tension on the microbicidal function of leukocytes in wounds and in vitro. Surgical Forum 1976;27:18-20.

Hunt 1972

Hunt TK, Pai MP. The effect of varying ambient oxygen tensions on wound metabolism and collagen synthesis. Surgery, Gynecology and Obstetrics 1972;135:561-7.

Kraus 1988

Kraus DH, Rehm SJ, Kinney SE. The evolving treatment of necrotizing external otitis. The Laryngoscope 1988;98:934-9.

Laden 2005

Mr Gerard Laden, Technical and Research Director, Hull Hyperbaric Unit, Hull and East Riding Hospital, Lowfield Road, Anlaby, East Yorkshire, United Kingdom. Personal correspondence 2005.

Lancaster 2000

Lancaster J, Alderson DJ, McCormick M. Non-pseudomonal malignant otitis externa and jugular foramen syndrome secondary to cyclosporin-induced hypertrichosis in a diabetic renal transplant patient. The Journal of Laryngology and Otology 2000;114(5):366-9.

Lucente 1982

Lucente FE, Parisier SC, Som PM, Arnold LM. Malignant otitis externa: a dangerous misnomer?. Otolaryngology - Head & Neck Surgery 1982;90(2):266-9.

Lucente 1983

Lucente FE, Parisier SC, Som PM. Complications of the treatment of malignant external otitis. The Laryngoscope 1983;93(3):279-81.

Mader 1980

Mader JT, Brown GL, Guickian JC. Mechanism for the amelioration by hyperbaric oxygen of experimental staphylococcal osteomyelitis in the rabbit. The Journal of Infectious Diseases 1980;142:915-22.

Mader 1982

Mader JT, Love JT. Malignant external otitis: cure with adjunctive hyperbaric oxygen. Archives of Otolaryngology 1982;108(1):38-40.

Parisier 1982

Parisier SL, Lucente R, Som P, Hirschman S, Arnold I, Roftman J. Nuclear Scanning in Necrostising Progressive 'Malignant' External Otitis. The Laryngoscope 1982;92:1016-20.

Reines 1980

Reines JM, Schindler RA. The surgical management of recalcitrant malignant external otitis. The Laryngoscope 1980;90:369-78.

Resouly 1982

Resouly A, Payne DJH, Shaw KM. Necrotzing otitis externa and diabetes control. The Lancet 1982;1:805-6.

RevMan 2004

The Nordic Cochrane Centre. Review Manager (RevMan) [Computer program]. Version 4.2.7. Oxford, England: The Cochrane Collaboration 2004.

Robinson 1994

Robinson S, Clark P. Necrotising (malignant) otitis externa. Australian Journal of Otolaryngology 1994;1(5):447-9.

Schulz 1995

Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. The Journal of the American Medical Association 1995;273(5):408-12.

Shupak 1989

Shupak A, Greenburg E, Hardoff R, Gordon C, Melamed Y, Meyer WS. Hyperbaric Oxygenation for Necrotizing (Malignant) Otitis Externa. Archives of Otolaryngologyâ€"Head & Neck Surgery 1989;115:1470-5.

Strauss 1982

Strauss M, Aber RC, Conner GH, Baum S. Malignant external otitis: long-term (months) antimicrobial therapy. The Laryngoscope 1982;92:397-406.

Tisch 2003

Tisch M, Lorenz KJ, Haarm M, Lampl L, Maier H. The treatment of necrotizing otitis externa with a combination of surgery, antibiotics, specific immunoglobulins and hyperbaric oxygen therapy. Results of the Ulm Treatment Concept [Otitis externa necroticans: Kombinierter Einsatz von chirurgischer Therapie, Antibiose, spezifischen Immunoglobulinen und hyperbarer Sauerstoff-therapie - Ergebnisse des Ulmer Therapiekonzepts]. HNO 2003;51(4):315-20.

Cover sheet

Hyperbaric oxygen as an adjuvant treatment for malignant otitis externa

Reviewer(s)	Phillips JS, Jones SEM
Contribution of Reviewer(s)	JP - lead reviewer, protocol development, design of search strategy, review preparation, quality assessment,

	data extraction and analysis SJ - protocol development, review preparation, quality assessment, data extraction and analysis
Issue protocol first published	2004 issue 1
Issue review first published	2005 issue 2
Date of last minor amendment	Information not supplied by reviewer
Date of last substantive amendment	23 February 2005
Most recent changes	Information not supplied by reviewer
Date new studies sought but none found	Information not supplied by reviewer
Date new studies found but not yet included/excluded	Information not supplied by reviewer
Date new studies found and included/excluded	Information not supplied by reviewer
Date reviewers' conclusions section amended	Information not supplied by reviewer
Contact address	Mr John Phillips Colney Lane Norwich Norfolk UK NR4 7UY Telephone: +44 1603 286286 Facsimile: E-mail: john.phillips@mac.com
Cochrane Library number	CD004617
Editorial group	Cochrane Ear, Nose and Throat Disorders Group
Editorial group code	ENT

Synopsis

There is no clear evidence to demonstrate the effectiveness of hyperbaric oxygen therapy in the treatment of malignant otitis externa

Malignant otitis externa is an uncommon, although potentially fatal, infection of the external ear canal including the surrounding soft tissue and bone. It is mainly found in the elderly or diabetics. Treatments include antibiotics, stringent diabetes control, the repeated removal of

dead tissue and surgical management. Hyperbaric oxygen therapy is increasingly being used in addition to these treatments where facilities exist. The review found no trials to demonstrate that the addition of hyperbaric oxygen therapy offers a better outcome than the treatments alone. Further research is required.

Keywords

Humans; Bacterial Infections[*therapy]; *Hyperbaric Oxygenation; Otitis Externa[*therapy