Acta Neurologica Belgica
https://doi.org/10.1007/s13760-024-02506-z

REVIEW ARTICLE

Oxygen as an abortive therapy in cluster headache: a narrative review and clinical practice aspects

Julie Van Houtte[1] · Nicolas Vandenbussche[1] · Eric Derom[2] · Jean Schoenen[3] · Jan Versijpt[4] · Koen Paemeleire[1]

Received: 13 December 2023 / Accepted: 8 February 2024
© The Author(s) under exclusive licence to Belgian Neurological Society 2024

Abstract

Cluster headache (International Classification of Headache Disorders third edition, ICHD-3 3.1) is a primary headache disorder affecting around 0.12% of individuals. It is characterized by severe headache attacks causing significant negative impact on the lives of patients. While administration of 100% oxygen is considered to be the first-choice acute treatment, undertreatment also exists. Reasons for undertreatment may entail problems with the correct prescription of oxygen, reimbursement issues or the practical implementation of home oxygen therapy. The aim of this manuscript is to review the scientific evidence on oxygen therapy for cluster headache and provide a practical guidance for both physicians and patients to optimize its use in an acute setting. The current evidence of the administration of 100% oxygen as a safe and effective treatment for cluster headache is strong. Based on several clinical trials and surveys, the recommended flow rates range between 12 and 15 L/min via a non-rebreathing mask, for at least fifteen minutes. The frequency of cluster headache attacks and thus the need for acute treatment can be very high. Fortunately, the Belgian social security system provides a full and lifetime reimbursement of oxygen therapy for cluster headache if the diagnosis and the need for this therapy has been certified by a neurologist, neurosurgeon or neuropsychiatrist.

Keywords Cluster headache · Treatment · Oxygen therapy · Clinical practice guidelines

Introduction

With cluster headache (CH) being an uncommon but not rare headache disorder, almost every practicing neurologist will encounter sooner or later a patient with this medical condition. As a consequence, it is important for general neurologists to have a profound understanding of the disorder and its most effective and safe therapies. As an abortive therapy, inhaled oxygen is an evidence-based, safe and effective treatment for CH attacks for everyday use by patients. It is therefore important for practitioners to have a thorough knowledge of the prescription and correct use of this treatment. This narrative review provides an overview of the rationale behind the use of inhaled oxygen in CH and offers practical guidance for its correct and optimal use.

✉ Julie Van Houtte
julie.vanhoutte@uzgent.be

[1] Department of Neurology, Ghent University Hospital, Corneel Heymanslaan 10, 9000 Ghent, Belgium

[2] Department of Respiratory Medicine, Ghent University Hospital, Ghent, Belgium

[3] Headache Research Unit, Department of Neurology, University of Liège, Liège, Belgium

[4] Department of Neurology, Brussels University Hospital, Jette, Belgium

Methods

A PubMed search was conducted using (a combination of) different keywords: “cluster headache”, “treatment” and “oxygen therapy”. Relevant full-text articles were selected based on their title and abstract. If no abstract was available or it did not provide enough information, the full text was retrieved. For issues concerning cost and reimbursement price and financing in Belgium, online government files and websites of commercial oxygen providers were consulted.

Epidemiology of cluster headache

CH is one of the so-called trigeminal autonomic cephalalgias (TACs). According to the third edition of the International Classification of Headache Disorders (ICHD-3), the

Published online: 18 March 2024

diagnosis can be made if a patient has experienced at least five attacks of severe unilateral orbital, supraorbital and/or temporal pain, lasting between fifteen and 180 min when untreated, and occurring at a frequency between one attack every other day and eight per day. In addition, the diagnosis of CH requires that the pain must be associated with a sense of restlessness or agitation and/or at least one cranial autonomic symptom ipsilateral to the headache (lacrimation and/or conjunctival injection, nasal congestion and/or rhinorrhoea, eyelid oedema, forehead and facial sweating or miosis and/or ptosis). In the majority of patients, attacks tend to occur in periods lasting seven days up to several weeks or months, separated by pain-free periods of at least three months. This episodic version of CH (ICHD-3 3.1.1) should be distinguished from chronic CH (ICHD-3 3.1.2), which occurs in 10–15% of patients and is characterized by attacks occurring for more than 1 year without remission, or remission periods lasting shorter than three months [1]. CH is the most frequent disorder within the group of TACs with an estimated prevalence of 1 in 1000 (around 0.12%) patients and a male-to-female ratio between 2.5:1 and 3.5:1 [2]. The age of onset most frequently lies between 20 and 40 years. Several studies have shown a strong correlation with (a history of) smoking. Also, a family history of CH leads to a 14-fold increase in the risk of developing this disorder in first-degree relatives [3–5].

