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SPRING 2020

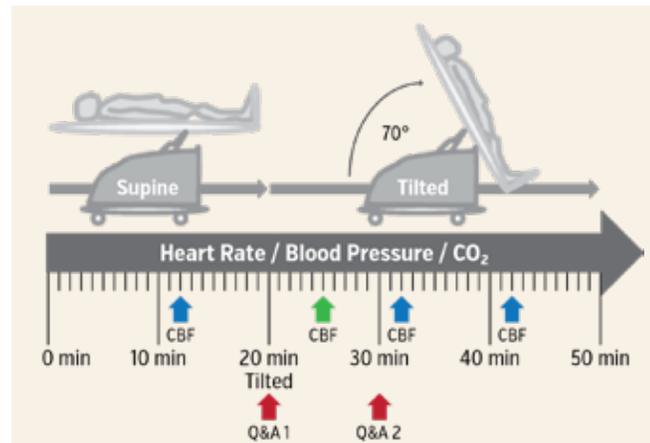
Could Improved Testing for Orthostatic Intolerance Lead to Better Clinical Care for People with ME/CFS?

By Kathryn Boorer, PhD

THE ME/CFS COMMUNITY has become very familiar with the term “orthostatic intolerance” (OI), but what exactly does this mean, and what do the most recent data tell us about this condition? When they stand up, people with OI report symptoms such as dizziness, changes in vision, headaches, nausea, and fainting as well as cognitive impairment, attention disorders, depression, and problems with spatial relationships (sensing where your body is in space). OI can also lead to release of the fight-or-flight hormone adrenaline into the bloodstream, increasing heart rate and blood pressure, among other symptoms. Orthostatic symptoms with a sustained increase in heart rate of at least 30 beats per minute (40 beats in adolescents) within 10 minutes without a decrease in blood pressure is termed postural tachycardia syndrome or POTS.

Diagnosis of OI in people with ME/CFS can be made by performing the head-up tilt test. During the test, a patient lies on a bed, which is then tilted at 70 degrees while blood pressure, heart rate, and other functions are monitored using a finger sensor that measures changes to blood flow. A reduction in blood flow to the brain, also known as a reduction in cerebral blood flow (CBF), is assumed to play a role in the symptoms of OI. A technique called Doppler imaging (a type of ultrasound test) can be performed during the tilt test to measure CBF, potentially allowing more accurate diagnosis of OI.

A new study published by Linda van Campen, MD, Frans Visser, MD, and colleagues sheds light on why so many people with ME/CFS are unable to maintain an upright standing position. The authors used extracranial Doppler imaging to measure whether orthostatic symptoms in people with ME/CFS are associated with



Head-up tilt test with extracranial Doppler imaging.

Patients were laid flat on a bed for 20 minutes and were then tilted head-up to 70 degrees for a maximum of 30 minutes. Heart rate and blood pressure were continuously recorded. Cerebral blood flow (CBF) measurements were made about 8 minutes before the patient was tilted and 12 minutes (mid-tilt) and 22 minutes (end-tilt) after the patient was tilted (blue arrows). Patients with POTS had additional images collected 5 minutes after they were tilted (green arrow). Patients were asked yes/no questions about 15 symptoms of OI. Questions were asked immediately after reaching the upright position and 10 minutes after being in the upright position (red arrows).

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a reduction in total CBF. The authors recruited 429 patients with ME/CFS (Fukuda and International Consensus Criteria classifications) and measured total CBF during a 30-minute head-up tilt test using extracranial Doppler imaging of carotid and vertebral arteries. During the tilt test, 247 patients had a normal heart rate and blood pressure response, 62 had delayed orthostatic hypotension (drop in blood pressure after being tilted upright), and 120 had POTS. Forty-four healthy controls were also assessed. Total CBF was measured before and after participants were placed in the upright position. Participants were also asked two sets of yes/no questions regarding their symptoms, one immediately after being placed in the upright position and another 10 minutes later.

Q&A 1: immediately after tilt

Did you develop, after being tilted:

- complaints of dizziness or lightheadedness?
- muscle weakness of your legs?
- a feeling of dyspnea or breathlessness?
- pain in the muscles of your neck or shoulders?
- a feeling of nausea?
- a tingling feeling in your right hand?
- a feeling of chest pain or pressure on your chest?
- low back pain?
- palpitations?
- a feeling of a pressure in your head or headache?

Are you, after being tilted, more fatigued in comparison to when you were lying down?

