Interventions for replacing missing teeth: hyperbaric oxygen therapy for irradiated patients who require dental implants

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This review should be cited as: Coulthard P, Esposito M, Worthington HV, Jokstad A. Interventions for replacing missing teeth: hyperbaric oxygen therapy for irradiated patients who require dental implants (Cochrane Review). In: *The Cochrane Library,* Issue 1, 2006. Oxford: Update Software.

A substantive amendment to this systematic review was last made on 17 May 2002. Cochrane reviews are regularly checked and updated if necessary.

Abstract

Background: Dental implants offer one way to replace missing teeth and associated tissues. Patients who have undergone radiotherapy and those that have also undergone surgery for cancer may benefit particularly from reconstruction with implants. Hyperbaric oxygen therapy (HBO) has been advocated to improve the success of implant treatment in patients who have undergone radiotherapy but this remains a controversial issue.

Objective: This review aims to compare success, morbidity, patient satisfaction and cost effectiveness of dental implant treatment carried out with and without HBO in irradiated patients.

Search strategy: The Cochrane Oral Health Group Specialised Register, the Cochrane Controlled Trials Register, MEDLINE and EMBASE were searched. In addition, the bibliographies of review articles were checked for studies outside the handsearched journals and personal references were searched. We also wrote to implant manufacturers and experts in the field.

Selection criteria: Randomised controlled trials of HBO therapy for irradiated patients requiring dental implants.

Data collection and analysis: No randomised trials were identified.

Main results: No data were available.

Reviewers' conclusions: Clinicians ought to make patients aware of the lack of reliable clinical evidence for or against the clinical effectivness of HBO in irradiated patients requiring dental implants.There is a definite need for RCTs to ascertain the effectivness of HBO in irradiated patients requiring dental implants. These trials ought to be of a high quality and reported as recommended by the CONSORT statement (http://www.consort-statement.org/). Each clinical centre may have limited numbers of patients and it is likely that trials will need to be multi-centred.

Background

Missing teeth and supporting oral tissues have traditionally been replaced with dentures or bridges permitting restoration of masticatory, phonetic function, and aesthetics. Dental implants now offer an alternative. These implants are inserted into the jaw bones to support a dental prosthesis and are retained because of the intimacy of bone growth onto their surface. This direct structural and functional connection between bone and implant surface, termed osseointegration, was first described by Branemark (Branemark 1977) and has undoubtedly been one of the most significant scientific breakthroughs in dentistry over the past 30 years.

Teeth are most commonly lost through dental disease but may also be lost as a result of trauma or be congenitally absent. In addition there are a number of people who have extensive loss of oral and facial tissues following surgery for cancer who are difficult to reconstruct and for whom osseointegrated implants may offer an improvement over previous treatments (Franzen 1995). These patients may have undergone radiotherapy in addition to their cancer surgery. Other patients may have undergone radiotherapy without having had surgery. Complications of this radiotherapy treatment include oral mucosal damage (mucositis), dry mouth (xerostomia) as result of salivary gland damage, and damage to bone (osteoradionecrosis) in the form of a reduction in vascularity and damage to bone cells. Although osteoradionecrosis may occur in other bones (sternum, skull, pelvis) it most commonly affects the mandible and is difficult to treat. Any surgical treatment involving the jaws following radiotherapy may show compromised healing, or even lead to osteoradionecrosis requiring partial jaw resection, and for this reason, placement of implants has been considered a relative contraindication in this group of patients. However, these patients are those that may particularly benefit from implant treatment.

Hyperbaric oxygen (HBO) therapy gained strong support for positive effects on compromised tissue following irradiation after its introduction for this use in the 1970s (Marx 1984). Granstrom later proposed that HBO therapy might improve osseointegration (Granstrom 1992). HBO therapy consists of exposing a patient in a special chamber to intermittent, short term 100% oxygen inhalation at a pressure greater than one atmosphere. A typical protocol developed for osteoradionecrosis is the Marx-University of Miami protocol (Marx 1984) which requires a patient to receive 20 HBO treatments of 100% oxygen at 2.4 atmospheres for 90 minutes before surgery, followed by a further ten HBO treatments of 100% oxygen at 2.4 atmospheres for 90 minutes after surgery.

