Treating primary headaches: cluster headache

Fabio Antonaci MD, PhD,
Headache Centre,
C. Mondino National Institute of Neurology Foundation, IRCCS,
University of Pavia, Italy
and
University Consortium for Adaptive Disorders and Head pain (UCADH)
Terminology in CH

**ATTACK**
the actual paroxysm of pain

**CLUSTER PERIOD**
period of time when attacks regularly recur

**REMISSION**
period during which no attacks recur, either spontaneously or by induction
Cluster headache: clinical picture

- Most frequent TAC: 1CH/25 migraines
- Incidence 9.8 patients/100,000 subjects/year
- Family history 2-6%
- 90% male, 25-30 years
- 10% chronic (>1 year)
- Main diagnostic criteria:
  - Unilateral, periocular pain, lasting from 15-180 min
  - Autonomic ipsilateral symptoms
  - Frequency: 1 attack/2 days to 8 attacks/day
EFNS guidelines on the treatment of cluster headache and other TACS (2006)

<table>
<thead>
<tr>
<th>ACUTE THERAPY</th>
<th>Treatment of choice</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cluster headache</td>
</tr>
<tr>
<td></td>
<td>100% Oxygen, 15 l/min (A)</td>
</tr>
<tr>
<td></td>
<td>Sumatriptan 6 mg s.c. (A)</td>
</tr>
<tr>
<td></td>
<td>Sumatriptan 20 mg nasal (A)</td>
</tr>
<tr>
<td></td>
<td>Zolmitriptan 5 mg nasal (A/B)</td>
</tr>
<tr>
<td></td>
<td>Zolmitriptan 10 mg nasal (A/B)</td>
</tr>
<tr>
<td></td>
<td>Zolmitriptan 10 mg oral (B)</td>
</tr>
<tr>
<td></td>
<td>Zolmitriptan 5 mg oral (B)</td>
</tr>
<tr>
<td></td>
<td>Lidocain intranasal (B)</td>
</tr>
<tr>
<td></td>
<td>Octreotide (B)</td>
</tr>
</tbody>
</table>

A denotes effective; B denotes probably effective;
Acute treatment

HIGH EFFICACY

- O2
- Sumatriptan subcutaneous (6 mg)
- Sumatriptan nasal spray (20 mg)
- Zolmitriptan oral / nasal spray (5 mg mg)

- IV/IM/SC dihydroergotamine mesylate 0.5mg – 1.0 mg
- Octreotide subcutaneous (100 mg)

LOW EFFICACY

- Ergotamine 1 mg – 2 mg oral or suppository
- DHE nasal spray
- Intranasal lidocaine
Oxygen

- 100% O2: 10 liters/ min for 15 to 20 minutes
- May delay rather than abort attack
- Efficacy 70% at 15 minutes
- Most effective when headache is at maximum intensity
- Main limitation is lack of accessibility and inconvenience
- Mask type and compliance
Sumatriptan subcutaneous

- No tachyphylaxis with repeated use
- Attack frequency not increased with prolonged use
- Not effective for preemptive or preventive treatment
- Overall and median time to pain relief longer in patient with chronic cluster headache
Intranasal cocaine and lidocaine

- Complete cessation of nitroglycerin induced attack [after 31 ± 3 min (cocaine) and 37 ± 7 min (lidocaine) 59 ± 12 min after placebo] (Costa et al., 2000)
Prophylactic treatment: when?

- Attacks are frequent, severe of rapid onset and often too short-lived for abortive medication to take effect
- Abortive treatment may only postpone the attack
- Treating frequent attacks abortively may result in overmedication
- Failing the cluster period early may prolong the suffering for months

(Mathew, 1992)
Prophylactic treatment: principles

- Start medication early in the cluster period;
- Continue the drugs until the patient is headache free for at least two weeks;
- Taper the drugs rather than abruptly withdrawing them;
- Restart the drugs at the next cluster period

(Mathew, 1992)
Prophylactic treatment: medication choice

- Previous drug response
- Prior adverse drug reactions
- Contraindication to drug use
- Type of cluster (episodic/chronic)
- Frequency and timing of attacks (nocturnal versus diurnal)
- Expected length of cluster period
- Age and lifestyle of the patient
## EFNS guidelines on the treatment of cluster headache and other TACS (2006)

