Cluster headache: review of the literature

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Authors' objectives
To review the efficacy of interventions used in the treatment of acute and chronic cluster headache.

Searching
MEDLINE (from 1966 to 1998) and the Cochrane Controlled Trials Register (Issue 2, 1998) were searched using the MeSH term 'cluster headache' and textwords 'migranous neuralgia' and 'Horton's neuralgia'. The papers found were then searched for further references. Only papers in English which stated the diagnostic criteria were included in the review.

Study selection

Study designs of evaluations included in the review
No inclusion criteria relating to the study design were stated. The included studies were randomised controlled trials (RCTs), controlled clinical trials (CCTs), and randomised and non-randomised crossover trials.

Specific interventions included in the review
Studies that assessed interventions for either the treatment of acute attacks or prophylaxis of cluster headache were eligible for inclusion.

The specific interventions included in the review were: pizotifen, 1 to 4 mg daily (1 study); prednisolone, 30 mg for acute attack, or 20 mg as prophylaxis (1 study); dihydroergotamine nasal spray, 1 mg (1 study); oxygen, 100%, 6 L/minute for 15 minutes (1 study); lithium 900 mg/day and verapamil 360 mg/day (1 study); sumatriptan, 6 mg and 100 mg (1 study); leuprolide, 3.75 mg (1 study); intranasal capsaicin (2 studies); sumatriptan, 100 mg 8-hourly for 7 days (1 study); melatonin, 10 mg/day for 14 days (1 study); lithium carbonate, 800 mg for 7 days (1 study).

Participants included in the review
No exclusion criteria relating to the participants were explicitly stated in the review. The participants had episodic cluster headache (n=269), cluster headache (type unspecified; n=60) and chronic cluster headache (n=197).

Outcomes assessed in the review
The primary outcome assessed was pain relief.

How were decisions on the relevance of primary studies made?
The author did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The author did not state that they assessed validity.

Data extraction
The author did not state how the data were extracted for the review, or how many reviewers performed the data extraction. The tabulated data were the drug and study reference number, study design, study group, treatment and control, pain relief and side-effects. The author also added comments on the quality of the studies.

Methods of synthesis
How were the studies combined?
The studies were discussed narratively according to the intervention. There was no attempt to combine the results of the different studies due to the number of different interventions examined.
How were differences between studies investigated?
The author did not explore any differences between the included studies.

Results of the review
Twelve studies (n=526) were included in the review: 3 RCTs (n=201), 1 randomised crossover trial (n=49), 4 CCTs (n=180) and 4 non-randomised crossover trials (n=96).

Management of acute attacks.
Oxygen (7 L/minute for 15 minutes) delivered by face mask was evaluated in one small, non-randomised crossover trial. The results indicated that 6 of the 19 patients treated reported an improvement.

Sumatriptan was investigated in a randomised crossover trial. When sumatriptan 6 mg was given subcutaneously, there was complete or nearly complete relief of headache and a reduction of conjunctival injection in 80% of the patients. A further study was then conducted to evaluate the dosage: sumatriptan 6 mg was compared with 12 mg subcutaneously. There appeared to be no advantage in the higher dose in terms of relief of symptoms, and more adverse reactions were noted.

Dihydroergotamine nasal spray was investigated in one small CCT. Half of the patients improved with treatment, but half also improved in the placebo group.

Intranasal capsaicin was evaluated in one RCT and one CCT. There were no data available on individual patients from the RCT. Six of the 19 patients with chronic cluster headache in the CCT reported either no attacks or a 50% reduction in pain.

Prophylactic management.
Pizotifen was evaluated in one non-randomised crossover trial. The results showed that 6 out of 28 patients indicated complete remission of their headaches, while a further 10 showed a 50% improvement.

Prednisolone was assessed in one non-randomised crossover trial. The outcomes provided in the trial were not defined clearly and there were insufficient data on the number of patients that responded to treatment.

Lithium and verapamil were assessed in a non-randomised crossover trial. The results indicated that half of the patients reported an improvement with verapamil, while 9 out of 24 patients reported an improvement with lithium.

Leuprolide was assessed in a CCT. Twenty-six out of 39 patients reported a global improvement in their headaches.

Melatonin was evaluated in one small RCT. The results showed that 5 out of 10 patients with episodic cluster headache reported an improvement, but neither of the patients with chronic headache reported any relief.

Lithium was assessed in one CCT. The results showed that 8 out of 13 patients showed an improvement of at least 50%.

Authors' conclusions
The mainstay of treatment remains prophylaxis, and abortive agents are used if there is a breakthrough. The choice of agents depends on various factors since some effective agents may not be appropriate for a particular patient. More than one drug may be used to achieve a reduction in the frequency of the attacks.

CRD commentary
The author provided an overview of the literature rather than a systematic review of the efficacy of the interventions used in the treatment of acute and chronic cluster headache. The review question was adequate, but it did not state clearly the types of study designs that were to be included in the review, or the types of outcome measures that should be assessed. The search was restricted to studies in English, and only two databases and references were searched. It is
therefore likely that studies could have been missed. The method of carrying out the review was unclear as it has not been reported. It was also unclear whether the author conducted any validity assessment; it is not possible to ascertain the quality of the studies included in the review or to weight the results by recourse to their quality. The author provided adequate details of the studies included, but for a number of these, data on subgroup of patients were missing and the outcome measures assessed were unclear. Contact with the authors of the primary studies was clearly warranted to clarify the results.

Overall, it is difficult to extrapolate the author's guideline from the results of the studies included in the review, as only three interventions (sumatriptan, pizotifen and leuprolide) showed any overall beneficial effect. The guideline to the treatment and prophylaxis of cluster headache should, therefore, be interpreted with caution.

**Implications of the review for practice and research**

**Practice:** The author recommended the following guidelines for treatment and prophylaxis.

- Treatment of acute attacks: oxygen, 7 L/minute for 15 minutes; sumatriptan, 6 mg subcutaneously as soon as the attack begins; intranasal dihydroergotamine to reduce the severity of the attacks.

- Prophylaxis of episodic attacks: verapamil, 360 to 480 mg/day; ergotamine 2 mg/day; a combination of verapamil and ergotamine; methylsergide, 2 mg three or four times daily; intranasal capsaicin, once daily; steroids, 60 mg dose reducing over 3 weeks. Prophylaxis of chronic cluster headache: verapamil and lithium; ergotamine, verapamil and lithium.

**Research:** The author stated that double-blind RCTs are needed to further assess the efficacy of pharmacological interventions for the treatment and prophylaxis of acute and chronic cluster headache.

**Bibliographic details**


**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Anticonvulsants /therapeutic use; Clinical Protocols; Cluster Headache /diagnosis /drug therapy /physiopathology /surgery; Diagnosis, Differential; Migraine Disorders /diagnosis; Randomized Controlled Trials as Topic; Review Literature; Serotonin Agonists /therapeutic use; Sumatriptan /therapeutic use; Valproic Acid /therapeutic use

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