



HEADACHE LITERATURE

Cochrane Database Syst Rev. 2008 Jul 16;(3):CD005219.

Normobaric and hyperbaric oxygen therapy for migraine and cluster headache.

Bennett MH, French C, Schnabel A, Wasiak J, Kranke P.

BACKGROUND: Migraine and cluster headaches are severe and disabling. Migraine affects up to 18% of women, while cluster headaches are much less common (0.2% of the population). A number of acute and prophylactic therapies are available. Hyperbaric oxygen therapy (HBOT) is the therapeutic administration of 100% oxygen at environmental pressures greater than one atmosphere, while normobaric oxygen therapy (NBOT) is oxygen administered at one atmosphere. **OBJECTIVES:** To assess the safety and effectiveness of HBOT and NBOT for treating and preventing migraine and cluster headaches. **SEARCH STRATEGY:** We searched the following in May 2008: CENTRAL, MEDLINE, EMBASE, CINAHL, DORCTIHM and reference lists from relevant articles. Relevant journals were hand searched and researchers contacted. **SELECTION CRITERIA:** Randomised trials comparing HBOT or NBOT with one another, other active therapies, placebo (sham) interventions or no treatment in patients with migraine or cluster headache. **DATA COLLECTION AND ANALYSIS:** Three reviewers independently evaluated study quality and extracted data. **MAIN RESULTS:** Nine small trials involving 201 participants were included. Five trials compared HBOT versus sham therapy for acute migraine, two compared HBOT to sham therapy for cluster headache and two evaluated NBOT for cluster headache. Pooling of data from three trials suggested that HBOT was effective in relieving migraine headaches compared to sham therapy (relative risk (RR) 5.97, 95% confidence interval (CI) 1.46 to 24.38, $P = 0.01$). There was no evidence that HBOT could prevent migraine episodes, reduce the incidence of nausea and vomiting or reduce the requirement for rescue medication. There was a trend to better outcome in a single trial evaluating HBOT for the termination of cluster headache (RR 11.38, 95% CI 0.77 to 167.85, $P = 0.08$), but this trial had low power. NBOT was effective in terminating cluster headache compared to sham in a single small study (RR 7.88, 95% CI 1.13 to 54.66, $P = 0.04$), but not superior to ergotamine administration in another small trial (RR 1.17, 95% CI 0.94 to 1.46, $P = 0.16$). Seventy-six per cent of patients responded to NBOT in these two trials. No serious adverse effects of HBOT or NBOT were reported. **AUTHORS' CONCLUSIONS:** There was some evidence that HBOT was effective for the termination of acute migraine in an unselected population, and weak evidence that NBOT was similarly effective in cluster headache. Given the cost and poor availability of HBOT, more research should be done on patients unresponsive to standard therapy. NBOT is cheap, safe and easy to apply, so will probably continue to be used despite the limited evidence in this review.



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Schmerz. 2008 Apr;22(2):129-32, 134-6.

Hyper- or normobaric oxygen therapy to treat migraine and cluster headache pain. Cochrane review

Schnabel A, Bennet M, Schuster F, Roewer N, Kranke P.

BACKGROUND: The aim of this systematic review was to assess the benefits and harms of supplemental oxygen (HBOT/NBOT) for treating and preventing migraine and cluster headaches. MATERIAL AND METHODS: All randomized trials comparing the effect of supplemental oxygen on migraine or cluster headache with those that exclude supplemental oxygen were included in this review. The systematic search included all relevant sources according to the paradigms of the Cochrane Collaboration. Data were analyzed with RevMan 4.2. RESULTS: Nine trials involving 201 participants satisfied the inclusion criteria. **HBOT was effective in relieving an acute migraine and seemed to be sufficient in the treatment of an acute cluster attack.** NBOT was effective in terminating acute cluster headache compared to sham treatment, but not in comparison to sublingual ergotamine. There was no evidence for any prophylactic effects. Serious adverse effects were not noted in the trials investigated. **CONCLUSIONS: There is some evidence that HBOT is effective for termination of acute migraine.** NBOT was similarly effective in cluster headache, however with sparse data. Because of costs and poor availability HBOT cannot be regarded as a routine therapy. Further indications in the case of treatment failure using standard therapy need to be defined based on data of future clinical trials.

J Headache Pain. 2005 Sep;6(4):294-7.

Management of cluster headache in the Emergency Department.

Di Sabato F, Giacobozzo M.

Although cluster headache (CH) is considered one of the most distinctive and painful primary headache disorders in clinical practice because of the brevity of each attack, its management is not always ergonomic or possible in the Emergency Department. In case of a previously competent diagnosis, the Emergency Department's team should send the patient to a headache centre where specialists in the management of CH can handle the pathology in the best way. In our headache centre we treat patients with CH attacks with a hyperbaric chamber, **confirming the effectiveness of hyperbaric oxygen in CH patients.**



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Cephalalgia. 2004 Aug;24(8):639-44.

A randomized, double blind study of the prophylactic effect of hyperbaric oxygen therapy on migraine.