History of oxygen therapy in cluster headache

Although the Dutch physician Nicolaas Tulp described CH-like syndromes already in the seventeenth century [6], the first post-war medical reports on the syndrome date from 1952 [7]. The pain itself and its associated symptoms were described in detail by Bayard Horton. He called the syndrome "histaminic cephalgia" as he noticed a certain provocative effect of histamine, suspecting vasodilation as a potential pathogenic factor. His personal experience of successful treatments with histamine desensitization, ergot preparations and oxygen led him to confirm his working hypothesis. Horton thought the effect of oxygen on CH attacks could be attributed to the vasoconstrictive effect of oxygen [7, 8]. In the years following his publication several studies on the effect of oxygen in CH were conducted. The first systematic study with oxygen was published in 1981 by Kudrow [9]. First he studied the success rate of the inhalation of 100% oxygen, at 7 L/min during fifteen minutes, in a group of episodic and chronic patients. Treatment turned out to be effective in 75% of the patients, as the responders became (almost) pain-free within fifteen minutes for at least seven out of ten attacks. Kudrow performed a second cross-over trial comparing the success rate of 100% oxygen with that of sublingual ergotamine. Pain relief was reached faster and more frequently using 100% oxygen compared to sublingual ergotamine, although the difference was statistically non-significant [9].

Efficacy of oxygen therapy in cluster headache

Experimental studies

Focusing on the efficacy of oxygen itself, Fogan in 1985 was the first to publish a double-blind randomized crossover study in nineteen male patients with CH comparing the efficacy of 100% oxygen versus compressed room air [10]. Patients were instructed to inhale one of the two gasses at a flow of 6 L/min via a non-rebreathing face mask for up to fifteen minutes at the onset of a cluster attack. The effect was evaluated using a questionnaire that patients had to fill in after each treatment and detailing the severity of symptoms, time of headache onset, time the patient first breathed from the cylinder and time to first noted effect. The primary outcome was the subjective evaluation of pain relief, scored from zero (no relief) to three (complete relief). Eleven out of the nineteen patients evaluated both gasses. Taking into account the data of the other eight patients, the authors concluded that the use of 100% oxygen yielded a significantly better relief score (9/16 having a substantial or complete relief in at least 80% of the attacks) compared to the use of room air (only 1/14 showing a substantial or complete relief in at least 80% of the attacks) [10].

The largest double-blind crossover study comparing 100% oxygen and room air was published by Cohen et al. in [11]. Of the 109 patients randomized 76 did receive treatment. Each patient received two cylinders, not knowing which one contained 100% oxygen and which one contained room air. They were instructed to treat four cluster attacks in an alternate way starting with cylinder 1 for the first one and 2 for the next and so on, at flow rates of 12 L/min during fifteen minutes through a nonrebreathing facial mask. Fifty-five patients with episodic CH and eighteen patients with chronic CH completed the cycle of four treated attacks, corresponding with a total of 148 attacks treated with room air and 150 attacks treated with 100% oxygen. Seventy-eigth percent of attacks treated with 100% oxygen met the primary endpoint, namely being pain-free at fifteen minutes, versus 20% of attacks treated with room air, a statistically significant difference. Concerning the secondary endpoints in this study, 100% oxygen was shown to be superior to room air, as summarized in Table 1.

