



Postural Hypotension

24th April, 2009

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QEH

Inter-hospital Geriatric Meeting

New case in admission ward

Mr. WY

- M/66
- ADLI
- Lives with wife
- NSND
- Walks unaided

PMHx

- 20+ years history of T2DM
 - metformin 1gm bd and diamicon 160mg bd
 - Recent A1c 7%
 - microalbuminuria
 - Background DMR FU HKEH
- HT on hydrochlorothiazide
- BPH FU by urologist
 - terazosin 1mg nocte

Dizziness spell and fell in the doorway of toilet at 6am

Found supine BP 150/80 mmHg and standing BP 95/51 mmHg in A&E

H'stix 6.8



Further history taking in ward

- **Postural dizziness** for few years
- Especially in the morning
- LOC x 2 in the past
- Worried to go out in case he felt dizzy

- The dizziness was so severe that he **felt fainted** on day of admission
- No LOC, witnessed convulsion or incontinence
- No head injury
- No chest pain / SOB / palpitation
- No vertigo, hearing loss or tinnitus
- No tarry stool, vomiting or diarrhea
- No recent URI, chest or urinary symptom
- Not taking herbs or over-the-counter drug

Physical examination



- SBP 140 → 90 mmHg from lying to sitting
- Without significant HR change
- Neurological exam found peripheral neuropathy (depressed pinprick sensation over glove and stocking distribution; absent ankle jerk; bilateral flexor plantar response)
- No clinical feature of Parkinsonism
- No focal neurological sign, peripheral neuropathy, cerebellar sign or gait disturbance
- No clinical feature of CHF
- No carotid bruit
- Abdominal examination: unremarkable
- PR: brownish stool
- H'stix in A&E was 6.8

Investigations

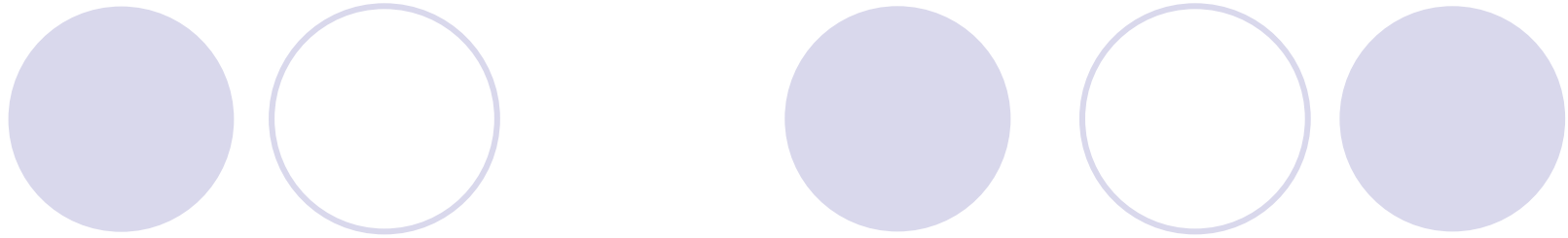


1. CBP, LFT, glucose, CaPO₄, lipid profiles, serum cortisol, B12, folate, VDRL, TSH were unremarkable
2. RFT 132/4.8/8.6/100
3. Short Synacthen Test: 153 → 617
4. Serial cardiac enzymes and ECGs: normal
5. Cardiac monitoring: no arrhythmia detected
6. 24-hour Holter study, echocardiogram and treadmill: all normal
7. CXR: no abnormality seen
8. ENT consulted: no pathology seen
9. CT brain: no abnormal attenuation

Tilt table test in 8/2003

- Significant postural BP drop during tilt table test
- BP 114 / 64 mmHg (lying) → 76 / 55 mmHg (70° tilt at 2 min)
- Pulse 76/min (lying) → 78/min (70° tilt at 2 min)
- Associated with dizziness and chest discomfort of similar character





Review of orthostatic hypotension (OH)

