

ETHICAL & RATIONAL MANAGEMENT OF VERTIGO

Drugs & other Modalities



Dr. Anirban Biswas
Neurotologist
Vertigo & Deafness Clinic
Kolkata, India

ETHICAL & RATIONAL MANAGEMENT OF VERTIGO

-drugs & other modalities

Drugs

Non specific
Symptomatic
therap

Specific therapy
to treat the
underlying
disorder

Maneuvers

For Benign
Positional
vertigo

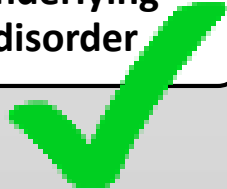
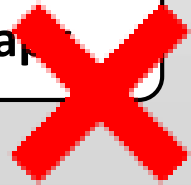
Physical Therapy

Non specific
Vestibular
Exercises-

Organ specific
Vestibular
Physiotherap

Cawthorne
Cooksey
Excercises?

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

Balance disorder patients are not just



Vertigo

or



Imbalance

-- they have a lot of other problems



Irrational behavior



Poor concentration



Forgetfulness

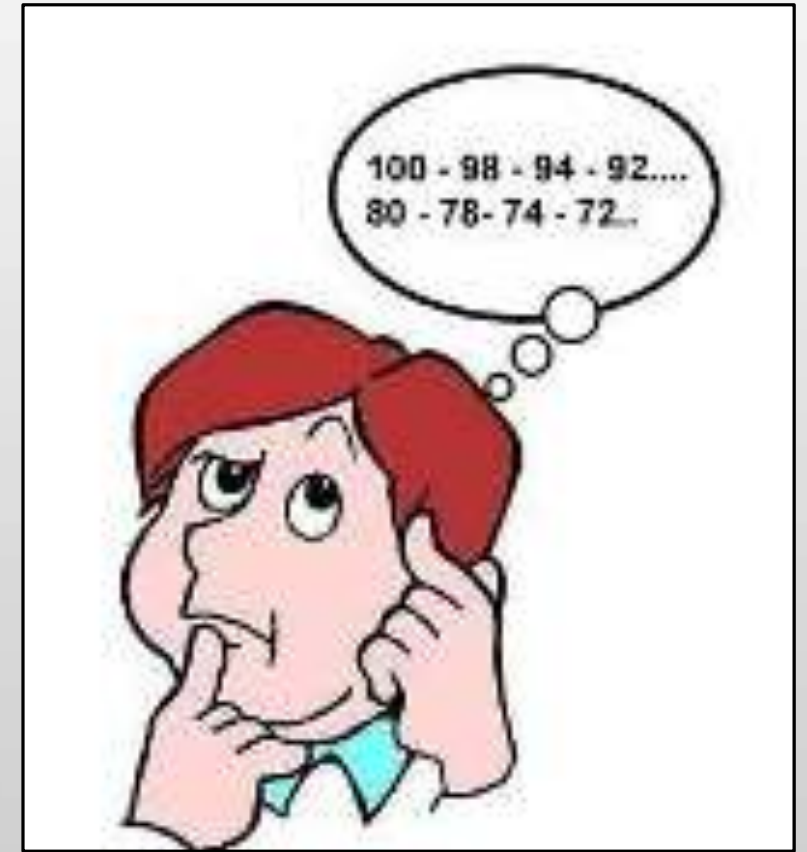
Balance disorder patients have **COGNITIVE** deficits and show poor cognitive skills in the domains of:-



