

Informed Consent Form

Date: _____

Study Name: Does taurine supplementation improve vascular function and orthostatic responses in Long COVID?

Researchers:

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Purpose of the Research:

COVID-19 has infected millions of people worldwide, and about 13% may develop what's called "Long COVID." The World Health Organization defines Long COVID as symptoms that continue or appear three months after the initial infection and last for at least three months without another clear cause. COVID-19 affects blood vessels because the virus uses a protein called ACE2 to enter cells, and ACE2 is found in the lining of blood vessels throughout the body. This can lead to problems with blood vessel function. Studies show that even young, healthy people who had COVID-19 can have reduced blood vessel function just a few weeks after infection. These problems with vascular function can also influence someone's ability to maintain their blood pressure when standing and thus cause dizziness and feelings of faintness.

Recent research suggests that people with Long COVID often have low levels of taurine, a natural substance in the body that helps regulate blood pressure and inflammation. Taurine is found naturally in meat, fish and dairy and our own bodies can make it. When taurine levels return to normal, symptoms tend to improve. Other studies show that taking taurine for 12 weeks can improve blood pressure and blood vessel health in people with early signs of high blood pressure. These improvements might also help with dizziness or lightheadedness when standing up, which is common in Long COVID. We will determine if taking taurine for 12 weeks can improve blood vessel health and reduce dizziness when standing in people with Long COVID. Research results will be presented at national and international conferences and will be published in relevant journals.

What You Will Be Asked to Do in the Research:

The total time commitment for the research project will be approximately 1.5 hours at each of 2 visits. There are two groups of participants, those who are taking 12-weeks of taurine supplementation (self-administered) and those who are not. For each lab visit (baseline and 12-weeks), all participants will be asked to refrain from smoking, caffeine and fatiguing exercise for at least 12 hours prior.

At the beginning of each visit your height and weight will be taken and you will be asked to complete 3 brief questionnaires while seated at a desk: COMPASS31, Symptom Tracker, and Energy Envelope. You can take these home with you if you find it too hard to complete at the time of your visit. You will also be requested to complete a 3-day diet record. Afterwards, you will be asked to lie down on a medical table to rest for 15 minutes. Your blood pressure will now be taken with an automated device on your upper arm. You will then have a blood pressure cuff wrapped around your forearm and small finger cuffs placed on your fingers which will inflate and hold onto them. You will then have an ultrasound picture of an artery in your arm taken for 5 minutes at rest, during 5 minutes of occlusion using the blood pressure cuff, and for 5 minutes of recovery when the pressure in the cuff will be released.

After the above protocols, you will rest for at least 10 minutes and then equipped for measurements of heart rate (HR) via electrocardiogram (ECG) consisting of three stickers attached to your upper body. Blood pressure will be monitored using a beat-by-beat non-invasive blood pressure device on the middle finger (NexFin). This device will squeeze your finger throughout the test. Blood pressure will also be taken before and after testing using a standard automated device. Brain blood flow will be measured using an ultrasound probe on your temple. This will be held in place with a plastic headband. Lastly, your breathing will be monitored with a strap around your chest and a small plastic tube below your nostrils. During these measurements, you will be asked to lie down on a table for 10 minutes, after which the table will be moved

to a 70 degree head-up position for 5 minutes. You will then be returned to the lying down position for at least 5 more minutes. You will be lightly strapped into place using large velcro bands for safety.

All of these tests will be completed at baseline and after 12 weeks. For those participants taking taurine, you will be asked to record how much taurine that you take every day. Throughout this 12 week period a researcher will connect with you by phone or e-mail to get your feedback and to coach you through the use of a Polar heart rate monitor to get 5 minutes of resting heart rate data from you. The monitor will be loaned to you at your first visit to the lab and you will receive instructions on how to use a cell phone application to retrieve and send the data to researchers. This data will be used to determine your heart rate variability, which is a marker of your nervous control of heart rate.

