Orthostatic Intolerance in EDS: the Basics

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Presenter Disclosure Information

Peter C. Rowe, MD

- No relationships to disclose
- Off-label uses of several drugs will be discussed, where possible supplemented by short-term physiologic studies
Orthostatic intolerance in EDS

Earlier webinars:
- EDS Society
  Orthostatic intolerance in EDS, 19 December 2018
  https://www.youtube.com/watch?v=7I3A3Vcbz_w8
- EDS ECHO 06/24/2019, 11/13/2019, 02/27/2020
- Connecting the Dots between EDS and POTS
  https://www.youtube.com/watch?v=srUJRRihvsE
Autonomic symptoms in EDS and controls

Orthostatic Intolerance

“Orthostatic” means “upright.”

The term “orthostatic intolerance” refers to a group of clinical conditions in which symptoms worsen with quiet upright posture and are improved (although not necessarily abolished) by lying down.

500-750 mL of blood pools in the lower half of the body on standing.

The normal response is a 10-20 beat increase in heart rate and better blood vessel constriction to return blood to the heart and brain.
Symptoms of Orthostatic Intolerance

Lightheadedness
Syncope
Diminished concentration
Headache
Blurred vision
Fatigue
Exercise intolerance

Dyspnea
Chest Discomfort
Palpitations
Tremulousness
Anxiety
Diaphoresis
Nausea
Due to reduced cerebral blood flow

<table>
<thead>
<tr>
<th>Lightheadedness</th>
<th>Dyspnea</th>
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<tbody>
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</table>
Due to higher levels of catecholamines (adrenaline and noradrenaline or epinephrine and norepinephrine)

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Tremulousness
Anxiety
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Nausea
Historical questions with high yield in OI

– Have you ever fainted?
– Do you feel lightheaded or unwell when you stand for more than 5 minutes?
– How do you feel in the following settings:
  • Waiting in line, shopping?
  • Standing at a reception, in chorus, at a service?
  • After taking a hot shower, bath, or sauna?
  • In a warm environment (in a hot room, on a hot day)?
– Do you study in a reclining position, with knees to chest, or feet under you?
– Do you fidget and move around when standing?
Diagnostic testing

- Orthostatic vital signs—HR and BP measured supine, sitting, and standing—often measured over < 2 minutes: insufficient to identify most forms of chronic orthostatic intolerance. Prolonged testing of ≥ 10 minutes usually needed.

- Standing test (usually 10 min after a variable time supine):
  - Passive Stand Test
  - Active Stand Test
Passive Standing Test

**Supine:** 5 min with BP and HR every minute

**Standing:** 10-15 min with feet positioned 6 inches apart, 6 inches from a wall, leaning slightly backwards against the wall.

HR & BP measured each minute

Symptoms recorded every 1-2 minutes

Hyatt KH, Jacobson LB, Schneider VS. Comparison of 70° tilt, LBNP, and passive standing as measures of orthostatic tolerance. Aviat Space Environ Med 1975;46:801-8.
Head-up tilt table testing

Supine: Obtain baseline HR and BP values

Stage 1: head-up tilt to 70° for ~ 45 min

Stage 2 (optional): return to supine for 10 minutes, then head-up tilt for 15 minutes with isoproterenol (1-2 mcg/kg/min).
pooling, vasoconstriction

↓ intra-vascular volume

Standing/Tilt test

↓ cerebral blood flow

↑ sympatho-adrenal response

OH
dOH
NMH
POTS
Normal HR and BP
Common forms of orthostatic intolerance

**POTS**
- BP / HR
- 51 bpm
- L. H., Fatigue, HA

**NMH**
- BP / HR
- HR Δ 9 bpm supine to peak during tilt
- LH, pale
- Tonic-clonic mvmts
- HR Δ 9 bpm supine to peak during tilt

Supine → Standing → Supine

Supine → 70° Tilt → Supine
POTS and NMH can occur together
Acrocyanosis is common in OI
Passive standing tests for the office diagnosis of postural tachycardia syndrome: New methodological considerations

Maria Roma, Colleen L. Marden and Peter C. Rowe
Division of General Pediatrics and Adolescent Medicine, Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Table 3. Proportion of POTS diagnoses that would be missed at each minute of an abbreviated standing test (full sample, N = 93).

