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O_2xygen

Oxygen as treatment for Cluster Headache attacks

The French version of the content of this document has been validated by the scientific committee of OUCH Belgium.

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Why should this treatment be preferred?

- Oxygen is, like Imitrex, a **vasoconstrictor** (it decreases the diameter of blood vessels) which will counteract the **vasodilation** (increase in the diameter of blood vessels) which "crushes" the trigeminal nervous system (trigeminal nerve: V1, V2, V3).
  On the other hand, during the attacks, many substances play a role in vasodilatation, including CGRP [1], a substance that we will hear more and more about therapeutically speaking. Both Imitrex and oxygen have been shown to reduce the amount of CGRP at the trigeminal level [2].
- If used properly, it is not very toxic. Oxygen is an alternative to be tried considering the acceptable side effects and the good effectiveness to treat on average 60% of attacks [3].
- Oxygen is effective in 60% of cases following clinical trials at >10 litres per minute, and experience has shown that **12** to **15** litres per minute bring greater effectiveness.
- Oxygen is 100% refunded in Belgium [4].

Contraindication for COPD

There is one case where oxygen **cannot be administered at all** (at the rate required for treatment):
People suffering from COPD (chronic obstructive pulmonary disease). Paradoxically, these people are at risk of respiratory arrest if they receive too much oxygen.
Consult a pulmonologist if you are in this case!
Since active smoking is fairly recurrent in patients with cluster headache, a prior check by a pulmonologist could rule out the presence of post-tobacco COPD, and therefore that contraindication.

Contraindications to Medication [5]

The use of medicinal oxygen **may increase** or reduce the desired or undesirable effects of other medications. Consult your doctor or pharmacist for more information. In particular, seek advice from your doctor or pharmacist if you are taking any of the following medications:

- **Amiodarone** (a medication used for the treatment of cardiac arrhythmias).
- **Bleomycin** or **actinomycin** (cancer drugs)**.** These medications can cause pulmonary damage that can be aggravated by oxygen therapy, possibly with fatal consequences.

[1] Calcitonin-Gene-Related-Peptide
[2] Goadsby PJ, Edvinsson L. Human in vivo evidence for trigeminovascular activation in cluster headache. Neuropeptide changes and effects of acute attacks therapies. Brain. 1994 Jun;117 (Pt 3):427-34.
[3] Cohen AS, Burns B, Goadsby PJ. High-flow oxygen for treatment of cluster headache: a randomized trial. JAMA. 2009 Dec 9;302(22):2451-7. Bennett MH, French C, Schnabel A, Wasiak J, Kranke P. Normobaric and hyperbaric oxygen therapy for migraine and cluster headache. Cochrane Database Syst Rev. 2008(3):CD005219.
[4] Except for a possible additional charge. See "Supplier" and "Legislation".
[5] Source : http://www.vivisol.be/assets/uploads/services/Notice_dinformation_FR_ver_062015.pdf

The following drugs **may increase** the harmful effects of medicinal oxygen:

- **Adriamycin** (a cancer drug).
- **Menadione** (a medication used to reduce the effects of anticoagulants).
- **Promazine, chlorpromazine and thioridazine** (medications used against serious mental disorders that cause patients to lose control of their behaviour and their actions (psychosis)).
- **Chloroquine** (a medication for malaria).
- **Some Corticosteroids:** hormones such as cortisol, hydrocortisone, prednisolone and many others (drugs that stimulate specific parts of the nervous system). **Be careful if you are taking Medrol!**
- **Furadantine** and similar antibiotics.

Possible side effects

- Used several times a day, irritation of the upper respiratory tract (nose - throat) may occur since the oxygen in the cylinder is dry.
- Dry cough (1/100)

However, these problems can be overcome by using an « aquapak ».

Inconveniences

- It is difficult to treat oneself outdoors because of the large quantities of oxygen required. The small cylinders that can be easily transported (B2, 400 litres, ±0.4 m3) are emptied by treating one or two attacks at the most and the larger cylinders (B5, B10, B20) are difficult to transport without a vehicle.

