

## Drug treatment of Vertigo

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Lecture handout:  
<http://tchain.com/cv/courses/cyprus2010/index.htm>

## Processes we might try to treat

- Vertigo in general (nystagmus)
- Menieres's disease
- Migraine (major source of dizziness)
- Motion sickness, emesis
- Compensation

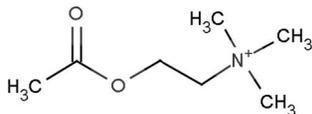
## Processes we might NOT try to treat with medications

- Sensory ataxia (such as gentamicin ototoxicity, blindness, B12 deficiency)
- BPPV (best managed with physical treatments)
- Malingerers (drug treatment facilitates them) – altho there are some tricks – the “tiny dose” approach.

## Main drug categories for vertigo

- Anticholinergic
- GABA agonists
- Everything else

## Anticholinergics



- Block central and peripheral ACH
- Reduce vertigo and nausea from peripheral vertigo
- Reduce central nystagmus (in very high doses)
- Numerous interesting side-effects ð

## Scopolamine Muscarinic antagonist



- Scopolamine (Transderm-Scop)
- Transderm does not require ingestion (but many other oral GI drugs do same thing – Levsin and Robinul for example). Nothing magic about patch.
- Apply every 3 days to skin surface
- Withdrawal syndrome and CNS side effects limit use

## Anticholinergic side effects (Locoweed poisoning)

- Confusion (similar to drug induced Alzheimer's)
- Dry mouth, loss of sweating
- Urinary hesitancy/stoppage. Constipation
- Blurry vision
- Cardiac conduction block
- Addiction



*Oxytropis lambertii*

## H1-antihistamines with strong anticholinergic properties

- meclizine (Antivert)
- dimenhydrinate (Dramamine)
- diphenhydramine (Benadryl)

Antihistamines must cross BB barrier -- i.e. Claratin, Allegra do not work for dizziness

## Antihistamine side effects

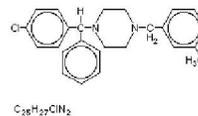
- Sleepiness
- Weight gain (big problem)

## Anticholinergic side effects

- Dry mouth and eyes
- Constipation
- Confusion

## Meclizine (antivert)

- 12.5 TID or 25 TID. Lasts about 8 hours. Available OTC.
- Limitation is sedation and anticholinergic side effects
- Pregnancy: category B. May be best drug



## GABA agonists (benzodiazepines)

- Modulate inhibitory transmitter GABA
- Reduce vertigo and nausea from peripheral vertigo
- Reduce nystagmus
- Sedation, addiction limit usefulness
- ? May impede compensation (no evidence in humans for this)

## Benzodiazepines that work

- Valium (diazepam, "Mothers little helper", 2mg)
- Ativan (lorazepam – 0.5 mg)
- Klonopin (clonazepam, 0.5 mg)



## Benzodiazepines to avoid

- Marginally useful benzodiazepines
  - Halcion (very short acting)
- Benzodiazepines to discourage
  - Alprazolam (xanax) (addiction)
  - Tranzene (too long acting)
  - Diazepam (Valium) in 5mg+ doses (addiction)

## Dosing: beer scale 1 glass of beer =

- 2 mg of diazepam
- 0.5 mg of lorazepam
- 0.5 mg of clonazepam



## Benzodiazepines Bottom line

Extremely useful drugs  
Treat dizziness and anxiety  
Addiction is the big problem

## Drugs of unclear utility (perhaps as a last resort)

- Beta-histine (Serc) – Placebo ? More coming under Meniere's (James and Burton, 2001)
- Baclofen (occasionally useful)
  - Reduces duration of vestibular responses
  - Taper up to 80 mg/day.
- Trimetazidine – (no experience)
  - Placebo ? Not enough data (Prescrire, 2000)

James AL and MJ Burton (2001). Cochrane Database Syst Rev 1: CD001873. Updated in 2009  
Trimetazidine: a second look. Just a placebo. Prescrire Int. 2000 Feb9(45):207-9

## Drugs of unclear utility (perhaps as a last resort)

- Alternative medications
  - Vertigo-HEEL (homeopathic)
  - Ginkgo-Biloba (very weak evidence)

## Meniere's drugs Menieres is a chronic disease Treatment needs to be long term

- Emergency kit
- Diuretics
- Calcium channel blockers
- Betahistine
- Placebos

## Meniere's Emergency kit

- Unpredictable vertigo and vomiting
- Author's approach
  - Sublingual lorazepam (1 mg)
  - Sublingual Ondansetron (8 mg)