A denotes effective; B denotes probably effective; C denotes possibly effective

<table>
<thead>
<tr>
<th>Preventive Treatment</th>
<th>Cluster Headache</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verapamil (A)</td>
<td></td>
</tr>
<tr>
<td>Steroids (A)</td>
<td></td>
</tr>
<tr>
<td>Lithium carbonate (B)</td>
<td></td>
</tr>
<tr>
<td>Methysergide (B)</td>
<td></td>
</tr>
<tr>
<td>Topiramate (B)</td>
<td></td>
</tr>
<tr>
<td>Ergotamin tartrate (B)</td>
<td></td>
</tr>
<tr>
<td>Valproic acid (C)</td>
<td></td>
</tr>
<tr>
<td>Melatonin (C)</td>
<td></td>
</tr>
<tr>
<td>Baclofen (C)</td>
<td></td>
</tr>
</tbody>
</table>
Cluster headache

**Transitional**
- Prednisone (60 mg daily for 3 days, then 10 mg decrements every 3 days) or Dexamethasone (4 mg b.i.d. for 2 weeks)

**Maintenance**
- Ergotamine tartrate (1 mg to 2 mg po/suppository daily) DHE 45 (0.5 mg to 1 mg sc/im 8 – 12 hrs)
- Occipital Nerve Block **
- Verapamil ** (240 mg to 720 mg/day)
- Methysergide (2 mg tid; up to 12 mg daily)
- Lithium carbonate (150 mg to 300 mg tid -> 1800 mg)

**Class-I evidence available**
Cluster headache, other preventive options

- Melatonin (10 mg)
- Topiramate (50 mg to 200 mg/day) open studies
- Gabapentin (900 mg to 2400 mg/day)
- Divalproex sodium (500 mg to 3000 mg/day)
- Occipital Nerve Block (92% response rate -> 50% reduction in attack frequency; 70% remission rate by 4 weeks)
Other treatments

- Gabapentin
- Olanzapine
- Baclofen 15-30 mg
- Cibamide 50 mg/day intranasal
- Capsaicin
- Magnesium sulphate IV
- Frovatriptan
Prophylactic treatment: association of drugs

Not recommended
- Metisergide + ergotamine
- Metisergide + valproate

Recommended
- Verapamil + ergotamine
- Verapamil + lithium carb.
  + ergotamine
- Verapamil + valproate
Single high-dose steroid treatment in episodic cluster headache

F Antonaci12, A Costa13, E Candeloro1, O Sjaastad1 & G Nappi13,5
1Department of Neurological Sciences, IRCCS C. Mondino, University of Pavia, 2University Centre for Adaptive Disorders and Headache (UCADH), Varenna and 3University Centre for Adaptive Disorders and Headache (UCADH), Pavia, Italy and 4Department of Neurology, St. Olavs Hospital, Norwegian University of Technology and Science, Trondheim, Norway and 5Department of Neurology and Otorhinolaryngology, La Sapienza University, Rome, Italy


Parenteral indomethacin (the INDOTEST) in cluster headache

F Antonaci, A Costa, S Ghirmai, G Sances1, O Sjaastad1 & G Nappi2
Department of Neurological Sciences, Institute of Neurology IRCCS C. Mondino, University of Pavia, Pavia, Italy, 1University Centre for Adaptive Disorders and Headache (UCADH), Pavia, Italy 2Department of Neurology, St Olav’s Hospital, Trondheim University Hospital, Trondheim, Norway, and 3Chair of Neurology, Department of Neurology and Otorhinolaryngology, University of Rome La Sapienza, Rome, Italy


What it does not work
Criteria for Refractory HA

Failure to an adequate trial of regulatory approved and conventional treatments according to local national guidelines (at least 4 preventative classes)

Goadsby et al. Cephalalgia 2006
Criteria for Refractory Cluster Headache

Adequate trial:
- Appropriate dose
- Appropriate length of time
- Consideration of medication overuse

Failed:
- No therapeutic or unsatisfactory effect
- Intolerable side effects
- Contraindications to use

Failure of at least 4 classes, where 3 should come from 1 to 3:
- 1-3: Verapamil, lithium and methysergide
- 4-6: Melatonin, topiramate and gabapentin

Goadsby et al. Cephalalgia 2006
Refractory cluster headache

- Combination therapy
- Hospitalization / headache specialist
- (repetitive IV DHE; IV methylprednisolone)
- Surgery
Surgical procedures for cluster headaches

- Sensory trigeminal pathway procedures
- Radiofrequency or glycerol rhizotomy
- Gamma knife radiosurgery
- Trigeminal root section
- Autonomic (parasympathetic) pathway procedures
- Occipital nerve stimulation (ONS)
- Hypothalamic stimulation

Dawn, Noon, Sunset, and Twilight, 1979 S. Dalí
(Spanish, 1904-1989)
Coming on...

- supraorbital nerve stimulation
- vagal nerve stimulation
- gamma knife surgery (TN, SPG) - 60%...
Thanks

fabio.antonaci@unipv.it