ETHICAL & RATIONAL MANAGEMENT OF VERTIGO

Drugs & other Modalities

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ETHICAL & RATIONAL MANAGEMENT OF VERTIGO

Drugs
- Non specific Symptomatic therapy
- Specific therapy to treat the underlying disorder

Maneuvers
- For Benign Positional vertigo

Physical Therapy
- Non specific Vestibular Exercises
- Organ specific Vestibular Physiotherapy
- Cawthorne Cooksey Exercises
- Tai Chi / Yoga / Virtual Reality
Objectives of management of vertigo

- **Provide symptomatic relief** – taking care of the inherent ill-effects of anti-vertigo drugs
- **Diagnose the cause of the vertigo and treat the cause of the vertigo** rather than merely suppress & camouflage the symptom of vertigo
- **Treat the co-morbidities** esp the psychological and cognitive impact of the balance disorder
- **Restore the deranged balance function** possible only by physical therapy in different formats
Vestibular physiotherapy

Physical therapy to restore normal balance function after it has been deranged by disease.

Acts by:-

1. enhancing the vestibular compensatory mechanism
2. improving the general balance function and sharpening the balancing skills of the subject
3. enhancing the functionality of a damaged part of the vestibular labyrinth or of a deranged mechanism in the vestibular system
What is new in today’s scenario ??

- **Our understanding of vestibular physiology has undergone immense refinement;** the morbidity of the balance disorder patient is now much better understood.

- **Any lesion in the vestibular system can be very precisely diagnosed with pin-point accuracy;** specific therapy is now available for most if not all balance disorders.

- **The pharmacology of the anti-vertigo drugs and their mechanism of action in the balance disorder patient is now much better known;** some drugs are now proved to be a complete hoax or just a placebo, some are found to have serious adverse effects and all jeopardise the vest compensatory mechanism.

- **Very specific treatment is available for most causes of balance disorders today;** management now involves treating the co-morbidities also.

- **Vestibular physiotherapy targeted to specific organs in the vestibular system is now a reality;** hence relevance of anti-vertigo drugs is much lesser now.

*Anirban Biswas, Neurotologist*
Balance disorder patients are not just

**or**

-- they have a lot of other problems

Vertigo

Imbalance

Irrational behavior

Poor concentration

Forgetfulness

Anirban Biswas,
Neurotologist
Balance disorder patients have COGNITIVE deficits and show poor cognitive skills in the domains of:

- Memory
- Concentration
- Arithmetic and reading
They also have psychological and emotional disorders
VERTIGO or IMBALANCE are just one of their many problems

A HOLISTIC MANAGEMENT is NEEDED

Anirban Biswas, Neurotologist
Vertigo / imbalance is just a **symptom** or manifestation of an underlying disorder; the causative pathology needs to be known for treatment.

Objective of management is to **correct the cause**, (not merely suppress the symptom) and to **promote balance restoration** by stimulating the deranged balance system and by enhancing vestibular compensation.

**Vestibular compensation** is a natural process but can be expedited by physiotherapy and **inhibited by CNS depressants and the anti-vertigo drugs**.

**Central disorders and bilateral vestibulopathy** usually **present with imbalance**; suppressing vestibular sensitivity by vestibular sedatives will **aggravate the imbalance** as CNS gets deprived of normal vestibular input.
Vertigo / imbalance and psychogenic as well as cognitive disorders are **co-morbid** conditions that need effective management.

Neurotropic agents / antioxidants / cognition enhancing drugs have a **positive** role in the management of balance disorders.

Prolonged use of anti-vertigo drugs is hazardous and detrimental to the balance system; **current recommendation for duration of therapy with anti-vertigo drugs is 3-5 days maximum 7 days**, 

Anirban Biswas, Neurotologist
The role of Vestibular sedatives-
decrease the sensation of head spinning

PROCLORPERAZINE
MECLIZINE
DIMENHYDRINATE

Provide symptomatic relief by -
- receptor blockage in cholinergic pathways
- inhibiting vestibular nuclei
- decreasing discharge rate in the vest nuclei
- sedating the CNS

CINNARIZINE
BETAHISTINE
DIAZEPAM

All these processes INHIBIT the central vestibular compensatory mechanism

Sensory conflicts that increase vertiginous symptom 

Anirban Biswas, Neurotologist
This is what the world believes today...

