Treatment of Intractable Angina Pectoris Utilizing Spinal Cord Stimulation

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Intractable angina pectoris affects approximately 5% to 15% of patients with ischemic heart disease. Current treatment options for refractory angina can be divided into 3 groups: pharmacological, nonpharmacological noninvasive, and invasive. The newest pharmacological treatment option for intractable angina pectoris is ranolazine. Nonpharmacological, noninvasive treatment options include enhanced external counterpulsation and transcutaneous electrical nerve stimulation. Invasive treatment options include revascularization procedures: coronary artery bypass grafting, percutaneous transluminal coronary angioplasty, and percutaneous laser revascularization. Spinal cord stimulation (SCS) as a palliative intervention for refractory angina has been underutilized in the United States. This case review describes application of SCS in a 43-year-old woman with a 10-year history of symptomatic ischemic heart disease who was unresponsive to all available treatment options for intractable severe chest pain. Following spinal cord stimulator placement, the patient reported no further angina, discontinued nitroglycerine, had improved sleep quality, and resumed full-time employment.

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Key words: Angina • Ischemic heart disease • Spinal cord stimulation • Enhanced external counterpulsation

In this time of modern medicine, most patients suffering from ischemic heart disease are successfully treated with anti-ischemic drugs and revascularization procedures. Anti-ischemic and anti-anginal medications diminish the oxygen demand or increase the myocardial oxygen supply through vasodilatation. Procedures that increase the oxygen flow to the ischemic myocardium not only alleviate symptoms but prolong life in certain groups of patients. Despite

the multitude of therapeutic applications in the treatment of disabling angina pectoris, there is a group of patients who are resistant to the conventional medical or surgical therapies.[1-3] These are patients who have exhausted all available therapies or who will not benefit from any existing strategies because of the nature of the condition, as in the case of small vessel disease.[4]

An estimated 300,000 to 900,000 people in the United States have refractory angina, and 25,000 to 75,000 new cases are diagnosed each year.[5] Mannheimer and colleagues[6] reported that approximately 5% to 15% of patients with angina meet the criteria for refractory angina. Any treatment that improves the quality of life for these patients without adversely affecting their prognosis should be considered.

Case Presentation

A 43-year-old, 190-pound, 5-foot 6-inch woman presented to the pain clinic with complaints of intractable chest pain. On the visual analog pain scale (1 to 10), the patient rated her chest pain as between 6 and 9. Her medical history included coronary artery disease since 1996; nontransmural myocardial infarction in 2002; and multiple cardiac procedures, including coronary angiograms with balloon angioplasty, placement of stents, and coronary artery bypass grafting in June 2002. She also had a history of hyperlipidemia, thoracic outlet syndrome, endometriosis, hemiplegic migraine, fibromyalgia, major depression, lumbar disc disease, secondary infertility, and recurrent menorrhagia. Her medications included amlodipine besylate (5 mg twice daily), atenolol (25 mg twice daily), aspirin (325 mg once daily), atorvastatin calcium (40 mg once daily), clopidogrel bisulfate (75 mg once daily), isosorbide dinitrate (30 mg once daily), isosorbide mononitrate (160 mg once daily), nitroglycerin (a 0.4 mg tablet as needed), and verapamil (120 mg sustained-release tablet once daily). Physical examination and laboratory data were unremarkable. Blood pressure was controlled. Electrocardiography showed sinus bradycardia, low-voltage QRS, and nonspecific T-wave abnormality. Chest radiography was unremarkable.

The patient was offered placement of a spinal cord stimulator, and she agreed to the following 2-part implantation procedure. In November 2005, she successfully underwent placement of 2 temporal percutaneous leads (Axxess® leads, Advanced Neuromodulation Systems, Plano, TX) (Figure 1), advanced with x-ray imaging to the epidural space at level T2 to T4 for trial. Correct placement was confirmed by test-stimulation and patient interview. The patient experienced paresthesia adequately covering the area of anginal pain. The leads were then affixed to the skin and connected to a temporary, external, portable neurostimulator. During the spinal cord stimulation (SCS) trial, the patient reported good control of the pain and had no angina episodes. The temporal percutaneous leads were easily removed 3 days later. Two weeks post-trial, permanent leads were implanted into the same epidural space at the T2 to T4 level. The leads were tunneled subcutaneously and connected to a rechargeable generator (Eon®, Advanced Neuromodulation Systems, Plano, TX), then placed in a subcutaneous pocket over the right supragluteal region. The procedure was performed in ambulatory surgery, and the patient's postoperative course was uneventful.

The neurostimulator was set to give constant, continuous paresthesic stimulation at the minimal level perceived by the patient. The stimulation parameters used by the patient were amplitude 5.8 mA and pulse wide of 225 microseconds at a frequency of 100 Hz. The patient used the SCS continuously. After surgery, the patient stated that her pain had abated and she had no subsequent episodes of angina. She stopped using nitroglycerin, reported improvement of sleep and functional status, and went back to work full time. In the following 18 months, the patient sustained the improvement in her symptoms.