Despite a growing body of evidence supporting HBO therapy (Larsen 1997;Granstrom 1999) it remains a controversial issue and some clinicians consider HBO ineffective (Keller 1997). The aim of this review was to compare dental implant treatment carried out with and without HBO in irradiated patients.

Objectives

This review aims to test the null hypothesis of no difference in success, morbidity, patient satisfaction and cost effectiveness between dental implant treatment for irradiated patients with and without HBO, against the alternative hypothesis of a difference.

Criteria for considering studies for this review

Types of studies

Randomised controlled trials were considered.

Types of participants

Patients who have had radiotherapy and who have missing teeth that require replacement with osseointegrated dental implants.

Types of intervention

HBO therapy compared with no HBO therapy

Types of outcome measures

Outcome measures of interest were:

- prosthesis failure if secondary to implant failure (binary)

- implant failure (mobility and implant removal of stable implants dictated by progressive marginal bone loss) (binary)
- marginal bone levels on intraoral radiographs using a parallel technique (continuous)
- adverse event (eustacian tube dysfunction, tympanic membrane rupture, ear or sinus or tooth pain, pneumothorax) (binary)
- mucosal health (ulceration) and osteoradionecrosis
- patient satisfaction (both binary and continuous on VAS scale)
- cost effectiveness

Search strategy for identification of studies

See: Cochrane Oral Health Group search strategy

To identify studies for inclusion or consideration in this review a detailed search strategy was developed for each database searched. These were based on the search strategy developed for MEDLINE but revised appropriately for each database. The search strategy combined a sensitive search strategy for RCTs revised from phases one and two of the Cochrane Sensitive Search Strategy for RCTs (as published in Appendix 5c in the Cochrane Reviewers' Handbook). The subject search used a combination of controlled vocabulary and freetext terms based on the following search strategy for searching MEDLINE:

- #1 randomized controlled trial.pt.
- #2 controlled clinical trial.pt.
- #3 randomized controlled trials.sh.
- #4 random allocation.sh.
- #5 double blind method.sh.
- #6 single blind method.sh.
- #7 latin square.ti,ab.
- #8 crossover.ti,ab.
- #9 (split adj (mouth or plot)).ti,ab.
- #10 or/1-9
- #11 (ANIMAL not HUMAN).sh.
- #12 10 not 11 #
- #13 clinical trial.pt.
- #14 exp clinical trials/
- #15 (clin$ adj25 trial$).ti,ab.
- #16 ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab.
- #17 placebos.sh.
- #18 placebo$.ti,ab.
- #19 random$.ti,ab.
- #20 research design.sh.
- #21 or/13-20
- #22 21 not 11
- #23 22 not 12
- #24 12 or 22

- #25 exp Dental Implants/
- #26 exp Dental Implantation/ or dental implantation.mp.
- #27 exp Dental Prosthesis, Implant-Supported/
- #28 ((osseointegrated adj implant$) and (dental or oral)).mp. [mp=title, abstract, registry number word, mesh subject heading]
- #29 dental implant$.mp. [mp=title, abstract, registry number word, mesh subject heading]
- #30 (implant$ adj5 dent$).mp. [mp=title, abstract, registry number word, mesh subject heading]
- #31 dental-implant$.mp. [mp=title, abstract, registry number word, mesh subject heading]
- #32 (((overdenture$ or crown$ or bridge$ or prosthesis or prostheses or restoration$) near (Dental or oral)) and implant$).mp. [mp=title, abstract, registry number word, mesh subject heading]
- #33 "implant supported dental prosthesis".mp. [mp=title, abstract, registry number word, mesh subject heading]
- #34 ("blade implant$" and (dental or oral)).mp. [mp=title, abstract, registry number word, mesh subject heading]
- #35 ((endosseous adj5 implant$) and (dental or oral)).mp. [mp=title, abstract, registry number word, mesh subject heading]
- #36 ((dental or oral) adj5 implant$).mp. [mp=title, abstract, registry number word, mesh subject heading]
- #37 25 - 36
- #38 24 and 37

The last search was carried out on the 8th May 2002.