Toxicity (do not panic)

- **More than two hours** at PpO2 > 0.5 bar [6]: there is a risk of inflammation of the pulmonary alveoli followed by a possible development of acute pulmonary oedema [7].
- At 100% oxygen, we die **after 100 hours** [8].

Risks related to oxygen

- Oxygen is a combustion agent, that means it greatly increases the risk of fire hazard and speeds it up. In the event of fire, the oxygen cylinders present an explosion risk. This is why you should not smoke in the vicinity of an oxygen cylinder, nor light a candle, etc…
- Avoid contact with fatty substances that could spontaneously ignite when in contact with oxygen (certain make-up, ...).

It should be noted that it is preferable to notify your insurer when you hold oxygen cylinders at home and in your car.

[6] PpO2: Oxygen partial pressure: 0.5 bar is equivalent to 50% oxygen at atmospheric pressure.
[7] Hyperoxia
[8] https://www.srlf.org/wp-content/uploads/2015/11/0201-Reanimation-Vol11-N1-p028_039.pdf

Conditions for efficiency

- It is necessary to treat the attack from the onset of the first symptoms, before the pain. The longer you wait, the longer the treatment, the greater the risk of failure [9].
- Prefer the seated position.
- Sufficient flow rate (12-15 litres per minute, based on patients' experience) should be used.
- A suitable mask system must be used.
- The further away the inhaled oxygen fraction is from 100%, the less effective the treatment will be.

Documents for reimbursement (Belgium)

For the first application, you need the authorisation of the medical adviser of your health insurance. This authorisation is based on a detailed report from a neurologist, neurosurgeon or neuropsychiatrist, together with the diagnosis of cluster headache and a justification for starting oxygen therapy because of the patient's clinical situation.
There is no standard form for claiming a reimbursement. If the request is made by the general practitioner, the latter must attach the specialist's report.

The authorisation has an **unlimited** period of validity. Furthermore, the patient must have a **monthly** prescription for the pharmacist that includes the following items:

- Medical gaseous oxygen in DCI [10] prescribed as required, with specific accessories adapted to a high flow rate.
- The dosage (in litres per minute).
- If necessary, the oxygen humidifier (aquapak).

Important note

If the delivery is carried out by a supplier who, for the rental of the gas cylinder, accessories and any oxygen humidifier, charges more than the maximum amount covered by the insurance, the pharmacist or hospital pharmacist may charge a supplement to the patient for these items. This supplement may not at any time exceed 20% of the maximum amount covered.

Type of intervention	**Maximum covered by the insurance (including VAT) paid to the pharmacist**	**Maximum supplement (max. 20%) that the pharmacist can charge the patient if the supplier (non-pharmacist) charges a higher amount for these items.**
Rental of O2 cylinder and regulator	**22,17 €**	**4,43 €**
Masks and/or nasal cannula	**2,54 €**	**0,51 €**
O2 delivery tubings	**1,70 €**	**0,34 €**
Single-use humidifier	**4,41 €**	**0,88 €**

[9] Discontinuation of treatment because the attack becomes unbearable and the use of Imitrex very tempting.
[10] International Common Denomination : http://www.riziv.fgov.be/fr/themes/cout-remboursement/par-mutualite/medicament-produits-sante/prescrire-medicaments/Pages/prescrire-dci-regles-prescripteur.aspx#.WlnsEajiZhE

Suppliers (Belgium)

- Francis Fléron (Liège, Namur, Luxembourg)
- Linde Homecare Belgium
- Oxycure Belgium (Billing the authorized surcharge to new customers)
- Oxysphair
- SOS Oxygene Benelux
- VitalAir
- Vivisol

Public pharmacies are responsible for oxygen in the case of the Cluster Headache.
The pharmacist has the choice of supplier, but if he or she chooses a supplier who charges a supplement at your expense, do not hesitate to ask him or her to change supplier.
Once the procedure has been established, do not hesitate to agree with your pharmacist so that you can order directly from the supplier to save time.

Attention: Not all suppliers deliver every day and not all suppliers deliver the same days of the week, depending on the region. Beware also of public holidays and long weekends. Plan ahead!

