The East of England
Priorities Advisory Committee
A function of PrescQIPP

GUIDANCE STATEMENT

Oxygen in cluster headaches

PAC recommendations

General recommendations on the treatment of cluster headaches:

1. A clear positive diagnosis of cluster headache should be made. Where necessary, advice from a specialist should be sought.
2. Use of a headache diary is recommended to help both in diagnosis and establishing the pattern (if any) of the condition. This will help planning the provision of treatment, e.g. is it episodic or chronic in nature.
3. Consider prophylactic treatment with verapamil. This may require further advice from, or referral to, more specialist services. This option should not preclude interim provision of acute treatment.
4. Consider options for acute treatment; subcutaneous triptan or nasal triptan and/or high-flow oxygen. The prescriber should have sufficient knowledge of the treatment being offered, and for unlicensed use be aware of the attendant responsibilities. In making choice of treatment, consideration should be given to the risks/benefits of the option, patient's ability to use the option and applicability of the option to the patient's needs and lifestyle.
5. Whichever treatment option is chosen, there should be regular follow-up to ensure both efficacy of the treatment and continued benefit. On-going use of a short attack headache diary detailing attack duration, frequency and response to treatment is recommended. Failure of one treatment option does not preclude the subsequent use of an alternative.
6. Oral analgesics, oral triptans or ergot treatments are ineffective in the treatment of acute cluster headaches and should not be offered.

Recommendations specific to oxygen for the treatment of cluster headaches:

1. High-flow oxygen should not usually be considered as a first line treatment option unless subcutaneous or nasal triptans are contraindicated or attack frequency is greater or equal to two attacks per day.
2. When using oxygen for the acute treatment of cluster headache, use 100% oxygen at a flow rate of at least 12 litres per minute with a non-rebreathing mask and a reservoir bag.
3. Demand valves should only be used as part of regional pilot study. Currently there is insufficient evidence on clinical and cost effectiveness and routine use is not recommended.
4. The frequency and duration of cluster headache episodes must be considered when determining the installation status of the Home Oxygen Supply.
5. Ambulatory provision is supported by NICE, however it should be appreciated that there are practical limitations to its use. Whilst portable, the (small) cylinders are still cumbersome. Capacity is limited, so for patients that experience frequent attacks, the number of cylinders required (to be transported) may limit use.
6. Home oxygen installations can present locational difficulties. All installations (including storage provisions for cylinders) must be risk assessed and actual placement options within the home setting may be limited.
7. Multiple static provisions (e.g. at home, work and other location) significantly reduce cost-effectiveness and should only be provided after a thorough evaluation of all options. This may be viewed as an option to avoid potential difficulties associated with portable supplies. However, the generally sporadic use pattern will significantly reduce the cost-effectiveness, e.g. if installation at one location remains unused.

Background

NICE Clinical Guidance (CG) 150, issued in September 2012 recommends the use of oxygen for the acute treatment of cluster headaches in over twelves as outlined below.[1]

Management, cluster headache, acute treatment

- Discuss the need for neuroimaging for people with a first bout of cluster headache with a GP with a special interest (GPwSI) in headache or a neurologist.
- Offer oxygen and/or a subcutaneous or nasal triptan for the acute treatment of cluster headache.
- When using oxygen for the acute treatment of cluster headache:
    - » Use 100% oxygen at a flow rate of at least 12 litres per minute with a non-rebreathing mask and a reservoir bag and
    - » Arrange provision of home and ambulatory oxygen.
- When using a subcutaneous or nasal triptan, ensure the person is offered an adequate supply of triptans calculated according to their history of cluster bouts, based on the manufacturer's maximum daily dose.
- Do not offer paracetamol, NSAIDs, opioids, ergots or oral triptans for the acute treatment of cluster headache.

Historically, the approach to treatment of cluster headache has varied across the NHS. To a certain extent, this has mirrored the situation for headaches in general.

This is recognised in CG150 in the statement: "*Many people with headache do not have an accurate diagnosis of headache type*".[1]

Headaches are classified as primary or secondary, with the commonest primary disorders (classified according to clinical pattern) being, tension-type, migraine and cluster, headaches. Secondary headaches are attributed to underlying disorders.