<table>
<thead>
<tr>
<th>Minutes upright</th>
<th>POTS diagnoses missed at each minute</th>
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<tbody>
<tr>
<td>%</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>(95% CI)</td>
</tr>
<tr>
<td>2</td>
<td>70 (60–78)</td>
</tr>
<tr>
<td>3</td>
<td>53 (43–63)</td>
</tr>
<tr>
<td>4</td>
<td>43 (33–53)</td>
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<tr>
<td>5</td>
<td>37 (27–47)</td>
</tr>
<tr>
<td>6</td>
<td>27 (19–37)</td>
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<tr>
<td>7</td>
<td>24 (16–33)</td>
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<tr>
<td>8</td>
<td>15 (9–24)</td>
</tr>
<tr>
<td>9</td>
<td>10 (5–17)</td>
</tr>
<tr>
<td>10</td>
<td>5 (2–12)</td>
</tr>
</tbody>
</table>

Similar findings in ME/CFS adults
What does it mean if you have lots of symptoms with standing, but the formal tests of heart rate and blood pressure are normal during a passive standing test or a head-up tilt table test?

Does this mean nothing is wrong?
What does it mean if you have lots of symptoms with standing, but the formal tests of heart rate and blood pressure are normal during a passive standing test or a head-up tilt table test?

Does this mean nothing is wrong?

NO!
Changes in CBF during 30 minutes of HUT compared to supine values in 44 HC and 429 ME/CFS

For all ME/CFS groups vs HC, P < 0.001.
(No differences in CBF supine pre-tilt)

van Campen CMC, Vergheut FWA, Rowe PC, Visser FC,
Clinical Neurophysiology Practice 2020;5
Treatment of Orthostatic Intolerance

• Step 1: Non pharmacologic measures

• Step 2: Treat contributory conditions

• Step 3: Medications
  – Monotherapy
  – Rational polytherapy
Inhalant allergies/asthma
Infection
Movement restrictions
Food allergies, MCAS
Migraines/CDH
GERD, abdo pain, nausea, IBS, MALS
Chiari type I or C-spine stenosis
Anxiety
EDS/JHS
Depression
Pelvic vein incompetence
CFS
JRA, Sjogrens, etc.
**Pharmacologic Therapy**

- **Vasoconstrictors**
  - Midodrine, dexedrine, methylphenidate, SSRIs, SNRIs; L-DOPS (Droxidopa)

- **Volume expanders**
  - Sodium (PO & occasionally IV), fludrocortisone, clonidine, OCPs, desmopressin

- **↓ HR**
  - ↓ Catecholamine release/effect
  - β-blockers, disopyramide, SSRIs, ACE inhibitor, ivabradine, pyridostigmine bromide
Management of orthostatic intolerance

• requires careful attention by the patient and the practitioner to the factors that provoke symptoms
• requires a willingness to try several medications before a good fit is achieved
• requires a realization that meds often can treat symptoms but do not necessarily cure OI
• management of OI is one part of a comprehensive program of care
Resources

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Diagnosis and Management in Young People: A Primer

Peter C. Rowe¹, Rosemary A. Underhill²*, Kenneth J. Friedman³, Alan Gurwitt⁴, Marvin S. Medow⁵, Malcolm S. Schwartz⁶, Nigel Speight⁷, Julian M. Stewart⁸, Rosamund Vallings⁹ and Katherine S. Rowe¹⁰

Open Access, so available to all free of charge
Ol in EDS references

• ME/CFS - Solve ME/CFS Initiative
  http://solvecfs.org/

• ME/CFS - International Association for CFS/ME
  www.iacfsme.org

• OI - Search “Dr. Peter Rowe” on YouTube for webinar on “Managing Orthostatic Intolerance”

• OI - Dysautonomia International is a non-profit
  www.dysautonomiainternational.org

• EDS - Ehlers-Danlos Society
  http://ehlers-danlos.com/
THANK YOU

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