Eιδικά θέματα της υπέρτασης
Υπέρταση και νόσος Parkinson

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Ιπποκράτειο ΓΝΑ
Declaration of Interest

✓None for this presentation
Our roadmap

- Parkinson disease essentials
- Parkinson disease and CVD link
- Parkinson disease and BP
- Treatment issues
Parkinson Disease phenotype

Typical appearance of Parkinson's disease
- Stood posture
- Masked facial expression
- Forward tilt of trunk
- Flexed elbows & wrists
- Reduced arm swinging
- Slightly flexed hips & knees
- Trembling of extremities
- Shuffling, short-stepped gait

Parkinson’s disease
- Non-motor disorders caused by Parkinson's disease
- Depression
- Sleep disorders
- Weight loss
- Forced closure of the eyelids (blepharospasm)
- Orthostatic hypotension
- Constipation, micturition disorders, sexual problems
- Difficulty speaking, excessive saliva, difficulty in swallowing, respiratory problems
- Bowing of the shoulders, swelling of the feet
- Increased sweating
PD pathophysiology

- Loss of dopaminergic neurons in Substantia Nigra pars compacta and Locus Coeruleus
PD pathophysiology

- Presence of Lewy Bodies
  - 1979 (Kosaka and Mehrain)

- Lewy bodies stained strongly with antibodies of α-synuclein
  - 1997 (Spillantini et al)

Neurotoxins
Genetic factors
Neuroinflammation
SYMPATHETIC CARDIONEUROPATHY IN DYSAUTONOMIAS

DAVID S. GOLDSTEIN, M.D., PH.D., COURTNEY HOLMES, C.M.T., RICHARD O. CANNON III, M.D., GRAEME EISENHOFER, PH.D., AND IRWIN J. KOPIN, M.D.

The New England Journal of Medicine
Predictors of PD

- 5888 adults aged 65 years and older who were followed longitudinally for 14 years from 1989-2003
- Carotid stenosis >50% and ECG abnormalities (ventricular conduction defect, major Q or QS abnormalities, minor Q or QS with ST-T-wave abnormalities, left ventricular hypertrophy, isolated major ST-T-wave changes, atrial fibrillation, and first degree atrioventricular block) were related to onset of PD

Change in cardiovascular physiology is a near-universal feature in PD, and may precede a diagnosis of PD.

The neuropathological changes seen in PD (Lewy-formations) in cardiac nerves years before motor manifestations of PD of incidental.

PD on levodopa Tx: higher arterial stiffness and diastolic dysfunction.

PD+OH: x1.6 for cardiac mortality and x3.2 for cerebrovascular mortality.

CVD risk factors modulation may modify progression in early PD.

3 determinants of cardiovascular characteristics in PD

1. Cardiac noradrenergic denervation

2. Extra-cardiac noradrenergic denervation

3. Arterial baroreflex failure resulting in OH post-prandial hypotension, BP lability, supine hypertension, fatigue and exercise intolerance
Baroreflex function

Normal baroreflex function
A. Resting state
- Normal cortical input
- Carotid sinus
- PNS: -
- SNS: +
- HR
- BP

B. Under stress
- Cortical input
- Carotid sinus
- PNS: +
- SNS: -
- HR
- BP

Baroreflex failure
A. Resting state
- Cortical input
- Carotid sinus
- PNS: -
- SNS: +
- HR
- BP

B. Under stress
- Cortical input
- Carotid sinus
- PNS: +
- SNS: -
- HR
- ↑BP
Factors involved BP variability

- Humoral factors
  (endothelial etc.)
- Vasomotion
- Behavioral factors
- Rhythmic influences
  (probably largely central)
- Environmental stimuli
- Mechanical factors
- Baroreflexes
- Arterial stiffness
- Other reflexes
- Genetic factors

- Ventilation
OH: Definition

Consensus guidelines

OH is defined as an orthostatic fall of at least 20 mmHg in systolic or 10 mmHg in diastolic BP within 3 minutes of standing.

