NHS England

Clinical commissioning policy: Hyperbaric oxygen therapy for malignant otitis externa (all ages)

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Clinical Commissioning Policy: Hyperbaric oxygen therapy for malignant otitis externa (all ages)

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Prepared by NHS England Specialised Services Clinical Reference Group for Hyperbaric oxygen therapy

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Contents

Policy statement

NHS England will not routinely commission hyperbaric oxygen therapy for malignant otitis externa (all ages) in accordance with the criteria outlined in this document.

In creating this policy NHS England has reviewed this clinical condition and the options for its treatment. It has considered the place of this treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources.

This policy document outlines the arrangements for funding of this treatment for the population in England.

Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

Plain language summary

About malignant otitis externa

Malignant otitis externa is a disorder that involves infection of and damage to the bones of the ear canal and at the base of the skull. Malignant otitis externa is caused

by the spread of an outer ear infection (otitis externa) also called swimmer's ear. It is not common (NHS Choices, 2015).

About current treatments

The goal of treatment is to cure the infection. The treatment is taking medicines that fight infections (antibiotics) for a long period of time. The medicines may be given through a vein (intravenously), or by mouth. In some cases, surgery might be needed to remove dead or damaged tissue in the skull.

About the new treatment

Hyperbaric oxygen therapy (HBOT) has been suggested as an adjuvant treatment (another treatment used together with the primary treatment) of malignant otitis externa. HBOT is delivered by giving a patient oxygen to breathe while in a pressurised chamber so that a higher level of oxygen can be dissolved in the patient's blood plasma. Inhaling oxygen at increased pressure is intended to improve oxygen supply to the infected tissue. During HBOT, the patient is in a pressure chamber, usually for 60 to 120 minutes at least once daily. On average, patients require between 15 and 30 treatments.

What we have decided

NHS England has carefully reviewed the evidence to treat malignant otitis externa with hyperbaric oxygen therapy. We have concluded that there is not enough evidence to consider making the treatment available at this time.

1 Introduction

About Malignant Otitis Externa

Malignant Otitis Externa (MOE) is an uncommon condition mainly found in the elderly or in diabetics (Phillips and Jones 2013). It is an aggressive infection involving the external ear canal and the surrounding skull base, mainly the temporal bone. It was first reported in the literature by Toulmouche in 1838.

Signs and symptoms of malignant otitis externa can include:

- severe ear pain and headaches
- exposed bone visible in the ear canal
- facial nerve palsy – where the face droops on the side of the affected ear (NHS Choices, 2015).

Occasionally, MOE can also be complicated by infections of the parts of the body near to the ear. This can cause parotitis, mastoiditis, jugular vein thrombosis, meningitis and death (Glamarellou 1992). *Pseudomonas aeruginosa* is the infective organism most commonly isolated from the aural drainage in more than 90% of MOE cases. Diagnosis is based upon clinical, microbiological and radiological findings (Ali et al 2010).

Current treatment

The mainstay of treatment for MOE has been prolonged antibiotic therapy, stringent diabetes control, the repeated removal of dead tissue by surgical management (Glamarellou 1992, Illing and Olaleye 2011, Phillips and Jones 2013).

Proposed intervention

HBOT is the breathing of 100% oxygen at pressures above one atmosphere absolute (ATA) (~100 kilopascals [kPa]). HBOT involves placing the patient in a compression chamber, increasing the environmental pressure within the chamber and administering 100% oxygen through a face mask or a transparent hood. In this way, it is possible to deliver a greatly increased partial pressure of oxygen to the tissues. Typically, treatments involve pressurisation to between 203 to 304 kilopascals (kPa) [two and three atmospheres absolute (ATA)] for periods between

60 and 120 minutes once or twice daily. A typical course might involve 15 to 30 such treatments (Phillips and Jones 2013).

Hyperbaric oxygen has been proposed as an adjuvant (additional) therapy for MOE and has been included in treatment pathways in places where a therapeutic pressure chamber is available (Shupak et al 1989). It is postulated that HBOT works by increasing oxygen supply to hypovascular tissues. This leads to efficient leukocyte (white blood cell) function which is essential for soft tissue and bone healing as well as infection resolution (Phillips and Jones 2013).

