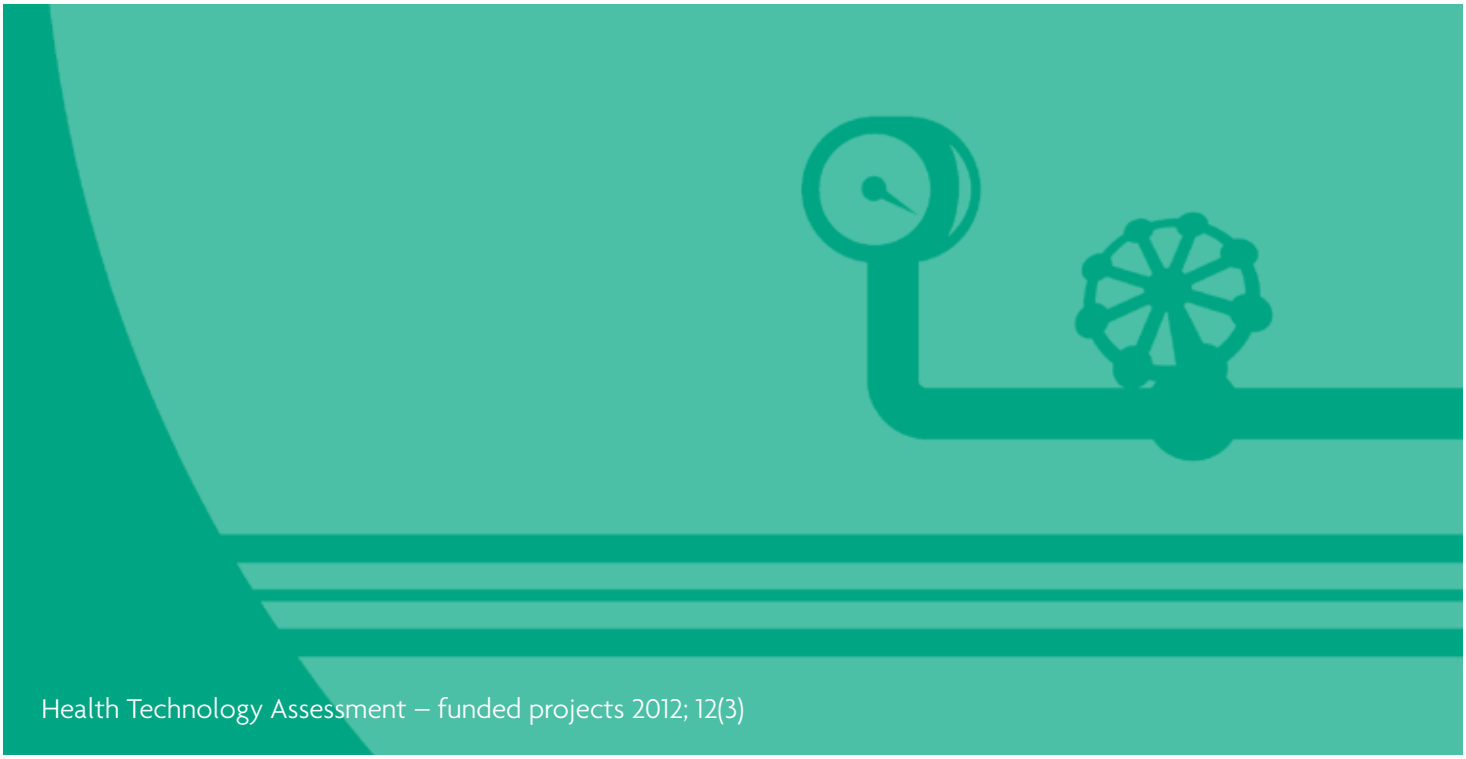
Sundhedsstyrelsen
Danish Health and Medicines Authority

HYPERBARIC OXYGEN TREATMENT OF INJURIES AFTER RADIOTHERAPY FOR HEAD AND NECK CANCER

– a health technology assessment
Summary

2012



Health Technology Assessment – funded projects 2012; 12(3)

Hyperbaric oxygen treatment of injuries after radiotherapy for head and neck cancer – a health technology assessment; Summary

URL: http://www.dacehta.dk

Key words: technology, patient, organisation, economy, health services research, health technology assessment, HTA, hyperbaric oxygen treatment, head and neck cancer, radiotherapy, late radiation tissue injury

