Study Protocol

Official Title: Simple Non-invasive Breathing Device to Improve Pulmonary Flow Pusatility in Single Ventricle Post Fontan

ClinicalTrials.gov ID (NCT number): STUDY22050151

Protocol Date: 1/1/24

Scientific Background

By replicating biphasic ventilation's benefits, Sniff-PEP breathing may prove to improve outcomes in Fontan patients. This research will furnish preliminary data encompassing CMR, biomarker studies, and QoL analyses on Sniff-PEP breathing's effects. With our multidisciplinary team's expertise, we are well-equipped to evaluate this promising intervention, laying the groundwork for broader, multi-institutional research endeavors.

Study Objectives

A. Specific Aims

Aim #1: To evaluate the acute effects of oPEP in Fontan patients undergoing clinically indicated echocardiogram

Hypothesis: oPEP use in Fontan patients will increase flow pulsatility in the inferior vena cava, hepatic veins, Fontan circuit and pulmonary arteries that will ultimately lead to increased cardiac output

Aim #2: To evaluate the effects of one month use oPEP in Fontan patients undergoing clinically indicated echocardiogram

Hypothesis: oPEP use in Fontan patients for a month will increase flow pulsatility in the inferior vena cava, hepatic veins, Fontan circuit and pulmonary arteries that will ultimately lead to increased cardiac output

Study Design & Methods

Dr. Shaji will be screening pediatric cardiology patients who will be having their appointments in the Lawrenceville locations. Of those patients who meet inclusion criteria, either he, Dr. Alsaied, or another appointed official will approach the patient and/or their guardians and discuss the study with them and provide them information. If they agree to participate in the study, then a demonstration will be done for the subject on how to use the device appropriately. The subject will be given their own personal device and will practice the breathing technique for the device. This device has been catalogued, never been used by another person, and sanitized. The patient will place the device between their lips and create a tight seal. Then, they will start by inhaling through their nose and exhaling through their mouth through the device. The subject will practice till they feel comfortable with the breathing maneuver. An initial research quality of life questionnaire will be given to the subject and their guardians for completion. Subject then will have his standard clinic echocardiogram. After completion of the standard echocardiogram protocol, the subject will perform the breathing exercise through the device. While breathing through the device, we will obtain echocardiogram measurements as detailed below:

a. Subcostal sagittal
i. Color Doppler of IVC and hepatic veins
ii. Pulse wave Doppler of IVC (distal to hepatic veins)
iii. Pulse wave Doppler of hepatic vein

b. Apical view
i. 2D of systemic outflow tract
ii. Color Doppler of systemic outflow tract
iii. Pulse wave Doppler of systemic outflow tract Doppler
iv. Continuous wave Doppler of neoaortic valve

c. Suprasternal coronal Notch view
i. If possible, 2D of SVC and RPA/LPA junction
ii. Color Doppler of SVC and RPA/LPA junction
iii. Pulse wave Doppler of SVC, RPA, and LPA

d. (if LPA not well seen in suprasternal coronal) Suprasternal sagittal view
i. Color Doppler of LPA
ii. Pulse wave Doppler of LPA

These echo measurements will then be confirmed or read by a cardiologist who will be blinded against the condition the patient is in (normal breathing vs breathing through oPEP). 20% of the measurements will be confirmed by another reader.

The patient will complete a brief questionnaire at baseline. We will instruct the patient to use the device 3-4 times daily for a duration of 10-15 minutes. After a period of

approximately 4 weeks, the patient will return to the Lawrenceville location and will have a repeat echocardiogram according to the protocol below:

a. Subcostal sagittal
iii. Color Doppler of IVC and hepatic veins
iv. Pulse wave Doppler of IVC (distal to hepatic veins)
v. Pulse wave Doppler of hepatic vein

b. Apical view
vi. 2D of systemic outflow tract
vii. Color Doppler of systemic outflow tract
viii. Pulse wave Doppler of systemic outflow tract Doppler
ix. Continuous wave Doppler of neoaortic valve

c. Suprasternal coronal Notch view
x. If possible, 2D of SVC and RPA/LPA junction
xi. Color Doppler of SVC and RPA/LPA junction
xii. Pulse wave Doppler of SVC, RPA, and LPA

d. (if LPA not well seen in suprasternal coronal) Suprasternal sagittal view
xiii. Color Doppler of LPA
xiv. Pulse wave Doppler of LPA

These echo measurements will again be confirmed or read by a cardiologist who will be blinded against the condition the patient is in (normal breathing vs breathing through oPEP). 20% of the measurements will be confirmed by another reader.
At this point, the subject and guardian will be given a follow up questionnaire and we will leave them with the device for their personal use if they choose to keep it. Otherwise, we will accept the returned device, catalogue return, and will disposed in an appropriate manner.

Eligibility Criteria

Inclusion Criteria:

- Patients with single ventricle with Fontan palliation
- Over the age of 8 years who would be cooperative with breathing through the oPEP device

Exclusion Criteria:

- Patients with Fontan palliation under the age of 8 years
- Patients who have interrupted inferior vena cava

- Patients with abnormal pulmonary artery anatomy

Statistical Considerations

The pulmonary pulsatility index, hepatic vein and portal vein pulsatility index, aortic valve VTI will be compared before and at the time of using the oPEP device. A repeated t-test will be used for within subject comparison. Since this is a pilot study we will plan to include 15 patients.