## Diuretics for Meniere's worth trying

- Evidence for efficacy is scanty (Thirlwell, 2006)
- Hctz+triamterine (Dyazide and Maxide)
- Acetazolamide (Diamox) – also helpful for
  - Migraine
  - Periodic ataxia
- Furosemide (Lasix)
  - Try to avoid as causes hearing loss and hypokalemia

Thirlwall, A. S. and S. Kundu (2006). "Diuretics for Meniere's disease or syndrome." *Cochrane Database Syst Rev* 3: CD003599

## Calcium Channel blockers for Meniere's – worth trying

- Author's experience – about 30% respond (placebo ?).
- Verapamil 120 SR (1 mg/lb). No evidence for efficacy.
  - Side effects – constipation
  - Excellent for migraine which often accompanies Menieres
- Flunarizine (*Sibellium*)
  - author has no experience, literature says weakly effective – Haid, 1988)

Haid, T. (1988). "Evaluation of flunarizine in patients with Meniere's disease. Subjective and vestibular findings." *Acta Otolaryngol Suppl* 460: 149-53.

## Betahistine (Serc)

- Evidence for efficacy is very weak, US (FDA) position is that it is a placebo (James, 2001)
- Readily available – popular worldwide
- Weak H1 agonist and H3 blocker (which results in some Histamine agonism)
- Author's experience – Useful for motion intolerance and Meniere's. Nearly always try.

James A L and MJ Burton (2001). "Betahistine for Meniere's disease or syndrome (Cochrane Review)." *Cochrane Database Syst Rev* 1: CD001873. Updated in 2009

## Placebos for Menieres

- Torok N. Old and new in Meniere's disease. *Laryngoscope* 87:1870-1877, 1977
- 600 treatments reviewed ranging from spinal fluid drainage to numerous medications.
- Nearly all had 60% efficacy (natural history)
- If it works ...

## Migraine treatments rationale

- Often good rationale for treating Migraine in vertigo patients
  - Migraine is a VERY common cause of vertigo
  - Migraine is highly comorbid with vertigo and Menieres -- > 50% lifetime prevalence (Radke et al, 2002)
  - Chicken-Egg – vertigo triggers migraine (Murdin et al, 2009)
  - Sensory hyperreactivity – makes vertigo worse
    - ┆ ALWAYS start medications at very low dose

Radtko et al. *Neurology*. 2002 Dec 10;59(11):1700-4  
Murdin et al. (2009). *Neurology* 73(8): 638-42.

## Migraine treatments Highly effective

- Anticonvulsants (topiramate, valproate)
- Calcium channel blockers (verapamil, flunarizine)
- Beta-blockers
- Antidepressants (venlafaxine, tricyclics)

Radtke et al. Neurology. 2002 Dec 10;59(11):1700-4  
Murdin et al. (2009). Neurology 73(8): 638-42.

## Migraine prevention treatments general rules

- They all
  - Are “off-label” use of other medications
  - Work between 50-75% of the time (often have to try several ones).
  - Take about 1 month to decide if they work
  - **have to be started slowly** (uptaper)
  - Work in small doses

Radtke et al. Neurology. 2002 Dec 10;59(11):1700-4  
Murdin et al. (2009). Neurology 73(8): 638-42.

## Anticonvulsants for Migraine Topiramate

- Topiramate 25 to 200 mg HS
  - Works 50% of the time at 100 mg HS
  - Tingling in fingers, taste perversion
  - Weight LOSS (5-10 lbs)
  - Word finding problems at higher doses

Brandes, J. L., J. R. Saper, et al. (2004). "Topiramate for migraine prevention: a randomized controlled trial." *Jama* 291(8): 965-73.

## Anticonvulsants for Migraine Valproate

- Sodium Valproate (250 to 1000 mg)
- Effective (Silberstein, 1996)
- Side effects – author rarely prescribes
  - Tremor
  - Weight GAIN
  - Hair LOSS

Silberstein (1996). "Divalproex sodium in headache: literature review and clinical guidelines." *Headache* 36(9): 547-55.

## Calcium Channel Blockers for migraine

- Verapamil SR 120 to 360 HS
  - Effective, about 1-2 mg/lb (Solomon, 1989)
  - Start with 120 SR HS
  - Constipation means enough to work
  - 2 weeks
  - Occasional palpitations, edema
- Verapamil is also an excellent drug to prevent cyclic vomiting (migraine variant resembling Menieres).

Solomon, G. D. (1989). "Verapamil in migraine prophylaxis--a five-year review." *Headache* 29(7): 425-7.