Language: English summary of the full report in Danish

Format: pdf
Version: 1.0
Version date: September 6 2012

Issued by: Danish Health and Medicines Authority, Denmark, September 2012

Design of report template: National Board of Health and 1508 A/S
Layout of the report: Rosendahls-Schultz Grafisk A/S
Design and layout of front page: Wright Grafics

Electronic ISSN: 1601-586X

This report should be cited as follows:
Forner L, Lee A, Kruse M, Jansen EC, Sørensen J
Hyperbaric oxygen treatment of injuries after radiotherapy for head and neck cancer – a health technology assessment; Summary
Copenhagen: Danish Health and Medicines Authority, Danish Centre of Health Technology Assessment (DACEHTA), 2012
Health Technology Assessment – funded projects 2012; 12(3)

Series title: Health Technology Assessment – funded projects
Series editorial board: Diana Reerman & Line Holt

For further information please contact:
Danish Health and Medicines Authority
Danish Centre of Health Technology Assessment (DACEHTA)
Axel Heides Gade 1
DK-2300 Copenhagen
Denmark

Phone: +45 72 22 74 00
E-mail: dacehta@sst.dk
Home page: www.dacehta.dk

The English summary can be downloaded at www.dacehta.dk

What is Health Technology Assessment?

Health Technology Assessment (HTA) contributes to decision making in the health care sector. A HTA collects and assess existing knowledge about a given health technology. A health technology is defined broadly as procedures and methods for prevention, diagnostics, treatment, care and rehabilitation including devices and medicine. An example could be a new method to treat patients. Focus is on healthcare, patient, organisational and economical aspects. New research can be conducted if the number of sufficient studies is limited to elucidate one or more of these aspects.

The HTA results in a report that can contribute to better planning, quality enhancement and prioritizing in the health care sector. The target group is decision-makers in the health political field. The primary users are therefore administrations and politicians and other decision-makers in the health political field. The HTA contributes to decisions within administration as well as political management as to which services should be offered in the health care sector and how they should be organized.

Health technology assessment is defined as:

- HTA is a comprehensive systematic assessment of the prerequisites and consequences of applying a health technology

- HTA is a research-based, application-oriented assessment of relevant existing knowledge about problem areas applying a technology within the field of health and illness.

The project is funded by a HTA-fund that was terminated in 2007. The purpose of the fund was to spread out knowledge and use of HTA locally. The funded HTA-reports are prepared in collaboration with an external interdisciplinary project group. The project group systematically reviews the existing literature, contributes with data collection and produces the chapters and conclusions of the report. The project management is placed at the National Board of Health who is also responsible for the editing of the final report. The report has been submitted to an external reference group and is also externally peer-reviewed.

Find more information about HTA at www.sst.dk/mtv under HTA toolbox:
“Handbook of Methods for Health Technology Assessment”
“Health Technology Assessment – Why? What? When? How?”

Summary

Introduction

This HTA was launched at the initiative of the Danish Head Neck Cancer group (DAHANCA) calling for an assessment of hyperbaric oxygen treatment (HBO treatment) of osteoradionecrosis (ORN) in the lower jaw, with the primary purpose of describing and providing evidence for this treatment modality. Also outside of Denmark, HBO treatment has been much debated due to a French randomized study from 2005 concluding that hyperbaric treatment has no clinical effect on ORN of the lower jaw. The results of the French study had far reaching consequences for state-funded treatment for ORN patients. Subsequently, the study has received extensive criticism and therefore, at the present moment, it seems essential to provide additional evidence.

ORN is a condition when bone (osteo) and surrounding soft tissue die (necrosis) in the wake of radiation therapy (radio). ORN of the lower jaw is in this HTA defined as "exposure of the lower jaw bone due to radiation therapy in a period of more than three months."

ORN of the lower jaw occurs in approximately 0.5-15% of previous head and neck cancer patients receiving radiation therapy. The disease occurs either spontaneously or following a surgical trauma to the radiated bone, e.g. a tooth extraction. In principle, the disease can be present in any bone exposed to radiation therapy. Most often, however, the disease occurs in the lower jaw which is frequently extensively damaged after radiotherapy. This is due to the fact that the lower jaw has a less dense supply of blood vessels which reduces blood circulation and thus also oxygen tension in the tissue.

