Tension-type headache
Comorbidities EHF-summerschool
Belgrade – May 2012

Conflicts of Interest: Lectures for Pfizer, Berlin-Chemie, Allergan, Merck
Member of advisory boards in: ATI, Medotech, Neurocore, and Linde Gas ltd. Director in LTB, EHMTIC and Vicepresident in EHF

A gift to The Danish Cluster Headache Foundation and located in the Danish Headache Centre. Painted by Maiken Hejnfeldt, a patient with chronic cluster headache for more than 20 years.
• Agenda

✓ What is the problem
✓ Goals: Optimal diagnosis and treatment
✓ Obstacles: Identification and mechanisms of chronification
✓ Management
✓ Discussion
International Headache Classification, (ICHD- II) (Cephalalgia 2004; 24[Suppl 1]: 1-160)

IHCD-II
14 subgroups

Group 1- 4
Primary headaches

- Migraine,
- TTH,
- Cluster headache,
- Other TAC’s

Group 5–12
Secondary headaches

- Medication
- Trauma, stroke,
- Neoplastic and systemic disorders

Group 13–14
Cranial neuralgias, etc

- Trigeminal neuralgia,
- Other cranial neuralgia and
- Facial pain disorders
Natural History

Headache

Remission
- Evolution to few or no attacks over years

Persistence
- Relative stable attack frequency

Progression
- Evolution to chronic headache
Prevalence of Tension-Type headache in the general population (days per year)

Lifetime prevalence: 86% (98% in females and 76% in males)

Lyngberg et al. Eur J Epidemiol 2005
Comorbidity

• Definition:
• Association with 2 or more disorders occurring together greater than chance alone

• Migraine: Depression, Anxiety, CVD, Stroke, asthma, Raynaud, restless legs syndrome and other headache disorders
Comorbidities and Differential diagnosis to Tension-Type headache

- Migraine
- A secondary headache
- GI problems
- Sleep disorder
- Depression
- Anxiety
- Medication-Overuse headache
Comorbidity of headache and gastrointestinal complaints.
The Head-HUNT Study

AH Aamodt, LJ Stovner, K Hagen & J-A Zwart
Norwegian National Headache Centre, Trondheim University Hospital, Department of Neuroscience, Faculty of Medicine, Norwegian University of Science and Technology, Norway

Cephalalgia


Associations between headache, including migraine, and gastrointestinal (GI) symptoms were studied in a large questionnaire-based cross-sectional study (the Head-HUNT Study). The headache questionnaire was completed by 43,782 individuals, who answered all the questions concerning nausea, reflux symptoms, diarrhoea and constipation. In the multivariate analyses, adjusting for age, sex, educational level, medication use, depression and anxiety, a higher prevalence of headache was found in individuals with much reflux [odds ratio (OR) 2.4, 95% confidence interval (CI) 2.2, 2.6], diarrhoea (OR 2.4, 95% CI 2.1, 2.8), constipation (OR 2.1, 95% CI 1.9, 2.4) and nausea (OR 3.2, 95% CI 2.6, 3.8) compared with those without such complaints. All the GI symptoms investigated seemed to be approximately as common among persons with non-migrainous headache as among migraine sufferers, but the association between headache and GI complaints increased markedly with increasing headache frequency. This may suggest that headache sufferers generally are predisposed to GI complaints.

Migraine, headache, gastrointestinal complaints, epidemiology, HUNT
Comorbidity of headache and gastrointestinal complaints Aamodt et al Cephalalgia 2008

- Hypothesis?

- Conclusion: “This may suggest that headache sufferers generally are predisposed to gastrointestinal complaints”

- Unidirectional or bidirectional relation?

- GI-questionnaire?