DATABASES SEARCHED

- Cochrane Oral Health Group Specialised Register
- The Cochrane Controlled Trials Register: Cochrane Library 2002 Issue 2
- MEDLINE 1966 - May 2002
- EMBASE 1974 - May 2002
- The bibliographies of papers and review articles were checked for studies outside the handsearched journals. Personal references were also searched.

LANGUAGE

Non-English papers were to be included.

UNPUBLISHED STUDIES

It was the intention to write to authors of identified RCTs in order to obtain further information about the trials and to attempt to identify unpublished or ongoing studies. We also wrote to 55 manufacturers of oral implants and contacted three experts in the field of HBO.

HANDSEARCHING

Several journals relevant to this review were handsearched as part of the Oral Health Group's ongoing journal handsearching programme (www.cochrane-oral.man.ac.uk).

Methods of the review

STUDY SELECTION

The titles and abstracts (when available) of all reports identified through the electronic searches were scanned independently by two reviewers (PC,ME). For studies appearing to meet the inclusion criteria, or for which there was insufficient data in the title and abstract to make a clear decision, the full report was obtained. The full reports obtained from all the electronic and other methods of searching were assessed independently by two reviewers to establish whether the studies met the inclusion criteria or not (PC,ME). Any disagreements were to be resolved by discussion. A third reviewer (HW) was to be consulted if there was unresolved disagreement. All studies meeting the inclusion criteria were to undergo validity assessment and data extraction. Any studies to be rejected at this or subsequent stages were to be recorded in the table of excluded studies, and reasons for exclusion recorded.

QUALITY ASSESSMENT

- It was planned to undertake a quality assessment of included trials independently and in duplicate by two reviewers (PC,ME) as part of the data abstraction process.
- Three main quality criteria were to be examined:

- 1) Allocation concealment, recorded as;
- (A) Adequate
- (B) Unclear
- (C) Inadequate
- (D) Not used
- 2) Blind outcome assessment
- (A) Yes
- (B) No
- (C) Unclear
- (D) Not Possible
- 3) Clear explanation of completeness of follow-up by group, recorded as;
- (A) None
- (B) Yes
- (C) No
- as described in the Cochrane Reviewers' Handbook.

- Further quality assessment was to be carried out to assess the definition of exclusion/inclusion criteria, adequate definition of success criteria and comparability of control and treatment groups at entry.
- The quality assessment criteria was to be pilot tested using several articles. The agreement between the quality assesments was to be measured using the Kappa statistic.

DATA EXTRACTION

Data was to be extracted by two reviewers (PC,ME) independently using specially designed data extraction forms. The data extraction forms were to be piloted on several papers and modified as required before use. Any disagreement was to be discussed and a third reviewer (HW) consulted where necessary. Authors were to be contacted for clarification or missing information whenever possible. Data was to be excluded until further clarification was available if agreement could not be reached.

For each trial the following data was to be recorded:

- Date of the study, year of publication, country of origin and source of study funding.
- Details of the participants including demographic characteristics, source of recruitment, criteria for inclusion and of their cancer treatment.
- Details on the type of intervention.

- Details of the outcomes reported, including method of assessment (where measurement scales were used it was to be recorded whether or not they had been validated), and time intervals.

DATA SYNTHESIS

For dichotomous outcomes, the estimate of effect of an intervention was to be expressed as relative risks together with 95% confidence intervals. For continuous outcomes, means and standard deviations were to be used to summarise the data for each group.

Clinical heterogeneity was to be assessed by examining the types of participants, interventions and for all outcomes in each study. Only if there were studies of similar comparisons reporting the same outcome measures was meta-analysis to be attempted. Relative risks were to be combined for dichotomous data, and weighted or standardised mean differences for continuous data as appropriate, using a fixed effects model. The significance of any discrepancies in the estimates of the treatment effects from the different trials were to be assessed by means of Cochran's test for heterogeneity. If any significant statistical heterogeneity ($P<0.1$) were detected, it was planned to re-assess the significance of the treatment effects by using a random effects model.

