
Research Submission

Inhaled Oxygen and Cluster Headache Sufferers in the United States: Use, Efficacy and Economics: Results From the United States Cluster Headache Survey

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Objective.—To present results from the United States Cluster Headache Survey concerning the use of inhaled oxygen as acute treatment for cluster headache (CH).

Background.—Several small clinic and community-based investigations have indicated that more than 50% of CH patients have never used oxygen for the treatment of their headaches. This statistic is alarming and the reasons why they have not tried oxygen have not been determined.

Methods.—The United States Cluster Headache Survey is the largest study ever completed looking at CH sufferers living in the United States. The total survey consisted of 187 multiple choice questions, 84 questions dealt with oxygen use, efficacy and economics. The survey was placed on a website from October to December 2008.

Results.—A total of 1134 individuals completed the survey (816 male, 318 female). Among them 868 patients had episodic CH while 266 had chronic CH. Ninety-three percent of survey responders were aware of oxygen as a CH therapy; however, 34% had never tried oxygen. Forty-four percent of patients had to suggest oxygen to their physicians to get prescribed. Twelve percent of physicians refused to prescribe oxygen. Fifty percent using oxygen never received training on proper use. Forty-five percent had to find their own source for oxygen. On prescriptions only 45% specified flow rate, 50% stated CH as diagnosis and 28% indicated mask type. Seventy percent of the surveyed population felt oxygen was effective but only 25% was presently using oxygen. Potential reasons for this finding include: oxygen is slow to onset; prescribed oxygen flow rates are too low for efficacy and most CH patients need to raise flow rates during attacks to achieve response. The efficacy of oxygen does not vary by the age of the patient, gender, the number of CH attacks per day, and smoking history. Episodic CH responds better and faster to inhaled oxygen than chronic CH. Oxygen plus a triptan may be more efficacious and faster at aborting a CH than a triptan alone. Sixteen percent of CH patients state that oxygen is unaffordable while 12% are getting welder grade oxygen because of costs of medical grade oxygen, and this form of oxygen could be potentially dangerous to the individual user.

Conclusions.—Oxygen is underutilized by CH patients living in the United States. Current recommended oxygen treatment regime is not meeting the needs of many CH patients. Prescribed oxygen flow rates are too low for efficacy. Oxygen can be expensive and very difficult to obtain. Physicians need to be better educated on the use of inhaled oxygen for CH.

Key words: cluster headache, oxygen, medical cost, acute treatment

Abbreviations: CH cluster headache, DHE dihydroergotamine

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Cluster headache (CH) is a primary headache disorder marked by excruciating attacks of short lived one-sided head pain with associated autonomic features. It is felt to be one of the most severe headache conditions that humans experience. Oxygen inhalation therapy is recognized as one of the 2 most effective abortive treatments for CH outside of injectable sumatriptan.¹ Oxygen therapy was first proposed for CH by Bayard Horton in the 1950s² and was made a mainstream treatment for CH by Kudrow in the early 1980s.³ For many years the recommended inhaled oxygen flow rate for acute CH treatment was 7 liters per minute (L/minute). Recently, the first randomized placebo-controlled study of high flow oxygen at a rate of 12 L/minute was completed showing statistically significant improvement over placebo.⁴ Other studies have shown efficacy up to 15 L/minute in CH patients who did not respond at lower flow rates.⁵ Presently, inhaled oxygen given via a non-rebreather face mask at rates of 7 to 12 liters per minute for 20 minutes is the recommended dosing schedule and delivery system for acute CH treatment. As many CH sufferers have significant cardiovascular risk factors and thus may develop contraindications to the use of triptans, inhaled oxygen is an extremely valuable treatment tool for this primary headache syndrome. The high number of CH patients who present to dedicated headache clinics having never tried oxygen therapy is surprising. Equally surprising is if they have utilized oxygen, it was given via a nasal cannula or at a delivery flow rate below what is suggested. At present we have no published data on the use of inhaled oxygen in any large CH population and specifically nothing from the United States. The goal of this present study was to abstract data from the United States Cluster Headache Survey, the largest survey ever completed looking at CH patients living in the United States, to better understand oxygen usage by this population.⁶ Questions that were looked at included: What is the percentage of CH patients who have actually tried oxygen therapy? What is actually being prescribed to CH patients by physicians? What is the efficacy of oxygen therapy? And what is the financial cost of oxygen therapy for CH patients?