Purpose

The purpose of the present report is to critically evaluate existing literature and own data with a view to examining the evidence for the effect of HBO treatment on ORN, used as sole treatment or in addition to surgical treatment. The intention of the report is to summarize relevant knowledge on:

Target audience

The HTA target audience is decision makers within the public health care system, defined as hospital management, referral authorities and other public policy makers such the Danish Health and Medicines Authority as well as regional health authorities. Moreover, the HTA is relevant for health care professionals involved in HBO therapy as well as health care professionals dealing with delayed effects of cancer treatment.

Demarcation

The description and analysis of HBO treatment confines itself to patients with ORN in the lower jaw.

Method

In order to elucidate the central research questions, systematic literature searches have been conducted within all four central HTA elements comprising technology aspects,

patient perspectives, organisational aspects and economic aspects. Because of the limited number of quality studies, studies of lesser quality were also included in the review of the literature. Moreover, primary data collection and analysis has been completed with respect to all four above mentioned HTA elements. Detailed description of the methods used may be found in the individual chapters of the HTA and its annex.

Technology

The technology element assesses the effect of HBO treatment on ORN based on a review of the existing literature as well as on data from a cohort of ORN patients treated with and without HBO in Copenhagen and Aarhus in the period 1994-2010. The same cohort is used for the analyses of whether HBO treated patients more often suffer from a relapse of their cancer or from a new cancer, and whether HBO treated patients have a lower mortality. This analysis is accompanied by a literature review.

The analysis of the technology element answers the following questions:

- Is there a clinical effect of HBO treatment of ORN patients, used as sole treatment or in addition to surgical removal of the damaged bone tissue?

There is only very limited evidence in the literature of the clinical effect of HBO in ORN patients. Only one randomized study was identified. Due to the design of the identified study it is, however, not possible to conclude that HBO has a lack of clinical efficacy on ORN.

Based on own data from the cohort of HBO treated ORN patients, it can be concluded that there is a statistically higher healing frequency among the HBO treated than the non-HBO treated. These results must of course be interpreted with the limitations of the cohort study in mind.

- Is mortality reduced in HBO treated ORN patients compared with ORN patients not receiving HBO treatment?

Due to the limited information in the literature, it is not possible to draw to a conclusion on the effect of HBO treatment on mortality.

Our data show that there is no difference in mortality rates between HBO treated and non-HBO treated patients.

- Is there an increased incidence of cancer (relapse or new cancer) in HBO treated ORN patients compared with ORN patients who not receiving HBO treatment?

Studies disclosing cancer-promoting effects of HBO treatment do exist in the literature. A review of the complete literature in this field does, however, not provide supporting evidence for concluding that HBO treatment in itself causes an increased incidence of cancer or an accelerated growth of existing cancer. As the existing literature primarily consists of animal experimental studies, the evidence for rejecting a cancer-promoting effect must be described as being poor.

The analyses of own data support the conclusion of the literature review. The cohort study did not find that HBO treated ORN patients more often are diagnosed with cancer than non-HBO treated ORN patients – whether a relapse of existing cancer or the onset of a new cancer. These results must of course be interpreted with the limitations of the cohort study in mind.

Patient

The patient element examines by means of own studies how ORN patients in two Danish available treatment options perceive HBO treatment. The characteristics of this particular group of patients are described in this study as well as how this affects their need for the organisation of HBO treatment. Furthermore, the study illustrates both opportunities and barriers experienced by ORN patients with regard to the organization of HBO treatment. The analysis is accompanied by a literature review.

The analysis of the patient element answers the following questions:

- How do ORN patients experience their disease?

ORN causes pain and discomfort affecting the daily lives of ORN patients. Patients experience problems in relation to speaking, chewing, swallowing, smelling and tasting. Eating becomes problematic and a subject of strong presence to both patients and relatives.

- What are ORN patients' experiences of HBO therapy?

HBO treatment, with hours of daily treatments for a long period of time and often far from the patients' home, is physically, mentally and socially demanding. Patients experience the stay in the pressure chamber as long, boring and not very pleasant. It is associated with discomfort and the feeling of being cooped up for a long time. They experience problems with pressure equalisation, nausea, cold/heat as well as noise. In multi-person chambers, patients moreover also feel discomfort in breathing inside the hood and uncomfortable sitting positions. Finally, there are transient inconveniences, e.g. problems with a changed sight.