Although an orthostatic fall of 30/15 mmHg =severe supine hypertension
Orthostatic symptoms in PD

Prevalence of OH (%)

Overall

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Age groups 20/10 criteria

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Age groups 30/15 criteria

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Symptomatic OH

Asymptomatic OH

Palma J, et al. Mov Disord 2015
the prevalence of OH increased with age, but not significantly with disease duration or L-dopa equivalent dose
Valsalva maneuver in PD+OH
Tilt table test in PD+OH

[Graph showing changes in systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) during a tilt table test. The graph indicates a near syncope event at SBP=75 mmHg.]
24-h BP profile in PD
Balancing the BP effects of PD

Hypotension
- Increased risk of fail and syncope
- Risk of dementia (PD+OH)
- Immediate risks

Supine hypertension
- No studies on CV risk
- Stroke (less smoking, catecholamine depletion)
- Long-term risks
Non-pharmacologic Treatment of Neurogenic Orthostatic Hypotension

- Treat anemia, dehydration and reduce or eliminate drugs that such as alpha-blockers (BPH), phosphodiesterase-5 inhibitors (ED) and alpha2 agonists (clonidine) and tricyclic anti-depressants.
- Elevate the head of the bed to reduce nocturnal diuresis and avoid supine hypertension.
- Lifestyle changes such as avoiding heat, exercise in the upright position and large meals.
- Encourage water intake (500 ml) which results in a marked increase in BP within 5-10 min, and the performance of counter-pressure maneuvers.
- Compression stockings (20 mmHg) waist-high if possible or abdominal binders.
Drugs for OH

- **Fludrocortisone** (0.1 mg - 0.2 mg QD): Clinical effects are seen in 1-2 weeks. Side effects include supine hypertension, lower extremity edema and low K.

- **Midodrine** (2.5 mg – 10 mg TID): Effect seen within 40 minutes of intake with peak effect noted at 2 hours. Side effects include supine HTN, “goose bumps”, skull pruritis and urinary retention.

- **Droxidopa** is a promising drug with seemingly less supine HTN; however, its long-term efficacy remains unproven.

- **Other therapies:**
  - Pyridostigmine (30-60 mg TID): Enhances ganglionic transmission resulting in increased sympathetic outflow in addition to enhancing vagal tone.

- Erythropoietin, desmopressin, indomethacin and caffeine
Supine hypertension

✓ Lifestyle changes
Mind the head during the night
✓ Pharmacologic therapy
  Bed time trans-dermal nitroglycerin patch with removal at least 30 minutes before getting up
✓ Bed time short-acting calcium channel blockers, hydralazine or Losartan
✓ Avoid daytime use of alpha blocker, beta blockers with alpha blocking properties and diuretics
Key points in PD for a cardiologist

- PD and CVD symptoms is a clinical scenario not to be missed in hypertensives
- Administration of CV (antihypertensive) drugs in PD especially if OH present with caution regarding 24-h effect
- Lifestyle measures to address hypertension and OH + drugs by individualization
Ευχαριστώ
LF and cardiac NE spillover

LF and LF/HF detects baroreflex failure, not cardiac innervation

Case presentation

- Past medical history: Parkinson’s disease diagnosed 9 years ago, cognitive problems with some psychotic symptoms, constipation and orthostatic hypotension.
- Medications:
  - Carbidopa-levodopa 25-100 mg 2.5.tabs in am, 2.5 tabs at noon and 1.5 tab in the evening
  - Clozapine 50 mg at bed time
  - Flodrocortisone 0.5 mg per day
  - Midodrine 10 mg TID
  - Mirtazapine 15 mg, half a tablet per day
  - Consulted to consume salt
PD+OH: neuropharma tests

HR response to BP changes - baroreflex

Vital Signs and Physical Exam

Supine: BP 140/82 mmHg, HR 62 BPM
Standing 1 min: BP 78/42 mmHg, HR 70 BPM (dizzy)
Standing 3 min: BP 68/38 mmHg, HR 68 BPM (near sync)

General appearance: Flat affect, minimal communication
Chest: Clear to auscultation
Cardiovascular exam: No NVD, no murmurs
Extremities: No tremor, no edema
Neurologic exam: Mild rigidity in all extremities
ECG and Echocardiogram: Unremarkable
Labs: Unremarkable