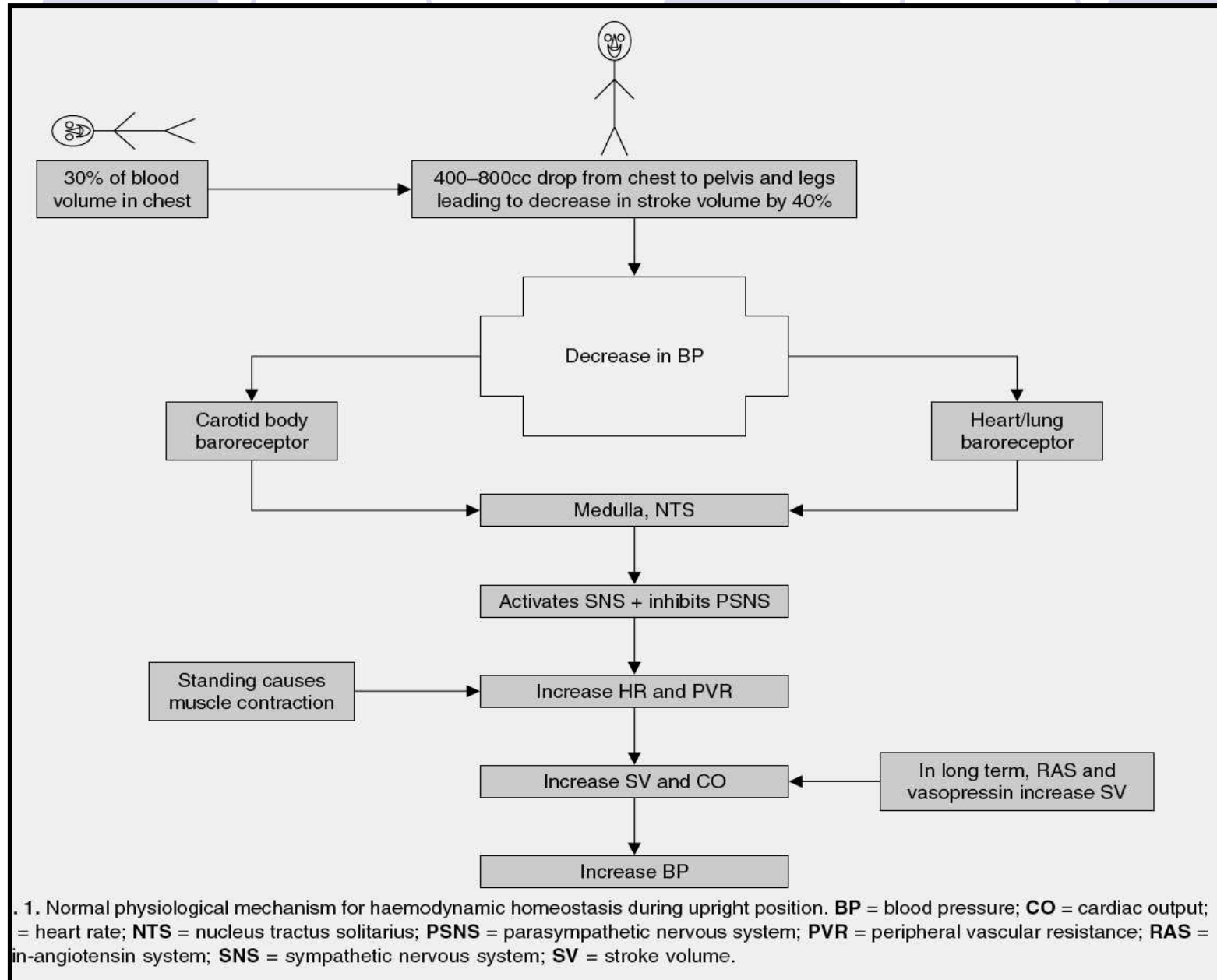


Orthostatic Hypotension: Definition

- American Autonomic Society Criteria:
 - Fall of systolic BP of at least 20 mmHg or diastolic BP of at least 10 mmHg within 3 min of standing (or 60 degree tilt).
 - May be Symptomatic or Asymptomatic
 - Schatz IJ et al. *Neurology* 1996; 46: 1470

What happens on standing?

Hajjar J. Postural blood pressure changes and orthostatic hypotension in the elderly patient. *Drugs Aging* 2005; 22: 55-68



What is the Prevalence of OH in different settings?

- Cross-sectional prevalence of OH in unselected elders aged 65 years or older has been reported – 5% to 30% (Lipsitz 1989; Mader et al 1987; Caird et al 1973; Johnson et al 1965; Rutan et al 1992; Masaki et al 1998; Tilvis et al 1996)
- Higher in institutionalized populations – 10-33% (Palmer et al 1983; Aronow et al 1988; Lock et al 1997)
- Highest in acute care setting – close to 70% (Weiss A et al 2002)

Approach to OH

A decorative graphic at the top of the slide consists of two groups of three circles. The first group on the left has a solid light purple circle on the left, a white circle with a light purple outline in the middle, and a solid light purple circle on the right. The second group on the right has a solid light purple circle on the left, a white circle with a light purple outline in the middle, and a solid light purple circle on the right.