Relation between Reflux symptoms, headache and age (Aamodt et al 2008)
Table 3: Prevalence odds ratio (OR) of different gastrointestinal complaints (dependent variables) related to headache frequency and compared with headache-free subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total</th>
<th>Reflux symptoms (n = 47 046)</th>
<th>Diarrhoea (n = 45 453)</th>
<th>Constipation (n = 46 283)</th>
<th>Nausea (n = 45 478)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No.</td>
<td>OR* (95% CI)</td>
<td>No.</td>
<td>OR* (95% CI)</td>
</tr>
<tr>
<td>Headache-free</td>
<td>32 965</td>
<td>8215</td>
<td>1.0 (ref.)</td>
<td>3806</td>
<td>1.0 (ref.)</td>
</tr>
<tr>
<td>All headache types</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>&lt;7 days/month</td>
<td>14 500</td>
<td>4886</td>
<td>1.7 (1.6, 1.8)</td>
<td>2973</td>
<td>1.8 (1.7, 1.9)</td>
</tr>
<tr>
<td>7–14 days/month</td>
<td>2 729</td>
<td>1116</td>
<td>2.3 (2.0, 2.5)</td>
<td>669</td>
<td>2.2 (2.0, 2.4)</td>
</tr>
<tr>
<td>&gt;14 days/month</td>
<td>1 189</td>
<td>517</td>
<td>2.2 (1.9, 2.5)</td>
<td>313</td>
<td>2.3 (2.0, 2.7)</td>
</tr>
<tr>
<td>Migraine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;7 days/month</td>
<td>4 361</td>
<td>1450</td>
<td>1.7 (1.5, 1.8)</td>
<td>921</td>
<td>1.8 (1.7, 2.0)</td>
</tr>
<tr>
<td>7–14 days/month</td>
<td>1 125</td>
<td>469</td>
<td>2.3 (2.0, 2.6)</td>
<td>280</td>
<td>2.0 (1.8, 2.4)</td>
</tr>
<tr>
<td>&gt;14 days/month</td>
<td>350</td>
<td>165</td>
<td>2.6 (2.1, 3.3)</td>
<td>106</td>
<td>2.7 (2.0, 3.3)</td>
</tr>
<tr>
<td>Non-migrainous headache</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;7 days/month</td>
<td>10 139</td>
<td>3436</td>
<td>1.8 (1.7, 1.8)</td>
<td>2052</td>
<td>1.8 (1.7, 1.9)</td>
</tr>
<tr>
<td>7–14 days/month</td>
<td>1 604</td>
<td>647</td>
<td>2.2 (2.0, 2.5)</td>
<td>389</td>
<td>2.3 (2.0, 2.6)</td>
</tr>
<tr>
<td>&gt;14 days/month</td>
<td>839</td>
<td>352</td>
<td>2.0 (1.8, 2.4)</td>
<td>207</td>
<td>2.2 (1.9, 2.6)</td>
</tr>
</tbody>
</table>

*Odds ratio adjusted for sex, age, education, depression, anxiety and use of medication calculated in multiple logistic regression. $P$-trend value <0.0001 for all the variables. The gastrointestinal symptoms were considered to be present if the were some or many of the symptoms.
Other possible explanations might be that GI complaints lead to headache, or, vice versa, that the GI complaints represent manifestations of the GI component of migraine. In the study of Meucci et al. there were completely normal endoscopic findings in 90% of migraineurs with nausea/vomiting or other dysmotility-like symptoms, and their symptoms were considered related to their migraine attacks and not to any GI disorder (11). The GI symptoms may also represent side-effects caused by medicines against headache. It is well known that opioid analgesics may cause constipation and nausea, and various GI symptoms are common side-effects of NSAIDs. Furthermore, psychological factors may also be a common dynamic.
Sleep disorders?

- Problem: Pain affect sleep / Impaired sleep induce pain

- Sleep apnoea 2-4% affect of the general population

- Morning headache? (ICHD-II)

- Cross sectional study in Norway 40,000 adults (Kristiansen et al JHHP 2011)

- Prevalence of fTTH and CTTH, 18.7% and 2.1% resp in SOA persons vs 31.6% and 1.6% resp in Non-SOA persons

- Conclusion: No association between SOA and tension-type headache when controlled for frequency of headache

Females had the headaches and men had SOA but other sleep disorders are not studied in relation to TTH
Psychological comorbidities in tension-type headache

- Depression (OR 1.9-2.4)
- Anxiety (OR 2-3)
- Neuroticism (1.0-1.8)
- Other?