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



Some undisputed basics relevant to therapy

- 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**



Some undisputed basics relevant to therapy

- 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,**



The role of Vestibular sedatives-

decrease the sensation of head spinning

PROCLORPERAZINE

CINNARIZINE

MECLIZINE

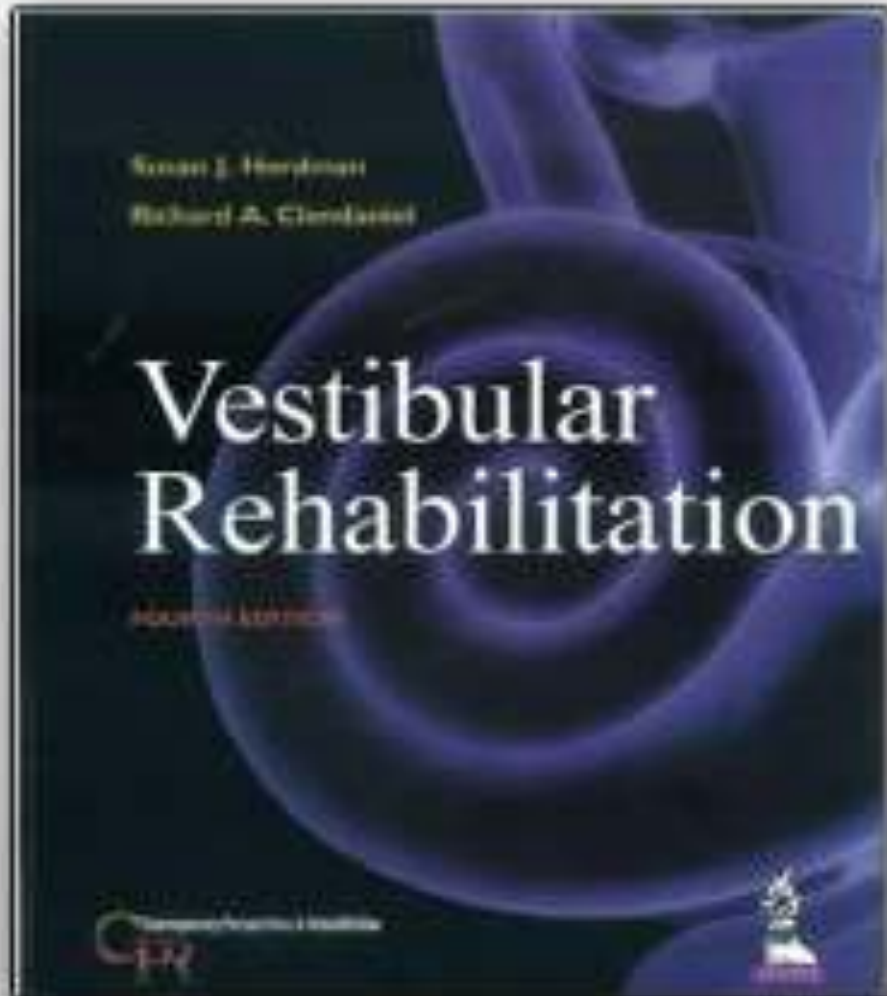
Outcome of prolonged use of vestibular sedatives:--

- Poor vestibular compensation
- Complete balance function **not** restored
- Persistence of imbalance

All these **INHIBIT** the central vestibular compensatory mechanism

*Sensory conflicts that increase vertiginous symptom **enhances** compensation*

This is what the world believes today...



valacyclovir offer no therapeutic advantage.³⁶ There is a consensus that drugs exerting a “sedative effect” on the vestibular system should be used for only the first 24 hours.¹⁰ Some drugs commonly used for treatment of vertigo, nausea,

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10. Baloh RW, Kerber KA. *Clinical Neurophysiology of the Vestibular System*. Fourth ed. New York: Oxford University Press, 2011.

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. PPPV.....1%
- Labyrinthitis.....1%
- Cervical vertigo.....1%
- Cervical column lesions.....1%
- Vestibulopathy -?Ototoxicity.....1%
- Central vertigo due to oculomotor or other CNS diseases like extrapyramidal/ cerebellar disorders/ NPH5%

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

Specific therapy for BPPV



BPPV

Specific therapy for VESTIBULAR NEURITIS

VESTIBULAR NEURITIS

Specific therapy for VERTIGINOUS MIGRAINE

**MIGRAINE RELATED
VERTIGO**

Specific therapy for PHOBIC POSTURAL VERTIGO

**PHOBIC POSTURAL
VERTIGO**

Specific therapy for LABYRINTHITIS

LABYRINTHITIS

Specific therapy for MENIERE'S DISEASE

MENIERE'S DISEASE

RESEARCH

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)

BMJ 2016; 352 doi: <https://doi.org/10.1136/bmj.h6816> (Published 21 January 2016)

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.