Legislation (Belgium)

Explanations on the INAMI website :
http://www.inami.fgov.be/fr/themes/cout-remboursement/par-mutualite/medicament-produits-sante/remboursement/oxygene/Pages/default.aspx#Rembourser_l%E2%80%99oxyg%C3%A9noth%C3%A9rapie_de_courte_dur%C3%A9e

Royal Decree of 17 September 2012:
http://www.ejustice.just.fgov.be/mopdf/2012/09/20_3.pdf#page=5

How to properly treat the Cluster Headache attack with oxygen?

Oxygen can work for you, even if you have tried it in the past without success!

It should be noted that the 7 litres per minute of old clinical trials and recommendations are now widely considered to be too low.
A flow rate of **12 to 15 litres per minute** is strongly recommended.

It is essential to use a material that delivers **100% oxygen**, WITHOUT ANY OUTSIDE AIR (See the section "Oxygen fraction inhaled depending on equipment used" at the end of this booklet).

It is also **very important** to begin using oxygen **as soon as possible**, at the first sign of an attack, **before the pain sets in**.
The sooner you start, the sooner you can abort the attack.

Do not use oxygen therapy while lying down! The **sitting position** is the best for good breathing.

Breathing techniques vary: find the one that works best for you!
It is always best to get as much oxygen into the lungs as possible and then exhale as much air as possible.
Try to breathe faster and deeper than usual and exhale fully.
Twenty minutes of breathing oxygen in is the maximum **recommended** time for a session. If this does not abort the attack, wait five to ten minutes and try again. (Don't lack courage!)

Follow the demo and practice away from attacks, calmly, without stress 😉

Hyperventilation

Various definitions:

- Hyperventilation is a breathing mode in which the breathing in is strongly accentuated. Hyperventilation or respiratory acceleration and amplification is a non-physiological ventilation, i.e. with modification of the normal partial pressures of blood gases. During hyperventilation, the partial pressure of carbon dioxide in the lungs (and consequently in arterial blood) will decrease. At the blood pH level, this will produce respiratory alkalosis. (Wikipedia).
- Increased pulmonary ventilation due to anxiety, physical activity or illness (larousse. fr).
- Hyperventilation results from a change in breathing that causes an abnormally high flow oxygen compared to normal breathing and a reduction in the amount of carbon dioxide (CO2) in the blood. (psychomedia. qc. ca).
- Hyperventilation is used in clinical practice to promote the onset of signs suggestive of an epilepsy during or outside EEG registration. In case of hyperventilation, we know that a percentage of people predisposed to epilepsy get epileptic seizures and sometimes, the same result can also be found in people who are not predisposed to epilepsy [11].

Conclusion:

The very fact of treating our attacks with 100% oxygen puts us in conditions similar to hyperventilation. A fortiori, if the flow rate is very high and the breathing fast and ample. But... that's also the goal:

- Oxygen increase (O2) => vasoconstriction
- Carbon dioxide (CO2) reduction => vasoconstriction

Unfortunately, this metabolic imbalance is also one of the triggers of an epileptic seizure!
Thus, people predisposed to epilepsy (but who knows that?) will avoid exceeding the flow rate of 15 litres per minute (cylinders allowing it or valve on demand).
For the same reason, it is recommended to **suspend treatment after 20 minutes.**

Reasons to suspend treatment (even before 20 minutes):
Tingling in fingertips, feeling of abnormal tiredness (not from the attack itself), feeling of close syncope.

[11] (Mazzucchi E, Vollono C, Losurdo A, Testani E, Gnoni V, Di Blasi C, Giannantoni NM, Lapenta L, Brunetti V, Della Marca G. Hyperventilation in Patients With Focal Epilepsy: Electromagnetic Tomography, Functional Connectivity and Graph Theory - A Possible Tool in Epilepsy Diagnosis? J Clin Neurophysiol. 2017 Jan;34(1):92-99. doi: 10.1097/WNP.0000000000000329.
Salvati KA, Beenhakker MP. Out of thin air: hyperventilation-triggered seizures. Brain Res. 2017 Dec 27. pii: S0006-8993(17)30579-6. doi: 10.1016/j.brainres.2017.12.037.)