A recent randomized, double-blind, crossover trial compared the effect of 100% oxygen at different flow rates for the treatment of CH attacks. Oxygen-naïve patients with CH were randomized to either a flow of 7 L/min or 12 L/min using an oxygen container with a fixed flow rate valve. The authors found no differences in the effects of oxygen at a flow rate of 12 L/min compared to 7 L/min. Although a

Table 1 Number of attacks (percentages) treated with room air or 100% oxygen meeting the stated endpoints, adapted from [11]

		Room air	100% oxygen
Number of attacks treated		148	150
Primary endpoint	Pain-free at 15 min	29	116
Secondary endpoints	Pain-free at 30 min	19	78
	Reduction in pain at minute 15	25	88
	Reduction in pain at minute 20	28	93
	Reduction in pain at minute 30	28	93
	Reduction in pain at minute 60	38	95
	Need for rescue medication from 15 min	76	30
	Overall response to the treatment and overall functional disability	18	75
	Effect on associated symptoms	40	81

higher percentage of successfully treated attacks was seen at a flow rate of 7 L/min, more patients preferred the 12 L/min flow rate. No serious side-effects emerged in both treatment arms. The authors concluded that, since a subgroup of patients with CH responded well to 7 L/min, 7 L/min may provide a valuable alternative to a flow rate of 12 L/min, particularly when oxygen supplies are limited or costs are high. Limitations of the study were the small number of treated attacks for the analysis of the primary outcome and the lack of differentiation between patients with episodic and chronic CH [12].

Head-to-head comparison to other acute treatment options

Oxygen therapy is not the only acute treatment option for CH. Subcutaneous sumatriptan, nasal spray zolmitriptan and non-invasive vagal nerve stimulation have all been reported to be effective for the treatment of CH attacks [3, 13]. Unfortunately, no head-to-head randomized controlled trials of oxygen versus another active comparator are available. Using a network meta-analysis, Medrea et al. looked at the effects of acute treatment options for CH. High-flow oxygen was the most effective therapy for headache response at 15 and 30 min, with injectable sumatriptan having the next highest efficacy. High-flow oxygen (15 L/min) was more effective than low-flow oxygen (6 or 7 L/min), nasal spray zolmitriptan and non-invasive vagal nerve stimulation [14].

Observational studies

Petersen et al. [13] conducted a survey among 400 Danish patients with CH, investigating the effect of 100% oxygen for the acute treatment of CH attacks and comparing it with triptans. Two hundred and eighty-four patients used 100% oxygen as an acute therapy at the moment of the survey. Seventy-four percent were classified as good responders to oxygen, but only 29% of oxygen users had complete relief of pain (Table 2). The maximum delay in which pain relief had to be reached was not specified in this survey. The mean oxygen flow was 12.6 L/min. In a logistic regression analysis, a favorable outcome with 100% oxygen was associated with episodic CH, moderate pain intensity and fewer years with CH. An increased likelihood of a complete response to 100% oxygen was associated with episodic CH, male sex, moderate pain intensity, and fewer years with CH. Oxygen flow rate was not associated with a complete response. Lastly, the authors also reported that, in 119 patients with CH who used both sumatriptan injections and oxygen, the proportion of 100% responders and 50% responders was significantly higher with sumatriptan injections compared to oxygen.

In two other surveys, the effectiveness and tolerability of 100% oxygen and triptans were compared. Schindler et al. [15] analyzed the findings of the online "Clusterbusters Medication Use" survey, conducted between May and July 2012. From the 558 participants who completed the survey, 493 were identified

Table 2 Comparison of the effect of 100% oxygen to that of subcutaneous sumatriptan in a Danish cluster headache survey [13]

	Number of patients reaching at least 50% response[1]	Number of patients reaching 100% response[2]
Group using oxygen alone: $n = 284$	210 (74%)	82 (29%)
Group using subcutaneous sumatriptan alone: $n = 138$	121 (88%)	79 (57%)

[1]Defined as having answered "completely, the pain is gone" or "some, the pain is halved or more"

[2]Defined as having answered "completely, the pain is gone"

as adult patients with a diagnosis of CH confirmed by a neurologist or headache specialist. The patients with episodic CH accounted for 67.1%. In the group that tried both treatments and only responded to one of these, significantly more participants responded to subcutaneous sumatriptan than to 100% oxygen. However, focusing on those using oxygen flow rates > 10 L/min, there was no significant difference in efficacy between 100% oxygen and subcutaneous sumatriptan. Likewise, the difference in response rate was not significant between 100% oxygen at flow rates > 10 L/min and subcutaneous sumatriptan in participants who had only tried one of both treatments.