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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.

Specific therapy for VESTIBULAR SEIZURES

VESTIBULAR SEIZURES

Specific therapy for VESTIBULAR PAROXYSMIA

VESTIBULAR PAROXYSMIA

Specific therapy for SENSORY ATAXIA

**SENSORY ATAXIA /
POSTERIOR COLUMN LESIONS**

Specific therapy for BILATERAL VESTIBULOPATHY

OTOTOXICITY

Specific therapy for CENTRAL VERTIGO

CENTRAL VERTIGO

Managing the main COMORBIDITIES

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??

COGNITION & maintenance of balance

Maintenance of balance involves:-

-understanding (acquiring knowledge) of ongoing reality through the visual, proprioceptive and vestibular senses *-perception,*

-establishing coherence between these different sensory inputs and by comparing with previously stored experiences *– 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 *–execution of a programmed response*

This is a real cognitive process



COGNITION & maintenance of balance

(contd)

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

COGNITION & maintenance of balance

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*

COGNITION & Vestibular Compensation

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.



The vestibular –psychiatric interrelationship :-

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.

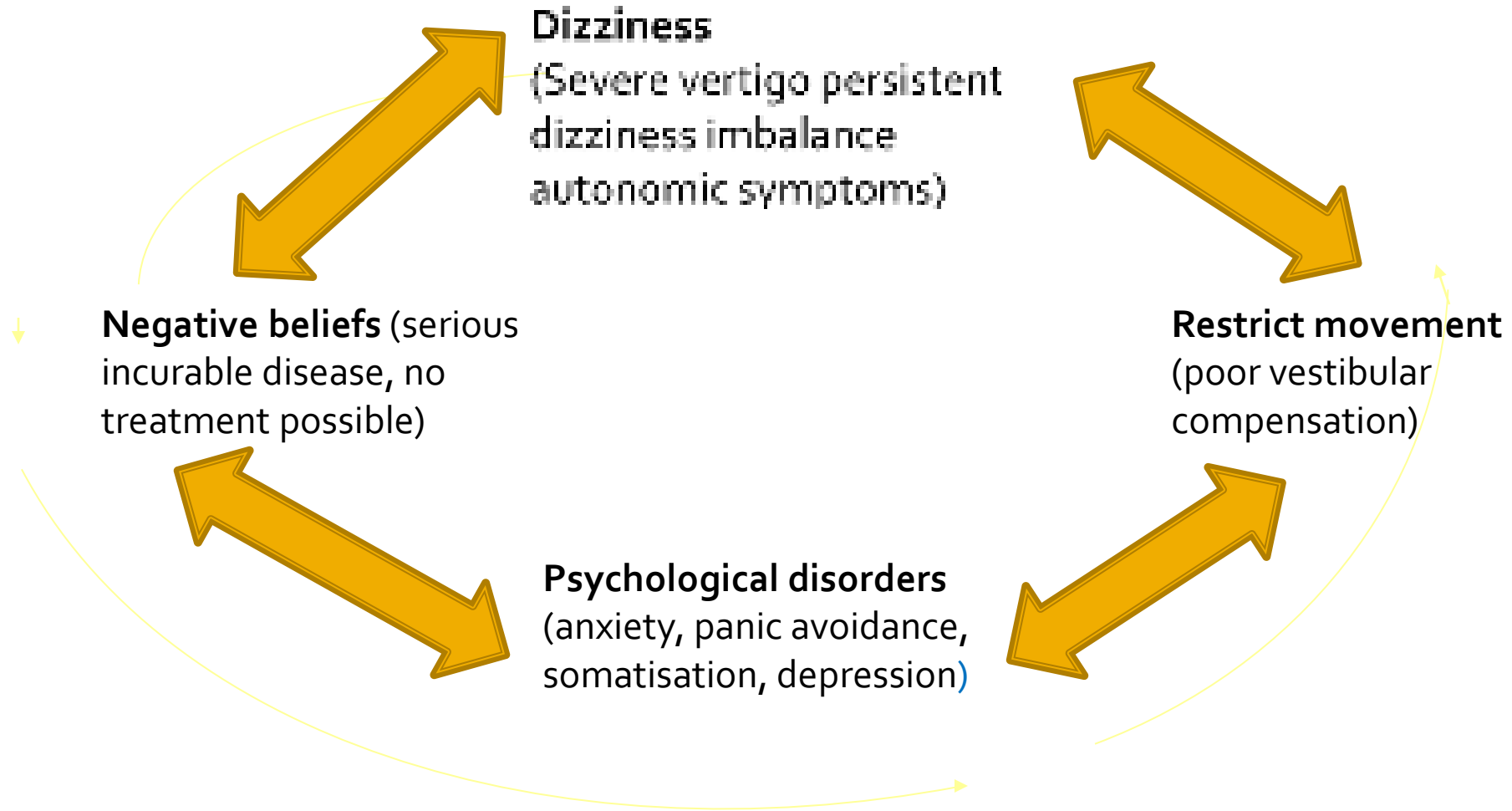
The vestibular –psychiatric interrelationship (Contd.) :-