- Acute vs chronic

- Acute OH develops over a relatively short time
- requires immediate attention

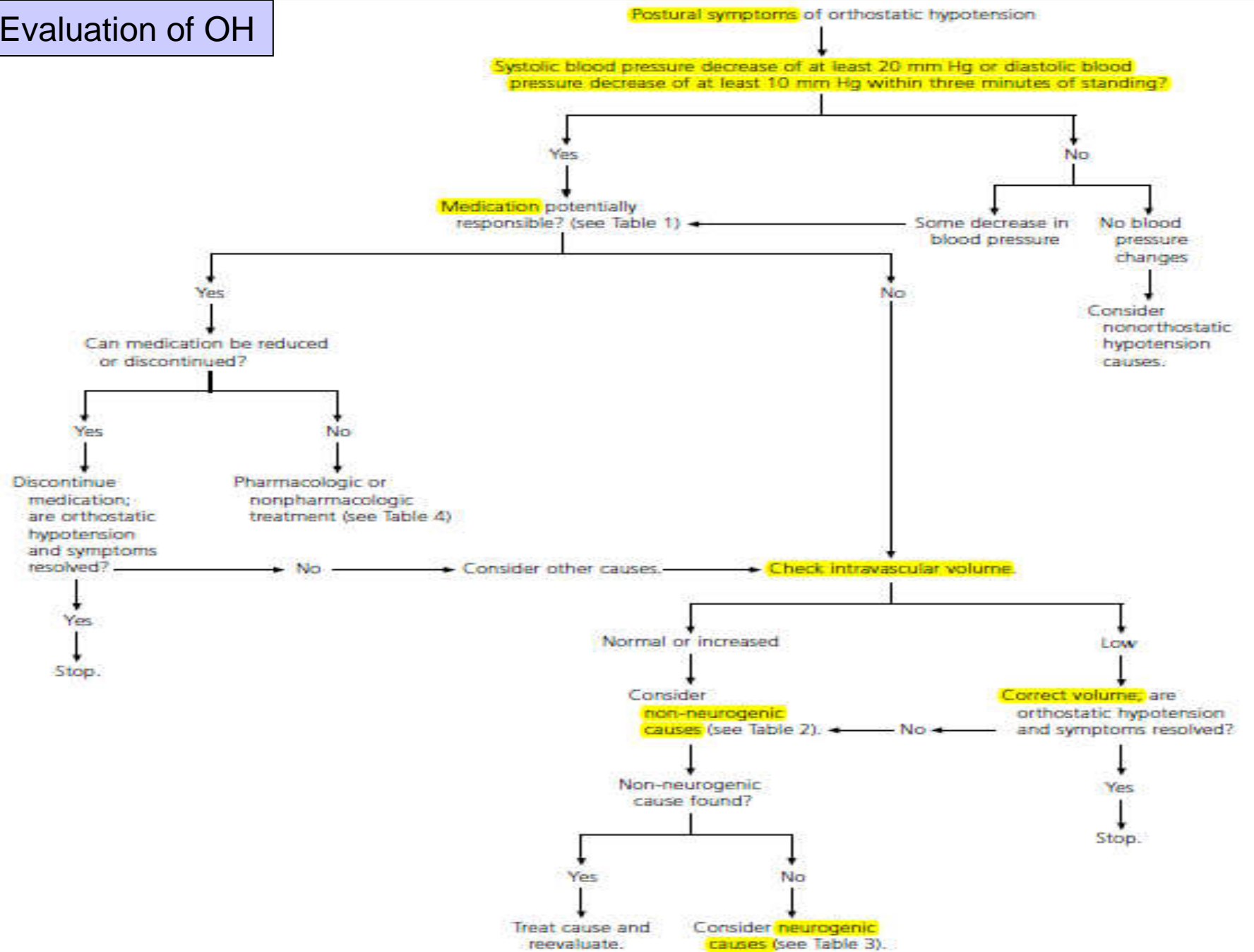
- Causes

- Medications
- Non-neurogenic
- neurogenic

Causes of orthostatic hypotension

- Acute:
 - Primary
 - Acute dysautonomia
 - Secondary
 - Volume
 - Volume depletion
 - Acute blood loss
 - sepsis
 - Neuromuscular
 - Spinal cord lesions
 - Acute stroke