## Antidepressants for Migraine Venlafaxine

- Venlafaxine 37.5 XL (Effexor)
  - Small amounts effective (Turkish study !)
  - Start with 1/3 capsule, increase 1/3 every week
  - About 10% of time, increase to 75 after 1 mo.
  - Don't go beyond 75
  - Side effects –
    - ┆ Nausea, tremor, strange dreams, withdrawal
  - Generic is more difficult to dose (no capsule)

Bulut, S., M. S. Berilgen, et al. (2004). "Venlafaxine versus amitriptyline in the prophylactic treatment of migraine: randomized, double-blind, crossover study." *Clin Neurol Neurosurg* 107(1): 44-8

## Antidepressants for Migraine Tricyclics

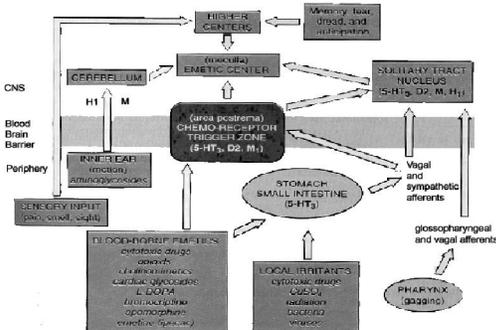
- Amitriptyline (10-50) mg or Nortriptyline
  - Works well, cheap, poorly tolerated
  - Problems
    - ‡ Sedation
    - ‡ weight GAIN – 25 lbs is common
    - ‡ Anticholinergic
  - Start with 10 mg HS.

Bulut, S., M. S. Berilgen, et al. (2004). "Venlafaxine versus amitriptyline in the prophylactic treatment of migraine: randomized, double-blind, crossover study." *Clin NeuroNeurosurg* 107(1): 44-8

## Emesis



## Vomiting is complex



## Drugs used for treatment of emesis

### MOST IMPORTANT

- Dopamine blockers
- 5-HT<sub>3</sub> antagonists
- Anticholinergics
- H<sub>1</sub> antihistamines
- Benzodiazepines
- THC – (Marinol) (rarely used)

## Commonly used phenothiazine antiemetics dopamine blockers

prochlorperazine  
(Compazine)  
5, 10 and 25 mg forms,  
including rectal suppositories.  
Pregnancy -- unknown



promethazine (Phenergan).  
12.5, 25, 50 mg forms,  
including rectal suppositories  
12.5 BID prn oral dose  
typical. Pregnancy Cat. C



## Commonly used phenothiazine antiemetics dopamine blockers

- Powerful drugs
- Major side effects
  - Extrapyramidal
- Use if you have a big vomiting problem



## ondansetron (Zofran) 5HT3 receptor antagonist

- Dose: 32 mg IV, 4-8 mg PO. MLT form
- Category B in pregnancy



**Dr. Hain's drug of choice to use prior to nauseating PT session.**  
Costs a LOT but generic is available

## Last resort vomiting treatments

- Butyrophenones
  - Haloperidol, droperidol sublingually
  - Very effective, but risk of heart block
- Combinations of
  - 5HT3 blocker, Benzo, antihistamine, anticholinergic, dopamine blocker, THC
- Verapamil (good for cyclic vomiting)

## Compensation

### Compensation -- subtypes

- Static compensation – recovery from tone imbalance (vertigo).
  - Largely automatic and not likely to be modified by drugs.
- Dynamic compensation (oscillopsia) – readjust gain.
  - Takes some time, modifiable by medications.

### Compensation -- goals

- Facilitate compensation for static vestibular lesions or central problems. (i.e. vestibular neuritis, bilateral loss)
- Halt compensation for transient vestibular lesions (i.e. Menieres attack).

### Drugs that accelerate dynamic compensation (in animals)

- Amphetamines
- Bromocriptine (Dopamine agonist)
- ACTH (adreno-corticotrophic hormone)
- Caffeine
- TRH

Modified from Brandt, 1991

## Drugs that retard dynamic compensation in animals

- Phenobarbital (sedative, Barbituate)
- Dopamine antagonists (e.g. Lisuride, Thorazine)
- ACTH antagonists (e.g. steroids). Steroids seem to help in people !
- Diazepam, (GABA agonist, Valium). No evidence for this in people.

Modified from Brandt, 1991

## No pain – no gain ? or: Do rat studies apply to people ?

- Drugs that make people more comfortable often impede compensation in animals.
- Animal studies suggesting that medications impede compensation are generally not replicable in people.

## Summary

- Large and complex pharmacology
  - Vertigo
  - Migraine/Meneires
  - Emesis
  - Compensation
- Nearly always will there be an opportunity to explore a different avenue with any particular patient

## More details

Hain TC, Yacovino D. Pharmacological Treatment of Dizziness. Continuum Neurotology Issue (Tusa R editor), 2006.

[www.dizziness-and-hearing.com](http://www.dizziness-and-hearing.com)

Lecture handout: <http://tchain.com/cv/courses/cyprus2010/index.htm>