While physical and organisational conditions seem to be crucial for patient safety and satisfaction, the importance of the type of pressure chamber (multi or single person) is less certain. The comfort seems better in the individual chamber than in multi person chamber. On the other hand, time spent with other ORN patients also seems essential. While time together with other ORN patients may be met through interaction outside the chamber, it appears that the joint stays in the multi-person chamber support patients' experience of belonging to a community.

- What impact do other patients and staff have?

While patients experienced some nervousness prior to the first treatment, subsequent treatments were experienced as familiar and acceptable. Good information prior to treatment, daily routines and involvement in a community are important factors for patient safety. A limited number of staff and their courtesy have implications both for safety and confidence in the treatment. Additionally, a positive interaction with other patients supports the experience of being part of a community as well as it nourishes the hope of an effect of the treatment.

- What are the patient experienced effects of HBO therapy?

Upon end of HBO treatment, patients experience incipient improvements in terms of less pain, increased mouth sensitivity, improved saliva production and a less dry mouth. All informants, except one, valued the treatment and would recommend it to others. The informant that didn't value HBO therapy was treated in an individual chamber and at a hospital different to the hospital where he was treated for ORN. This particular informant reported experiences of loneliness and a lack of belonging.

- What causes patients to accept and accomplish a treatment described as physically, mentally and socially demanding, without knowing if their health problems will be addressed?

Patients' acceptance of HBO therapy is influenced by both past experiences with illness and treatment, their current problems with their ORN disease as well as the expectation that their health problems will be alleviated through HBO treatment. Their uncertainty regarding the effect of HBO treatment give rise to persistent attempts to be confirmed in the possible effect of this treatment modality, e.g. through awareness of own experiences as well as conversation with staff and other HBO treated patients.

Both the completion of and the satisfaction with a lengthy and intensive course of treatment seem to be supported through the fulfilment of a universal need for affiliation. This need is addressed through awareness and confidence in staff as well as the safety of the treatment and its effect.

Organisation

The organisational element describes two available treatment options in Denmark: the multi person chamber at Rigshospitalet and the individual chamber at Aarhus University Hospital. Moreover, the results from a questionnaire survey directed at referring oncologists, otorhinolaryngology surgeons and maxillofacial surgeons are presented. Finally, the organisational element compares the Danish HBO capacity with other countries as well as it discusses the potential for adapting the organisation of HBO treatment in Denmark to an increasing demand. The analysis is accompanied by a literature review.

The analysis of organisational aspects answers the following questions:

- How is HBO treatment in ORN patients organised in Denmark?

HBO treatment for ORN takes place at two locations in Denmark: in the multi person pressure chamber at Rigshospitalet and the individual pressure chamber at Aarhus University Hospital. The treatment consists of daily outpatient treatments over a period of 5-6 weeks and, possibly, with daily follow-up treatments over a period of two weeks. Patients living far away from the treating hospitals or with special needs are admitted to hospital.

- How is the physical environment of HBO treatment and what are the safety requirements to HBO treatment?

The pressure chamber at Rigshospitalet is a multi-person chamber with room for seven patients. Intensive treatment takes place with personnel and equipment inside the chamber. The pressure chamber at Aarhus University Hospital is an individual chamber with room for a single patient. Both staff and equipment are outside the chamber during intensive treatment. As treatment involves pure oxygen under a pressure, a series of security measures have been described.

- Which personnel resources are involved in the HBO treatment?

While both pressure chambers organisationally are affiliated to anaesthesiological departments, the education and the skills of staff vary at the two HBO treating hospitals due to the different types of pressure chambers. In the technically complex multi-person chamber, up to 21 patients are treated on daily basis which means that there is a need for a larger organization with permanent staff with both anaesthesiological and

special expertise such as diving skills. As treatment can take place within the pressure chamber, staff must, in addition to training in HBO therapy, have updated skills into becoming pressurised. An individual pressure chamber is technically much simpler. Here, there is no opportunity for staff to be in the chamber and, thus, no need for diving skills or competencies into becoming pressurised. However, the small and varying number of treatments in the individual pressure chamber requires flexibility of the involved staff as they will a varying number of hours with HBO therapy.

- What is the use of HBO treatment for ORN, including referral patterns?