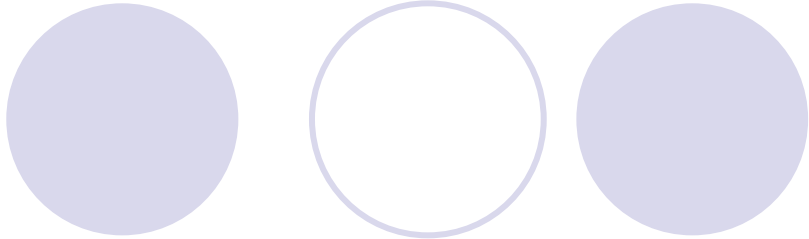
Evaluation of OH



Drugs



- Alpha and beta blockers
- Antihypertensives
- Bromocriptine
- Diuretics
- Insulin
- MAO inhibitors
- Marijuana
- Minor tranquilizers

- 
- Narcotics/sedatives
 - Nitrates
 - Phenothiazines
 - Sildenafil (Viagra)
 - Tricyclic antidepressants
 - Vasodilators
 - Vincristine (Oncovin)

Non-neurogenic etiologies

Cardiac pump failure

- Aortic stenosis
- Bradyarrhythmia
- Myocardial infarction
- Myocarditis
- Pericarditis
- Tachyarrhythmia

Reduced intravascular volume

- Adrenal insufficiency
- Burns
- Dehydration
- Diabetes insipidus
- Diarrhea
- Hemorrhage
- Salt-losing nephropathy
- Straining with heavy lifting, urination, or defecation
- Vomiting

Venous pooling

- Alcohol consumption
- Fever
- Heat (e.g., hot environment, hot shower or bath)
- Postprandial dilation of splanchnic vessel beds
- Prolonged recumbency or standing
- Sepsis
- Vigorous exercise with dilation of skeletal vessel beds

Neurogenic etiologies

Spinal cord problems

- Syringomyelia
- Tabes dorsalis
- Transverse myelitis
- Tumors

Peripheral nervous system problems

- HIV/AIDS
- Alcoholic polyneuropathy
- Amyloidosis
- Diabetes mellitus
- Dopamine beta-hydroxylase deficiency
- Guillain-Barré syndrome
- Paraneoplastic syndrome
- Renal failure
- Vitamin B₁₂ or folate deficiency

Other neurogenic etiologies

- Brain-stem lesions
- Brain tumors
- Carotid sinus hypersensitivity
- Cerebral vascular accidents
- Dysautonomias
- Multiple sclerosis
- Multiple system atrophy
- Neurocardiogenic syncope
- Parkinson's disease
- Pure autonomic failure
- Syringobulbia

Investigation of OH

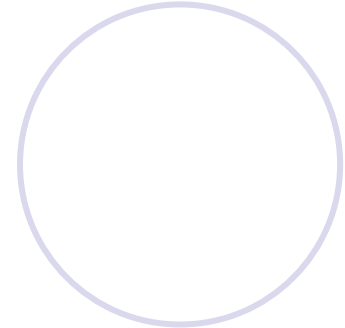
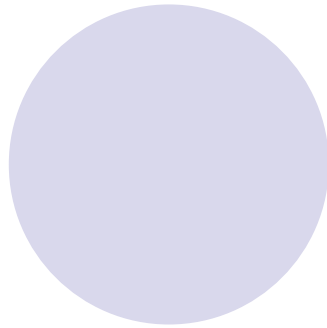
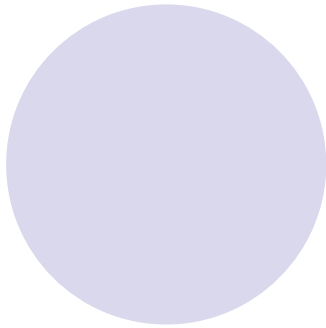
European Federation of Neurological Societies (EFNS) guidelines on the diagnosis and management of orthostatic hypotension

European Journal of Neurology 2006; 13: 930-936

Recommendations (level C):

1. Structured history taking
2. Detailed physical examination
3. 12-lead ECG recording
4. Routine laboratory testing
5. BP measurements whilst supine and upright
6. Cardiologic referral, if heart disease or abnormal ECG is present or suspected
7. Passive head-up tilt testing (HUT) if the active standing test is negative
 - Especially if the history is suggestive of OH, and in patients with motor impairment, as in PKD, MSA and spinal cord lesions
 - Tilt tables with foot board support, and if available, devices providing non-invasive, automatic and ideally continuous heart rate and BP measurements are recommended
8. Further ANS screening tests, with other appropriate investigations, depending on the possible aetiology of the underlying disorder

What do you recommend for
treatment of the patient's
symptomatic OH?