- The risk for depression and anxiety increase in parallel with headache frequency in both migraine and TTH
Psychological comorbidity?  
Lyngberg et al (in prep)

<table>
<thead>
<tr>
<th></th>
<th>Migraine</th>
<th>Migraine adjusted</th>
<th>TTH</th>
<th>TTH adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality of Life - psychological health</td>
<td>0.002</td>
<td>0.04</td>
<td>&lt; 0.0001</td>
<td>0.0003</td>
</tr>
<tr>
<td>Quality of Life - physical health</td>
<td>0.0005</td>
<td>0.06</td>
<td>&lt; 0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Depression</td>
<td>0.02</td>
<td>0.31</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Neuroticism</td>
<td>0.03</td>
<td>0.43</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>
Major depression
Headache individuals from general population

Multivariat:
Migraine:
p = 0.31
Tension-type headache:
p < 0.0001
Neuroticism/ depression headache individuals from general population
Tension-type Headache and Psychiatric Comorbidity

Bernadette Davantes Heckman, PhD, and Kenneth A. Holroyd, PhD

Figure 1. Baseline (BL) mood or anxiety disorder diagnosis moderates improvements in headache-related disability (Headache Disability Inventory) with placebo; estimated values and 95% confidence intervals. X-axis is measured in months. A, No mood or anxiety diagnosis. B, Mood or anxiety diagnosis. Tx—treatment.
"My doctor's great, but I'm just not getting better!! "He's just too busy!"
Case

- 44 year old lady referred with a chronic refractory headache
- No familial history to headache
- Otherwise healthy
- Diagnostic strategy?
- Therapeutic strategy?
- Prognosis?
The 8 most important questions to ask a headache patient

<table>
<thead>
<tr>
<th>Have you one or several different types of headache? Describe them one by one</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>How long does your headaches last? (seconds, minutes, hours, days)</td>
<td></td>
</tr>
<tr>
<td>How frequent are your headaches?</td>
<td></td>
</tr>
<tr>
<td>What is the intensity of pain?</td>
<td></td>
</tr>
<tr>
<td>What do you do during a headache attack?</td>
<td></td>
</tr>
<tr>
<td>Where is the pain located?</td>
<td></td>
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<tr>
<td>Are there any associated symptoms?</td>
<td></td>
</tr>
<tr>
<td>Do you take medication?</td>
<td></td>
</tr>
</tbody>
</table>
### The 8 most important questions to ask a headache patient

<table>
<thead>
<tr>
<th><strong>Have you one or several different types of headache? Describe them one by one</strong></th>
<th><strong>One type, I think, vary in intensity</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>How long does your headaches last? (seconds, minutes, hours, days)</td>
<td>Constant, all day</td>
</tr>
<tr>
<td>How frequent are your headaches?</td>
<td>Constant lasted for more than 40 years, started as episodic at the age of 4</td>
</tr>
<tr>
<td>What is the intensity of pain?</td>
<td>Moderate to severe</td>
</tr>
<tr>
<td>What do you do during a headache attack?</td>
<td>Try to function, but have to lie down during severe pain</td>
</tr>
<tr>
<td>Where is the pain located?</td>
<td>Holocranial</td>
</tr>
<tr>
<td>Are there any associated symptoms?</td>
<td>No but Photophobia, phonophobia, sometimes nausea when it is severe</td>
</tr>
<tr>
<td>Do you take medication?</td>
<td>Yes, I have to, on a daily basis</td>
</tr>
</tbody>
</table>
Diagnostic diary or headache calender for at least 4 weeks
TIME LINE FOR HEADACHE DURATION and MOST LIKELY DIAGNOSIS

- SUNCT or TN: Seconds
- CPH: Minutes
- Cluster Headache: ½-3 Hours
- Migraine: 4-72 Hours
- TTH: Days/weeks
- MOH: Months
Key points for chronification

- Frequent intake of pain killers and antimigraine drugs may induce *medication overuse headache*

- Sustained administration of pain killers, triptans or opiates produces neuroadaptive changes

- These neural adaptations might be responsible for hyperexcitability of the trigeminal system and engagement of descending facilitation

- Enhanced descending facilitation may manifest as loss of diffuse noxious inhibitory control

*De Felice et al Curr Opin Neurol 2011*
Clinical features (medication overuse headache, MOH)

- Daily or almost daily headaches
- Medication overuse

**Medication intake**

- Mon
- Tue
- Wed
- Thur

• Dull diffuse headache
• With or without associated symptoms
• Wake up with headache
• Superimposed migraine-like attacks
• Increased frequency of attacks

Migraine?
ICHDI-II - “Medication-Overuse Headache”

II revision, 2006

... a system whereby medication overuse headache became a default diagnosis in all patients with medication overuse would encourage doctors all over the world to do the right thing, namely, to take patients off medication overuse as the first step in a treatment plan.

