Treatment of Cluster Headache

A Double-blind Comparison of Oxygen *v* Air Inhalation

Lance Fogan, MD, MPH

• **Nineteen men, aged 20 to 50 years, were treated in a double-blind crossover study comparing oxygen *v* air inhalation at 6 L/min via nonrebreathing face masks for 15 minutes or less, for up to six headaches. Patients scored their own degree of relief for each treatment as none, slight, substantial, or complete relief. The average (±SE) relief score for all oxygen-treated patients was 1.93 ± 0.22 out of a possible total score of 3.0, and for air the treatment relief score was 0.77 ± 0.23. This difference is highly statistically significant by an analysis-of-variance *F* test; it documents that patients with cluster headache can benefit from oxygen inhalation during acute attacks.**

(*Arch Neurol* 1985;42:362-363)

Patient Study Results

Patient	Oxygen: No. of Treatments	Oxygen: Substantial or Complete Relief, %	Oxygen: Relief Score*	Air: No. of Treatments	Air: Substantial or Complete Relief, %	Air: Relief Score*
1	2	50	2.0	0	...	...
2	5	80	2.6	5	0	0.0
3	5	60	1.4	5	0	0.4
4	2	50	1.0	5	20	1.0
5	5	100	2.2	5	40	1.2
6	0	...	...	1	0	0.0
7	0	...	...	5	0	0.0
8	6	83	2.3	0	...	...
9	5	0	0.4	0	...	...
10	4	100	3.0	5	0	0.0
11	1	100	3.0	5	100	2.5
12	9	44	1.2	0	...	...
13	5	20	0.4	4	50	1.3
14	0	...	...	10	70	1.5
15	5	20	0.6	2	50	1.0
16	5	100	3.0	1	0	0
17	5	100	3.0	0	...	...
18	5	80	2.4	5	0	0
19	5	100	2.4	5	60	1.8

*The relief score is an average of the scores of the subjective relief of all of that patient's headaches achieved by that treatment (air or oxygen), divided by the total number of treatments. A score of 0 indicated no pain relief; 1, slight relief; 2, significant relief; and 3, complete relief. The specific data for each patient are required to make these calculations. They are available from the author on request.

In its classic presentation, the cluster headache (Horton's headache or histaminic cephalalgia) is a distinctive headache syndrome characterized by one to several attacks recurring each 24 hours, over several weeks to months, with headache-free periods in between the headache clusters. These headache-free periods may last from months to years. The throbbing, excruciating, unilateral pain almost always occurs over the same orbitotemporal region, and it is associated with ipsilateral scleral injection, lacrimation, nasal stuffiness, and, less often, partial Horner's syndrome. The pain lasts 30 minutes to several hours; it occurs at any time of the day and night, but onset one to two hours after falling asleep is very common (coincidental with rapid eye movement sleep).[1] Prodrome, scintillations, emesis, and focal motor and sensory symptoms are absent. Male patients suffer these headaches five to ten times as often as female patients. It is nonfamilial. Persons of all ages are afflicted with cluster headaches, but the range between 20 and 50 years predominates. All races are represented.[2] Although many patients experience their clusters at the same time of the year, all seasons seem to be associated.

A universal characteristic is that alcohol intake precipitates a cluster headache if the person is in the midst of his cluster, but the alcohol will not have this effect if the person is between clusters. Sublingual nitroglycerin[3] and subcutaneously injected histamine[4] have similar provocative effects. Alcohol dilates arteries, and most authorities agree that the cluster headache pain is due to dilatation of various areas of the carotid arterial tree.[5] Oxygen inhalation had been suggested anecdotedly as an occasionally helpful therapy in recent decades.[6] Inhalation of 100% oxygen is believed to relieve pain in cluster headache by causing arterial constriction, thus reducing arterial blood flow

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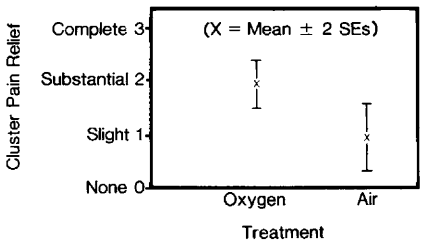
From the Department of Neurology, Southern California Permanent Medical Group, Panorama City, and the Department of Neurology, UCLA School of Medicine.

Reprint requests to Department of Neurology, Southern California Permanente Medical Group, 13652 Cantara St, Panorama City, CA 91402 (Dr Fogan).