METHODS

Author RF originally conceived the United States Cluster Headache Survey, and author TDR was asked to contribute as a headache specialist. The questions were then developed and finalized by both authors with input from directors and members of the US Organization for the Understanding of Cluster Headache (OUCH), of whom all were CH sufferers themselves. The survey was tested with randomly selected episodic and chronic CH sufferers of different ages and gender who were members of OUCH prior to finalization and implementation. Previous surveys of CH patients in the literature were evaluated for their deficiencies and unaddressed key questions. The survey questions were structured to be mutually validating and amenable for cross tabulation. The survey was simultaneously promoted on the internet by US OUCH and clusterheadaches.com on their respective websites, by a dedicated survey web page promotion linked to searches using the phrases “cluster headache” and “cluster headache therapies” and by search advertising promotions on other key headache therapy websites. In parallel, the survey was promoted by the American Headache Society in its monthly newsletter to member neurologists, a mailing to leading headache neurologists and clinics in the United States using the American Headache Society and the American Medical Association neurologist headache specialist lists asking physicians to suggest that their CH patients participate in the survey, and issuance of approximately 9000 emails by US OUCH and clusterheadache.com to their website users. Surveys were completed on a first come, first serve basis and were thus accumulated on a randomized basis from interested participating sufferers. The resulting survey results were not dominated by any one geographic area, one specific medical practice or one type of medical practice. Only patients who were diagnosed with CH by a neurologist were able to complete the survey. The diagnosis of CH was not validated by the authors. The total survey consisted of 187 multiple choice questions of which 84 questions dealt specifically with oxygen usage, efficacy and economics. The survey was placed on an internet website from October 12, 2008 to December 2008. Only fully completed surveys were included in the data analysis.

Incomplete surveys were automatically rejected by the survey service computer. The study was approved and given exempt status by the Geisinger IRB.

Statistical Analysis.—The service that programmed the survey, tabulated the results and established statistical validity was InfoSurv in Atlanta, GA, USA. The direct and cross-tabulated results were then analyzed by author TDR. When statistical analysis was warranted the Fisher's exact test or the chi-square test was used for categorical data. Statistical significance was defined as $P < .05$. All P values were 2-tailed. SPSS software package for Windows version 18 (Chicago, IL, USA) was used for statistical analysis.

RESULTS

A total of 1134 individuals completed the survey. There were 816 male responders and 318 female responders. Among them 868 patients had episodic CH while 266 had chronic CH. Ages of survey responders were as follows: less than 20 years (7 responders), 21-30 years (137 responders), 31-40 years (311 responders), 41-50 years (384 responders), 51-60 years (238 responders), and 61 years plus (57 responders). Every state was represented in the survey.

A. Oxygen Usage.—Ninety-three percent of the surveyed patients were aware of oxygen being an acute therapy for CH; however, 34% had never tried oxygen. The younger the age of the CH patient the less likely they were to have tried oxygen. Seventy-one percent of those surveyed who were under the age of 20 years had never tried oxygen therapy vs only 24% of those who are currently between 51 and 60 years of age. Only 50% of the surveyed population had tried oxygen alone to abort a CH. In addition, only 25% were currently using oxygen as a sole abortive greater than 80% of the time. Of those who had utilized oxygen 81% stated oxygen was started as acute treatment for their CH months to years after the initial diagnosis of CH was made. At the time of the survey only 25% of CH patients were using oxygen to treat their CH.

B. Who Prescribed Oxygen and Reasons Why Oxygen Was Never Prescribed.—There was an equal distribution (28% each) of physician type (general practitioner, general neurologist, headache specialist)

who initially prescribed oxygen. Forty-four percent of the surveyed patients had to first suggest oxygen therapy to their physician to get it prescribed. About 12% of physicians refused to prescribe oxygen for their CH patients. Reasons cited included: did not believe it would work (44%), did not know that oxygen was used to treat CH (32%), and stated that the medical literature was not convincing enough to prescribe oxygen (16%).

