Migraine: The Future
Current and Emerging Treatments

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MIGRAINE TRUST
Disclosures

• No industry disclaimers, Dr Callum Duncan (Consultant Neurologist Aberdeen) has given me some of the materials and information on updates of new treatments.

• I am a nurse specialist working in headache clinics in Northampton General Hospital outpatients department.
History milestones

• Aspirin
• Ergotamine tartrate *(ergot)* 1940s
• Dihydroergotamine mesylate *(DHE)* 1950s
• Merthyrsergide 1959
• Triptans 1980s
• **Sumatriptan 1990s**
• Preventative drugs, last 15-20 years
• Still no cure.
Where are we now?
Migraine Management

• Consider:
  – Modifiable lifestyle triggers
  – Abortive treatment
  – Preventative treatment
Modifiable Lifestyle Triggers

- The case for the sensitive migraine brain

- Normal life events trigger or are associated with attacks in those predisposed
Abortive treatment

Treatment taken when the headache is mild is more likely to be effective
What is available now?
Abortive Treatment

- High dose Aspirin 900mg
- Non-steroidal anti inflammatory drugs (non-specific analgesic)
  Ibuprofen 400 mg increase to 600mg if not effective
- Paracetamol 1g
- Anti-emetics – effective for headache as well as nausea.
  metoclopramide 10mg or Prochlorperazine 10mg.
- Triptans – First choice Sumatriptan 50mg or 100mg others may be tried if not effective. (Zolmatriptan 5mg nasaly or injection Sumatriptan 6mg)

- Avoid opioids and combination analgesics!

- Limit to 10 days per month (2 days per week) to avoid the development of medication overuse headache
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 (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 ......
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
What is available now?
Preventative Treatment

Cupboard 1
- Propranolol
- Amitriptyline / Nortriptyline
- Topiramate

Cupboard 2
- Gabapentin / Pregabalin
- Candesartan
- Venlafaxine / Duloxetine
- Flunarizine
  (requires hospital prescription)
- Sodium Valproate
  (not in women of childbearing age)

Cupboard 3
- Botox
- Lisinopril
- Pizotifen
Greater Occipital Nerve Block
The future available now
BOTOX® for Chronic Migraine

- UK licence for Chronic Migraine
  - ≥15 days headache of which ≥8 days are migraine

- Approved by NICE (2012) for chronic migraine where:
  - ≥15 days headache of which ≥8 days are migraine
  - Medication overuse has been addressed and
  - Failed >3 prophylactics

- Now a standard treatment option
BOTOX® for Chronic Migraine

PREEMPT - fixed-site fixed-dose injection paradigm

Frontalis (4 x 5 U)
Procerus (1 x 5 U)
Corrugator (2 x 5 U)
Occipitalis (6 x 5 U)
Temporalis (8 x 5 U)
Trapezius (6 x 5 U)
Cervical paraspinal group (4 x 5 U)
Neurostimulation

- Non-invasive
  - Cephaly
  - TMS
  - Gammacore
- Invasive
  - SPG
  - ONS
Non-invasive devices
Cefaly

Cefaly is positioned on the forehead using an adhesive electrode. Precise impulses are produced, which act on the trigeminal nerve in order to reduce pain and prevent migraine attacks.
Cephaly

- Not available on the NHS
- Can be purchased directly from manufacturer
  - £249 for device, £50 for 3 month supply of re-usable electrodes
- Preventative treatment
- Evidence limited to
  - 1 small manufacturer sponsored sham controlled trial (PREMICE)
  - Post marketing data
eNEURA TMS stimulation

Brief pulse of energy, such as transcranial magnetic stimulation (TMS), may be effective in interrupting or short-circuiting the progression of migraine. eNeura technology utilizes single-pulse Transcranial Magnetic Stimulation, or sTMS. The **SpringTMS®** delivers each treatment in a millisecond (1/1,000 of a second).
eNEURA TMS stimulation

• Not widely available on the NHS (individual funding requests can be made)
• Can be purchased from manufacturer through private sector
  – Free 3 month trial followed by £158 / month
• Abortive treatment
• Evidence limited to
  – 1 small manufacturer sponsored sham controlled trial
  – Post marketing data
Gammacore

Non-invasive vagus nerve stimulator (nVNS) that produces a mild electrical signal to treat migraine and cluster headaches.
Gammacore

- Not widely available on the NHS for migraine but is funded for cluster headache. (individual funding requests can be made)
- Can be purchased from manufacturer through private sector
- 93 day devices with top up card system
- Abortive or Preventative treatment
- Ongoing randomised trials in migraine and cluster headache
Invasive neurostimulation
Occipital Nerve Stimulation
The future
Role of specialist nurses

• Personal view but numbers of specialist nurses are growing.

• Specialist nurses influencing treatments representation NMC NICE helping with clinical trials clinical findings and observations.

• Having access to rescue treatments and advice more readily will be beneficial.
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists

• Key receptor in migraine pathway
  – Animal models show stimulating trigeminal sensory fibres evoke CGRP mediated vasodilation of dural vessels
  – Migraine associated with increasing CGRP serum concentrations
  – These can be reversed by triptans coinciding with pain relief
  – Initial studies show CGRP receptor antagonists can abort migraine attacks (Erenumab) three weeks ago declined for Funding)

• The CEGEPANTS
  • Olcegepant, Telcagepant, MK3207, B144370A
  • Looked promising as an abortive treatment, but also trailed as a preventative
  • As effective as triptans
  • No vascular effects, ? No medication overuse
  • Problems with liver enzymes but newer trials have overcome this and closer to licence.
Ditans

- Serotonin-5-HT1F receptor agonist
  - 5-HT1F receptors are not expressed in the vasculature, and activation of this subtype of receptors has no vascular effects
  - Triptans are serotonin 5-HT\textsubscript{1B} and 5-HT\textsubscript{1D} receptors agonist

Only Lasmiditan has progressed through phase 111 trials

- Promising for Triptan non responders.

? Cost effectiveness

- Role most likely to be for Triptan non responders or those with adverse cardiovascular profile
Calcitonin Gene-Related Peptide (CGRP) Monoclonal antibodies

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- Monoclonal antibodies are now used for a wide variety of conditions

- Promising effect in phase 2 trials, but high placebo rate

- Licensed medication but not funded NHS England and Wales

- Expensive
The future is promising!

- Botox now available if criteria is met.
- Devices
- Range of possible new abortive treatment options
- Monoclonal antibodies
- Growing number of specialists in the field and research is helping understanding of migrane and treatment options.
Thank you for listening.

• Questions??