Use of Pulsed Electromagnetic Fields For Ischemic Cardiomyopathy Therapy (EFFECT Trial): A Randomized, Double-Blind, Parallel, Placebo-Controlled, Prospective Trial

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Background

- Revascularization (CABG or PCI) has been the standard care for patients with refractory angina from ischemic heart disease (IHD). However, many patients are not candidates for PCI or CABG due to diffuse coronary disease or total occlusion of the coronary arteries, high surgical risk or lack of conduits.
- Following the applications of electrical stimulation to enhance healing of recalcitrant bone fractures and chronic wounds, newly developed signals and revised protocols with pulsed electromagnetic fields (PEMF) have been shown in clinical studies to enhance microvascular blood flow, promote endothelial cell growth, angiogenesis and hemodynamics post infarct.
- First clinical trial conducted, thus far, to assess PEMF safety & efficacy in pts with ischemic cardiomyopathy.

Aims:

- The study is a randomized, parallel, placebo-controlled and prospective pilot trial to assess PEMF therapy in pts with ischemia refractory angina for:
- *Safety*
- *Efficacy* on perfusion, function & clinical symptoms
- *Sustainability* after completion of the therapy
- Regional myocardial perfusion and function (primary outcome). Patient angina and exercise tolerance (secondary outcome).

Methods

Patient Selection:
Pts undergoing evaluation and TX for chronic IHD. All pts signed a consent form approved by the IRB.
- 33 patients randomized into 2 groups:
- TX Group: 15 patients with PEMF TX for 3 mon.
- Sham group: 17 patients with Sham PEMF TX for 3 mon.

Inclusion criteria:
- Pts between 30 – 70 yrs old
- Coronary stenosis > 70% on catheterization
- The coronary disease cannot be revascularized
- Ischemia on echocardiography or SPECT imaging.

Exclusion criteria:
- Coronary stenosis <70% by catheterization.
- Good candidates for revascularization.
- Unable to sign consent.
- With pacemaker/AICD.
- Stent placement < 1 month

PEMF Application

- The PEMF device cleared for pain and edema (SofPulse, Ivivi Technologies, Inc., Northvale, NJ) produces a low power, pulsed radio frequency (PRF) signal consisting of a 4 msec burst of 27.12 MHz sinusoidal waves repeating at 5/sec. The incident amplitude of the signal is 0.05 Gauss peak to peak (for reference, the earth's magnetic field is 0.5 Gauss). The signal is delivered to the tissue target via a single turn circular electrical coil 8 inches in diameter, fitted in a garment worn around the chest, situated over the patient's heart. No heat or muscle stimulation is produced.
- The procedure is repeated for 30 min twice a day for 3 months. The 1st Tx was conducted at CCF. Subsequently, all patients were treated and trained by experienced homecare RN at patient's home for 1 week. After the 1-week period, the patients used the device at home by themselves.
- The PEMF signal was configured to modulate calmodulin-dependent NO and growth factor (e.g., FGF-2) production.

Assessment of Safety

- The initial treatment was conducted at CCF. Hemodynamics (HR, blood pressure) was mentored at baseline, every 5 min during the 30 min treatment and 30 min after treatment. ECG was acquired at baseline, 15 min during, immediately post and 30 min post treatment.
- Any clinical symptom, hemodynamic response, arrhythmias, or ECG changes was documented. Chemistry labs (C18) and cardiac enzymes (CPK, MB and TnP) were checked at baseline and 24 hours after the 1st treatment. High sensitive CRP was measured at baseline, after 1, 3-mon treatment and 2 mon after completion of the therapy.
- 24 hrs home-telemetry monitoring was performed on all patients for 1 week pre- and 1 week post-treatment. Hemodynamic monitoring was performed at patients home by homecare RNs at all visits in these 2 weeks.

Cardiac Imaging

- SPECT imaging (Tc99m-mibi) & Echocardiogrphy were performed at baseline, 1-mon, 3-mon during PEMF TX and 2 mon after completion of the TX using standard protocols.
- The perfusion defect was quantified as percentage of LV compared with normal database using a standard software package (QGS/QPS).

Clinical Evaluation

- All patients underwent clinical evaluation for medical history, symptoms of angina, functional capacity using Seattle Angina Questionnaire (SAQ). All pts received clinical guideline recommended standard care for IHD (beta-blockers, ACE inhibitors or ARBs, calcium charnel blockers, etc). Clinical evaluation was conducted at baseline, 1-month, 3-months during TX and 2 months after completion of PEMF therapy.

Results

Two pts in Sham group (VT) and 1 pt in TX group (MI) dropped out due to complications unrelated to PEMF Tx. No adverse effects from PEMF Tx were noted.

Clinical Characteristics: No significant differences between groups.

Labs and Hemodynamics: No significant differences between groups.

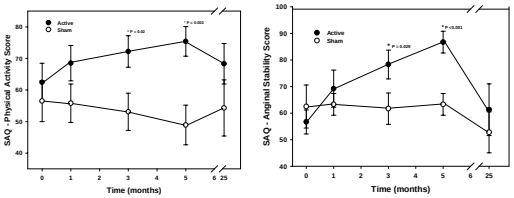
Symptoms: Significant improvements in SAQ scores for angina severity and physical limitations were noted during PEMF Tx and 2 months after Tx in the active group vs no effects in the Sham group.

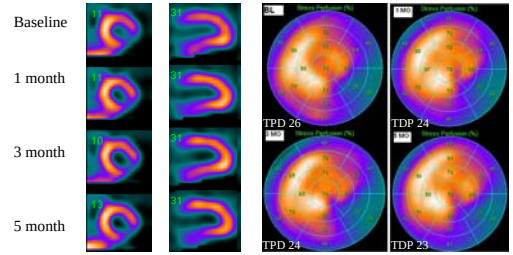
SAQ scores evaluated 25 months (average) after completion of trial showed all improved scores in the active group returned to baseline (see graphs), suggesting continued PEMF therapy is indicated. All contactable patients, except 5 in the sham group, desired to restart PEMF Tx.

Echo: No significant differences between groups.

SPECT: No significant differences between groups. However, 3 pts in the Tx group had 12-25% increase in perfusion (see images) compared to sham group.

SAQ Scores





Conclusions

- This is the first study using PEMF in pts with IHD. The trial shows that PEMF therapy is safe to use and effective improving angina severity and physical capacity in pts with IHD and failed medical therapy & revascularization options.
- Treated patients showed steady improvement in clinical symptoms which persisted at two months after cessation of PEMF therapy. This clinical improvement disappeared approximately 25 months post PEMF, suggesting a longer Tx regimen may be warranted.
- This unique device is non-invasive, non-pharmacological and self-operable at home.
- Future studies are needed to confirm angiogenesis, investigate mechanistic effects, quantitate perfusion changes and clinical outcomes in larger trials.

References

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