C. Prescribing Patterns for Oxygen.—Fifty percent of the survey responders stated that when oxygen was prescribed to them for the first time they received no information on how to conduct or perform oxygen therapy. If they did get some training only 15% received it from their treating physician while 44% received instruction from a home care/oxygen delivery service. On the prescription itself only 45% of prescribers specified a specific flow rate for oxygen. Only 50% of the prescriptions noted CH as the diagnosis and only 28% specified a specific delivery system/mask type. Once prescribed only 55% of patients were told by their physicians where to go to get their oxygen. The remainder used the phone book, internet or found out how to obtain oxygen from peers who had CH. More than 50% of survey responders stated that it was difficult to actually find a source for their oxygen.

D. Oxygen Delivery Systems Prescribed.—About 11% of patients were using a nasal cannula to deliver oxygen while 29% were using a face mask without a non-rebreather bag system. Only 53% were actually using the preferred non-rebreather face mask system. Seven percent were not using a mask or cannula although what was being used was not specified.

E. Oxygen Flow Rates Utilized.—The oxygen flow rates that were initially prescribed to the patients by physicians were as follows: 7 L/minute 23%, 8 to 12 L/minute 51%, 13 to 15 L/minute 18%, and 16 L/minute and above 8%. The surveyed patients did not always adhere to the initial prescribed oxygen flow rates as 17% used 7 L/minute, 25% used 8 to 12 L/minute, 25% used 13 to 15 L/minute and 13% used 16 L/minute or greater. In regard to current oxygen flow rates being used by survey responders during an individual CH attack: 41% start and 34% end using 7-10 L/minute, 17% start and 14% end using 11-12 L/

minute while 28% start and 52% end using 13 L/minute or higher flow rates (Table 1). Most CH patients will raise oxygen flow rates during CH treatment to try to achieve complete relief from pain.

F. Efficacy of Inhaled Oxygen (Table 2).—Seventy percent of survey responders stated that inhaled oxygen was an effective treatment for their CH. Oxygen effectiveness did not vary by age class: ages 21-30 years (70% stated effective), ages 31-40 years (73% stated effective), ages 41-50 years (70% stated effective), ages 51-60 years (69% stated effective), and ages 61 plus years (67% stated effective). Under age 20 years oxygen was 100% effective but only 2 individuals answered this survey question so not a significant result. The efficacy of oxygen appeared to be fairly consistent regardless of the number of CH attacks per day: 69% of patients with 1-2 attacks per day stated oxygen was effective vs 72% of those with 7-8 attacks per day. The highest efficacy was in those with 5 to 6 attacks per day (75% stated efficacious) but there was no statistical significance difference in the number of attacks per day and response to oxygen. In regard to the time on inhaled oxygen (whatever flow rate that patient would individually utilize) to have complete relief of CH pain: 17% stated between one and 10 minutes, 34% between 11 and 20 minutes, 22% between 21 and 40 minutes, and 27% over 40 minutes. Thus, in 49% of patients oxygen took 21 minutes or longer to provide complete head pain relief. The CH patients at the extremes of age seemed to have a faster response to inhaled oxygen as the largest percentage of patients aged 21-30 years and 61 plus years could fully abort a CH within 6-10

Table 1.—Starting and Ending Oxygen Flow Rates for Cluster Headache Attacks

	7 L/minute	8-12 L/minute	13 L/minute or Higher
Starting flow rate during CH attack	41%	17%	28%
Ending flow rate during CH attack	34%	14%	52%

CH = cluster headache.