Anirban Biswas,
Neurotologist
More than 95% patients of vertigo/imbalance are due to-

- BPPV
- Vestibular neuritis
- Migraine related vertigo
- Psychogenic vertigo e.g., PPV / PPPD / Spont MdDS
- Labyrinthitis
- Meniere’s disease
- Vestibular siezures
- Sensory ataxia/posterior column lesions
- Ototoxicity
- Central vertigo due to oculomotor or other CNS diseases like extrapyramidal disorders
More than 95% patients of vertigo/ imbalance are due to:

- BPPV ........ 26%
- Vestibular neuritis ........ 4%
- Migraine related vertigo ........ 21%
- Psychogenic vertigo e.g., PPV/PPPD/Spont MdDS ........ 19%
- Labyrinthitis ........ 1%
- Primary otolithic disorders ........ 9%
- Ménière's disease ........ 1%
- Vestibular siezures/ vest paroxysmia ........ 1%
- Sensorineural deafness/posterior disorder ........ 1%
- Bilateral vestibulopathy -?Ototoxicity ........ 1%
- Central vertigo due to oculomotor or other CNS diseases like extrapyramidal/ cerebellar disorders/ NPH ........ 5%

Specific therapies exist for all of them and none require long continued non-specific therapy with anti-vertigo drugs.
Specific therapy for BPPV
Specific therapy for VESTIBULAR NEURITIS

VESTIBULAR NEURITIS
Specific therapy for PHOBIC POSTURAL VERTIGO
Specific therapy for LABYRINTHITIS

LABYRINTHITIS
Specific therapy for MENIERE’S DISEASE
Efficacy and safety of betahistine treatment in patients with Meniere’s disease: primary results of a long term, multicentre, double blind, randomised, placebo controlled, dose defining trial (BEMED trial)

Discussion

Principal findings

For patients with Meniere’s disease, unpredictable vertigo attacks are the most unpleasant symptom, leading to not just physical but also psychological strain. Clinical experience and several studies have supported a potential beneficial effect of prophylactic drug treatment with betahistine on the attacks of vertigo as well as on vestibular and, to a lesser degree, audiological symptoms. However, according to a Cochrane review of betahistine for Meniere’s disease or Meniere’s syndrome, there is insufficient evidence to say whether betahistine has any effect.
The key findings of the BEMED trial are as follows:

- A significant decline of attack rates in each treatment arm was observed over the nine month treatment period.
- The effects of two different doses of betahistine could not be distinguished from a patient reported effect caused by placebo intervention in terms of the incidence of attacks as well as vestibular and audiological function and quality of life. **Therefore, the results do not give clear evidence that patients have a relevant clinical reduction in the number of attacks after nine months of treatment with betahistine at a daily dose of 48 mg or 144 mg, compared with a placebo (sham) intervention.**
- There were no safety concerns, and betahistine was well tolerated even in the high dose group of 144 mg betahistine per day.

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Specific therapy for VESTIBULAR SEIZURES

VESTIBULAR SEIZURES
Specific therapy for VESTIBULAR PAROXYSMIA
Specific therapy for SENSORY ATAXIA

SENSORY ATAXIA /
POSTERIOR COLUMN LESIONS
Specific therapy for BILATERAL VESTIBULOPATHY
Specific therapy for CENTRAL VERTIGO
VERTIGO — are there definite COGNITIVE & PSYCHIC aspects that need effective management? Is mental stress / anxiety an issue in balance disorders?

If so what is the logic and why and how to manage them??
Maintenance of balance involves:

- understanding (acquiring knowledge) of ongoing reality through the visual, proprioceptive and vestibular senses \textit{perception},

- establishing coherence between these different sensory inputs and by comparing with previously stored experiences \textit{integration & memory recall}

- integrating the inputs in the brain to comprehend the reality about the stability of the ground & the surroundings

- executing a motor action based on the integrated inputs to maintain stability and prevent a fall \textit{execution of a programmed response}

\textit{This is a real cognitive process}
Maintenance of balance involves:

- Adaptation to the ongoing reality and storing in the brain (memorisation of) experiences learnt pertaining to the maintenance of balance.

- Prediction of the expected response by comparing with the previously stored experiences.

