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Cold room air inhalation to abort cluster headaches: an exploratory study

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Abstract Research has shown that inhalation of pure oxygen is effective in aborting cluster headache. This article advances the hypothesis that cooling is the critical ingredient behind the effectiveness of oxygen inhalation, rather than the oxygen concentration. To test this hypothesis, eight cluster headache participants used a device that delivered cooled room air as a means to abort headache attacks. Additionally, six of the subjects administered pure oxygen so that comparisons could be made to the air-cooling device. The proportion of cases in which subjects attained effective relief from cluster headache pain by use of the air-cooling device was significantly higher than the proportion of cases in which subjects did not attain effective relief from headache pain. There was no significant difference between the proportion of headaches relieved by oxygen and the proportion of headaches relieved by the air-cooling device. This study raises questions about the mechanisms of action of oxygen inhalation for treating cluster headache, and indicates that future clinical investigations into the use of cold room air for treating cluster headache pain are warranted.

Key words Cluster headache • Oxygen • Cold room air

Introduction

Drawing upon the promising initial findings of Horton [1] and Friedman and Mikropoulus [2], Kudrow [3] conducted a controlled crossover investigation to compare the effectiveness of 100% oxygen inhalation and sublingual ergotamine tartrate in the relief of cluster headache symptoms. Eighty-two percent of patients who used oxygen and 70% of patients who used ergotamine tartrate obtained headache relief. This difference was not statistically significant. Within the 15-minute treatment period, oxygen and ergotamine tartrate produced a similar rate of relief. However, the peak response to oxygen inhalation was within 6 minutes, while the peak response to ergotamine tartrate was 10–12 minutes. According to Kudrow [4], this suggests oxygen deficiency as a factor in the cause of cluster headache.

In 1985, Fogan [5] conducted a follow-up study to confirm that Kudrow's success in relieving cluster headache pain resulted from 100% oxygen inhalation and not from: (1) the effects of breathing pressurized gas, (2) an increased focus on breathing, and (3) the breathing mask. Fogan investigated 19 male subjects in a double-blind crossover study that compared 100% oxygen inhalation and compressed room air inhalation, each administered by mask for 15 minutes at 6 liters per minute through six headache attacks. Fogan found a significant difference between the relief scores for 100% oxygen (56%) and compressed room air (7%).

After years of research and study, the exact cause of cluster headache remains unknown and new treatments continue to be developed [6–8]. Since 1968 the use of 100% oxygen has become a somewhat standard treatment. Yet, why 100% oxygen aborts cluster headaches remains uncertain.

During the preparatory stages for this investigation, it was noted that oxygen in the presence of moisture causes a sizeable drop in temperature. A 122-cm length of standard diameter oxygen tubing was dipped in water. The water was then drained out of the tubing, leaving only the moisture that adhered to the wall of the tubing. When the proximal end of the tubing was connected to a tank delivering 100% oxygen at 7 liters per minute, the temperature at the distal end of the tubing dropped 6.7° C in less than 30 seconds. In another trial, a moist gauze sponge was held at the distal end of a 46-cm length of standard diameter oxygen tubing. In this uncontained environment, 94% oxygen at 4 liters per minute caused a temperature drop of 11.1° C in less than two minutes.

When oxygen is used to abort cluster headaches, the oxygen flows over moist membranes. Cold temperatures will cause blood vessels to constrict. Is it pure oxygen or a local cooling that accounts for the headache relief? This exploratory study was designed to address this question.

Subjects and methods

Subjects

Seven men and three women, ranging in age from 39 years to 71 years, volunteered. Subjects had diagnoses of cluster headache, according to the International Headache Society classification [9], upon interview by a registered nurse and confirmation by treating physicians. Additionally, cluster headache attacks had to exceed 15 minutes in duration [10]. Five subjects experienced episodic headaches and all were in an active cluster phase; the remaining five reported chronic headaches. The University of West Florida (UWF) Institutional Review Board approved this study, and informed consent was obtained from each subject prior to participation.

Apparatus

A cold-air device was developed to deliver room air cooled to approximately 5° C to a non-rebreathing mask at 6 liters/minute. Subjects were given a device, provided with detailed instructions for use, and then were observed during a nonheadache state to verify proper application. During actual treatment, subjects operated the devices themselves in their homes, absent of investigator supervision.

Procedure

Subjects were asked to refrain from all medication prior to each study trial. They were informed that the investigation was examining the efficacy of a less cumbersome, safer, and less expensive alternative to oxygen inhalation and chemical therapy for aborting cluster headache attacks.

When headache pain reached a "moderate" level [10], subjects placed the device on a table, sat upright in a chair, affixed the mask, and breathed the cool air from the device. Subjects inhaled only slightly more deeply than normally and at their normal breathing rate. Subjects continued to breathe the cool air for 15 minutes or until the headache was aborted. After 15 minutes, if the headache continued, the subjects were then allowed to use their usual headache relief method.

Subjects rated their level of relief in a headache diary, using a scale that ranged from 0 to 3, where 0 was labeled as "no or minimal relief", 1 was "slight relief", 2 indicated "substantial relief", and 3 corresponded to "complete relief." Subjects recorded the time of headache onset, the time treatment was initiated, the time when a change in headache relief was detected and the corresponding relief rating. After treating 10 headache attacks, subjects returned their diaries and devices to the investigators. Subjects treated no more than two headache episodes on a given day.