The rebound effect

After having aborted an attack with oxygen, many patients report that they must continue to inhale oxygen for several minutes more, often at a lower flow rate, to prevent a rebound of the attack (the same attack that starts again after 5 to 10 minutes).
This phenomenon is very variable. Some find that one or two minutes are sufficient and others continue for up to 10 to 15 minutes. Experiment for yourself, vary the time and the flow rate, find out what suits you best by trial and error.

How many attacks can I treat with an oxygen cylinder?

Pure oxygen is compressed into white metal cylinders. There are different cylinders types depending on the volume of oxygen contained at 200 pressure bars.

Most common models:

- 400 litres (B2),
- 1000 litres (B5),
- 2100 litres (B10),
- 4200 litres (B20),

Commonly used models:

B5 "portable" and B10 at home. The B2 model is unsuitable because it is too small in volume. The B20 model is extremely heavy and practically impossible to install on the first floor without an elevator but it is suitable for the ground floor.

How many attacks can be treated depending on the type of cylinder?

This question cannot be answered precisely but by using the examples below, we can estimate an average based on the type of cylinder and its use.

It should be noted that the "full" cylinders are not always filled at 200 bars. This is due to the fact that they are filled with the "hot-filled" method, which increases the pressure. When cooling, the initial pressure decreases slightly (often 180 to 190 bars)
Let's take the most common case of a **B10** cylinder and consider that the gauge reads 180 bars when received:

- Capacity in litres: 10,5 litres
- Pressure: 180 bars

Cylinder capacity in litres of gaseous O2: 10,5 litres x 180 = 1890 litres of gaseous O2.
Which gives according to your consumption:

- Flow rate of 12 litres per minute: for 20 minutes: 1890 l / (12 l x 20) ±= 7 attacks (7,875).
- Flow rate of 12 litres per minute: for 15 minutes: 1890 l / (12 l x 15) ±= 10 attacks (10,5).

Plan ahead and order (at least) two cylinders (B10 or B20) at the beginning. Then, as soon as one cylinder is empty, order the next one, so as to cover the weekend,the holidays and... the eventual forgetfulness.

Transport of oxygen

There are no specific rules for individuals. However, you will be sure:

- to close the valves, even if the cylinders are empty.
- to handle the cylinders with care.
- not to smoke.
- to fasten the cylinders to prevent them from rolling or being thrown out in the event of braking or an accident.

- to balance the loads if there are several cylinders.
- not to leave your vehicle in full sunlight.
- to leave a window slightly open to guarantee ventilation.
- not to carry more cylinders than necessary.
- to inform your insurer that you are transporting gas cylinders for medical use.
- to affix the appropriate signage to warn (e. g. rear side window) the rescue services of the presence of oxygen on board in the event of an accident.

Oxygen in foreign countries

Do you want to go on holiday abroad?

What should you do to get an oxygen supply to your holiday destination?

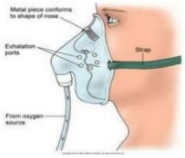
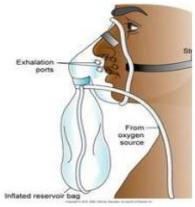
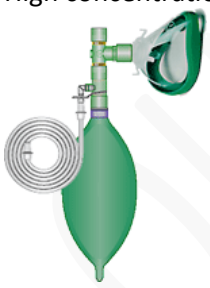
You must contact your **mutual insurance company** 5 weeks before your departure.

This one works with one of the following companies:

- MUTAS, International assistance (https://www.mutas.be/assistance-internationale)
- Mondiale Assistance, newly formed Allianz Global Assistance (https://www.allianz-assistance.be/fr/)

They are the ones who will contact the local supplier (the same as your supplier in Belgium or another, depending on the situation) to make the necessary arrangements.

Oxygen fraction inhaled depending on equipment used [12]:

nasal cannula 	20 to 44% depending on flow rate
Simple face mask (ventilation set of holes)  	30% to 60% depending on breathing speed and flow rate
High concentration mask (partial: ventilation holes or complete: valves leaking)  	Respectively ± 60% and ± 80%.
High concentration mask kit O2UCH 	100%
On demand valve 	100%

[12] https://www.slideshare.net/reply2raghavendra/oxygen-therapy-and-toxicity

Additional information: Trigeminal nerve