Therefore, the appropriate management and treatment of headache must be based on a clear differential diagnosis: NICE CG150 places diagnosis as one of the key priorities for implementation of the guidance.[1] The management and treatment of cluster headache should be seen and made within the overall management of headache disorders as outlined in CG150.[1]

Cluster headache

- The pain associated with cluster headache is excruciating and highly debilitating for affected patients.
- Any option for acute treatment should be accessible, fast-acting and effective.
- Prophylactic treatment should be effective in preventing or suppressing attacks.

In looking at treatment recommendations it will be assumed the following process has been followed:

1. Assessment to identify patients whose headache disorder may be classified as secondary, i.e. there is an underlying cause, which may require further investigation and/or referral.
2. Consideration has been given to the patient's use of a short attack headache diary detailing attack duration, frequency and response to treatment to aid diagnosis (this will also be useful in assessing the benefits/effectiveness of any treatment advised).
3. Possibility of medication overuse headache has been considered if there is a background history of migraine.
4. A positive diagnosis has been made, using the diagnosis chart (as per CG150), and where necessary, with advice from a more specialist source, e.g. a GPwSI.
5. If it is a first bout of cluster headache, the need for neuroimaging has been discussed with a GPwSI or neurologist.

It should be noted that the treatment options for cluster headache are both limited, and are generally based on only moderate to low levels of evidence.

One of the acute treatment options given in CG150 is unlicensed in all patients (nasal triptan), and two (subcutaneous and nasal triptan) are unlicensed in patients under 18 years.[2] The BNF for children recommends that treatment for cluster headache be initiated by a specialist.[3]

NICE CG150 recommends theuse of 100% oxygen at a flow rate of at least 12 litres per minute.[1] The recommended duration of use is up to 20 minutes per bout, for up to four hours daily.[2,4] The use of oxygen is only recommended for acute attacks and has no prophylactic effect. The NICE recommendation for ambulatory provision is not based on evidence, but on the Guideline Development Group's (GDG) informal consensus. This method of provision may present either access issues or restrict patient activity as a portable cylinder only has the capacity to provide full treatment for one acute attack and other suitable treatment delivery modalities are not transportable.

The treatment options for prophylaxis are even more limited. Verapamil is the only prophylactic treatment for cluster headache recommended by NICE[1] and is the first-line prophylactic treatment option in the 2011 European Handbook of Neurological Management, at a daily dose of 240-960mg.[5] However, it is unlicensed for this indication and NICE advises that prescribers unfamiliar with its use for cluster headache should seek specialist advice before starting it, including advice on electrocardiogram (ECG) monitoring.[1] Specialist advice is also required for cluster headache that does not respond to verapamil and if treatment for cluster headache is needed during pregnancy.[1]

The evidence for use of oxygen as an acute treatment for cluster headache is based on moderate and low quality evidence. However, all evidence for oxygen at 12L/min is of moderate quality and demonstrates good efficacy.[1] There are no direct comparison trials so there is no evidence to guide clinical preference as to primary choice. There is no evidence as to whether there is effectiveness of either used as a secondary treatment following failure of the alternative used as a primary choice.

When to discontinue oxygen in the management of cluster headaches:

- No clinical benefit from the use of oxygen.*
- Inability to utilise oxygen therapy effectively.
- Prolonged periods of "remission" (Note: oxygen can be reinstated in case of recurrence but is charged at a daily rate, not oxygen usage).
- Development of condition, or introduction of medication/therapy, that contraindicates concurrent use of oxygen.
- Persistent activity alongside oxygen use that presents unacceptable hazards.

*Defined as failure to abort cluster headache attacks determined by treatment of at least five independent attacks with treatment given at the onset of the attack; treatment success considered to be greater than 30% response in attenuation of severity and/or duration in three out of five attacks'

Table 1. Summary of points to consider for given treatment options

Therapy	Positive aspects	Negative aspects
Subcutaneous triptan	• Licensed in >18s • Moderate level of evidence • Excellent and rapid efficacy • Portable • No issue with frequent use	• Patients may not like parenteral self-administration
Nasally administered triptan	• Moderate level of evidence • Good efficacy • Portable • No issue with frequent use • Easy to use	• Unlicensed application
High-flow domiciliary oxygen	• Moderate level of evidence • Good efficacy • No issue with frequent use	• Even though ambulatory provision is available, portability is still an issue • Intrusive in the domestic setting • Possible supply issues • Unpredictable need may exacerbate either supply, or storage issues • Unsuitable for patients with co-existing respiratory disease, particularly COPD