Table 2.—Efficacy of Inhaled Oxygen

Category	% Stating Effective	P Value or Non-Significant (NS)
Total population	70	
Age class in years		
21-30	70	
31-40	73	NS
51-60	69	
61 plus	67	
CH attacks/day		
1-2	69	
3-4	71	
5-6	75	NS
7-8	72	
CH subtype		
Episodic CH	73	<.006
Chronic CH	62	
Gender		
Male	70	NS
Female	72	

CH = cluster headache.

minutes after oxygen initiation compared to those aged 31 to 60 years who needed on average 11 to 15 minutes to abort a CH. Only one patient under age 20 responded to this survey question so the number is too small to interpret. The majority of surveyed CH patients (75%) do not use oxygen alone to abort a CH attack. Only 25% use oxygen as a sole abortive greater than 80% of the time. If oxygen is used with another abortive medication (triptans or dihydroergotamine [DHE] or other) over half (55%) will use the additional abortive when they realize that oxygen will not take away that particular headache, while 38% will take the other abortive before using oxygen. When using oxygen plus another abortive 52% of survey responders will have complete headache relief within 20 minutes of taking the combined abortives while only 13% need more than 45 minutes to have relief compared with 27% when using oxygen alone. Interestingly, 37% of the surveyed patients had complete relief of their CH within 15 minutes of using combined treatment vs only 28% when a non-oxygen abortive was used alone. The abortives that were used in combination with inhaled oxygen included: injectable sumatriptan 36%, triptan nasal spray (sumatriptan or zolmitriptan) 12%, oral triptan (sumatriptan,

zolmitriptan, rizatriptan) 18%, DHE 2% and other non-specified abortive 32%.

G. Cluster Headache Subtype and Oxygen.—

There were some differences in oxygen response between episodic and chronic CH patients. Seventy-three percent of episodic CH patients stated that inhaled oxygen was effective vs 62% of chronic CH patients and this was a statistically significant difference ($P < .006$). Thirty-six percent of episodic CH patients had never tried oxygen vs 28% of chronic CH patients. Chronic CH patients were more likely to be currently using oxygen to treat CH (34%) than episodic CH patients who were in an active cycle (23%). Patients with episodic CH seem to get complete relief of CH faster with inhaled oxygen than chronic CH patients as 38% of episodic CH patients had complete pain relief within 15 minutes of oxygen treatment vs 28% of chronic CH patients which is a statistically significant difference ($P < .02$).

H. Gender and Oxygen.—Almost the same percentage of male and female CH patients stated that oxygen was an effective therapy (70% vs 72%). Male CH patients appear to respond faster to inhaled oxygen than female CH patients. Nineteen percent of male CH patients had complete relief of a CH on oxygen after 10 minutes or less of treatment vs 11% of the female CH patients surveyed and this was a statistically significant difference ($P < .05$). Fifty-one percent of female CH patients start with oxygen flow rates of 7 to 10 L/minute while 45% of men start at 13 L/minute or higher, and thus this may have led to faster response times in men.

I. Smoking History and Oxygen.—Smoking history did not appear to alter the effectiveness of inhaled oxygen. Seventy-eight percent of surveyed patients who had no personal smoking history and no secondhand smoke exposure from their parents stated that oxygen was effective compared to 70% of the entire population surveyed as a whole of which 73% had a personal smoking history. Of current oxygen users 96% of patients with a smoking history stated oxygen was an effective abortive vs 97% of non-smoking patients.

J. Economics of Oxygen Usage.—In regard to the costs of oxygen therapy for CH, 65% of surveyed patients stated that their costs were under \$1000 per

year, while 31% had costs between \$1000 and \$6000 per year and 2.5% of the surveyed population spent between \$8000 and \$12,000 per year on oxygen. These costs were before reimbursement from insurance. Complete out of pocket expense after insurance reimbursement showed the majority (87%) spent under \$1000 per year, while 13% spent between \$1000 and \$12,000 per year.

At present 64% of survey responders stated that their medical insurance covers oxygen therapy for CH. Seventy-six percent of the same surveyed group stated that injectable sumatriptan is covered by their insurance. Sixty-one percent noted that it was not difficult to get reimbursement from their insurance carrier for oxygen, while 7% stated it was very difficult. In order to get reimbursement 44% stated that the patient or their physician had to submit medical literature to the insurance carrier. Fifty-one percent of the CH patients in the United States stated they can easily afford their oxygen while 16% stated it is unaffordable. Twelve percent stated they have purchased non-medical grade oxygen (welders or research grade) and the main reasons for doing this were: that the non-medical grade oxygen was a lower cost than commercial grade oxygen (66%), cannot afford to go to the doctor to get a prescription for oxygen (22%), and my physician will not prescribe oxygen (18%).