Sensitivity analyses were to be undertaken to examine the effect of randomisation, allocation concealment and blind outcome assessment on the overall estimates of effect. In addition, the effect of including unpublished literature on the review's findings were also to be examined.

Where possible it was intended to undertake subgroup analyses in respect of the nature of surgery (alteration of vascular supply), the method of radiotherapy delivery (external beam or brachytherpy), the radiotherapy technique (accelerated, hyperfractionated, other), the radiotherapy dose, the time from radiotherapy to implant placement, nature of bone for implant placement (maxilla or mandible or bone grafted), the time from implant placement to implant restoration and loading, and the hyperbaric oxygen protocol.

Description of studies

Following the screening of more than 600 studies, no randomised controlled trials were identified by the search strategy for inclusion in this review.

Methodological quality

No randomised trials were available for quality assessment.

Results

No data were available.

Discussion

The question of whether or not HBO is effective for implant success in irradiated patients is important. HBO therapy requires significant patient compliance and involves financial cost per patient treatment and expensive equipment. It is not without risk of adverse effect. There are many scientific papers written about the subject, including a number of review articles, (Granstrom 1998;Esposito 1998) but randomised controlled trials are lacking. The randomised controlled trial, more than any other study design, provides the most reliable evidence for treatment effectiveness.

Reviewers' conclusions

Implications for practice

Clinicians ought to make patients aware of the lack of reliable clinical evidence for or against the clinical effectivness of HBO therapy in irradiated patients requiring dental implants.

Implications for research

There is a definite need for RCTs to ascertain the effectivness of HBO therapy in irradiated patients requiring dental implants. These trials ought to be of a high quality and reported as recommended by the CONSORT statement (http://www.consort-statement.org/). Each clinical centre may have limited numbers of patients, it is likely that trials will need to be multi-centred.

Acknowledgements

We wish to thank Sylvia Bickley (Cochrane Collaboration) for her assistance with literature searching and Emma Tavender (Cochrane Collaboration) for her help with the preparation of this review.

Potential conflict of interest

None known.

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Cover sheet

Interventions for replacing missing teeth: hyperbaric oxygen therapy for irradiated patients who require dental implants

Reviewer(s)	Coulthard P, Esposito M, Worthington HV, Jokstad A
Contribution of Reviewer(s)	Conceiving, designing and coordinating the review (PC) Developing search strategy and undertaking searches (ME,AJ,PC) Screening search results and retreived papers against inclusion criteria (ME,PC) Writing the review (PC) Providing general advice on the review (ME,HW,AJ)
Issue protocol first published	2002 issue 2
Issue review first published	2002 issue 3
Date of last minor amendment	25 September 2001
Date of last substantive amendment	17 May 2002
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
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Cochrane Library number	CD003603
Editorial group	Cochrane Oral Health Group
Editorial group code	ORAL

Sources of support

External sources of support

- The PPP Foundation UK
- Swedish Medical Research Council (9495) SWEDEN
- Jubileumsfonden (The Sahlgrenska Academy at Goteborg University) SWEDEN

Internal sources of support

- University Dental Hospital of Manchester UK
- The Sahlgrenska Academy at Goteborg University SWEDEN
- University of Oslo NORWAY

Synopsis

There is no strong evidence to show if hyperbaric oxygen can improve healing of dental implants for people who require them after radiotherapy cancer treatment.

Ordinarily, bone in the jaw grows around a dental implant that replaces a missing tooth. However, radiation therapy for cancer may cause damage to the bone and gums which can complicate healing dental implants. Hyperbaric oxygen involves people breathing pure oxygen in a specially designed chamber (such as used for deepsea divers suffering pressure problems after resurfacing). It is thought that this oxygen might improve the healing of bone and tissues. However the review found no trials to show the effects on people who required dental implants after radiotherapy.

Keywords

Humans; *Dental Implants; *Hyperbaric Oxygenation; *Radiotherapy