Is your vision less sharp since you have been tilted?

Do you hear me differently, after being tilted, in comparison to when you were lying down?

Are you less concentrated while standing, compared to when you were lying down?

Did you start to sweat after being tilted?

Please visit the online version of *The Chronicle* at <https://solvecfs.org/spring-2020-chronicle-1> to see **Q&A 2: 10 minutes after being in upright position**

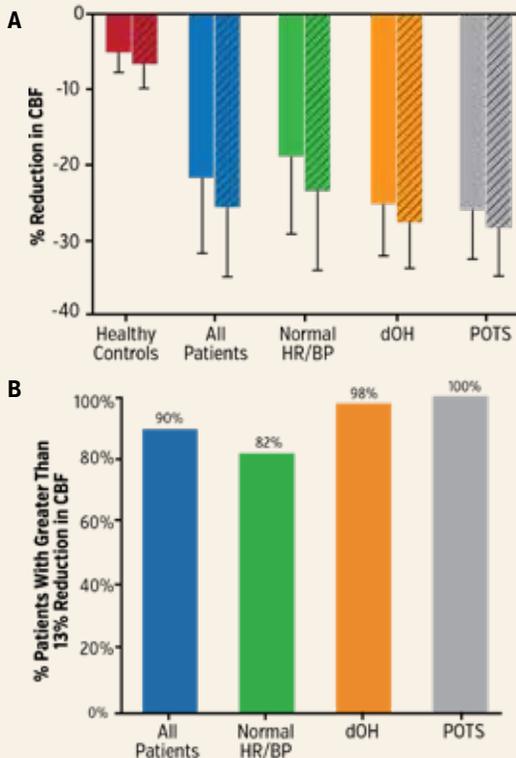
FINDINGS

- Compared with healthy controls, patients with ME/CFS had an approximate 3-fold reduction in CBF while in the upright position
- Patients with delayed orthostatic hypotension and those with POTS had the largest reduction in CBF
- Almost all patients (90%) had an abnormal reduction in CBF, i.e., a more than 13% reduction in CBF
- Abnormal reductions in CBF were seen in 3 subgroups of patients:
 - » 82% with a normal heart rate and blood pressure response
 - » 98% with delayed orthostatic hypotension
 - » 100% with POTS
- There was a significant correlation between degree of CBF decline and the number of OI symptoms that occurred during the tilt test
- Patients who denied having symptoms of OI in daily life (but who had OI based on clinical signs) had reductions in CBF within the range experienced by patients with OI symptoms
- Patients who had no OI symptoms had similar reductions in CBF to those of healthy controls

WHAT IS THE SIGNIFICANCE OF THESE FINDINGS? Van Campen and colleagues have shown that almost all patients with ME/CFS who report symptoms of OI during the tilt test have reductions in CBF. Importantly, this includes patients who report symptoms of OI but who have a *normal* heart rate and blood pressure response to the tilt test—the largest and most often misclassified group—as well as those who stated they had *no* symptoms of OI in daily life.

“The results of our study may explain why so many patients, including those considered “normal” in the head-up tilt test, cannot maintain an upright standing position and provides direction for treatments for OI. Getting this information out on a broad platform would help improve the way physicians look at OI symptoms in ME/CFS patients—hopefully.”

HOW WILL THESE FINDINGS BENEFIT PEOPLE WITH ME/CFS? The results of this study open the door to more accurate diagnosis and more effective treatments for ME/CFS. For example, treatments that increase blood volume can be tailored to patients who have reductions in CBF. With additional testing, extracranial Doppler during the head-up tilt test may become the gold standard for assessment of OI in patients with ME/CFS. ■



Reduction in cerebral blood flow in patients with ME/CFS.

(A) Reduction in CBF at the end of the tilt test was significantly greater in patients with ME/CFS than in healthy controls: 26% in the overall ME/CFS group [24% in patients with a normal heart rate and blood pressure response, 28% in those with delayed orthostatic hypertension, and 29% in those with POTS] versus 7% in healthy controls. The dotted bars represent mid-tilt; the hatched bars represent end-tilt.

(B) Most patients with ME/CFS had a greater than 13% reduction in CBF (abnormal blood flow).

Abbreviations: BP, blood pressure; dOH, delayed orthostatic hypotension; HR, heart rate; POTS, postural tachycardia syndrome.

Adapted from van Campen, C.M.C. et al. *Clin Neurophys Prac.* 2020;5:50-58.

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