Management of our patient, Mr. WY

- Clinical admission to medical ward
- Clinical evaluations not suggestive of GIB, hypovolemic or cardiogenic shock; neurological examination was unremarkable as before
- Stopped terazosin and hydrochlorothiazide
- Taught on drinking adequate amount of fluid, slowly arise from supine to seated position and to raise the head of the bed by 20 degrees

TREATMENT OVERVIEW



- Treat the underlying cause
- Stop offending drug
- Non-pharmacological
 - Education
 - Prevention
- Pharmacological
 - Increase central blood volume
 - E.g. NaCl tablets, fludrocortisone
 - Enhance vasoconstriction
 - E.g. midodrine
- Goal of therapy is to eliminate symptoms

Selected Nonpharmacologic Treatments

EFNS guidelines on the diagnosis and management of orthostatic hypotension

Implement

1. Dorsiflex feet several times before standing
2. Physical maneuvers
 - Crossed legs (tension of buttock, thigh, calf muscles)
 - leaning forward (reduce orthostatic difference between the heart and brain)
 - squatting
3. Make slow, careful changes in position
4. Increase salt and fluid intake
 - 8 g (150mmol) of sodium chloride daily
 - Water repletion 2-2.5 L/day
5. Elevate head of bed 5 to 20 degrees
6. Wear compression stockings
7. Eat small, frequent meals

Selected Nonpharmacologic Treatments

EFNS guidelines on the diagnosis and management of orthostatic hypotension

AVOID

1. Standing motionless
2. Prolonged recumbency
3. Rising quickly after prolonged lying or sitting
4. Large meals (splanchnic vasodilatation)
5. Alcohol consumption / Vigorous exercise / Heat, hot baths, and hot environment (cutaneous vasodilatation)
6. Dehydration
7. Coughing spells / Straining with urination or defecation (increasing intrathoracic pressure further decreases venous return to heart)