DISCUSSION

Inhaled normobaric oxygen has been recognized as an effective acute treatment for CH for about 50 years but its actual use in CH patients in the general population outside of dedicated headache centers has never been truly determined.² CH is such a severe condition that if patients do not have adequate acute treatment they can develop suicidal ideations and some individuals will act on these thoughts. Inhaled oxygen is an essential acute therapy for CH patients not only because it is effective, but in many instances CH patients who are known heavy cigarette smokers will eventually develop medical contraindications to the other primary CH abortives triptans and DHE, thus leaving oxygen as a sole abortive choice. In addition, because prescribing information limits the use of injectable sumatriptan to 2 doses per day due to

potential adverse reactions and 53% of survey respondents report more than 2 CH attacks per day,⁶ the need exists for an abortive such as oxygen that can be safely used for as many attacks per day as a sufferer may have. Several small clinic and community-based investigations have indicated that more than 50% of CH patients have never used oxygen for the treatment of their headaches.^{7,8} This statistic is alarming and the reasons why they have not tried oxygen have never been determined. To date, we have no large population-based studies looking at CH and inhaled oxygen usage. The United States Cluster Headache Survey is the largest study ever completed looking at CH sufferers living in the United States. A large percentage of the survey was dedicated to questions about inhaled oxygen and its overall usage, efficacy, prescribing characteristics and costs. The survey responders were from a selected population drawn from CH support groups and treating physicians. This type of epidemiologic investigation has been done previously by Bahra et al⁷ in a mostly UK investigation but the present study is novel based on its size of the studied CH population and its focus on oxygen therapy. The data are important not only for treating physicians and CH patients but also for the governmental agencies (Centers for Medicare and Medicaid Services) who are currently now reviewing if oxygen should garner a specific reimbursement code for CH treatment.

Greater than 90% of CH sufferers living in the United States are aware that oxygen is an acute treatment for CH but one-third of the population has never tried oxygen. Several reasons for this fact can be deemed from this study. First, 12% of the survey patients' physicians are refusing to prescribe oxygen therapy for their CH patients. Almost 50% stated they do not believe oxygen works for CH. This may reflect their prescription patterns for oxygen which in many instances are not the recommended treatment protocol (delivery system or flow rate) and thus would not lead to a positive abortive effect. CH patients are still being prescribed nasal cannula as a delivery system instead of a non-rebreather face mask and are being prescribed too low of flow rates and are not being told to increase the flow rates if the lower flow rates are not effective. One-third of physi-

cians are not prescribing oxygen for CH patients because they did not know this was actually a therapy for CH, perhaps indicative of a problem with physician instruction during their training. In defense of academic neurology there are very few lectures given to neurology residents and other medical trainees dedicated to headache alone and as CH is somewhat rare it may be omitted from these lectures altogether. Unfortunately, this may affect patient care. Part of the resistance to prescribe oxygen, or the lack of recognition of oxygen's usefulness in CH, by physicians could relate to the deficiency of placebo-controlled trials with inhaled oxygen in the medical literature. This has recently changed, however, with the study by Cohen et al⁴ published in JAMA in late 2009, which noted statistically significant improvement in CH with high flow oxygen vs placebo. The present survey was completed prior to the publication of this trial, and thus how it will affect physician prescribing patterns in the future is unknown. For most CH patients, oxygen, if prescribed, is not given for months to years after the initial diagnosis of CH is made. This again may reflect the lack of awareness of oxygen as a treatment or the lack of belief that oxygen actually works in CH by the physicians treating these patients. Almost half of the surveyed patients had to first suggest oxygen as a treatment to their physicians. Interestingly, the younger the CH patient the less likely they are to have utilized oxygen, which is opposite of what one would think as newer physicians in training should be more aware of inhaled oxygen as CH treatment although as stated above that may not be the case. This may also reflect the fact that younger CH patients are not seeking out medical care for their CH. Seventy-one percent of the survey patients under the age of 20 years are not currently seeing a neurologist. Second, oxygen may actually get prescribed to patients but multiple barriers have been set up that precludes them from actually getting the oxygen. More than 50% of survey responders stated that it was difficult to actually find a source for their oxygen. In addition, 45% received no information about a source for oxygen from their prescribing physician. If a CH patient is able to find a source for oxygen in most instances, their prescriptions are not complete lacking a prescribed flow rate or delivery system, and