5. Vestibular disorder patients have very high incidence of abnormality in psychometric test.

6. Better clinical

7. **Correction of psychic and cognitive deficits is a part of the therapy & much better treatment outcomes are obtained when these factors are attended to** has been established between systems.

A vicious cycle.....



Psychological disorders commonly encountered in dizziness patients :-

- **Anxiety**
- **Helplessness**
- **Agoraphobia**
- **Somatisation (hypochondria)**
- **Depression**
- **Conversion disorders**



MANAGEMENT

1. **Reassurance** : explanation about

- benign nature of pathology
- dizziness & psychopathology interrelationship
- high prevalence of disorder

2. **Psychotherapy**

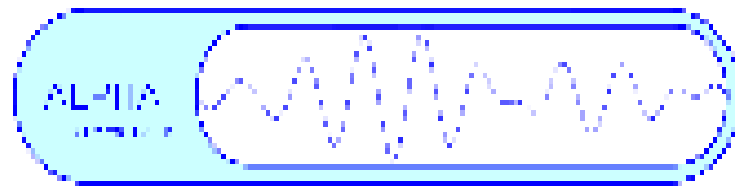
- cognitive behavioral therapy
- psychotherapy

3. **Pharmacotherapy**

- benzodiazepins
- antidepressants



A new medication claimed to be non-CNS depressant to reduce stress and manage sleeplessness



Mental Relaxation

Combination of LACTIUM & L-THIANINE

- **LACTIUM** is an bioactive decapeptide having relaxing properties, derived from milk



- **L-THEANINE** is naturally occurring amino acid mainly found in Green tea leaves



Claimed to be World's only proven anti-stress therapy



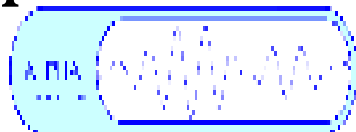
L-THEANINE

Safety approved by



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, etc.*
- pharmacologically recommended for acute vertigo
- has antihistaminic(H1), anticholinergic(M1), and antidopaminergic(D1),
- best drug for symptomatic relief in acute vertigo.
- vegetative symptoms that accompany acute vertigo like nausea, vomiting are greatly relieved.

**too many side-effects that
clinicians need to be aware of**

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*

Adverse effects of Cinnarizine in long term use in high dosage

A close-up photograph of a person's mouth with the tongue extended. The tongue is a deep red color and exhibits significant dryness and cracking, particularly on the surface, which is characteristic of xerostomia. The surrounding oral tissue also appears somewhat dry.

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



BETAHISTINE 24-1440mg/day

- Provides symptomatic relief by *? sedating ? stimulating* the vestibular 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

Source



ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

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

Betahistine dihydrochloride affects the histaminergic system. Betahistine dihydrochloride acts both as a partial histamine H₁ receptor agonist and histamine H₂ receptor antagonist in neuronal tissue, and has negligible H₃ receptor activity. Betahistine dihydrochloride increases histamine turnover and release by blocking presynaptic H₂-receptors and inducing H₂-receptor downregulation.