In a second online survey conducted by Pearson et al. and published in 2019, 1604 adult CH patients were analyzed, the majority of them living in North America and presenting with an episodic CH. Overall, 100% oxygen and triptans were both completely or very effective in 54% of respondents and again no significant differences in response rate could be reported. In a subgroup of patients aged 65 years and older, 100% oxygen was completely or very effective in 56% of these patients versus 61% for triptans, but these results were not further analyzed because of the small sample size. Next to the efficacy this survey also analyzed the data on complication rate of the different therapies. Significantly less physical or medical complications were reported with 100% oxygen compared to triptans with an overall odds ratio of 6.71 (95% CI 4.67–9.65) [16].

Modes of delivery

To optimize the effect of oxygen inhalation it is important to use the optimal oxygen delivery system. Petersen et al. conducted a single-blinded placebo-controlled crossover study comparing the efficacy of a simple face mask (15 L/min), an O_2ptimask (non-rebreathing mask with a 3 L reservoir, 15 L/min), a demand valve delivering 100% oxygen or a demand valve delivering compressed air (21% oxygen and 79% nitrogen). Blinding of the type of mask was not possible, but the gas cylinders of which three contained 100% oxygen and one contained compressed air, were identical. These four treatments were used in a random sequence, except the placebo which was always placed as the last option to make sure patients having less than four attacks used as much active treatments as possible. A time window of at least three hours between treatments was requested to eliminate a possible carryover effect of the previous treatment and reduce the risk of treating a rebound headache. Fifty-seven patients (30 with episodic CH and 27 with chronic CH) were included. Ten patients had four cluster attacks and used the four treatments. After fifteen minutes of treatment, the percentage of patients who became pain-free or rated a two-point decrease on a five-point rating scale was not significantly different between all four treatments, including placebo. By analyzing the treatment efficacy of the first attacks only, the demand valve oxygen was significantly better than the O_2ptimask and borderline better than the simple mask. Moreover, patients treating their first attack with demand valve oxygen had a significantly lower risk of completing the crossover study (meaning experiencing four attacks) compared to those treating with a simple mask or an O_2ptimask [17, 18].

It should be underlined that demand valve oxygen may not be affordable for all patients as it easily costs $300 or even more, which is about sixteen to 100 times more than an O_2ptimask or a simple mask, respectively [17–19]. In a review of the different delivery systems, Oude Nijhuis et al. also concluded that the demand valve oxygen and the non-rebreathing mask seemed to be the most promising systems in effectively reducing pain in CH attacks, though more qualitative comparative trials should support this statement. Taking into account the use and the financial aspects the non-rebreathing mask is the most frequently used oxygen delivery system in clinical practice nowadays. Also the fraction of inspired oxygen (FiO2) is an important factor in favor of this type of mask. The FiO2 is the concentration of oxygen in the gas mixture, for example, is this 21% in room air. When inhaling 100% oxygen from a device, the oxygen will still be mixed with room air and the FiO2 will never be 100%. Using a non-rebreathing mask values of 45–95% can be achieved depending on the flow rate (the higher the flow rate the higher the fiO2) [20, 21].

Guidelines

Looking at the European and American guidelines for the treatment of CH, oxygen is recommended as the first-choice treatment for the acute treatment of attacks. Oxygen 100% 6 to 12 L/min has a level A recommendation (established as effective) from the American Headache Society, next to sumatriptan 6 mg subcutaneous injection and zolmitriptan nasal delivery. In the European Federation of Neurological Societies guideline from 2006, 100% oxygen 12 to 15 L/min also has a level A recommendation, just as sumatriptan 6 mg subcutaneous injection and sumatriptan 20 mg nasal delivery [22, 23]. Also according to the recent guidelines of the European Academy of Neurology, published in March 2023, sumatriptan 6 mg subcutaneous injection and Oxygen 100% at a flow of at least 12 L/min during 15 min are the first options for the acute treatment of CH attacks. These EAN guidelines also make strong recommendations for the use of sumatriptan 20 mg nasal spray and zolmitriptan 5 mg nasal spray, though they have the disadvantage of a slower onset [24].