Cost effectiveness

No economic evidence for oxygen in the treatment of cluster headache was identified by NICE in their review. Instead, they used national data from the Primary Care Commissioning publication on Home Oxygen Service where it was estimated that the Home Oxygen Service costs around £175 per new person and around £69 per six month check-up, based on the 2008/9 Reference Cost data obtained from 20 submissions for an outpatient 'Oxygen Assessment and Review' service. These submissions comprised various service setups and the Home Oxygen Service can be expected to have smaller unit costs because of its scale, and the comparatively low resource usage of the half-hour six month check-ups.

This information relates to the provision of oxygen for various conditions (e.g. chronic obstructive pulmonary disease) and no specific cost could be determined for people with cluster headache by NICE.

The following data are aimed to give some indication of potential treatment costs and patient numbers in respect of using Home Oxygen Therapy to abort cluster headache attacks.

Recommended flow rate is >12 LPM (range 12-15 LPM) and the likely duration of uninterrupted treatment is 20 minutes. This gives an oxygen usage of >240 litres (range 240 – 300 litres) per treatment.

Each installation of oxygen will attract both an installation and training charge and site risk assessment. Thereafter, the installation will attract a regular six monthly risk assessment charge, rental charge per cylinder in the installation, and charges for replenishment of the cylinder holding.

Please note:

- The installation and training charge is a “one-off” initial charge.
- The “rental” and risk assessment charges are ongoing, and a daily rate will apply whether the oxygen is used or not.
- Refill charges will depend on the level of usage and the size (number of cylinders) of the installation.
- Urgent supplies carry an additional fee.

A static cylinder holds; (DF) 1360 litres, or ~ 4 to 5 treatments, (ZH) 2400 litres or ~ 8 to 10 treatments. A portable (CD) cylinder holds 430 litres, or ~ 1 treatment

Cluster headache attacks can be highly variable with the range quoted in NICE CG150[1] being from one attack every other day to eight per day. Similarly, duration of attacks can be from 15 to 180 minutes. Attacks occur during a cluster headache “bout”, with bouts occurring on an episodic basis with remission periods of > one month (range “a few weeks” to several months), or on a chronic basis with short (<one month) or almost non-existent remission periods. 80 – 90% of patients fall into the episodic categorisation.

If we assume one bout every three months, with two attacks per day during the bout and that the bout lasts for three weeks then the number of treatments required will be: 42 per bout or 168 per year. If the installation comprises 5 x ZH cylinders, this will provide 40 treatments and would necessitate four refill activities in the year.

Cost (approximate) breakdown based on the above would be:

- Basic cost of ongoing provision (rental) excluding use = £200
- First year additional installation costs = £110
- Oxygen usage costs = £100

Addition of portable provision would result in significant cost increase. The “rental” costs would be at a similar level, but the refill activity may be at a higher level. The cylinder capacity is much reduced equating to approximately one cylinder being required for each attack, and the refill costs are approximately 40% higher.

Comparative costing

Unfortunately, the manner of provision of HOS does not render the costs associated with use tractable to a “cost per treatment” basis, whereas the subcutaneous or nasal administration methods involve the use of discrete treatment units.

One option would be to consider the cost of providing treatment for one year if not actually used.

For the two triptans we could assume that four treatments are prescribed, and for oxygen (a) a standard domiciliary only (excluding portable) supply is installed and (b) a standard domiciliary plus portable supply is installed.

Treatment	Supply	Cost	
Subcutaneous triptan	1 x 2 treatment pack 1 x 2 refill pack	£42.47 £40.41	Total £82.88

Treatment	Supply	Cost	
Nasal triptan (note cost is the same for two strengths available)	2 x 2 dose unit	£23.60 (£11.80 each)	
Static only oxygen	5 x static cylinders	£210 **	
Static oxygen plus portable supply	5 x static cylinders 4 x portable cylinders	£210 £132	Total £342 **

**plus additional £60 for first installation

Provision of oxygen therapy

There are safety and logistical considerations as well as cost considerations that are associated with oxygen therapy for cluster headaches.

