

Pharmacological Interventions for dizziness

Timothy C. Hain, MD

Northwestern University Medical School
Chicago, Illinois, USA

First a caution

- 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)
- A lot of these medications may be placebo's

Processes we might try to treat

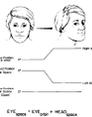
- Vertigo (nystagmus)
- Motion sickness, emesis
- Compensation

Processes we might NOT try to treat with medications

- Sensory ataxia (such as ototoxicity)
- BPPV (best managed with physical treatments)
- Malingering (drug treatment facilitates them)



Neurotransmitters

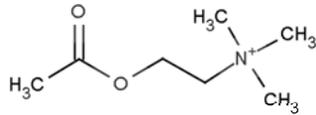


Neurotransmitter	Peripheral	Central
Acetylcholine	Excitatory	Excitatory
GABA	?	Inhibitory
Histamine	?	Excitatory ?
Dopamine	?	Excitatory
Norepinephrine	?	Modulator ?
Glutamate	?	Excitatory
Serotonin	(stomach)	Excitatory ?

Main drug categories

- 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 →

Scopolamine Muscarinic antagonist



- Scopolamine (Transderm-Scop)
- Does not require ingestion (many other oral GI drugs do same thing – Levsin for example)
- 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 would not work

Antihistamine side effects

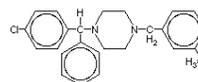
- Sleepiness
- Weight gain

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



C₂₅H₂₇ClN₂



GABA agonists (benzodiazepines)

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

Benzodiazepines

- Diazepam (Valium, “Mothers little helper”)
- Lorazepam (lorazepam)
- Klonopin (clonazepam)



Benzodiazepines

- Marginally useful drugs
 - Halcion (very short acting)
- Drugs to avoid
 - Alprazolam (xanax) (addiction)
 - Tranzene (too long acting)
 - Valium in large doses (abuse)

Dosing: beer scale 1 glass of beer =

- 2 mg of Valium
- 0.5 mg of Ativan
- 0.5 mg of Klonopin



Benzodiazepines Bottom line

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

Diuretics

- Dyazide and Maxide (Hctz+triamterine)
 - Menieres
- Diamox (acetazolamide)
 - Menieres
 - Migraine
 - Periodic ataxia

Drugs of unclear utility (perhaps as a last resort)

- Beta-histine (Serc) →
- Baclofen
- Memantine
- Alternative medications
 - Vertigo-HEEL
 - Ginkgo-Biloba

Betahistine (Serc)

- FDA position is that it is a placebo
- Available from compounding pharmacies and overseas (though made in US)
- Weak H1 agonist and H3 blocker (which results in some H agonism)
- Author's experience – definite utility for motion intolerance and Meniere's.

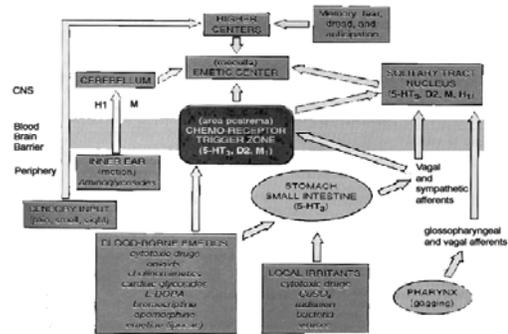
•Kingma H, Bonink M, Meulenbroeks A, Konijnenberg H. Dose-dependent effect of betahistine on the vestibulo-ocular reflex: a double-blind placebo controlled study in patients with paroxysmal vertigo. *Acta Otolaryngologica* 117(5):641-6, 1997

Emesis



FIGURE 1. – Egyptian lady vomiting.

Vomiting is complex



Drugs used for treatment of emesis

MOST IMPORTANT

- Dopamine blockers
- 5-HT3 antagonists
- Anticholinergics (OTC)
- H1 antihistamines
- Benzodiazepines

Commonly used phenothiazine antiemetics dopamine blockers

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

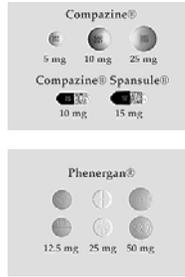


promethazine (Phenergan).
12.5, 25, 50 mg forms, including rectal suppositories
12.5 BID prn oral dose typical. Pregnancy Cat. C



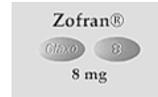
Commonly used phenothiazine antiemetics dopamine blockers

- Powerful drugs
- Major side effects
- 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

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
 - 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 Neurology Issue (Tusa R editor), 2006.

www.dizziness-and-balance.com