Eftedal OS, Lydersen S, Helde G, White L, Brubakk AO, Stovner LJ.

In a double blind, placebo-controlled study to assess the prophylactic effect of hyperbaric oxygen therapy on migraine, 40 patients were randomly assigned to a treatment group receiving **three sessions** of hyperbaric oxygen, or a control group receiving three hyperbaric air treatments. The patients were instructed to keep a standardized migraine diary for eight weeks before and after the treatment. Thirty-four patients completed the study. Our primary measure of efficacy was the difference between pre- and post-treatment hours of headache per week. **The results show a nonsignificant reduction in hours of headache for the hyperbaric oxygen group compared to the control group.** Levels of endothelin-1 in venous blood before and after treatment did not reveal any difference between the hyperbaric oxygen and control groups. We conclude that the tested protocol does not show a significant prophylactic effect on migraine and does not influence the level of endothelin-1 in venous blood.



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Cephalalgia. 2002 Nov;22(9):730-9.

Hyperbaric oxygen treatment of active cluster headache: a double-blind placebo-controlled cross-over study.

Nilsson Remahl AI, Ansjön R, Lind F, Waldenlind E.

Sixteen patients, 12 with episodic and four with chronic cluster headache (CH) according to the International Headache Society criteria (1), participated in the study. They were randomly selected to start with one out of two different hyperbaric treatments in a double-blind, placebo-controlled, cross-over study design. Both gases were administered by mask inside a multiplace hyperbaric chamber for 70 min at 250 kPa (2.5 ATA) in two sessions 24 h apart. Active treatment was 100% oxygen (HBO treatment), while placebo treatment was 10% oxygen in nitrogen (hyperbaric normoxic placebo = sham treatment) corresponding to breathing air at sea level. All patients were decompressed on air. The patients documented the number of headache attacks and their degree of severity according to a modified VAS scale (level 0-4, where level 0 = no headache and level 4 = very severe headache). A headache index (HI = sum of (number of attacks times degree of severity)) was calculated for the run-in week prior to and the week after each separate treatment. A treatment was regarded as effective if it reduced the HI by >50%. Blood samples were taken from the external jugular vein before and during hyperbaric treatment (after 30 and 70 min), 1 day and 1 week after each treatment for analyses of calcitonin gene-related peptide (CGRP), vasoactive intestinal peptide (VIP) and neuropeptide Y (NPY) and in a few patients also endotheline and nitrate. No difference between HBO and sham treatment on the HI or the prophylactic effect was observed in our study. However, 83% of the episodic CH patients and 25% of the chronic ones responded to either of the two treatments with at least 50% reduction of HI or remission for shorter or longer periods. This response rate exceeds an expected high placebo response due to the study procedure. Two episodic CH patients still experienced remission on follow-up 1 year after sham treatment. Five patients reported mild or moderate CH attacks during the sham treatment, and none during the HBO treatment. Changes in neuropeptides, endotheline and nitrate levels did not differ systematically when comparing the two different hyperbaric treatments or with respect to responders and non-responders. We conclude that **two HBO sessions were not more effective than two sham treatments in reducing the HI and interrupting the CH period when given in a well-established cluster period or in chronic CH. The hyperbaric condition itself seems effective in reducing the HI, at least in patients with episodic CH, although a powerful placebo response can not be ruled out.**



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Headache. 1998 Feb;38(2):112-5.

Hyperbaric oxygen in the treatment of migraine with aura.

Wilson JR, Foresman BH, Gamber RG, Wright T.

Cephalalgia is one of the most common medical complaints and the search continues for relief. Early treatments for migraine included inhalation of 100% oxygen. It has been theorized that the increased levels of oxygen in the blood act as an alpha-adrenergic agent to alleviate headache pain through vasoconstriction and local metabolic effects. The presence of muscle tenderness during some migraine headaches has also been established. The purpose of this study was to document relief of cephalalgia through use of a visual analog pain scale, algometry, and manual palpation. Female subjects with confirmed migraine were randomly assigned to begin with either the control (100% oxygen, no pressure) or hyperbaric treatment (100% oxygen, pressure). Manual palpation and algometry of 10 sites were done, bilaterally, by a trained specialist. Pain was evaluated with a visual analog scale. Resolution of tenderness and edema following both treatments was observable by manual palpation while algometry showed no differences between the two. Subjective pain was significantly decreased following hyperbaric oxygen treatment but not following the control treatment. Results suggest that hyperbaric oxygen treatment reduces migraine headache pain and that the patient's subjective assessment was the best indicator of relief.

Undersea Hyperb Med. 1997 Jun;24(2):117-22.

Hyperbaric oxygen in chronic cluster headaches: influence on serotonergic pathways.

Di Sabato F, Rocco M, Martelletti P, Giocovazzo M.