The safety, logistical and cost issues around the various models of supply have been considered by the East of England Home Oxygen Group. A summary of the issues and the consensus recommendations from the group can be found in Appendix 1.

Authors

John Reuben; Prescribing advisor, NHS Norfolk on behalf of PAC

Gemma Dowell, PAC author

Document history

PAC approval date	13 March 2017
Version	1
Consultation process	PAC members East of England Home Oxygen group East of England clinicians
QA process	Sue Smith, Senior Clinical Pharmacist, PrescQIPP

References

1. National Institute for Health and Care Excellence (NICE). Clinical Guidance 150. Headaches in over 12s. Updated November 2015. https://www.nice.org.uk/Guidance/CG150
2. Joint Formulary Committee. British National Formulary (online) London: BMJ Group and Pharmaceutical Press; January 2017. Available at: https://www.evidence.nhs.uk/formulary/bnf/current Last accessed 24/01/2017
3. Joint Formulary Committee. British National Formulary for Children (online) London: BMJ Group and Pharmaceutical Press; January 2017. Available at: https://www.evidence.nhs.uk/formulary/bnfc/current Last accessed 24/01/2017.
4. Organisation for the understanding of cluster headaches (OUCH) UK. . Available at: https://ouchuk.org/treatments. Last accessed 24/01/2017.

5. European Academy of Neurology. EFNS guideline 2011. Cluster headache and other trigemino-autonomic cephalagias. Available at: https://www.eaneurology.org/fileadmin/user_upload/guidline_papers/EFNS_guideline_2011_Cluster_headache_and_other_trigemino-autonomic_cephalgias.pdf
6. British Thoracic Society (BTS) Guidelines for Home Oxygen Use in Adults. June 2015. Available at www.brit-thoracic.org.uk

Assessment against ethical and commissioning principles

Treatment assessed	High flow oxygen to treat cluster headaches
East of England PAC recommendation	See summary box on page 1.
Clinical effectiveness	NICE concluded that all evidence for oxygen at 12l/min is of moderate quality and demonstrates good efficacy.[1] As they didn't identify any evidence for the effectiveness of ambulatory oxygen, this recommendation was based on GDG informal consensus.[1] Of the clinical evidence reviewed by NICE, one trial compared oxygen to ergots (ergotamine is rarely used now due to its poor oral absorption and side-effect profile) and two moderate quality trials were identified comparing 100% oxygen to air. 100% oxygen has been found to be more clinically effective than air at reducing pain at 30-60 minutes for around 60% of patients.[1,5] Both studies reported data on reduction in pain at 30 minutes, however data from one study could not be meta-analysed because the results were not reported in a useable format. Data on adverse events was reported differently across studies and could not be meta-analysed. None of the studies reported functional health status or health related quality of life data. No evidence was identified comparing oxygen to triptan therapy.[1]
Cost effectiveness	See pages 4,5,6
Equity	No issues arising

Needs of the community	Reports give the approximate prevalence as 1:1000 (0.1%) of the population, which appears to hold across differing demographics. With the highly patient-variable presentation of cluster headache, it is difficult to predict how many patients may have, or need, active treatment during a year. Further, it is difficult to predict which patients may need a home oxygen service (HOS). Looking at current HOS provision to cluster headache patients, the position is still variable, the reasons for this are: • Completion of clinical code on the HOOF (home oxygen order form) is poor, making identification through this route inadequate • CCGs have, hitherto, adopted differing advice in respect of HOS provision for cluster headache • Actual provision of HOS in terms of supply parameters is also variable (for example flow rates from 4LPM to 15LPM), making identification through this route difficult, or impossible. Using a compound of identification parameters (HOOF clinical codes, flow rate and treatment duration etc), an estimate of current HOS provision for cluster headaches gives a figure of approximately 1:13000 of the population (approximately 8% of the numbers predicted by prevalence)
Need for healthcare (incorporates patient choice and exceptional need)	Patient preference may be for a non-pharmaceutical treatment option. Patients who do not benefit from or cannot use (due to allergy or contraindication) other pharmacological treatments, may require oxygen as a first-line therapy.
Policy drivers	NICE clinical guideline 150.
Disinvestment	Not applicable.