Patients are referred from maxillofacial, oncological and otorhinolaryngological surgical wards. A survey among referring departments shows that the majority of departments refer their ORN patients to HBO treatment and that the common view is that HBO treatment is beneficial to patients. The study also shows that there is a critical attitude to the lack of evidence of HBO treatment and that local culture and attitudes among health professionals can be decisive for referral patterns. These circumstances may imply that some ORN patients not are informed about HBO therapy as a relevant treatment option. In particular, the facilities of the multi-person pressure chamber unit as well as transport condition seem to be important for referral patterns.

- What is the current HBO capacity in Denmark and in comparable countries, and how could a possible increased demand for HBO treatment be taken into account?

The Danish HBO capacity is small compared with other countries. While both chambers offer acute treatments, the majority of the capacity is used for elective treatments due to the fact that HBO therapy implies a long course of daily treatments. Besides treatment for ORN, which occupy the majority of the HBO capacity, a variety of other disorders are also treated with HBO therapy, e.g. radiotherapy damages to the bowel and the bladder, problematic wounds and bone inflammation.

The number of treatments has been increasing over the past 15 years. Today, there is a total of approximately 5,000 therapy sessions every year and the current capacity is close to being utilised. Meanwhile, both in Denmark and internationally it is the expectation that there will be an increased demand for HBO therapy in the treatment of ORN as well as in other radiotherapy damages and diabetic foot ulcers. These expectations are substantiated by changes in treatment regimes, new research findings and an increased awareness of HBO therapy among patients and health care professionals.

While it is not possible to expand the capacity of the pressure chamber at Rigshospitalet, it is the intention to increase the capacity at Aarhus University in connection with the relocation to a new university hospital. Additionally, an individual pressure chamber has been established at Odense University Hospital in March 2012.

Economy

The HTA economic element assesses the costs of treatment for ORN as well the cost-effectiveness of HBO treatment.

The analysis of economically aspects answers the following questions:

- What are the costs of treatment for ORN patients receiving HBO treatment and ORN patients not receiving HBO treatment, respectively?

Based on data from a cohort study it is estimated that HBO treatment of ORN aggregates to about 50,000 DKK more than conventional ORN treatment. This amount includes consumption of health care services up to five years after the date of diagnosis. Nearly two-thirds of the amount is costs related to HBO treatment, while approximately one third are costs related to subsequent health care costs.

- Is HBO treatment of ORN cost-effective?

The cost-effectiveness analysis estimates the costs for getting a patient completely healed, measured by the clinical measure CTC. The analysis shows that HBO treatment results in an additional cost of 286,000 DKK per additionally healed patient. Whether this is considered to be cost-effective is a question of political priorities.

Final recommendations

Based on the conclusions of the report, the following advice to the audience may be given:

- As the analyses in the present report suggest that there is a clinical effect of HBO therapy of ORN, it is important to support the completion of the ongoing randomized trial initiated concurrently with this HTA
- HBO treatment in Denmark should continuously be offered to ORN patients, until at least two randomized studies have concluded that HBO treatment has no favourable outcome. At present, there are no alternatives to HBO treatment
- Referring authorities and other relevant agencies should be informed about the fact that, at the present moment, there is no documentation of a cancer promoting effect of HBO treatment
- The principles for referral to HBO therapy for ORN patients should be compiled in interdisciplinary clinical guidelines with a view to standardising treatment of ORN on a national basis
- Information on this treatment modality should be provided to relevant patient and professional forums with a view to increasing the visibility of HBO treatment
- Information to ORN patients on HBO treatment should be provided to ORN patients prior to and during the course of treatment with view to ensuring patient confidence and acceptance of HBO treatment.

Future research should focus on the following areas:

- Completion of the ongoing randomized study
- Launch of studies seeking to identify the mechanisms of action in HBO therapy
- Examination of whether HBO treatment might have a greater potential in specific situations depending on factors such as disease characteristics, co-morbidities and lifestyle
- Continuation of the monitoring of cancer incidence among HBO treated and non-HBO treated ORN patients. Including a study of factors that might influence the cancer incidence of ORN patients as well as diagnostic initiatives that might minimise this risk
- Promotion of research into possible alternatives to HBO therapy.

www.dacehta.dk

National Board of Health
Documentation of Quality & Health
Danish Centre for Health Tecnology Assessment (DACEHTA)
Islands Brygge 67
2300 København S
Phone no 7222 7400

dacehta@sst.dk
www.dacetha.dk