- Innovating (usually by intuition) newer strategies to maintain balance when similar experiences are not stored in the brain or when contradictory inputs are received in the brain.

All these too are real cognitive processes.
Maintenance of balance as well as the process of vestibular compensation is all about:-

- learning and re-learning (*acquiring knowledge*) how to make best use of the available inputs

- evolve strategies (*reasoning using past experiences stored in memory*) about how to stay erect and prevent a fall

- achieve a goal by contracting some body muscles (*executing an action*) both in health as well as in disease

*all of which together is a COGNITIVE process*
Compensation and Adaptation involves:-

- Intelligently utilising the available inputs to maintain balance after a vestibular damage has taken place
- Evolving newer strategies to maintain balance as requisite inputs are not available after a vestibular damage

Both these are COGNITIVE processes
PSYCHIC impact of BALANCE DISORDERS

- 64% of vertigo patients had psychiatric symptoms
  - Kenna, Hallam, Hinchcliff Otolaryngol 1991
- 45% of vertigo patients had panic symptoms
  - Cleark, Hirsch, Smith Am J. Psychiatry 1994

Studies show: -

22 to 67% incidence of anxiety & agoraphobia in dizziness patients

39 to 88% incidence of vestibular abnormality in panic patients.
1. Psychiatric patient (esp. schizophrenics) more susceptible to motion sickness
2. Schizophrenic patients have higher incidence of abnormal findings on vestibular function test
3. Dizziness/instability is one of the common features of panic attacks
4. Incidence of definite psychiatric disorder very high in patients with proved vestibular dysfunction.
5. Vestibular disorder patients have very high incidence of abnormality in psychometric test.

6. Better clinical outcome provided when psychotropic drugs are combined with vestibular drugs in many patients of vertigo.

7. Neuroanatomical connections have been established between vestibular and autonomic systems.

Correction of psychic and cognitive deficits is a part of the therapy & much better treatment outcomes are obtained when these factors are attended to.
A vicious cycle

Dizziness
(Severe vertigo persistent dizziness imbalance autonomic symptoms)

Negative beliefs (serious incurable disease, no treatment possible)

Psychological disorders (anxiety, panic avoidance, somatisation, depression)

Restrict movement (poor vestibular compensation)
Psychological disorders commonly encountered in dizziness patients:

- Anxiety
- Helplessness
- Agoraphobia
- Somatisation (hypochondria)
- Depression
- Conversion disorders
1. **Reassurance**: explanation about
   - benign nature of pathology
   - dizziness & psychopathology interrelationship
   - high prevalence of disorder

2. **Psychotherapy**
   - cognitive behavioral therapy
   - psychotherapy

3. **Pharmacotherapy**
   - benzodiazepins
   - antidepressants
A new medication claimed to be non-CNS depressant to reduce stress and manage sleeplessness

Combination of LACTIUM & L-THIANINE

Mental Relaxation
• **LACTIUM** is a bioactive decapeptide having relaxing properties, derived from milk

• **L-THEANINE** is a naturally occurring amino acid mainly found in Green tea leaves
Claimed to be World’s only proven anti-stress therapy

Lactium + L-Theanine

Safety approved by FDA and GRAS
Claims from the manufacturers

- Effective and safe formula for managing stress & disturbed sleep
- Clinically proven efficacy and safety in numerous trials
- Clinically proven to reduce physical, physiological and psychological symptoms of stress (e.g., digestive, cardiovascular, intellectual, social & emotional symptoms)
- Stimulates brain alpha waves and induces relaxation within 40 mins
Manufacturers produced literature showing that the drug:

- Reduces Cortisol level – Major biomarker of stress

- Improves sleep quality & restores natural sleep

- Completely safe and no scary adverse effects (*does not cause sedation, habituation, addiction, dependence, memory impairment etc.*)
The antivertigo drugs - an analytical if not a cynical review
Finding out the least harmful one !!

1. Dimenhydrinate
2. Diazepam
3. Prochlorperazine
4. Promethazine
5. Cinnarizine
6. Betahistine
7. Meclizine
8. Ginkgo biloba
PROCHLORPERAZINE

- belongs to the phenothiazine group of antipsychotics – known to induce extrapyramidal disorders like PARKINSONISM, chorea, dystonia with oculogyric crisis, spasticity, opisthotonus, torticollis, laryngospasm, etc.
- pharmacologically recommended use
- has antihistaminic (H1), anticholinergic (muscarinic M1), antidopaminergic (D2) effects.
- best drug for providing symptomatic relief in acute vertigo.
- vegetative features that accompany acute vertigo like nausea, vomiting are greatly relieved.