Appendix 1

East of England Home Oxygen Group consensus on provision of home oxygen for the treatment of cluster headaches

The British Thoracic Society (BTS) guidelines for Home Oxygen Use in Adults have (June 2015) been revised.[6] Within this there are recommendations relating to oxygen use in the treatment of cluster headache. Broadly speaking the recommendations made within the guidelines correlate with the views expressed in this document and the NICE guidance (CG150).

The BTS recommended flow rate is more prescriptive at 12L/min. However, the document also makes reference to higher flow rates (14-15L/min) being effective in patients that had been unresponsive to lower flow rates. From this, it would be fair to assume that:

Our recommendation ≥12L/min is correct, and appropriate

We advised that the use of ambulatory/portable oxygen was unlikely to be a viable or useful option; BTS guidance makes no specific recommendation in terms of ambulatory supply, reference is predominantly in relation to "home" provision. We therefore confirm our advice.

- Perhaps more contentiously, the BTS guideline recommends the provision of oxygen on an attack basis, with withdrawal during remission periods. Whilst the reasoning for this approach is understandable, we believe there are problems in practice:
  - This would be inappropriate for the 10% of patients with chronic cluster headache, where remission periods are often short or even non-existent
  - This may also be inappropriate for patients that do not have pre-warning ("aura") of CH attacks, or where this occurs very shortly (≤4 hours) prior to development of the attack.
  - As there are costs associated with equipment installation, urgent service request, and removal, this has to be balanced against the "rental" costs of non-used equipment. It is likely that for patients that have a number of repeat episodes within a year, the costs of continued provision may be less than repeated installation/removal events.

Our recommendation would be that: the frequency and duration of cluster headache episodes must be considered when determining the installation status of the Home Oxygen Supply.

- In addition to the economic considerations, due regard must also be given to the safety issues around continued provision. The installation must be maintained as originally placed by the oxygen contractor. We have noted in our main guidance the domestically "intrusive" nature of the equipment. Particularly for patients where episodes are infrequent, the willingness and ability to ensure continued safe installation must be considered.
- It may be possible to mitigate this by:
  - Having contractor assessed and approved alternative storage provisions for reserve cylinders.
  - Reducing cylinder holdings during remission periods (also economically advantageous).
  - Whilst ensuring the supply is accessible and convenient to meet patient needs, siting in the least disruptive location.

Demand valve

- The standard recommendation is to provide high-flow (≥12L/min) via a 100% non re-breathing mask with reservoir. Recently, the contractor has been able to make available a "demand valve" delivery system. As the name implies, this allows oxygen flow only during the inspiration phase of the breathing cycle. The advantages of this are:
  - Reduction in wastage associated with continuous oxygen flow.

  - Prolongation of the supply delivered from oxygen cylinders.
  - Reduction in the potential oxygen saturation of surrounding materials (including clothes) from “waste” oxygen.
  - As the supply is either fully on or fully off, there is no need to regulate (or specify) flow rate.

Whilst this looks a promising and potentially cost-effective development, we would make the following recommendations:

- Whilst in-use patient feedback indicates satisfactory performance in terms of pain relief as compared with delivery via 100% non re-breathing mask and reservoir, we would like to see an initial short-term pilot use/study within our region to confirm this performance equivalence.
- The effectiveness of high-flow oxygen in treating the individual patient must be established using the standard delivery format before contemplating the use of the demand valve.
- Requests for the demand valve will be restricted to Home Oxygen Assessment and Review (HOS-AR) services that have been commissioned to provide HOS assessment and review for cluster headache patients.
- In the initial stages, selection of patients should be based on:
  - Proven effective relief of CH by the use of high-flow oxygen.
  - Ability and willingness to use the demand valve mouthpiece delivery system.
  - Frequent or prolonged use of oxygen to treat CH episodes which places high demand on cylinder holdings and/or replenishment.
  - Frequent requests for emergency cylinder replenishments.
- Initial exclusion factors:
  - No prior assessment using standard delivery format.
  - Inability or unwillingness to use the demand valve mouthpiece delivery system.
  - Patients that have few, infrequent attacks.
- Continued availability of this delivery format will be conditional on:
  - Proven clinical effectiveness in use.
  - Patient acceptability.
  - Proven cost-effectiveness.

Approved MOPB April 2017, review April 2022 or following PAC review of the document