thus they may not be able to obtain the oxygen because of incomplete prescription data. Additionally, as the majority of CH patients are given no instruction on oxygen utilization, they may be too apprehensive to have an oxygen tank in their home or place of work with no idea what to do with that tank. Finally, cost presumably is a reason behind the low oxygen utilization rates, as 16% of the surveyed population stated that oxygen was unaffordable.

In regard to the effectiveness of inhaled oxygen for CH, the majority of patients (70%) felt it was helpful. This percentage matches up well with other studies, both open label and placebo-controlled trials looking at oxygen treatment for CH.^{3,4,7} From the survey results inhaled oxygen efficacy does not appear to vary by patient age, the number of CH attacks per day and smoking history. Very few studies have looked at oxygen response and CH subtype and gender. In the present study, patients with episodic CH statistically had higher efficacy rates with inhaled oxygen than chronic CH patients. In addition, episodic CH patients statistically responded faster to oxygen than chronic CH patients. Kudrow's³ original study on inhaled oxygen also noted less effectiveness in chronic CH patients than in episodic CH patients. Schürks et al⁹ looking at 246 clinic and non-clinic based CH patients noted a higher efficacy of inhaled oxygen in episodic CH patients vs chronic CH patients but this was not a statistically significant difference. Oxygen flow rates utilized were not documented in the manuscript. The cause of the probable greater efficacy of inhaled oxygen in episodic CH patients is unknown. Chronic CH patients are more likely to be smokers so that could be a potential cause of lack of oxygen effect, but in the present survey smokers and non-smokers had equal efficacy to inhaled oxygen.¹⁰ In another headache clinic study, it was found that smokers actually responded better to oxygen than non-smokers.¹¹ Chronic CH patients as a whole may respond less to CH abortives than episodic CH patients as this trend was also noted in a large placebo-controlled trial looking at intranasal zolmitriptan.¹²

Regarding gender, both male and female CH patients had equal efficacy to inhaled oxygen but men

responded faster to oxygen: men were statistically more likely to be pain free after 10 minutes of oxygen therapy compared to women. This finding has not been published previously. Interestingly men used higher flow rates at the outset of attacks than women and that may have led to the faster response times. Rozen et al in 1999¹³ did show in a clinic-based study of CH a gender difference in response to oxygen as only 59% of female cluster patients responded, whereas 87% of men did. This study, however, was with relatively low flow rates of oxygen (7 L/minute), thus a possible reason why women responded less to oxygen than in the present survey study. In Kudrow's landmark study on oxygen, male and female patients showed equal efficacy to inhaled oxygen at 7 L/minute.³ Schürks et al⁹ looking at 246 CH patients noted a higher efficacy of oxygen in female vs male CH patients but this was not a statistically significant difference.

If oxygen is so effective for CH then why are only 25% of the survey responders currently using oxygen and in the ones who are treating with oxygen why are only 25% using it as their sole abortive? This is not the first study to show that even when oxygen is effective for CH, many sufferers do not continue to use it. Gallagher et al in 1996¹⁴ noted in 60 CH patients that 76% responded to oxygen but only 31% continued to utilize oxygen. Several items from the present survey responses may help us better understand this issue. First, oxygen may indeed be helpful for CH but its effectiveness and ease of use just does not compare with other abortive choices like injectable sumatriptan which is very effective, quick to onset and does not require special equipment and a tremendous effort to even locate. Second, the goal of acute CH treatment is fast and effective relief, as the duration of CH is relatively short from 15 to 180 minutes.¹⁵ Overall the CH survey responders suggested that inhaled oxygen is fairly slow to have an abortive effect as 49% noted that they needed over 21 minutes to completely stop a headache. How many of these patients actually had spontaneous resolution of their CH without any effect from oxygen cannot be obtained from the survey data. This relatively long duration to effect may reflect the flow rates that are being prescribed to patients: it is possible the rates are

