How do we treat migraine?
New SIGN Guidelines

Managing your migraine
Migraine Trust, Edinburgh 2018

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Chair SIGN Guideline 155
Migraine: A Feature-full Headache

- **Premonitory**
  - Mood changes
  - Fatigue
  - Cognitive changes
  - Muscle pain
  - Food craving

- **Aura**
  - Fully reversible
  - Dull headache
  - Neurological changes: Nasal congestion
  - Visual symptoms: Muscle pain

- **Early Headache**
  - Unilateral
  - Throbbing
  - Nausea
  - Photophobia
  - Phonophobia
  - Osmophobia

- **Advanced Headache**
  - Fatigue
  - Cognitive changes
  - Muscle pain

- **Postdrome**

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**Time**

- Preheadache
- Mild
- Moderate
- Severe
- Post headache

**Headache**
Definitions

• Episodic Migraine
  – Low frequency: 1-9 migraines per month
  – High frequency: 10-14 migraines per month

• Chronic
  – Headache (Tension type or Migraine) 15 or more days per month, for more than 3 months.

• Medication Overuse Headache
  – Headache 15 or more days per month that has evolved along with the frequent use of acute medication, for more than 3 months.
  – Usually chronic migraine pattern
  – Not all patients fitting this criteria have MOH, ie some have frequent headache and current treatment is ineffective
Migraine Management

• Consider:
  – Modifiable lifestyle triggers
  – Acute treatment
  – Preventative treatment
• The case for the sensitive migraine brain

• **Normal life events** trigger or are associated with attacks in those predisposed
(2) Acute treatment

**Aura**
- Fully reversible
- Neurological changes: Visual somatosensory

**Early Headache**
- Dull headache
- Nasal congestion
- Muscle pain

**Advanced Headache**
- Unilateral
- Throbbing
- Nausea
- Photophobia
- Phonophobia
- Osmophobia

- Treatment taken when the headache is mild is more likely to be effective
(2) Acute treatment

**Aura**
- Fully reversible
- Neurological changes
- Visual somatosensory

**Early Headache**
- Dull headache
- Nasal congestion
- Muscle pain

**Advanced Headache**
- Unilateral
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**Headache**

Limit acute treatment to 10 days per month or 2 days per week to prevent medication overuse headache.
Avoid opioids and combination analgesics.

*Time*

- Preheadache
- Mild
- Moderate
- Severe
- Post headache
**Acute Treatment (SIGN)**

- **High dose Aspirin (900mg): NNT 8.1**
- **Non-steroidal anti-inflammatory drugs**
  - Ibuprofen 400mg: NNT 7.2
  - Increase to 600mg if not effective
- **Paracetamol 1g: NNT 12**
- **Antiemetics**
  - Effective for headache as well as nausea
  - Metroclopramide 10mg or Prochlorperazine 10mg
- **Triptans**
  - First choice Sumatriptan 50mg (NNT 6.1) or 100mg (NNT 4.7)
  - Others should be offered if not effective
  - Should consider nasal or injectable if severe headache or early vomiting
Triptans

Serotonin 5-HT$_{1B}$ and 5-HT$_{1D}$ receptors agonists

- Rapid onset short duration triptans
  - Almotriptan 12.5mg
  - Eletriptan 40mg or 80mg
  - Rizatriptan 10mg
  - Sumatriptan 50mg or 100mg (nasal / injectable)
  - Zolmatriptan 5mg (oral / nasal)

- Slow onset long duration triptans
  - Frovatriptan 2.5mg
  - Naratriptan 2.5mg

  Frovatriptan half life 26 hours
  Naratriptan half life 6 hours

*Response to triptans is ideosyncratic*

*i.e. If one does not work try another and another and .......*
Triptan side effects

• Most patients have few problems
  Not “strong” medications

• Common side effects
  – Sensations of tingling, heat, heaviness, pressure, tightness of throat or chest
  – Flushing
  – Dizziness
  – Feeling of weakness, fatigue
  – Nausea and vomiting
Which triptan?