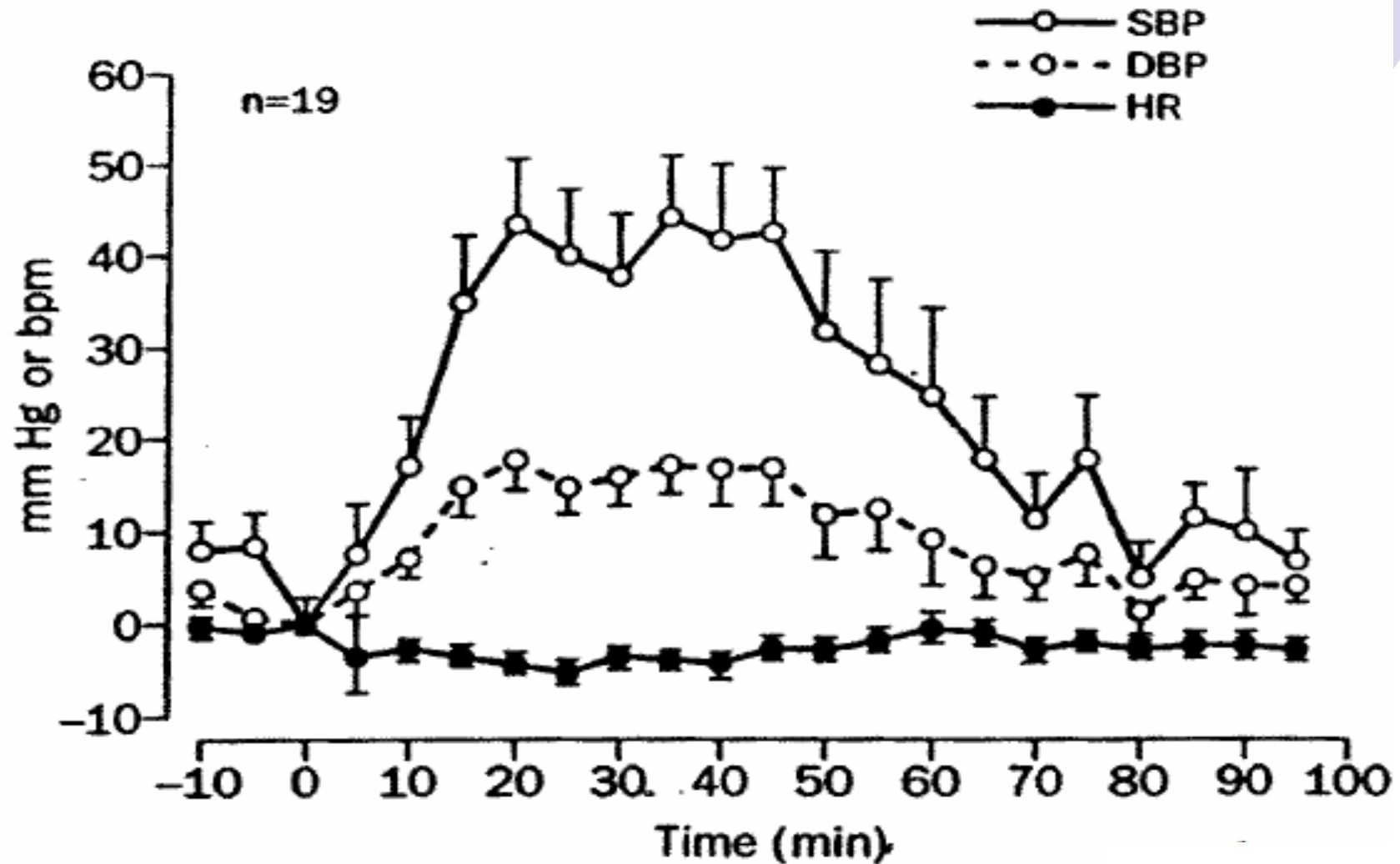


Water ingestion

- Ingestion of ~ 500mL of water
- SBP increase of > 30 mmHg in some patients within 5 minutes
- The peak effect occurs after 20-30 minutes
- Effect lasts for up to 1 hour.
- There is some inter-patient variability
- The mechanism is not established

Jordan J et al. The pressor response to water drinking in humans : a sympathetic reflex? *Circulation* 2000; 101:504-509.

Oral Water Raises BP



Jordan J et al. The pressor response to water drinking in humans : a sympathetic reflex? *Circulation* 2000; 101:504-509.



Fludrocortisone acetate

- Synthetic mineralocorticoid
1. Increases central blood volume
 2. Enhances blood vessel sensitivity to catecholamines
 3. Enhances NE release from SNS neurons

Fludrocortisone acetate

Recommendations (level C)

EFNS guidelines on the diagnosis and management of orthostatic hypotension

- First line drug
- Monotherapy
- 0.1 – 0.2 mg / day
- Combination of a high salt diet, head-up tilt sleeping (20-30cm) and a low dose of fludrocortisone is an effective means of improving OH
- Side Effects:
 - Supine hypertension
 - Edema and congestive heart failure
 - Hypokalemia
 - Headache



Midodrine

- Peripherally acting α_1 adrenoreceptor agonists
- Arteriolar and venous constrictor
- Prodrug of active metabolite, desglymidodrine
- Excreted in urine
- Duration of action is approximately 4 hours

Midodrine

Recommendations (level A)