Betahistine dihydrochloride may increase blood flow to the cochlear region. Pharmacological testing in animals has shown that the blood circulation in the stria vascularis of the inner ear improves, probably by means of a relaxation of the particularly spastic vessels of the microcirculation of the inner ear.

Betahistine dihydrochloride also normalizes function of the vestibular nuclei. Betahistine dihydrochloride was also found to have a beneficial effect on vestibular nuclei activity in lateral and medial vestibular nuclei.

EMA / Public Health
 European Medicines Agency, 2, rue d'Arlon, 1205 Brussels, Belgium

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Betahistine is a vestibular SUPPRESANT

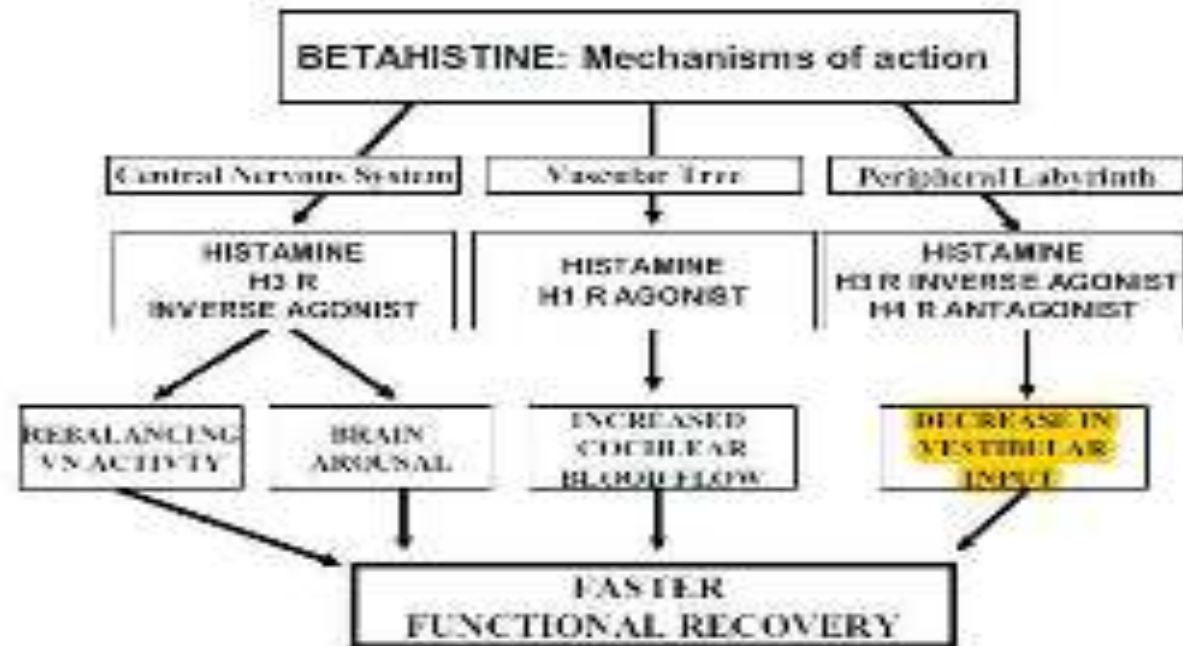
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M. Lacour / Vertigo, vestibular compensation, and betahistine.

Betahistine treatment in managing vertigo and improving vestibular compensation: Clarification

Michel Lacour
TUM, MZM, GPO, Universität Erlangen-Nürnberg, Germany, 2010

M. Lacour / Vertigo, vestibular compensation, and betahistine.



DILEMMA

- 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).

The chequered history of Betahistine

- 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

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Serc (betahistine)

[Timothy C. Hain, MD](#)

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

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 .