- **Trying for the first time ....**
  - Sumatriptan 50-100mg

- **Side effects ....**
  - Almotriptan (least side effects)
  - Frovatriptan (slow onset)
  - Naratriptan (slow onset)

- **Early vomiting ....**
  - Nasal
  - Injectable

- **Inadequate response ....**
  - Add anti emetic
  - Add Non-steroidal (Naproxen 500mg)
  - Add Paracetamol

- **Severe headaches ....**
  - Rizatriptan
  - Eletriptan
  - Nasal / Injectable
  - Combine with NSAID / Paracetamol

- **Recurrence ....**
  - Eletriptan (fastest acting / most potent)
  - Combine with long acting NSAID
  - Frovatriptan (long acting)
  - Naratriptan (long acting)
Stepped vs Stratified

- High dose Aspirin / NSAID
  - During attack
  - Across attacks
- Triptan
- Mild
- Moderate
- Severe

Vary treatment depending on severity of the attack.
Rescue treatment

• If partly effective can repeat after 2 hours
• If ineffective for that attack don’t use same treatment
• Consider ....
  – Triptan if 1st line treatment is high dose NSAID
  – Rectal Diclofenac
  – Injectable

• May have to ride the headache out ....
  – Status Migrainosis = Migraine > 3 days
  – Injectable Sumatriptan / Injectable anti-emetic / iv Aspirin
  – Steroid taper (anecdotal evidence only)
  – Regular use of analgesics can result in medication overuse headache
Medication Overuse Headache

• Medication overuse headache results from a desire to treat pain and carry on with work and home life!

• 2 common patterns:
  – Transformed migraine
    • Gradual increase in frequency of headache with increasing medication use, perhaps with anticipation that the next headache is starting
  – Daily persistent headache
    • Persistent headache in a person with known migraine with ongoing frequent medication use
      – After a particularly bad headache
      – After a headache that has responded poorly to treatment
      – After treatment of non-headache pain eg shoulder injury
MOH (SIGN)

• Mediation overuse headache needs managed
  – Not all people “overusing” acute medication have medication overuse headache
  – Not clear what the best strategy is

• Evidence to support
  – Abrupt withdrawal of “overused” medication and then need for preventative treatment assessed after a delay
  – Abrupt withdrawal and start a preventative at the same time
  – Start a preventative without withdrawal

*Strategy should be tailored to each individual person*
(3) Preventative treatment

• Aim is to adjust threshold for developing headache
Preventative Treatment

• Reserve for frequent disabling headaches
  – e.g. 3-4 migraines per month

• Start low, go slow, aim high

• Minimum effective, maximum tolerated dose

• Use adequate dose for at least 2-3 months

• Combinations can be effective

• Not a cure!
  – Good response is 50% reduction in headache frequency or severity
Do prophylactic medications work in MOH?

No
• Based on observational studies
• Previously ineffective treatments become effective if tried again after medication withdrawal

Yes
• Topiramate and Botox randomised controlled trials
• No difference between those who overused abortive medication and those who did not

In practice ....
For the majority frequent analgesic / triptan use increases headache frequency and reduces the effectiveness of preventative treatment
Prophylaxis: 1\textsuperscript{st} line (SIGN)

- **Propranolol**
  - Often require 80mg twice daily
  - Main side effects: lethargy, reduced exercise tolerance
  - Don’t use in asthma
  - Other beta blockers can also be effective

- **Tricyclic anti-depressants**
  - Amitriptyline / Nortriptyline (aim for 1mg / kg)
  - Main side effects: dry mouth and day time sedation
  - Amitriptyline is useful if sleep is an issue
  - Nortriptyline is much less likely to cause day time sedation

- **Topiramate** (should have used at least 1 previous preventative medication)
  - Aim for 50mg twice daily, but higher doses can be helpful
  - Can be very effective, but problems with tolerability
  - Small number develop significant cognitive / depressive side effects
Other Prophylaxis (SIGN)

- **Candesartan**
  - Angiotensin receptor blocker
  - Generally very well tolerated

- **Sodium Valproate crono**
  - Main issue is weight gain
  - Should not use in women of child bearing age

- **Flunarizine**
  - Unlicenced in UK

- **Botox**
  - Not recommended for episodic migraine
  - Recommended for the prophylactic treatment of chronic migraine where medication overuse has been addressed and patients have been appropriately treated with 3 or more oral migraine prophylactic treatments
Valproate and women (SIGN)

• Sodium valproate is associated with an increased risk of foetal malformations and poorer cognitive outcomes in children exposed to valproate *in utero*.

• For women who may become pregnant sodium valproate should only be considered as a prophylactic treatment when:
  – other treatment options have been exhausted
  – patients are using adequate contraception.