A. Headache present on ≥15 days/month

B. Regular overuse for >3 months of one or more acute/symptomatic treatment drugs as defined under sub form 8.2
   1. Ergotamine, triptans, opioids or combination analgesic medications on ≥10 days/month on a regular basis for >3 months

   2. Simple analgesics or any combination of ergotamine, triptans, analgesics, opioids on ≥15 days/month on a regular basis for > 3 months without overuse of any single class alone

C. Headache has developed or markedly worsened during medication overuse
Pathophysiology of Medication-overuse Headache: Implications from Animal Studies

Saknun Bongsebandhu-phubhakdi · Anan Srikiatkhachorn

- Increase frequency of cortical spreading depression
- Increase expression of 5-HT2A receptor
- Decrease in diffuse noxious inhibitory control
- Enhance nociceptive facilitation
- Increase expression of CGRP, substance P and nNOS in trigeminal ganglia
- Decrease nociceptive threshold – Latent sensitization
- Enlargement of receptive field
- Decrease nociceptive threshold
Pain sensitivity during and after long term exposure to opioids or triptans

After Vera-Portocarrero LP et Porreca F 2008
Medication overuse headache

- **Prevalence:** 1–2% of adult population
- **Outcome:** Is treatable and preventable
- **Treatment:** Cessation of overuse
- **Success rate:** 60–93% (Mig and triptans) but 40–45% in TTH
- **Depression:** > 50% improved after detox
- **Prognosis:** Good, 65–69% success after 1 year
- **Cost-effective:** Cost of triptans reduced with 68% after 1 yr

Gaist et al; Katsarava et al, Zeeberg et al, Shah et al
Effect of detoxification and multidisciplinary treatment in medication overuse headache

*** p<0.001

Tension-type headache
Migraine

Visit 1
Final visit

Zeeberg et al 2007
Identification and outcome of MOH: A typical headache calendar

<table>
<thead>
<tr>
<th>JAN.</th>
<th>FEB.</th>
<th>MARTS</th>
<th>APRIL</th>
<th>MAJ</th>
<th>JUNI</th>
<th>JULI</th>
<th>AUG.</th>
<th>SEPT.</th>
<th>OKT.</th>
<th>NOV.</th>
<th>DEC.</th>
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</thead>
<tbody>
<tr>
<td>1</td>
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<td>31</td>
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</tr>
</tbody>
</table>
Mechanisms of chronification

- Genotype
- Phenotype-shift over time
- Increased pain sensitivity
- MOH
- Inactivity
- Psychosocial factors, depression
Psychological treatments at DHC
Groups of 8 patients, nine sessions, 2 hours each

1. Stress and tension, how to recognize and control
2. Biofeedback
3. Pain behaviour, pain accept
4. Cognitive restructuring
5. Feelings, how to handle
6. Thoughts, avoid negative circles
7. Communication
8. Problem solving methods
9. Summary, plan ahead
Important elements in a multidisciplinary headache team

- Medication
- Lifestyle and exercise
- Psychology
- Patient education

Jensen et al Cephalalgia 2010,
Outcome in so-called refractory headache patients after treatment in a multidisciplinary center. Effect on the headache frequency ($p<0.001$) and reduction of absence from work with $60\%$ ($p<0.001$) ($N=1326$)

Days/month

Jensen et al Cephalalgia 2010
Conclusions and perspectives

• In general, migraine and TTH has a good prognosis

• It is very rewarding to treat headache patients

• Stress and depression are important comorbidities to chronic TTH

• Depression and anxiety are pronounced coexisting Migraine and TTH, not in migraine alone

• Medication overuse is a very important and potentially preventable risk factor

• Increased focus on prevention of Chronification
Generally I'm very brave, only today I happen to have a headache!