Treatment reimbursement in Belgium

An important and practical issue is the choice and use of the different available gas cylinders. To enable and optimize

Table 3 Overview of the monthly cost price for the rental of the material needed for oxygen treatment [26]

Type of compensation	Maximum amount paid by the social security	Maximum supplement for the patient
Gas cylinders and flow meters	€22.17	€4.43
Oxygen masks	€2.54	€0.51
Oxygen hoses	€1.70	€0.34
Humidifier	€4.41	€0.88
Total	€30.82	€6.16

Table 4 Belgian prices of the first choice acute treatments in cluster headache

	100% oxygen	Subcutaneous sumatriptan 6 mg	Sumatriptan nasal spray 20 mg	Zolmitriptan nasal spray 5 mg
Price per package	Minimum: €4.26 Maximum: €6.25	€33.00	€67.40	€28.53
Doses per package	5	2	6	2
Daily price (gross)	Minimum: €1.70 Maximum: €2.50	€33.00	€22.47	€28.53
Daily price for the patient	€0.00	€8.68	€22.47	€28.53
Daily price for the social security	Minimum: €1.70 Maximum: €2.50	€24.32	€0.00	€0.00

the treatment of a CH attack with high flow rates of 100% oxygen, at least 180–225 L are needed per attack. Two types of portable gas cylinders are in use in Belgium: the B2 type with a real volume of 2 L of water and the B5 type with a real volume of 5 L of water. Pressurized at 200 bar, these cylinders contain 400 L and 1000 L, providing enough oxygen to treat a minimum of two and five CH attacks, respectively [25]. The flow meter connected to the oxygen cylinder should allow flow rates up to 15 L/min. It is of note that the currently used equipment for long-term oxygen treatment therapy in respiratory patients (oxygen cylinders with standard flow meters, oxyconcentrators or liquid oxygen, and nasal cannulas) is not suitable for the oxygen treatment of patients with CH.

In Belgium, social security provides a full and lifelong reimbursement of oxygen therapy for CH if the diagnosis and the need for this therapy has been certified by a neurologist, neurosurgeon or neuropsychiatrist. Installation and rental of the material needed for the use of oxygen (gas cylinders, masks, etc.) is largely reimbursed with a maximum remaining cost for the patient of about €6 per month, as shown in Table 3 [26].

In Belgium, only subcutaneous sumatriptan is (partially) reimbursed for CH. Table 4 summarizes the costs for the most frequently used acute treatments of CH, with the daily price if a patient develops two CH attacks per day. In this case, the treatment consists of 100% oxygen. A flow rate of 12 L/min during fifteen minutes is administered. At that flow rate, one B5 gas cylinder, containing 1000 L of oxygen, allows to treat five CH attacks. Depending on the supplier the price of oxygen can vary and therefore the minimum and maximum prices are shown in Table 4. The price of the installation has not been taken into account since this is only a one-time cost [27, 28]. As seen in the table the gross daily price of 100% oxygen is low compared to all three triptans. Comparing the triptans mutually, subcutaneous sumatriptan is relatively affordable for patients but puts the largest burden on social security.

Table 5 Correct way of prescribing oxygen therapy in Belgium [26]

R/	Gaseous 100% medical oxygen for cluster headache
Dt/	10 000 L, July 2023
S/	12 to 15 L/min

Once reimbursement of 100% oxygen has been approved, prescriptions can be provided by any physician with a monthly extension and must contain a minimum of essential information, shown in Table 5. As for one CH attack patients need between 180 and 225 L of oxygen, it is appropriate to prescribe large volumes of oxygen. Usually, patients do not need a separate prescription for the rental of the material needed for the use of oxygen, but it can be provided to make sure that, for example, a correct mask is delivered [26].