• Before commencing treatment women should be informed of:
  – the risks associated with taking valproate during pregnancy
  – the risk that potentially harmful exposure to valproate may occur before a women is aware she is pregnant
  – the need to use effective contraception
  – the need to seek further advice on migraine prophylaxis if pregnant or planning a pregnancy.
Flunarizine

- Calcium channel antagonist
  - Widely used in Europe, Canada and South America and in Headache centres in the UK

- Issues
  - Not licensed in UK
  - Usually centrally dispensed from hospital pharmacy

- Effective
  - As effective as the 1st line agents
  - Most effective treatment in Hemiplegic migraine / basilar and vertiginous migraine
  - Long half life - clinical effect and side effects accumulate gradually
  - Easy to use - start 5mg daily for 1 month increasing to 10mg daily if required
  - Discontinuing - because of the long half life it can just be stopped and the clinical effect and any side effects gradually subside
A total of 31 injections across seven specific head and neck muscles, with a minimum dose of 155 U of BOTOX® injected per patient.
Mean ± standard error. The double-blind phase included 688 subjects in the BOTOX® group and 696 in the placebo group.

Headache days at baseline: 19.9 BOTOX® group vs 19.8 placebo group, p=0.498.

<table>
<thead>
<tr>
<th>Study week</th>
<th>BOTOX® (n=688)</th>
<th>Placebo (n=696)</th>
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Study week

Double-blind phase: BOTOX® vs. placebo

Open-label phase: All patients on BOTOX®

Mean change in frequency of headache days from baseline (days/28-day period)

p=0.019
p=0.047
p=0.007
p=0.01
p=0.008
p=0.01
p=0.007
p=0.047
p=0.011
p=0.019
p=0.019
Botox

• Effective and well tolerated

• Approved by NICE (National Institute for Clinical Excellence) 2012
  – for limited use in chronic migraine
  – Must have tried 3 preventatives
  – Must had addressed medication overuse
  – 2 treatments 3 months apart
  – >30% response continue treatment
  – Revert to episodic migraine stop

• Approved by SMC (Scottish Medicines Consortium) February 2017
Other Prophylaxis (SIGN)

• Evidence insufficient to make a recommendation
  – Pregabalin and SNRI Anti-depressants (Venlafaxine / Duloxetine)
  – Pizotifen
    • Only evidence is from old poor quality studies
    • Widely used in primary care

• Evidence of no benefit
  – Gabapentin
  – Pooled evidence from 6 trials showed no consistent benefit over placebo
Greater occipital nerve block

- Combination of steroid and local anaesthetic
  - 80mg Methylprednisolone and 20mg Lidocaine
- Useful as a bridging treatment or to give a period of respite
- Effect is temporary, but outlives the duration of the block
  - Benefit in 60% (usually for 4-6 weeks)
  - No effect in 40%
  - Small number transiently worse (<5%)
  - If effective ~80% of subsequent blocks effective
- In those without benefit multiple block procedure is worth considering
Preventative Medication: Summary

**First line**
- Propranolol
- Topiramate
- Amitriptyline/Nortriptyline

**Pizotifen**
(low quality evidence, but commonly used in primary care)

**Cupboard 2**
- Candesartan
- Flunarizine
- Sodium Valproate
  (should not be used in women who may become pregnant)
- Botox
  (Chronic Migraine only)

**Cupboard 3**
- Pregabalin
- Duloxetine
- Venlafaxine
  (no or inadequate evidence)

Greater occipital nerve blocks
(low quality evidence)
Menstrual Migraine

- **Pure Menstrual Migraine (PMM)**
  - Migraine *without aura*
  - On day 1±2 of menstruation (days -2 to +3)*
  - At least 2/3 menstrual cycles
  - No migraine at other times of the cycle

- **Menstrually-related Migraine (MRM)**
  - As PMM but additional attacks *with or without aura at other times of the cycle*

*day 1 = first day of bleeding; there is no day 0

Peri-menstrual Prophylaxis (SIGN)

<table>
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<tr>
<th>Triptan</th>
<th>NNT</th>
<th>Number of patients</th>
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<tbody>
<tr>
<td>Frovatriptan 2.5mg daily</td>
<td>7.22</td>
<td>633</td>
</tr>
<tr>
<td>Frovatriptan 2.5mg twice daily</td>
<td>3.90</td>
<td>584</td>
</tr>
<tr>
<td>Naratriptan 1mg twice daily (1mg not available in UK – use 2.5mg)</td>
<td>7.99</td>
<td>392</td>
</tr>
<tr>
<td>Zolmatriptan 2.5mg twice daily</td>
<td>4.98</td>
<td>80</td>
</tr>
<tr>
<td>Zolmatriptan 2.5mg 3 times daily</td>
<td>2.52</td>
<td>83</td>
</tr>
</tbody>
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Inadequate evidence for mefenamic acid, naproxen or hormonal treatment (oestrogen gels and oral contraceptives)