Anirban Biswas, Neurotologist
ADVERSE EFFECTS OF PROCHLORPERAZINE

- Extrapyramidal effects like acute dystonic reactions, oculogyric crises, pseudo parkinsonism and akathisia are the major drawbacks - more common in children and adolescents.
- can also cause a life threatening condition called neuroleptic malignant syndrome
- sublingual preparation sometimes causes local erosive cheilitis of lips and tongue (patient can swallow the tablet in such situation)
- Hypotension, esp orthostatic hypotension not uncommon
- anticholinergic effects are often very distressing for the patient
CINNARIZINE

• Provides good symptomatic relief

• Increases blood supply to the brain and inner ear

• Not known to have any teratogenic effect

• But has too many side-effects — hence best abhorred

Anirban Biswas, Neurotologist
Adverse effects of Cinnarizine in long term use in high dosage

Xerostomia
CINNARIZINE  25 to 75mg thrice daily

- labyrinthine sedative effect; hence provides reasonably good symptomatic relief.
- anti-vasoconstrictive effect
- reduces slugging phenomenon of blood in narrow blood vessels
- stabilises vascular endothelium
- Anticholinergic drug hence induces CNS depression
- Side effects like pedal oedema, drowsiness, extrapyramidal symptoms like Parkinsonism/tremor anticholinergic effects

Anirban Biswas, Neurotologist
BETAHISTINE  24-1440mg/day

- Provides symptomatic relief by **sedating**? **stimulating**? the vest labyrinth
- Increases blood flow to brain and inner ear
- Does not depress the CNS
- Only non-sedative anti-vertigo drug without any anti-cholinergic and anti-dopaminergic effects

but

- Mechanism of action **very confusing** and unclear
- Controversies in dosage (24 - 900mg/day)
- Proved to be a **placebo** only without any medicinal effect
What is it actually?

- H1 and H2 receptors have postsynaptic excitatory action on the vestibular system.
- H3 receptor presynaptic autoreceptor (reduces histamine)
- H4 receptors outside CNS have inhibitory vestibular action.

This drug has both excitatory and inhibitory actions, hence, delusion lies in its very existence.

It used to be advocated as a vestibular suppressant but now claimed to be a stimulant of the vestibular system.
What the manufacturers/promoters have understood about mechanism of action of BETAHISTINE

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

The mechanism of action of beta-histidine dihydrochloride is only partly understood. There are several plausible hypotheses that are supported by animal studies and human data.

Beta-histidine dihydrochloride affects the histaminergic system. Beta-histidine dihydrochloride acts both as a partial histamine H2 receptor agonist and histamine H1 receptor antagonist in neuronal tissue, and has negligible histaminergic activity. Beta-histidine dihydrochloride increases histamine turnover and release by blocking presynaptic H2 receptors and inducing H1 receptor down-regulation.

Beta-histidine dihydrochloride may increase blood flow to the cochlear region. Pharmacological testing in animals has shown that the blood circulation to the inner ear improves, possibly by means of a dilation of the precapillary sphincters of the microcirculation of the inner ear.
Betahistidine is a vestibular SUPPRESANT.

Betahistidine treatment in managing vertigo and improving vestibular compensation: Clarification.

M. Lacour / Vertigo, vestibular compensation, and beta histidine.
It was suggested that betahistine causes inhibition of activity in the vestibular nuclei (Timmerman 1994).

Betahistine reduces vestibular input (Lacour 2013)

But, vestibular sedatives cannot be prescribed for more than 3-5 days as per current consensus, so now touted as vestibular stimulant!

Doesn’t this leave us all the more deluded?
The chequered history of Betahistine

- Serc (brand name for betahistine) was approved by the US FDA about 50 years ago for roughly 5 years, but later approval was withdrawn.

- Subsequently, four double blind studies have been done reporting reduction of vertigo attacks with betahistine (Frew and Menon, 1976; Wilmot and Menon; 1976; Meyer, 1985; Mira et al, 2003).
A review suggested that it is presently still unclear if betahistine has any effect in Meniere's disease (James and Burton, 2001).