Risks and Discomforts:

- 1) Removal of the ECG stickers will be similar to removing a "band-aid" and might result in discomfort or mild rash.
- 2) The non-invasive blood pressure monitor squeezes the middle finger for the duration of the test and is calibrated once with an upper arm blood pressure measurement. This mild pressure might be considered uncomfortable. Similarly, the occlusion of the brachial artery using a blood pressure cuff for 5 minutes may also be uncomfortable. We can stop the test at any time, if you request.
- 3) The headband which holds the ultrasound probe in place may feel tight, but it can be loosened upon request. Should you feel any discomfort, please inform the researcher and the headband will be adjusted and/or the test will be ended.
- 4) Upright tilt may elicit symptoms such as dizziness or faintness. We will be constantly monitoring heart rate and blood pressure, and if systolic blood pressure drops to 70mmHg or lower, or if you experience symptoms of dizziness, light-headedness or nausea, the test will be stopped immediately, and you will be returned to the supine position
- 5) Post-exertional malaise is a concern for many patients with Long COVID. These protocols, on the whole, could be considered strenuous by some patients and initiate a symptom "crash." Please inform the researchers as soon as possible if this occurs after your lab visit. We do not anticipate that the dietary supplement could cause this, however, the transportation to the lab and the 90 minute testing period including a 5 minute head-up tilt could exacerbate your symptoms. Should a "crash" occur, we will encourage you to visit your chosen medical practitioner and will provide whatever information that he/she requires from our testing.

Benefits of the Research and Benefits to You:

You will receive \$50/visit for your participation in this research and \$20 for parking or transportation to the University (a total of \$70 for each visit). You will learn about your own blood vessel function and your body's responses to upright tilt. The data collected from this project will provide valuable insight into the use of taurine as an accessible and cost-effective supplement to improve symptoms and physiology in Long COVID.

Voluntary Participation:

Your participation in the study is completely voluntary and you may choose to stop participating at any time. Your decision not to volunteer will not influence the nature of your relationship with researchers, staff, York University, or collaborative clinicians either now, or in the future. Your anonymous data may also be used in future studies.

Withdrawal from the Study:

You can stop participating in the study at any time, for any reason, if you so decide. Your decision to stop participating, or to refuse to answer particular questions, will not affect your relationship with the researchers, York University, or any other group associated with this project. In the event you withdraw from the study, all associated data collected will be immediately destroyed wherever possible. If you withdraw from the study, you will still receive \$70 for your visit.

Confidentiality: All information you supply during the research will be held in confidence and unless you specifically indicate your consent, your name will not appear in any report or publication of the research. Data and information will be collected via handwritten notes and into data collection software (EndoPAT, LabChart and Excel). Your data will be safely stored in a locked facility and on an encrypted database and only research staff will have access to this information. By consenting to participate in this project, your data will be coded, archived on in-lab encrypted hard-drives and potentially used in future studies. At the end of all studies in the Edgell lab (August 1, 2042), your data will be confidentially shredded and/or deleted from databases. Confidentiality will be provided to the fullest extent possible by law. The data collected in this research project may be used in a de-identified format by members of the research team in subsequent research investigations exploring similar lines of inquiry. Such projects will still undergo ethics review by the HPRC, our institutional REB. Any secondary use of data by the research team will be treated with the same degree of confidentiality and anonymity as in the original research project.

Questions About the Research? If you have questions about the research in general or about your role in the study, please feel free to contact Dr. Heather Edgell either by telephone at (416) 736-2100, extension 22927 or by e-mail (edgell@yorku.ca). This research has been reviewed and approved by the Human Participants Review Sub-Committee, York University's Ethics Review Board and conforms to the standards of the Canadian Tri-Council Research Ethics guidelines. If you have any questions about this process, or about your rights as a participant in the study, please contact the Manager, Research Ethics in the Office of Research Ethics, York University (e-mail ore@yorku.ca). This office oversees the ethical conduct of research studies and is not part of the study team. Everything that you discuss will be kept confidential.

Legal Rights and Signatures:

I, _____, consent to participate in the project "Does taurine supplementation improve vascular function and orthostatic responses in Long COVID?" conducted by Dr. Heather Edgell and Dr. Andrea Josse. I have understood the nature of this project and wish to participate. I am not waiving any of my legal rights by signing this form. My signature below indicates my consent.

Signature
Participant

Date

Signature
Investigator

Date