EFNS guidelines on the diagnosis and management of orthostatic hypotension

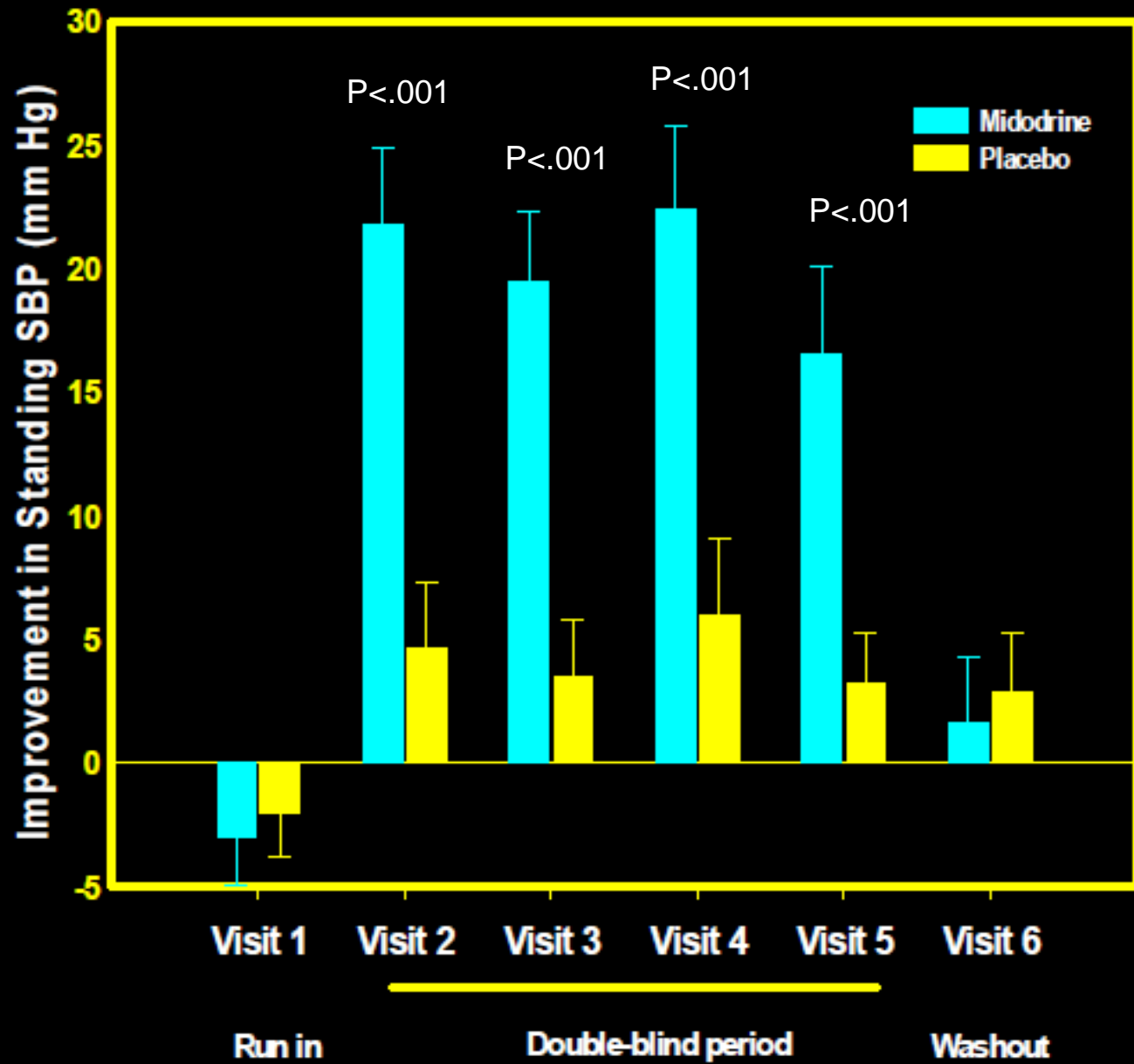
- Recommended for mono- or combined therapy (e.g. with fludrocortisone)
- 2.5mg - 10mg tds
- Side effects:
 - Piloerection
 - generalised pruritis
 - scalp or generalised paresthesia
 - supine hypertension
 - urinary retention
 - chills
- With caution
 - Hepatic dysfunction
- Contraindicated
 - Severe heart disease
 - Acute renal failure
 - Urinary retention
 - Pheochromocytoma
 - thyrotoxicosis

Phase III Midodrine study:

