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J Cardiovasc Pharmacol Ther 2006; 11; 271
DOI: 10.1177/1074248406296363

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Enhanced External Counterpulsation: A New Modality in the Treatment of Angina and Heart Failure

Rohit R. Arora, MD, FACC, and Ankur G. Shah, MD

As the population ages, more patients will suffer from refractory angina and heart failure. With advances in both the understanding of neurohormonal regulation and pharmacologic targets, the treatment of both has greatly evolved. However, despite treatment, some patients will remain symptomatic. Any intervention that can improve symptoms or outcomes is eagerly anticipated, with much recent attention given to enhanced external counterpulsation (EECP). However, the precise role the noninvasive technique will play in these disease states is uncertain.

While EECP has been used for more than 4 decades, its efficacy in heart failure is not as extensive compared to angina. Similar to the intra-aortic balloon pump, EECP is based on the principle of diastolic augmentation to increase coronary flow while simultaneously decreasing systolic afterload. Numerous small studies in patients with stable angina pectoris have shown improved cardiac perfusion imaging, a reduction of angina class, increases in exercise tolerance, a decrease in the use of nitroglycerin and increased time to ST segment depression on stress testing.

Even though these studies showed sustained improved effect as long as 5 years after treatment, they were inherently flawed. These were nonrandomized trials conducted with a limited number of patients and institutions, thus introducing bias, and they did not exclude the possibility of the placebo effect. The landmark trial that attempted to address these concerns was the Multicenter Study of Enhanced External Counterpulsation trial. This was a multicenter blinded study conducted in 7 university hospitals randomizing 139 patients to either full-dose EECP or a sham method with minimal pressures. At 1 month posttreatment, treated patients had a significant increase in time to ST segment depression on stress testing and significant decreases in angina frequency compared to nontreated patients. Although nitroglycerin use did decrease in both groups, there was no significant change between the 2 groups. No objective follow-up in angina frequency and/or ischemic testing was reported, but a substudy analysis at 1 year posttreatment demonstrated significant improvement in quality-of-life parameters.

These results, though, need to be considered with caution. Both groups had increases in exercise duration and decreases in nitroglycerin use, and while the decrease in angina frequency was statistically significant, a similar number of patients in each group showed a 0% to 25% level of improvement. Thus, the placebo effect may still have contributed to the results. Furthermore, cardiac perfusion imaging was not preformed, precluding comparison of the results to radiographic evidence of improved ischemia. Coupled with the fact that the double product (measure of heart rate × blood pressure) at the level of stress testing was not reported, the positive effects of EECP may have been transmitted via a peripheral effect (ie, exercise training).

The data from the International EECP Patient Registry (IEPR) studied the efficacy in the general population. Outcomes following 1097 patients (approximately 86% of patients were not candidates for further revascularization procedures), mostly with Canadian Cardiovascular Society Classification III or IV, showed a sustained significant decrease in weekly angina episode and dramatic reduction in angina class immediately posttreatment in addition to significant improvement in quality-of-life parameters at 2 years. Approximately 41% of patients remained event...
free during the 2-year period, and nitroglycerin use remained significantly decreased compared to baseline.\textsuperscript{11}

However, the optimization of medical management of patients from these studies is unknown. From clinical experience, patients are often not titrated to optimal doses of nitrates and/or β-blockers, especially those on triple antianginal therapy. Furthermore, only 70% of patients from the IEPR were on statins at 2 years and, similarly, only 72% were on aspirin. Given that most of these patients were at high risk for coronary events, these percentages were relatively low. After optimal medical management, would EECP still have such an impact?

In heart failure patients with left ventricular dysfunction, the increase in cardiac output and cardiac index by EECP can acutely increase right atrial mean pressures and pulmonary capillary wedge pressures, possibly precipitating an exacerbation.\textsuperscript{12} Data from the IEPR revealed that after 6 months, there was a significant increase in major adverse cardiac events, death, congestive heart failure, and cardiac hospitalization in patients with a history of heart failure, with an ejection fraction ≤35% portending a worse outcome.\textsuperscript{13} This was markedly evident in patients not able to complete the full course of EECP.\textsuperscript{14}

In patients with a left ventricular ejection fraction ≤35%, a small, nonrandomized prospective study did show a significant increase in peak VO\textsubscript{2} uptake and exercise duration at 6 months.\textsuperscript{15} The randomized, controlled Prospective Evaluation of EECP in Congestive Heart Failure trial demonstrated significantly increased exercise duration and improvement in New York Heart Association classification but no significant change in VO\textsubscript{2} or quality of life at 6 months.\textsuperscript{16} Consistent with previous studies, the discontinuation rate was greater in the treated group, but it is unclear if this was secondary to acute hemodynamic effects of EECP or other circumstances.

There is much uncertainty in how EECP delivers its beneficial effect. Studies have shown changes in neurohormonal regulation via production of NO and brain natriuretic peptide,\textsuperscript{7,8} improved systolic function,\textsuperscript{17} and improved endothelial function\textsuperscript{18} and have demonstrated an increase in angiogenic factors suggesting possible collateral formation.\textsuperscript{19} In both heart failure and angina, patients have been shown to have symptomatic improvement, but this does not imply longer life expectancy or decreased cardiovascular events. As of yet, the true effects of EECP have not been fully elucidated. Currently, in patients with angina who have exhausted other interventions or may not tolerate certain medications, EECP may be useful in improving symptoms; EECP is a Food and Drug Administration–approved, class IIb indication for refractory angina. However, until a well-controlled, randomized clinical trial with optimally managed patients can demonstrate a decrease in mortality/morbidity or exclude the placebo effect, EECP remains an adjunctive weapon in our arsenal to combat angina and heart failure but not a first-line defense.

References