too low to effectively stop a CH. Seventy-four percent of patients are being prescribed oxygen flow rates of 7 to 12 L/minute. Most CH patients do not follow the prescribed treatment guidelines for oxygen as almost all utilized flow rates higher than those prescribed by their physicians (Table 1). Over 50% of the CH patients end up using flow rates of 13 L/minute or higher for individual CH attacks and almost all patients will raise the flow rate during treatment to achieve efficacy. This survey was completed prior to the recent publication in JAMA of the randomized placebo-controlled trial documenting the efficacy of high flow oxygen for CH using 12 L/minute over placebo (room air).⁷ Thus, our survey results as well as the recent placebo-controlled study suggest that high oxygen flow rates seem almost essential for CH efficacy and possibly faster treatment response times and the old recognized flow rate of 7 L/minute documented by Kudrow in 1981³ in reality is too low for a large percentage of CH patients in the general population. The final reason why patients may not be using oxygen even though it is effective is the costs issue and the difficulty of obtaining oxygen once it is prescribed.

This is the first ever study to look at the economics of oxygen treatment for CH. One-third of the CH population in the United States need to spend more than \$1000 per year on oxygen treatment and a small percent spend upwards of \$12,000 per year. At present only 64% of survey responders state that oxygen is covered in some manner by medical insurance carriers and this compares to 76% coverage for injectable sumatriptan. Even though oxygen has been a recognized treatment for CH for almost half a century, still almost 50% of insurance carriers want medical literature submitted that supports the use of oxygen in CH before it will be approved for use. In many instances by the time the patient does get insurance clearance to use oxygen their cycle is already over and they have suffered unnecessarily. It is still commonplace for insurance companies to ask physicians about blood gas results or pulse oximetry results before oxygen will be approved for use for CH patients as if they were candidates for chronic obstructive pulmonary disease (COPD) respiratory therapy. Of course this has nothing to do with CH

patients who are not using oxygen for hypoxemia. At present 16% of CH patients in the United States cannot afford oxygen therapy, which is a serious issue for a patient population who has been known to take their lives during a CH attack. Twelve percent will get non-medical welding grade oxygen, which could be harmful to the user depending on the gas or gases the cylinder was previously filled with and trace gases still present in the cylinder. In addition, non-medical grade oxygen will definitely be less efficacious.

An interesting and unexpected finding from the survey is that oxygen may actually enhance the efficacy of non-oxygen abortives like triptans or DHE. When oxygen is combined with another abortive more patients have complete pain relief after a shorter duration of time compared to when the triptan or DHE is used alone. Thirty-seven percent of the surveyed patients had complete relief of their CH within 15 minutes of using combined treatment vs only 28% when a non-oxygen abortive was used alone. Of note however only 36% of these patients were using injectable sumatriptan, and thus it would be expected that oral triptan therapy and/or injectable DHE would have a slower time to pain relief than oxygen alone, so we cannot definitively state there is an enhanced treatment effect with oxygen. We are unable to determine from the available data if oxygen improves the response times of injectable sumatriptan alone which would more strongly suggest a treatment enhancing effect. In addition, these are all time estimates by patients who were not using stopwatches to determine true time to pain relief. A specific study looking at oxygen and its effect on non-oxygen CH abortives would need to be completed to substantiate our findings. The present study suggests that there may be a synergistic effect between oxygen and triptans and oxygen and DHE. This has not been previously reported from other CH studies and may change our thinking about using one abortive medication alone to treat an acute attack of CH. Interestingly in Horton's² original description of oxygen for CH he used a combination of oxygen and DHE so maybe an early demonstration of a synergistic effect.