Averaged degrees of pain relief experienced by patients with oxygen and air inhalation.

intracranially.[7] Kudrow[8] found oxygen inhalation highly successful in treating randomly selected cluster headache sufferers. He found it to be beneficial in a second cluster headache population in whom the effectiveness of oxygen inhalation and sublingual ergotamine tartrate was compared in a crossover-designed study.[8]

This communication is offered as an extension of Kudrow's research. In his study the following were not ruled out as factors in the headache relief and treatment success: the possible effects of the pressurized gas flow itself, the breathing mask, and the focus of the patients' attention on their own breathing. Our study incorporates the methodologic techniques of the double-blind approach in the use of air and oxygen.

PATIENTS AND METHODS

Between Jan 1, 1980, and Dec 31, 1982, 19 men aged 20 through 50 years, who suffered from cluster headaches as defined by the Ad Hoc Committee on Classification of Headache (1962),[9] formally consented to participate in this study. I examined each man and then they were immediately directed to the inhalation department of our medical facility. That department randomly assigned each patient a special study-coded "E"-size portable gas cylinder. These cylinders were of uniform shape, size, and color. They contained either 100% medically pure oxygen or compressed room air. Both gases are odorless, tasteless, and colorless. The cylinder contents could be differentiated by the cylinder's serial number only. The type of cylinder assigned was recorded and known only to the inhalation department. The patients and I were unaware of the cylinder contents until the conclusion of the study. Each patient was instructed that at the onset of his cluster headache, he was to breathe at a normal respiratory rate via a nonrebreathing face mask, at a flow of 6 L/min, for up to 15 minutes. If the headache continued beyond that time, he was to turn off the tank. Only at that point was he allowed to take a relatively short-acting analgesic if relief had not been achieved. He was instructed to complete a questionnaire for each headache treated concerning the following facts: the date, the time (to the minute) of the headache's onset, the time he first breathed from the cylinder, the time he first noted any effect on the intensity of the pain, if any, and the time he stopped the gas flow. He also recorded the quality of headache relief by indicating no relief, slight relief only, substantial relief, or complete relief.

The primary outcome criteria of the study were the patients' subjective evaluation of cluster headache pain relief; this relief was scored 0 for no relief, 1 for slight relief, 2 for substantial relief, and 3 for complete relief. This score was averaged over all headaches for the oxygen treatments and for the air treatments separately, thus yielding a summary score of the relief reflecting each patient's experience.

Patients were instructed not to take any headache prophylactic medications during the study, and they were not to take any other type of medications, unless these were cleared by me.

After a maximum of six individual cluster headaches were treated and reported as described above, the cylinder was returned to the inhalation department. A cylinder containing the other gas (air or oxygen) was then appropriately dispensed. The patient was instructed to carry out the same method of treatment for another maximum of six cluster headaches and to record the information in a similar fashion.

All report forms were returned to me. The patient was then allowed to choose to continue treating his cluster headaches with either the first or the second cylinder; this constituted the second phase of the study.

RESULTS

The study was designed to enable the patients to be crossed over (blindly) to the alternative cylinder. Six of the 19 patients' clusters ended before the study period ceased, but these six did produce valid data (two patients receiving air and four, oxygen). Another two patients were mistakenly given the same gas twice, and so an additional patient was exposed only to air and one only to oxygen. Eleven patients evaluated both gases.

To avoid losing the data on eight of the 19 patients, I used a general mixed-model analysis-of-variance program[10] to compute a maximum likelihood F ratio for this experiment. The test found a highly statistically significant difference between the relief scores of the air and oxygen treatments ($P < .01$, $F = 11.50$, $df = 1, 19$).

The Table lists each patient's experience in the study. Most perceived effects from one gas that often overlapped the effects of the other gas; but nine (56%) of the 16 who breathed oxygen perceived complete or substantial relief with the oxygen in 80% or more of their cluster headaches. Only one (7%) of the 14 patients who breathed air was similarly benefited. The average (±SE) relief score with oxygen was 1.93 ± 0.22 out of a possible 3.0, and it was 0.77 ± 0.23 with air (Figure).

Five patients of the 19 elected to continue in phase 2 of the study. All five selected the oxygen cylinder in a blind fashion. Complete details on each patient can be provided to any interested reader.

COMMENT

The cause and mechanism of cluster headache are, to date, speculative. Intracranial and extracranial arterial dilatation seems to occur during the cluster pain, but the reason is unknown. Oxygen constricts these vessels and decreases the flow therein. This knowledge supports the rationale for oxygen inhalation therapy for the individual headache.

This double-blind controlled investigation, using patients as their own controls, shows that oxygen inhalation can be a highly successful treatment for the individual painful cluster headache; its benefits clearly are superior to those of inhalation of compressed air. The study effectively rules out the likelihood that merely the act of breathing pressurized air, the effects of a face mask, or the effects of focusing the patient's attention on his breathing is the reason for the success of oxygen in previous reports.

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