Safety of oxygen therapy

In general, oxygen has proven to be a safe and well-tolerated therapy. Using non-humidified oxygen, dehydration of oral and nasal mucosa may occur, making it more susceptible to

inflammation and infection. Oxygen toxicity (characterized by complaints of dyspnea and coughing) or retinopathy only occurs in case of prolonged exposure, that is if a fraction of inspired oxygen higher than 50% is administered during at least 48 h. Using 100% oxygen first symptoms of tracheobronchial irritation can occur after 24 h of continuous exposure or after only three hours using hyperbaric oxygen. An important mechanism of action causing this toxicity is the formation of free oxygen radicals, which can interact with lipids, deoxyribonucleic acid (DNA), proteins, etc. [20, 29]. A possible adverse effect concerning the use of a non-rebreathing mask is a sense of claustrophobia, which is reported in a minority of patients. A very important safety measure patients have to take into account when using oxygen is to be careful with close contact with other flammable gases and fatty substances (for example several cooking oils) and to not smoke or use fire while using an oxygen delivery system [20]. In some medical conditions, especially in the case of chronic obstructive pulmonary disease (COPD), cystic fibrosis or severe restrictive pulmonary disorders, oxygen therapy must be used with caution due to the risk of oxygen-induced hypercapnia when using high flow rates [30, 31].

Another aspect of oxygen therapy is the sometimes observed rebound effect, characterized by a fast recurrence or increase in the frequency of attacks after an initial successful treatment of a CH attack. The mechanism of action of these rebounds is not yet clear, but one hypothesis for the rebound effect in oxygen therapy states that flow rates may have an influence on this effect. Indeed, in the trial of Kudrow, which used 100% oxygen at 7 L/min, 25% of patients reported rebounds, whereas only 4.4% (seven out of 158 patients) did in the study of Geerlings et al., where at least four of these seven patients used flow rates of 7 L/min or less. However, it seems unlikely that this is the only possible explanation, as a similar rebound effect is also seen in patients using sumatriptan subcutaneous injections, [9, 20].

Practical issues and conclusion

In summary, the current medical literature recommends the administration of normobaric 100% oxygen at flow rates of 12–15 L/min, using a non-rebreathing mask, for at least fifteen minutes as a first-choice acute treatment in CH. When used correctly and considering possible contraindications, it has been proven to be a safe treatment with only a few adverse effects. The financial aspects of oxygen therapy for patients within the Belgian social security system are advantageous compared to triptans, with almost full reimbursement for patients and yet a low burden on social security services.

Acknowledgements The authors would like to thank Lukas Nollet, resident Internal Medicine, for his appreciated contribution to this article.

Funding Not applicable.

Data availability Not applicable.

Declarations

Conflict of interest The author declares no conflict of interest.

Informed consent Not applicable.

References

1. Headache Classification Committee of the International Headache Society (IHS) (2018) The International Classification of Headache Disorders, 3rd edition. Cephalalgia 38(1):1–211
2. Hoffmann J, May A (2018) Diagnosis, pathophysiology, and management of cluster headache. Lancet Neurol 17(1):75–83
3. Burish M (2018) Cluster headache and other trigeminal autonomic cephalalgias. Continuum (Minneap Minn) 24(4):1137–1156
4. May A (2005) Cluster headache: pathogenesis, diagnosis, and management. Lancet 366(9488):843–855
5. Nesbitt AD, Goadsby PJ (2012) Cluster headache. BMJ 344:e2407
6. Koehler PJ (1993) Prevalence of headache in Tulp's Observationes Medicae (1641) with a description of cluster headache. Cephalalgia 13(5):318–320
7. Horton BT (1952) Histaminic cephalgia. J Lancet 72(2):92–98
8. Haane DY, Dirkx TH, Koehler PJ (2012) The history of oxygen inhalation as a treatment for cluster headache. Cephalalgia 32(12):932–939
9. Kudrow L (1981) Response of cluster headache attacks to oxygen inhalation. Headache 21(1):1–4
10. Fogan L (1985) Treatment of cluster headache. A double-blind comparison of oxygen v air inhalation. Arch Neurol 42(4):362–363
11. Cohen AS, Burns B, Goadsby PJ (2009) High-flow oxygen for treatment of cluster headache: a randomized trial. JAMA 302(22):2451–2457
12. Dirkx THT, Haane DYP, Koehler PJ (2018) Oxygen treatment for cluster headache attacks at different flow rates: a double-blind, randomized, crossover study. J Headache Pain 19(1):94
13. Petersen AS et al (2021) Real-life treatment of cluster headache in a tertiary headache center: results from the Danish cluster headache survey. Cephalalgia 41(5):525–534
14. Medrea I et al (2022) Network meta-analysis of therapies for cluster headache: effects of acute therapies for episodic and chronic cluster. Headache 62(4):482–511
15. Schindler EAD et al (2018) Survey analysis of the use, effectiveness, and patient-reported tolerability of inhaled oxygen compared with injectable sumatriptan for the acute treatment of cluster headache. Headache 58(10):1568–1578
16. Pearson SM et al (2019) Effectiveness of oxygen and other acute treatments for cluster headache: results from the cluster headache questionnaire, an international survey. Headache 59(2):235–249
17. O.B. (2008–2022) Ouch-Belgium winkel. https://ouch-belgium.be/nl/winkel-zuurstoftherapieapparatuur/. Accessed 6 June 2022
18. Petersen AS et al (2017) Oxygen therapy for cluster headache. A mask comparison trial. A single-blinded, placebo-controlled, crossover study. Cephalalgia 37(3):214–224