There are certainly several limitations to this study. First, even though this is a good representative sample of CH patients living in the United States it

certainly does not represent every, or nearly every, CH patient residing in this country. The suggested prevalence for CH is 0.4% of the general population, and thus there should be about 1.2 million individuals with CH in the United States and we only have data from 1134 individuals. It is possible, although not probable, that the remaining CH patients in the United States have a completely different response to oxygen, and thus these survey results should be interpreted with that statement in mind. Second, it is possible that the patients who answered the survey are a biased population based on the fact that they frequent CH websites. The survey responders may be more knowledgeable about CH and may even have harder to treat headaches than the general CH population because they search out the web for support and treatment options. On the other hand, as this is probably a more educated CH population, their experience with inhaled oxygen is better defined than those patients who do not have as severe CH and have only dabbled in CH treatment. Thus, the survey may more truly reflect the efficacy of inhaled oxygen and the hardships of obtaining it or getting a physician to prescribe it. Third, the study is lacking diagnostic validation. Even though all study participants had their headache diagnosis made by a neurologist, these medical specialists can still misdiagnose CH. It is possible that a certain percentage of survey responders had other trigeminal autonomic cephalalgias such as paroxysmal hemicrania or even had migraine with cranial autonomic symptoms.¹⁶ A large percentage of survey responders (80%) had never tried indomethacin, thus not ruling out paroxysmal hemicrania as a missed diagnosis. However, of those who did try indomethacin only 15% stated that it had some effect on their headache and less than 2% were currently using it. In regard to the CH subtype diagnosis of chronic vs episodic CH this also lacked diagnostic validation in our study as it was completely responder defined. Thus, any documented distinction between these subgroups in the survey results must be looked at with this issue in mind.

Finally, as this is a CH population from the United States it may only reflect experience with oxygen in this geographic region and the survey results cannot be extrapolated to CH patients world-

wide. The hope is that other large country-based population studies can be done with CH patients to get a true idea of inhaled oxygen efficacy, economics and usage and to see if the results are geographically similar or dissimilar.

CONCLUSION

Several key conclusions can be drawn from our survey:

1. Oxygen is underutilized for CH patients living in the United States.
2. Prescribed oxygen flow rates may be too low for efficacy and truly high flow oxygen of 12 L/minute or higher appears to be required for efficacy in many patients.
3. Oxygen in its current recommended prescribed form of 100% oxygen via a non-rebreather face mask delivered at 7-12 L/minute is not meeting the needs of many CH patients. This is reflected in the low percentage of CH patients using oxygen at all or solely as acute treatment. The potential reasons for this are numerous as based on the survey results. Oxygen is slow to onset compared with injectable sumatriptan. Oxygen, despite its much lower cost than injectable sumatriptan, can still be expensive and is difficult to obtain with sufferers often being left to find their own sources of oxygen.
4. Oxygen efficacy does not appear to vary by the age of the patient, gender, the number of CH attacks per day, and smoking history. Episodic CH responds better and faster to inhaled oxygen than chronic CH.
5. Physicians need to be better educated on the use of inhaled oxygen for CH. There appears to be a true lack of understanding about oxygen's efficacy and what is required to prescribe oxygen. More placebo-controlled studies looking at the efficacy of inhaled oxygen would certainly enhance physician acceptance of this treatment strategy.
6. Headache specialists and neurologists need to know that patients are pushing oxygen flow rates regardless of what is on their prescription and they are combining abortives to get better efficacy.

7. Oxygen plus a triptan or DHE may be more efficacious and faster at aborting a CH than a triptan or DHE alone. Thus, if a triptan is not very effective for a CH patient combining treatments with oxygen may make treatment response improved.
8. Medical insurance carriers need to recognize that inhaled oxygen is an effective treatment for CH and they need to make the process to obtain oxygen easier and more streamlined. Importantly, 12% of CH patients in the United States are getting welder grade oxygen because of the costs of medical grade oxygen and this form of oxygen could be potentially dangerous to the individual user.

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Category 1

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