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# [Intervention Review]

# Hyperbaric oxygen therapy for late radiation tissue injury

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# ABSTRACT

## Background

Cancer is a significant global health problem. Radiotherapy is a treatment for many cancers and about 50% of people having radiotherapy will be long-term survivors. Some will experience late radiation tissue injury (LRTI) developing months or years later. Hyperbaric oxygen therapy (HBOT) has been suggested as a treatment for LRTI based upon the ability to improve the blood supply to these tissues. It is postulated that HBOT may result in both healing of tissues and the prevention of problems following surgery.

# Objectives

To assess the benefits and harms of HBOT for treating or preventing LRTI.

# Search methods

We updated the searches of the Cochrane Central Register of Controlled Trials (CENTRAL; 2015, Issue 11), MEDLINE, EMBASE, DORCTIHM and reference lists of articles in December 2015. We also searched for ongoing trials at clinicaltrials.gov.

# Selection criteria

Randomised controlled trials (RCTs) comparing the effect of HBOT versus no HBOT on LRTI prevention or healing.

## Data collection and analysis

Three review authors independently evaluated the quality of the relevant trials using the guidelines of the *Cochrane Handbook for Systematic Reviews of Interventions* and extracted the data from the included trials.

#### **Main results**

Fourteen trials contributed to this review (753 participants). There was some moderate quality evidence that HBOT was more likely to achieve mucosal coverage with osteoradionecrosis (ORN) (risk ratio (RR) 1.3; 95% confidence interval (CI) 1.1 to 1.6, P value = 0.003, number needed to treat for an additional beneficial outcome (NNTB) 5; 246 participants, 3 studies). There was also moderate quality evidence of a significantly improved chance of wound breakdown without HBOT following operative treatment for ORN (RR 4.2; 95% CI 1.1 to 16.8, P value = 0.04, NNTB 4; 264 participants, 2 studies). From single studies there was a significantly increased chance of improvement or cure following HBOT for radiation proctitis (RR 1.72; 95% CI 1.0 to 2.9, P value = 0.04, NNTB 5), and following both surgical flaps (RR 8.7; 95% CI 2.7 to 27.5, P value = 0.0002, NNTB 4) and hemimandibulectomy (RR 1.4; 95% CI 1.1 to 1.8, P value = 0.001, NNTB 5). There was also a significantly improved probability of healing irradiated tooth sockets following dental extraction (RR 1.4; 95% CI 1.1 to 1.7, P value = 0.009, NNTB 4).



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There was no evidence of benefit in clinical outcomes with established radiation injury to neural tissue, and no randomised data reported on the use of HBOT to treat other manifestations of LRTI. These trials did not report adverse events.

#### Authors' conclusions

These small trials suggest that for people with LRTI affecting tissues of the head, neck, anus and rectum, HBOT is associated with improved outcome. HBOT also appears to reduce the chance of ORN following tooth extraction in an irradiated field. There was no such evidence of any important clinical effect on neurological tissues. The application of HBOT to selected participants and tissues may be justified. Further research is required to establish the optimum participant selection and timing of any therapy. An economic evaluation should be undertaken.

# PLAIN LANGUAGE SUMMARY

## Hyperbaric oxygen therapy for the treatment of the late effects of radiotherapy

## The issue

There is a risk of serious complications developing after radiation treatment (radiotherapy) for cancer (late radiation tissue injury (LRTI)). These problems can be very difficult to resolve and there is some doubt as to the best approaches to treatment. Hyperbaric oxygen therapy (HBOT) involves breathing oxygen in a specially designed chamber. It is used as a treatment to improve oxygen supply to damaged tissue (cells within the body) and support healing.

## The aim of the review

We searched medical databases for clinical studies aimed to find the evidence for or against the ability of HBOT, compared to either no treatment or alternative treatments, to improve these complications. The evidence was current to December 2015.

## What were the main findings?

There was some evidence that HBOT improved outcome in LRTI affecting bone and soft tissues of the head and neck, for radiation proctitis (inflammation of the lower part of the large intestine caused by radiotherapy treatment) and to prevent the development of osteoradionecrosis (bone death caused by radiotherapy treatment) following tooth extraction in an irradiated field. There was no such evidence of any important clinical effect on tissues in the nervous system.

## **Quality of the evidence**

The evidence was generally of moderate quality and limited by small numbers of participants, poor reporting of methods and results, and uncertainty as to the exact degree of improvement with HBOT.

#### What are the conclusions?

The application of HBOT to selected participants and tissues may be justified. Studies of radiation injury suggest that other tissues are also likely to respond (e.g. bladder). Further research is required to establish which people may respond and the best timing of such therapy. A study of costs would also be useful.