A controlled study was done with the aim of assessing the efficacy of hyperbaric oxygen (HBO2) in cluster headache and of studying the possible influence of this therapeutic approach on serotonergic pathways. Fourteen patients, aged between 26 and 56 yr, suffering from the chronic form of cluster headache were treated with HBO2 (n = 10) or environmental air (placebo) (n = 4) during the 15 sessions of exposure (lasting 30 min each) in the hyperbaric chamber. The influence of this procedure on serotonergic pathways of pain was monitored by means of study of serotonin binding to mononuclear cells before and after the treatment for both subgroups. All of the treated 14 chronic cluster headache patients completed the study. In the subgroup treated with the placebo, no particular modifications on the number of attacks and of analgesic consumption as well as no change in the specific binding curve of serotonin to mononuclear cells were observed, whereas in the subgroup treated with HBO2 the clinical effectiveness and the appearance of plateau in the binding curves indicated that the oxygen therapy could act through serotonergic pathways.

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Headache. 1996 Apr;36(4):221-3.

Effect of hyperbaric oxygen on the immunoreactivity to substance P in the nasal mucosa of cluster headache patients.

Di Sabato F, Giacobazzo M, Cristalli G, Rocco M, Fusco BM.

Exposure to hyperbaric oxygen has been shown to be effective in cluster headache, but the mechanism of the action is still not clear. Primary nociceptive neurons, containing neuropeptides such as substance P and particularly those innervating the nasal mucosa, could be involved in the pathogenesis of cluster headache. The present study evaluated the effect of an exposure to hyperbaric oxygen on the content of substance P in the nasal mucosa of patients affected by cluster headache. The results were compared with those observed in another group of cluster headache patients who underwent a placebo procedure. The samples of nasal mucosa were analyzed by immunocytochemical methods. A qualitative analysis of the slides was carried out by an operator under "blinded conditions". A marked decrease in the content of immunoreactivity for substance P was found in the patients exposed to hyperbaric oxygen. The decrease was statistically significant when compared with the findings of the placebo procedure. The results of the present study indicate that an influence on the content of peripheral neuropeptides could be involved in the mechanism of action of the beneficial effect of hyperbaric oxygen in cluster headache.

Curr Opin Neurol. 1995 Jun;8(3):243-7.

Treatment of cluster headache and its variants.

Stovner LJ, Sjaastad O.

In cluster headache, subcutaneous administration of sumatriptan has been established as an efficient, safe and well tolerated treatment for acute attacks. For prophylactic treatment, capsaicin (intranasal administration) and leuprolide (a synthetic slow-release gonadotrophin-releasing hormone) seem to be promising. Hyperbaric oxygen therapy seems to be effective in acute attacks, but it is of interest mostly because of its apparent interruption of the cluster period in some patients. In chronic paroxysmal hemicrania, which clinically resembles cluster headache, indomethacin is still necessary for diagnosis, and it is the treatment of choice in most patients. However, because of its potential side effects, alternative treatments should be sought.



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Headache. 1995 Apr;35(4):197-9.

A preliminary report on hyperbaric oxygen in the relief of migraine headache.

Myers DE, Myers RA.

Oxygen inhalation was early advocated as a treatment for migraine headache. It has been theorized that the efficacy of raising blood oxygen levels in vascular headache is mediated by vasoconstriction and metabolic effects. Hyperbaric oxygen can provide a much greater level of blood oxygenation than can provide a much greater level of blood oxygenation than normobaric oxygen, and in recent studies it has been used in the treatment of cluster headache. The purpose of this study was to compare the effects of hyperbaric oxygen and normobaric oxygen in migraine. Twenty migraineurs were divided randomly into two groups and studied in a hyperbaric chamber during a typical headache attack. Global headache severity was measured by a verbal descriptor scale before and after exposure to oxygen. One group received 100% oxygen at 1 atmosphere of pressure (normobaric) while the other received 100% oxygen at 2 atmospheres of pressure (hyperbaric). One of the 10 patients in the normobaric group achieved significant relief of headache symptoms, while 9 of 10 in the hyperbaric group found relief. Based on a chi-square test, this difference is significant at the $P < .005$ level. Those patients who did not find significant relief from normobaric oxygen were given hyperbaric oxygen as above. All nine found significant relief. The results suggest that hyperbaric (but not normobaric) oxygen may be useful in the abortive management of migraine headache. Possibilities for the mechanism of this effect, in addition to vasoconstriction, include an increase in the rate of energy-producing and neurotransmitter-related metabolic reactions in the brain which require molecular oxygen.

Pain. 1993 Feb;52(2):243-5.

Hyperbaric oxygen therapy in cluster headache.

Di Sabato F, Fusco BM, Pelaia P, Giacobazzo M.

Preliminary reports have shown that hyperbaric oxygen (HBO) interrupts cluster headache (CH) attacks. In the present study, 6 of 7 patients with episodic cluster headache who were treated with hyperbaric oxygen experienced an interruption of the attack. In 3 of 6 responders the florid period of the cluster headache was interrupted. The other 3 patients remained without pain attacks for a period lasting from 3 to 6 days. In 6 different patients, a placebo treatment had no effect. The present findings clearly indicate that hyperbaric oxygen has not only a symptomatic effect on a single attack of cluster headache, but it also could prevent the occurrence of subsequent attacks.