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Safety and Effectiveness of Enhanced External Counterpulsation in Improving Angioplasty Restenosis

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Summary

Clinical restenosis following coronary artery angioplasty (PTCA) occurs in up to 30% of patients within 6 months of treatment. Endothelial dysfunction in diseased and/or mechanically injured arteries may be a key factor in the process. Enhanced External Counterpulsation (EECP) is an effective noninvasive treatment for coronary artery disease (CAD), which has recently been shown to augment nitric oxide (NO) production. Thus, we postulated that EECP would reduce the restenosis rates after PTCA through its effects on endothelial function. 24 patients (pts) one-month post successful PTCA were randomized to EECP (15 pts) or Control (9 pts). At 6 month follow-up MACE and recurrence of ischemia in the PTCA related regions demonstrated by scintigraphy were observed in 13% of the EECP treated group and in 44% of the Control group ($p < 0.10$). This pilot study suggests that further investigation of EECP in reducing restenosis is warranted.

Introduction

Enhanced External Counterpulsation (EECP) is an effective noninvasive treatment for coronary artery disease (CAD). It utilizes 3 sets of pneumatic cuffs applied to the lower extremities that inflate sequentially from the calves to the thighs at the onset of diastole to provide diastolic

augmentation and increase venous return. The pressure is released at the onset of systole to produce presystolic unloading, and increase cardiac output. EECP therapy has been shown to improve angina and exercise tolerance [1], and its efficacy in producing sustained benefits over a long-term period after treatment has also been documented [2,3]. Recently the role of EECP in modifying neurohumoral derangements and endothelial dysfunction associated with cardiovascular disorders has been studied and it has been found that EECP augments nitric oxide (NO) production[4] and normalizes brachial artery reactivity[5].

Coronary artery angioplasty has become a mainstay therapy in interventional cardiology. Even though the initial success rate (90 – 95%) makes angioplasty an effective treatment for CAD, the high rate of restenosis following PTCA remains a major limitation. The mechanisms of restenosis have been extensively studied and it appears that NO deficiency in diseased and/or mechanically injured arteries may contribute to the process of restenosis. Improving endothelial function may then be a key concern in preventing restenosis. Therapies targeted at augmenting nitric oxide offer new potential opportunities for therapeutic intervention and prevention of restenosis after angioplasty[6].

Since there is preliminary evidence that EECP therapy improves endothelial function by increasing shear stress, we postulated that it might also reduce restenosis rate after elective angioplasty through improvement of endothelial dysfunction and nitric oxide synthesis. This study was designed to investigate the safety and efficacy of EECP therapy applied one month following coronary artery angioplasty.

Methods

Patients (pts) were randomized to either EECP treatment or a Control group one month after successful PTCA. Exclusion criteria included: congestive heart failure, aortic insufficiency, myocardial infarction within the previous 3 months, significant ventricular ectopic activity or atrial fibrillation, severe occlusive peripheral vascular disease, active deep vein thrombophlebitis, uncontrolled systemic hypertension (BP > 180/110 mm Hg), and clinically significant bleeding diathesis (patients treated with aspirin, clopidogrel, or warfarin were included). Patient's baseline demographic and clinical characteristics, as well as angiographic data were recorded.

The EECP group received one hour of EECP treatment daily for a total of 35 hours. All patients were monitored by continuous electrocardiogram, finger plethysmograph and oximetry during EECP treatment. The greatest external compression used to maximize the diastolic/systolic waveform ratio (Effectiveness Ratio) was 225 – 275 mm Hg. Medica-

tions were maintained unchanged throughout the course of the study. No other interventions were performed during the study.

The Control group received usual therapy. Follow-up radionuclide stress scintigraphy was performed at six months post PTCA in both groups. Study endpoints included major adverse cardiovascular events (MACE) - MI, death, angiographic restenosis, target vessel revascularization (TVR) or positive radionuclide tests in the regions related to previous PTCA vessels, indicating restenosis within 6 months after angioplasty.

Statistical analysis was performed using the chi-squared tests for discrete variables and the student's t test for continuous variables, significance $p < 0.05$.

Results

This study enrolled 24 pts (15 males, 9 females; 58 ± 10 years old). Of the 24 pts, 11 had previous revascularizations in addition to the current PTCA, and 7 had myocardial infarctions prior to study entry. Comparisons of patient characteristics of the study groups are shown in Table 1-3:

Table 1. Clinical characteristics of the study groups	**EECP GROUP**	**CONTROL GROUP**
Number of patients	15	9
Sex	F=7, M=8	F=2, M=7
Age	60±7 years	55±13 years
History of MI	33%	13%
History of revascularization *	67%	11%
Clinical presentation with unstable angina	18%	0%
Diabetes	14%	38%
Smoking	21%	25%
High cholesterol	79%	75%
Hypertension	43%	25%

* $p<0.05$; values are expressed in mean ± SD.

Table 2. Angiographic characteristics	**EECP GROUP**	**CONTROL GROUP**
Number of lesions	17	10
Lesion type A	0%	22%
Lesion type B	47%	22%
Lesion type C	53%	56%
Lesion diameter (mm)	3.3±0.4	2.9±0.3
Lesion length (cm)	1.8±0.8	2.0±1.2

* $p<0.05$; values are expressed in mean ± SD.

The six month follow-up of MACE and angiographic restenosis, target vessel revascularization (TVR) or positive radionuclide tests in the regions related to previous PTCA vessels for the EECP and Control groups is shown in Table 3.

Table 3. Events	**Death**	**Angina Restenosis TVR**	**MACE**
EECP	0	2	2/15 (13%)
Control	2	2	4/9 (44%)

Conclusions

In this preliminary trial of the effect of EECP on clinical restenosis after coronary angioplasty, MACE and recurrence of ischemia demonstrated by radionuclide scintigraphy were observed in 13% of the EECP treated and in 44% of the Control group ($p < 0.10$). The trial size enrollment was underpowered to demonstrate a statistically significant difference between groups. However, there is a definite trend suggesting that EECP therapy may reduce post PTCA restenosis rate. No adverse consequences or safety issues were identified with EECP treatment. This result suggests that further investigation of EECP in reducing restenosis is warranted.

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