Six of the subjects had previously used oxygen to obtain headache relief. After completion of all data collection with the cold-air device, these subjects were approached and asked to continue data collection to evaluate the effectiveness of oxygen therapy for their next five cluster headache attacks (they were not informed of this possibility in advance). All agreed to do so. This allowed the investigators to conduct a quasi comparison between the two different treatment conditions.

Results and discussion

During the study, two subjects had to be excluded. One man with episodic cluster headache went into remission; another man, who experienced chronic cluster headache, decided to remain on his current pain control regimen. Data from the 8 remaining subjects were analyzed to determine the proportion of cases in which varied degrees of relief were obtained (Table 1).

The cold room air device provided significant relief (combining relief categories 2 and 3) in 85% of the cluster headache attacks and only slight to no relief in 15% of evaluated attacks (z=5.162; p<0.0005).

Results for oxygen therapy were similar. The therapy was effective in 83% of the cluster headache attacks and ineffective in 17% (z=5.10; p<0.0005).

For the 68 observations in which cold room air was effective (out of 80 total possible), the mean relief score was 2.69. For the 25 observations in which oxygen was effective (out of 30 total possible), the mean relief score was nearly identical (2.72). A two-tailed t test indicated that the difference between the two means was not statistically significant (t=.073, df=91).

Table 1 Relief of cluster headache by cold room air and 100% oxigen. A total of 8 subjects recorded the degree of pain relief provided by cold room air during 10 episodes of cluster headache; 6 of the subjects subsequently reported the relief afforded by 100% oxygen during 5 further attacks. Values are numbers of attacks relieved

	Degree of relief[a]							
	Cold room air				100% oxygen			
Subject	0	1	2	3	0	1	2	3
1	0	6	4	0	0	4	1	0
2	0	0	0	10	0	0	0	5
3	0	1	0	9	0	0	0	5
4	0	0	2	8	0	0	0	5
5	0	2	8	0	0	0	2	3
6	0	0	0	10	–	–	–	–
7	0	3	7	0	0	1	4	0
8	0	0	2	8	–	–	–	–
Total	0	12	23	45	0	5	7	18
Percentage	0%	15.0%	28.8%	56.3%	0%	16.7%	23.3%	60.0%

[a] Degree of relief: 0, No or minimal relief; 1, slight relief; 2, substantial relief; 3, complete relief

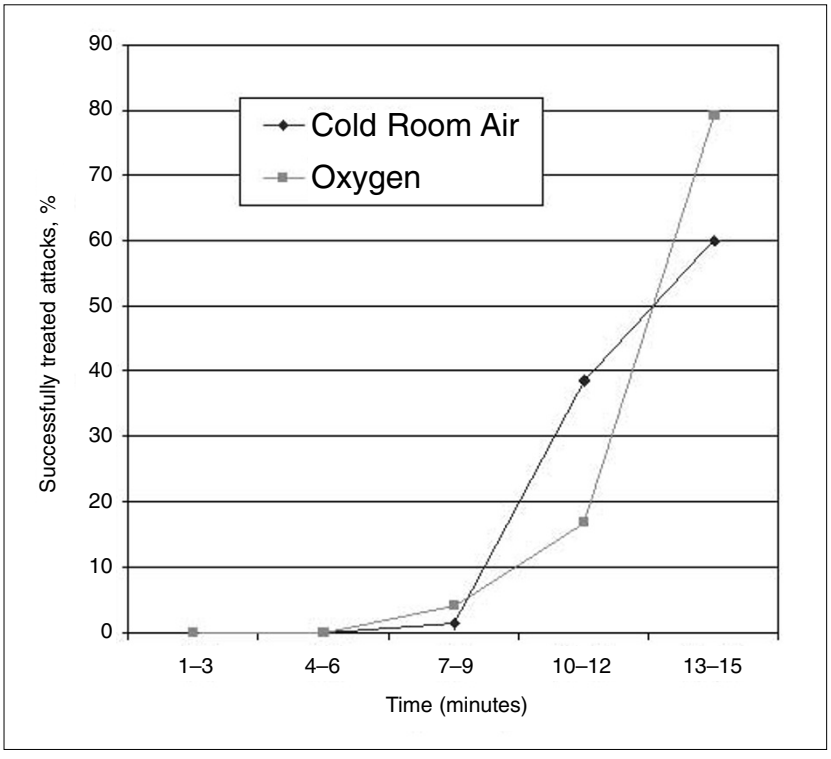

Fig. 1 Time to achieve significant improvement (relief rating, 2–3), reflected as a percentage of all successfully treated attacks

The time required for significant pain relief (a rating of either 2 or 3) with cold room air treatment varied from 6 to 15 minutes. The response rate for oxygen treatment varied from 7 to 15 minutes. Overall, the headache relief patterns for cold room air and oxygen were similar (Fig. 1). No subjects reported the occurrence of rebound cluster headache attacks.

In contrast to Fogan's study [5] that indicated a significant difference between the relief scores of 100% oxygen and compressed room air, this study suggests that room air

can be effective in relieving the pain of cluster headache, if chilled. There was no significant difference in level of relief scores, suggesting that it is the cold temperature and not the pure oxygen that provides relief of cluster headache pain. These encouraging but preliminary findings indicate that further clinical investigations into the use of cold room air as a viable treatment for cluster headache attacks are warranted. In this work, sample sizes should be increased and the treatments being compared should be alternated to guard against order and sequence effects.

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