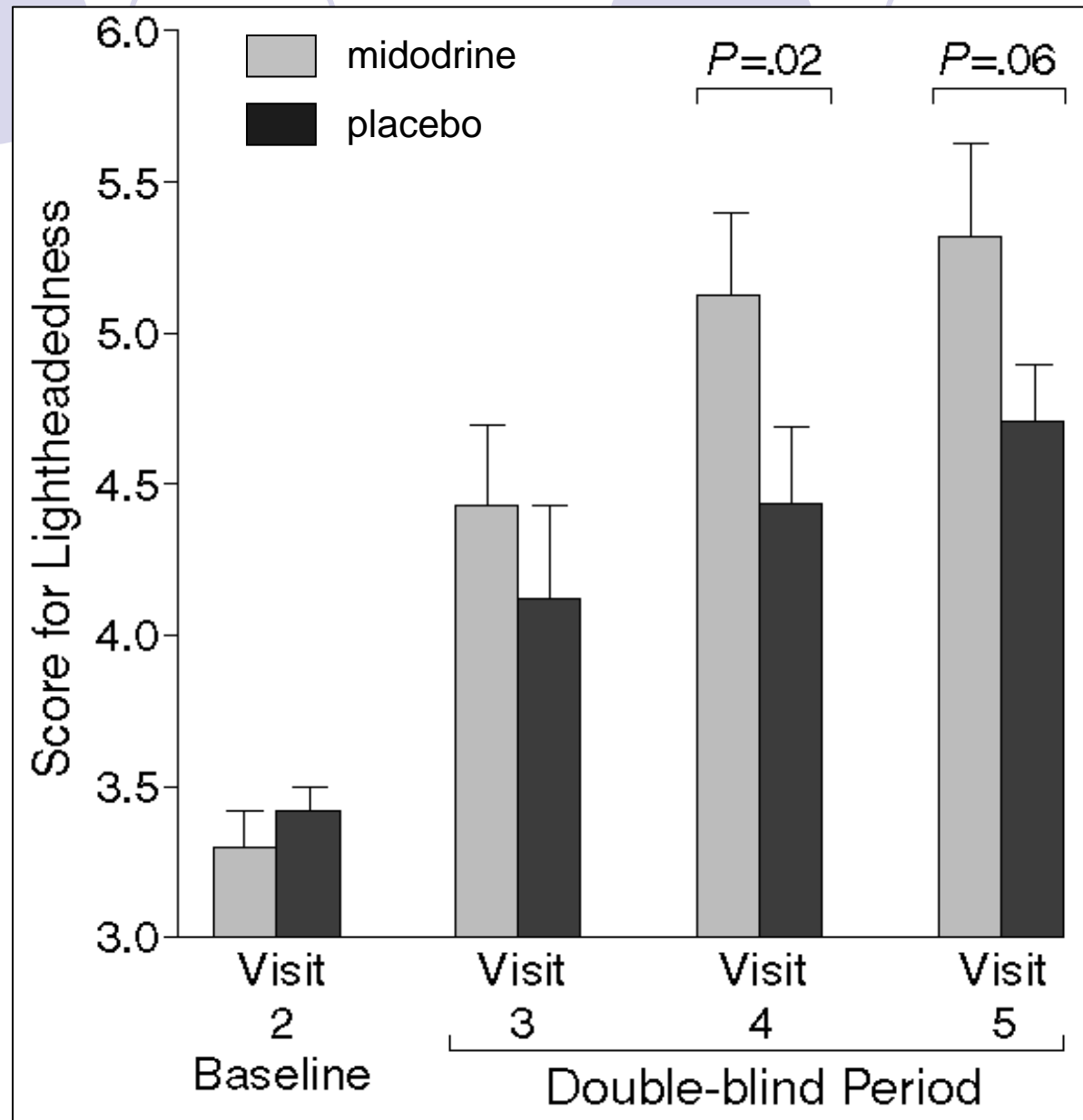
Efficacy of Midodrine vs Placebo in Neurogenic orthostatic Hypotension:
A Randomized, Double-blind Multicenter Study

Low et al. JAMA 277: 1046-1051, 1997

- Midodrine 10 mg tid
- 171 patients in 25 centres
- 139 completed the trial
- Primary endpoints
 - Improvement in standing SBP
 - Improvement in symptoms of lightheadedness



Less dizziness



Supplementary Agents

- **Caffeine**
 - Typical dose used 100-250mg tds (1 cup of coffee 85 mg; 1 cup of tea 50mg)
 - Modest pressor effect; tachyphylaxis
- **Erythropoietin**
- **Pyridostigmine**
- **Dihydroxyphenylserine**
- **β adrenoreceptor antagonists**
- **Somatostatin analogue**
 - 25 – 50 μ g half an hour before a meal to reduce postprandial hypotension (recommendation level C)
- NSAIDs (eg, indomethacin 25 to 50 mg po tid) (inhibit prostaglandin-induced vasodilation)
- Dihydroergotamine
- MAOI with tyramine
- α 2-adrenoreceptor antagonists (yohimbine)

Outcome of our patient (During the follow-up)



- Following cessation of terazosin and hydrochlorothiazide, patient's orthostatic symptoms disappeared
- Home BP monitoring
 - Supine BP 184-197/71-78mmHg
 - Standing BP 127-137/66-73mmHg
- Symptoms of BOO are only slightly worse
- Impression: Orthostatic fall in BP remains, probably due to underlying diabetic neuropathy



What do you recommend now?

- A. Lisinopril 10mg daily
- B. Atenolol 25mg daily
- C. Fludrocortisone 0.1mg daily
- D. No pharmacologic intervention at this time. Advise patient and family to report any recurrence of symptoms



A. Lisinopril 10mg daily

- Problems of this gentleman
 - Supine hypertension
 - Diabetes
 - Microalbuminuria
- Next FU:
 - Supine BP: 156-168/68-78mmHg
 - No appreciable change in upright BP
 - Without recurrence of symptoms



Bring home messages

- OH is a common condition in geriatric population
- OH can present atypically in elderly patients
- Causes of OH in a patient can be multifactorial
- Etiology of OH: acute vs chronic; medications / non-neurologenic / neurogenic
- Treatment: non-pharmacological, pharmacological
- Adjustment of anti-hypertensives might help