RESEARCH

CROSSREF OPEN ACCESS



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)

Christine Adnan,^{1,2} Carolin Simone Fischer,¹ Judith Wagner,¹ Robert Gjurkov,⁴ Ulrich Mansmann,³ Michael Strupp^{1,3} On behalf of the BEMED study group

WHAT THIS STUDY ADDS

Long term prophylactic treatment with betahistine dihydrochloride (at daily doses 2x24 mg or 3x8 mg) does not change the time course of vertigo episodes related to Meniere's disease compared with placebo

Placebo intervention as well as betahistine treatment showed the same reduction of attack rates over the study's nine month treatment period

Reliable and valid instruments that measure subjective vertigo symptoms (in particular, vertigo attacks caused by Meniere's disease) are lacking; derivation of definite or probable attacks caused by Meniere's disease, on the basis of raw patient recordings in vertigo diaries, is methodologically challenging and requires prespecified rules

<https://doi.org/10.1136/bmj-2022-074826>

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DIMENHYDRINATE

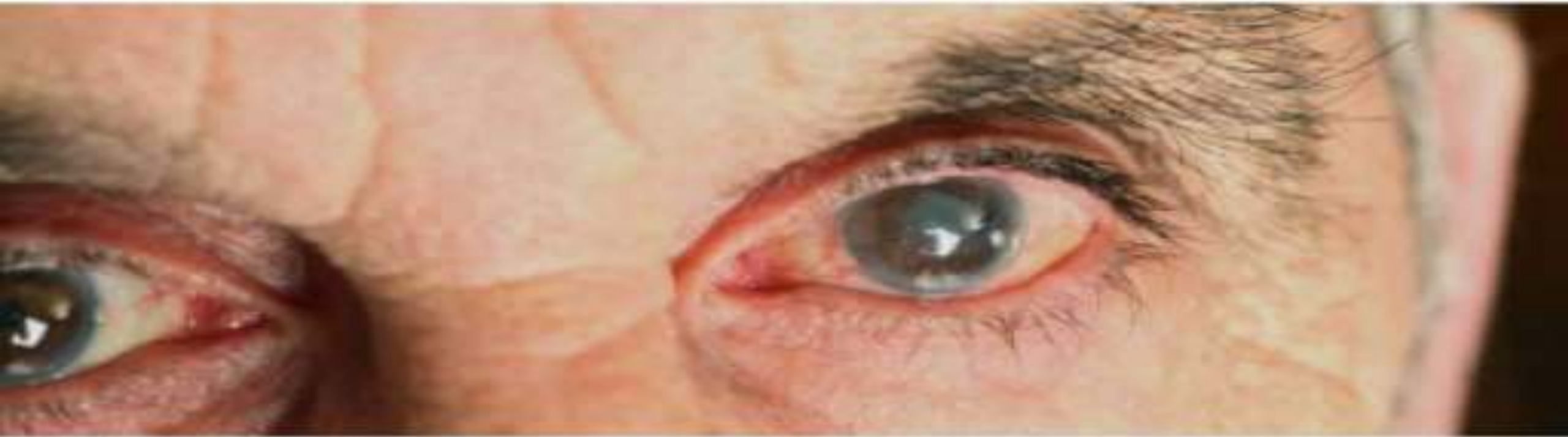
- ▶ Conventional antihistaminic with high anti-cholinergic activity.
- ▶ Mechanism of action: inhibits spread of hyperactive vestibular input via MLF to centers for vegetative regulation in medulla -*e.g-centers for heart rate, respiration, vomiting, sweating etc.*
- ▶ Thus very effective in acute vertigo with pronounced vegetative symptoms
- ▶ Absence of extrapyramidal features is the biggest advantage of this antiemetic.

Adverse effects of DIMENHYDRINATE in recommended therapeutic dosage



Highly sedative-impairs psychomotor skill. Concomitant use of alcohol or other CNS depressant should thus be discouraged.

Adverse effects of DIMENHYDRINATE in long term use



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



**FIXED DRUG COMBINATION OF
CINNARIZINE AND DIMENHYDRINATE**

Cinnarizine + Dimenhydrinate - Summary of Literature review

- 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

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 camouflage 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

A photograph of a theater stage. A large white screen is the central focus, displaying the words "THANK YOU" in a bold, red, sans-serif font. The screen is framed by dark red curtains. Above the screen, a curved architectural element features a logo on the left and some faint, illegible text on the right. The foreground shows rows of dark red theater seats, mostly empty, receding into the distance.

THANK YOU

ultra