Reviewed by the "Cochrane database“, in 2009 which concluded insufficient evidence to prove its action.

A recent study of hydrops also found that betahistine had no effect (Gurlov et al, 2012).

Currently not approved by FDA for use in USA
So to summarize, evidence is weak for betahistine being an effective treatment of Meniere's. Our guess is that it is mildly effective, and fortunately it has very few adverse effects (see following).
Betahistine increases cerebral and inner ear blood flow

• The increased blood flow is due to its action both on H1 and H3 receptors

• The much hyped H1 agonistic action is pretty weak; this action was observed only at levels which were 100 fold higher than therapeutic.

• Moreover this action is negated by the antihistaminic group of drugs

• However due to its H3 antagonistic effect, some increase in vestibulo-cochlear blood flow may be possible

Anirban Biswas, Neurotologist
BETAHISTINE and vest. comp

Betahistine has been shown to enhance vestibular compensation and facilitate recovery of balance function in a 1995 study by Tighilit et al.

But this study was on cats and not a human study and dose used was 100 times the recommended therapeutic dose for humans.
Placebo and betahistine have same results.
Discussion

Principal findings

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- There were no safety concerns, and betahistine was well tolerated even in the high dose group of 144 mg betahistine per day.
Conventional antihistaminic with high anti-cholinergic activity.

Mechanism of action: inhibits spread of hyperactive vestibular input via MLF to centers for vegetative regulation in medulla - *e.g.*, centers for heart rate, respiration, vomiting, sweating etc.

Thus very effective in acute vertigo with pronounced vegetative symptoms.

Absence of extrapyramidal features is the biggest advantage of this antiemetic.

Anirban Biswas, Neurotologist
Highly sedative-impairs psychomotor skill. Concomitant use of alcohol or other CNS depressant should thus be discouraged.
Better avoided in patients having enlarged prostate, glaucoma, emphysema, chronic bronchitis. – *applies to other anticholinergics too like cinnarizine meclizine*
Adverse effects of DIMENHYDRINATE in long term use

At very high doses it can affect color discrimination, night vision, visual reaction time, stereopsis.
A new entrant in the anti-vertigo drug market

CINNARIZINE + DIMENHYDRINATE

FIXED DRUG COMBINATION OF CINNARIZINE AND DIMENHYDRINATE

Anirban Biswas, Neurotologist
1) first line drug for symptom control in VERTIGO in different disorders

2) high Anti-vertiginous efficacy for the fixed combination in various vestibular disorder

3) more efficient in reducing vertigo and associated vegetative symptoms than the routinely prescribed Betahistine

4) as effective as Betahistine in Meniere’s disease

5) no signs of a possible detrimental influence of the 4-week treatment with the fixed combination compared with Betahistine in terms of recovery of caloric responsiveness and abatement of rotation-induced nystagmus.

6) Does not impair alertness
The current consensus on management-

- Diagnose the cause of the balance disorder and treat the cause of the vertigo rather than camouflage the symptom of vertigo by eternal continuation of anti-vertigo drugs/ vestibular sedatives

- Treat holistically taking care of the co-morbidities like psychological and cognitive problems induced by the balance disorder

- Ethical and rational treatment consists of:-
  - diagnosing the cause and
  - treating the cause by

Specific drug therapy *not* non-specific anti-vertigo drugs

Manoeuvres for positional vertigo

Vestibular physiotherapy
Yoga/ Taichi / VR / Organ specific PT

Anirban Biswas, Neurotologist
Take home message:-

- Today the UNDERLYING PATHOLOGY AND SITE OF LESION CAN BE DIAGNOSED very accurately in most if not all patients of vertigo

- RESTRICT use of symptom relieving anti-vertigo drugs to 3-5 days and only for acute vertigo; only use drugs that are efficacious and has a logical mech. of action

- TREAT the underlying disorder causing the vertigo, rather than camouflaging the symptom of vertigo

- EXPEDITE vestibular compensation through organ targeted physical therapy as this is the only way to restore balance

- TREAT the concomitant PSYCHOLOGICAL and COGNITIVE impairment for a complete recovery

Anirban Biswas, neurotologist
THANK YOU