There are no national evidence-based policies or guidance for the management of patients with MOE.

2 Definitions

Avascular: characterized by or associated with a lack of blood vessels.
Case reports: An uncontrolled observational study involving an intervention and an outcome in a single patient.
Case series: Reports of several patients with a given condition, usually covering the course of the condition and the response to treatment. There is no comparison (control) group of patients.
Computerised tomography (CT): a *scan* that uses X-rays and a computer to create detailed images of the inside of the body.
Granulation tissue: new connective tissue and microscopic blood vessels that form on the exposed surfaces of a wound during the healing process.
Hypovascular: characterized by or associated with fewer blood vessels than normal.
Immunocompromised: inability to respond normally to an infection due to an impaired or weakened immune system.
Jugular vein thrombosis: an extremely rare vascular disease.
Leukaemia: a cancer which starts in blood-forming tissue, usually the bone marrow.
Lymphoma: is an uncommon cancer that develops in the lymphatic system, which is a network of vessels and glands spread throughout the body.

Mastoiditis: result of an infection that extends to the air cells of the skull behind the ear. Specifically, it is an inflammation of the mucosal lining of the mastoid antrum and mastoid air cell system inside the mastoid process. The mastoid process is the portion of the temporal bone of the skull that is behind the ear which contains open, air-containing spaces.

Meningitis: an infection of the protective membranes that surround the brain and spinal cord (meninges).

- **Neoplasia:** the presence or formation of new, abnormal growth of tissue.
- **Post-transplantation immunosuppression**: drugs or medicines that lower the body's ability to reject a transplanted organ.

Parotitis: an inflammation of one or both parotid glands, the major salivary glands located on either side of the face in humans. The parotid gland is the salivary gland most commonly affected by inflammation.

Pulmonary: relating to the lungs.

Retrospective study: A research study that focuses on the past and present. The study examines past exposure to suspected risk factors for the disease or condition.

Splenectomy: is a surgical procedure to remove the spleen

Systematic review: A review that summarises the evidence on a clearly formulated review question according to a predefined protocol, using systematic and explicit methods to identify, select and appraise relevant studies, and to extract, analyse, collate and report their findings.

3 Aims and objectives

This policy aims to consider the evidence underpinning the use of HBOT for malignant otitis externa.

The objectives are to consider whether:

- the evidence base supports HBOT as a routine adjuvant treatment in the management of malignant otitis externa
- the evidence base identifies the place of HBOT in the care pathway for the management of malignant otitis externa.
- there is a subgroup of patients who are most likely to benefit

- the evidence identifies a treatment schedule that is most effective in achieving best outcomes
- HBOT is cost effective as an adjuvant treatment for malignant otitis externa.

4 Epidemiology and needs assessment

MOE is an uncommon condition mainly found in the elderly or in diabetics (Phillips and Jones 2013). It is generally suspected in diabetic patients with pseudomonal otitis externa, especially when pain is a prominent feature. Recent reviews have quoted the prevalence of diabetes in MOE cases as 90% to 100% (Berenholz, Katzenell and Harell 2002, Mani et al 2007). Other immunocompromised states also represent risk factors for MOE development (with or without diabetes) (Shpitzer et al 1993), including human immunodeficiency virus (HIV) infection, acquired immunodeficiency syndrome (AIDS), neoplasia, leukaemia, lymphoma, splenectomy and post-transplantation immunosuppression (Hollis and Evans 2011). MOE is more common in males than females (Phillips and Jones 2013).

The mortality of MOE has been reported to be as high as one third, but when cranial nerves are affected it may be as high as 80% (Phillips and Jones 2013).

Chawdhary, Liow & Whiteside (2015) undertook an analysis of Hospital Episode Statistics in the UK and found a six-fold increase in the number of cases from 1999 (n=67) to 2013 (n=421).

5 Evidence base

Summary of evidence

NHS England commissioned a review of the published evidence on the use of HBOT treatment for malignant otitis externa. To aid in the search for clinically relevant literature, experts in the field of HBOT guided the development of a Population, Intervention, Comparison, Outcome (PICO) framework. Key findings were:

Clinical effectiveness

- The literature search for this rapid evidence review found one systematic review (Phillips and Jones 2013), one retrospective controlled study (Sabra et al 2015)

and one case series (Saxby et al 2010) which assess the use of HBOT in the management of MOE.

