Treatment of Migraine Associated Vertigo

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Migraine Pathophysiology

• Baseline sensory hyperexcitability (thicker sensitive brains)
• Environmental events push past a threshold leading to:
  • Electrical changes (cortical spreading depression – CSD) occurs in brain.
  • Causes aura (aura is no longer attributed to vasospasm)

The “new” migraine process

• CSD
  • Trigeminal nucleus caudalis (TNC) stimulation
  • Release of inflammatory neuropeptides (CGRP)
• CGRP →
  • Vasodilation
  • “sensitization” (allodynia) in trigeminal circuit
• Pain and sensitization leads to positive feedback.

Treatments for Migraine

• Abortive agents
  • Triptans, Ergots
• Symptom agents
  • Analgesics
  • Antiemetics
• Prevention
  • Interrupt the feedback loop

Abortive medications

Triptans bind to serotonin 5-HT_{1B} and 5-HT_{1D} receptors

• Reduce pain by blocking TNC and reduce secondary sensitization
• Usually very effective for headache phase
• Can block some sensory triggers and prodrome (e.g. nausea) if taken prophylactically

Available Abortive Agents

• Pre-triptan era – agents little used now
  • DHE, Ergotamine, Isomethptene (Midrin)
• Triptans – first was sumatriptan (now generic)
• Common features of triptans:
  • Highly effective, minimal side effects
  • Highly expensive, highly marketed
  • Can be addictive
Triptans – pharmacokinetics

- Rapid/powerful agents
  - rizatriptan (Maxalt), eletriptan (Relpax)
- Moderate
  - Sumatriptan (Immitrex), zolmitriptan (Zomig)
- Weak/slow
  - Naratriptan (Amerge), frovatriptan (frova)

Prophylaxis is more important

- Unpredictable vertigo spells may prevent driving or be dangerous
- Migrainous vertigo rarely responds to vestibular suppressant medications
- Often helps to treat underlying sensory amplifications

Prophylaxis of Migraine – 2008
Mechanism of most of these is not well understood, but they all work about 75% of the time. They all take weeks-months to work.

- CSD blockers
- Anticonvulsants
- Mysterious mechanism agents
- Beta blockers
- L-channel calcium channel blockers
- Neurochemical modulators
- Antidepressants

Sanchez-Del-Rio et al. (2006).

Anticonvulsants – probably raise threshold for CSD

- Topiramate (Topamax)
- Gabapentin (Neurontin)
- Sodium Valproate (Depakote)
- Levetiracetam (Keppra)

Anticonvulsants: Topiramate (Topamax)

- Very effective – about 75%
- Dose: 25 mg to 150 mg, Start with 25, increase weekly
- Associated with weight loss!
  - Large doses – speech disturbance
  - Tingling in hands and feet too
  - Expensive – $1/dose.

Sanchez-Del-Rio et al. (2006).

Beta Blockers

- Very effective - 75%
- Mechanism – not entirely clear --
- Any beta blocker works (not just central ones)
  - Propranolol 60 LA (category C)
  - Metoprolol 50 XL (category C)
  - Atenolol 50-100/day (Category D)
- Side effects
  - Fatigue, Slow pulse, Hypotension, impotence
- 1 month to work
L-channel Calcium Channel Blockers -- Verapamil

• Very effective (75%)
• Mechanism – not well understood
  • Perhaps block TNC (Akerman, 2003)
  • Perhaps relates to genetics (calcium channel gene)
• Verapamil dose 120-240 SR.
• Takes 2 weeks to work
• Constipation main side effect – increase dose if not constipated after 2 weeks.

Antidepressants
Venlafaxine (Effexor) 80% effective

• Mechanism – not very clear -- Dual SNRI and SSRI
• Very useful in managing the sensory amplifications seen in migraine.
• Cheap and very effective (Bulut, Berilgen et al. 2004)
• Start with 12.5 mg, increase slowly to maximum of 75 mg
• Side effects are minor, high doses have withdrawal syndrome

Antidepressants – less used amitriptyline/nortriptyline

• Tricyclic group
• Messy agents
  • Central antihistamine, antihistamine, norepinephrine, serotonin
  • Accumulate in body
  • Weight gain – 25 lbs – not unusual

Summary

• The migraine process is complex and includes electrical, vascular and neurochemical processes and a positive feedback loop
• Migraine can be effectively treated with agents that interrupt this loop.