19. De Block M (2020) AR – KB 13.05.2020 – MB – BS 19.05.2020. 2020. https://www.riziv.fgov.be/SiteCollectionDocuments/niet_implanteerbare_medische_hulpmiddelen_vergoedingsvoorwaarden.pdf. Accessed 12 June 2022
20. Oude Nijhuis JC, Haane DY, Koehler PJ (2016) A review of the current and potential oxygen delivery systems and techniques utilized in cluster headache attacks. Cephalalgia 36(10):970–979
21. Fuentes S, Chowdhury YS (2023) Fraction of Inspired Oxygen. In: StatPearls. Treasure Island (FL) ineligible companies
22. May A et al (2006) EFNS guidelines on the treatment of cluster headache and other trigeminal-autonomic cephalalgias. Eur J Neurol 13(10):1066–1077
23. Robbins MS et al (2016) Treatment of cluster headache: the american headache society evidence-based guidelines. Headache 56(7):1093–1106
24. May A et al (2023) European academy of neurology guidelines on the treatment of cluster headache. Eur J Neurol 30(10):2955–2979
25. Nv O.B. Oxycure-fles voor Medische zuurstof (2015) Gebruiksaanwijzing met bijsluiter gasvormige zuurstof Air Products. https://www.oxycure.be/wp-content/uploads/2019/11/10-Oxycure-zuurstofflessen-B2-B5_NL.pdf. Accessed 14 June 2022.
26. RIZIV (2022) Kortdurende zuurstoftherapie. https://www.inami.fgov.be/nl/themas/kost-terugbetaling/door-ziekenfonds/geneesmiddel-gezondheidsproduct/terugbetalen/zuurstof/Paginas/default.aspx. Accessed 13 June 2022
27. Vandenbroucke F (2014) AR - KB 22.05.2014 - MB - BS 26.06.2014. https://www.inami.fgov.be/SiteCollectionDocuments/zuurstofconcentrators_zuurstoftherapie_indicaties_vergoedingsvoorwaarden.pdf. Accessed 18 August 2022
28. RIZIV.fgov. (2022) "Goedkoopste" en "goedkope" geneesmiddelen. 2022. https://webappsa.riziv-inami.fgov.be/SSPWebApplicationPublic/nl/Public/PriceComparison?baseId=1983. Accessed 18 August 2022
29. Thomson L, Paton J (2014) Oxygen toxicity. Paediatr Respir Rev 15(2):120–123
30. Abdo WF, Heunks LM (2012) Oxygen-induced hypercapnia in COPD: myths and facts. Crit Care 16(5):323
31. Allardet-Servent J et al (2019) Benefits and risks of oxygen therapy during acute medical illness: Just a matter of dose! Rev Med Interne 40(10):670–676

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.