- A variety of outcomes were reported including pain, ear discharge, complications of HBOT and mortality.
- Sabra et al (2015) carried out a retrospective controlled study to assess the usefulness of HBOT as an adjunctive treatment in diabetic patients with MOE. 28 patients received ciprofloxacin (antibiotics) only while 15 patients were treated with ciprofloxacin and HBOT. HBOT was administered at 2.5 ATA (~253 kPa) for 90 minutes per session every other day for two months. All the patients were evaluated clinically (in terms of ear discharge, granulations, and pain severity) and radiologically by a temporal bone computed tomography scan. The patients were followed up for at least two months.
- The authors reported the following in patients treated with ciprofloxacin plus HBOT versus those treated with ciprofloxacin only: an improvement in pain in 86.7% vs. 32.1% of patients at one month after 15 sessions (no p-value was reported); freedom from pain in 46.7% vs. 0% of patients at one month and 93.3% vs. at 28.5% two months ($p<0.001$ for both follow up periods); the absence of purulent ear discharge in 80% vs. 0%[1] ($p<0.001$) at one month and 93.3% vs. 28.5% ($p<0.001$) at two months (Sabra et al 2015).
- The systematic review did not identify any RCTs; it described four case reports and five case series which included a total of 73 patients (range was not reported). The authors reported that the individual papers described the use of HBOT as adjuvant therapy with antibiotics in the majority of cases. Most regimens used 20 to 40 doses of hyperbaric oxygen treatment. Each treatment was of 90 minutes duration at 2.5 ATA (~253 kPa). However due to the poor quality of studies, lack of randomisation or other controls, they were unable to assess statistically the effectiveness of treatment with HBOT compared with other treatments (Phillips and Jones 2013).
- The retrospective case series of patients with a diagnosis of MOE, referred to a hyperbaric unit for treatment over a period of six years, conducted by Saxby et al included 17 patients. All the patients received HBOT once daily on Monday to Friday on a standard 90-minutes schedule at 243 kPa (2.4 ATA).They reported

[1] Not reported to one decimal place therefore inconsistent with other results

that 12 patients (70%) were disease-free at follow up, so were considered cured of their disease; this included four patients who had died of other causes but were symptom-free at the time of death. Three patients (18%) died from MOE, one after a recurrence of their disease. Two further patients (12%) had recurrent disease, both successfully treated with a second cycle of HBOT and antibiotics (Saxby et al 2010).

Safety

- The study carried out by Sabra et al did not report any complications associated with HBOT. The case reports and case series described in the Cochrane review did not report any complications or adverse events related to hyperbaric oxygen treatment (Phillips and Jones 2013).
- However, the retrospective review conducted by Saxby et al reported that five out of 17 patients (29%) had complications attributable to HBOT; acute pulmonary oedema (n = 2), seizure (n = 1), tympanic membrane perforation (n = 1) and claustrophobia (n = 1).

Cost-effectiveness

No studies on cost-effectiveness were identified.

Conclusion

The published literature on the use of HBOT in MOE is limited to very small un-randomised studies; it is therefore not robust enough to make blanket recommendations.

The evidence for the clinical effectiveness of HBOT as adjunctive treatment in the management of MOE is limited to small case series and retrospective studies. Although the reported results suggest that this intervention may be effective, the studies have a number of limitations. For this reason the results may not be reliable or generalisable.

In summary, while HBOT may be useful as an adjunct in the management of MOE, there is insufficient evidence to make clear recommendations particularly in comparison to alternative treatments. The low prevalence of MOE is likely to make

randomised control trials of HBOT in this indication very difficult to complete. However study designs that encompass a more systematic approach to the diagnosis, standard care, outcome measures and place of HBOT in the care pathway would help to reduce the uncertainty.

6 Documents which have informed this policy

This document replaces the present NHS England Clinical Commissioning Policy (2013): Hyperbaric Oxygen Therapy: NHSCB/D11/P/a: https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2013/10/d11-p-a.pdf

7 Date of review

This document will be reviewed when information is received which indicates that the policy requires revision.

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