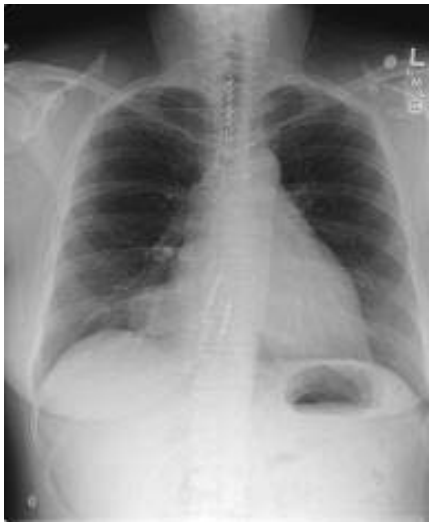

Figure 1. *Thoracic epidural placement of 2 quadrupolar leads showing the electrodes in a staggered position with tips at T1 to T2.* www.medreviews.com

Discussion

Current treatment options for refractory angina can be divided into 3 groups: pharmacological, nonpharmacological noninvasive, and invasive. The newest pharmacological treatment option for intractable angina pectoris is ranolazine. In 2006, the Food and Drug Administration approved sustained-release ranolazine, which decreases ischemia without negatively impacting hemodynamic parameters. When used alone, ranolazine significantly improves exercise duration time, time

to angina, and time to 1 mm ST-segment depression at both trough and peak.[7] When used as a concomitant pharmacological therapy (with amlodipine, beta-blockers, or nitrates), ranolazine significantly improves exercise duration, reduces incidence and severity of angina, and decreases nitroglycerin use.[8,9] Ranolazine is generally well tolerated but is contraindicated in patients with severe renal impairment or a known history of ventricular tachycardia.[10,11] Ranolazine is not currently used as a first-line treatment, pending elucidation of the complete clinical implications of its potential to prolong the QT interval, but it is recommended when standard-of-care anti-anginal drugs fail.

Nonpharmacological, noninvasive treatment options include enhanced external counterpulsation (EECP) and transcutaneous electrical nerve stimulation.[12-14] EECP may be a suitable alternative for patients in whom conventional drug therapy and invasive treatments are contraindicated. Inflatable cuffs are used on the legs to treat anginal pain, increasing the rate of blood return to the heart and the resting blood pressure, and lowering the pressure against which the heart must pump. EECP offers a promising, noninvasive, and safe option that significantly reduces anginal episodes, improves anginal symptoms and quality of life, and extends time to exercise-induced ischemia. It is of interest to note that reported safety and efficacy outcomes for EECP are similar to those for SCS.[3,12-25] The American College of Cardiology and the American Heart Association have classified both EECP and SCS at class IIb level of evidence (usefulness/efficacy is less well established by evidence opinion), and therefore presently recommend the use of these techniques "only in patients who cannot be managed adequately by medical therapy and who are not candidates for revascularization (interventional and/or surgical)."[16] Further positive study results are needed for a definitive recommendation.[12-19]

Transcutaneous electrical nerve stimulation was first used as a neuromodulation (afferent stimulation) treatment in patients with refractory angina in the late 1970s. The anti-anginal effect is attributed to reduced myocardial ischemia. Today, transcutaneous electrical nerve stimulation is typically used to determine whether myocardial ischemia is the actual origin of a patient's pain and, as appropriate, to pilot SCS therapy and compliance.

Invasive treatment options include revascularization procedures: coronary artery bypass grafting, percutaneous transluminal coronary angioplasty, and percutaneous laser revascularization. These first-line treatment options are continually evaluated and improved, increasing life expectancy in the ischemic heart disease patient. However, these modalities may not be viable options in the care of refractory angina patients. Alternative treatment options include transmyocardial laser revascularization and angiogenesis. However, these procedures require anterior thoracotomy and general anesthesia, and they result in clinical outcomes of debatable benefit.[26]

The American Heart Association currently considers SCS a possible treatment of refractory angina. Thus far, it has a class IIb indication (usefulness/efficacy is less well established).[16] However, SCS is a minimally invasive procedure proven to be efficacious and safe (Table 1).

Eddicks and colleagues[27] reported the first placebo-controlled randomized study (n = 12 responders), in which improvement in functional status and symptoms occurred as a result of standard or subthreshold stimulation, compared with a low-output or placebo stage. Additionally, a retrospective analysis of efficacy and cost benefit by Yu and coworkers[28] concluded that SCS treatment not only reduced angina and improved patient quality-of-life, but also decreased the rate and duration of hospitalizations, saving hospital care costs. The authors stated that "The total cost of the SCS procedure was recovered within 16 months after implantation, which is less than 40% of the device life span."

SCS has been used for almost 40 years in the treatment of chronic pain conditions, including failed back syndrome, phantom limb pain, complex regional pain syndrome, peripheral neuropathies, radiculitis, postherpetic neuralgia, and pelvic and rectal pain. This type of treatment for chronic intractable angina pectoris was first reported in 1987 by Murphy and Giles.[29] Neuromodulation or SCS of the upper thoracic and low cervical regions has been used for the past 2 decades in Europe to relieve anginal symptoms, and investigators in the United States report similar good results of SCS in the treatment of refractory angina pectoris.[25,26,29-34] This case provides additional evidence and support for utilizing SCS in the treatment of refractory angina pectoris in patients with end-stage coronary artery disease.

SCS is based on the principles enunciated in the gate-control theory of pain proposed by Melzack and Wall in 1965.[35] This theory postulates that SCS activates large-diameter afferent fibers via application of an externally applied electric field that "closes the gate" to pain transmission. SCS blocks pain by stimulating the dorsal columns that inhibit transmission through the pain-conducting spinothalamic

Table 1
Spinal Cord Stimulator Use in Refractory Angina Pectoris: Efficacy and Safety

Investigators	Angina Episodes	Myocardial Ischemia Incidence (ECG)	Canadian Cardiovascular Society Angina Class	Sublingual Nitrate Use	Safety
Eliasson T et al[20] (N = 19)	Decreased ($P < .05$)	Decreased	Not available	Not available	No serious adverse effects
de Jongste MJ et al[3] (N = 10)	Decreased (group median; $P < .03$)	Decreased (group median; $P = .04$)	Not available	Decreased (group median; $P = .02$)	No serious adverse effects
Mannheimer C et al[21] (N = 53)	Decreased ($P < .001$)	Not available	Not available	Decreased ($P < .0001$)	No serious adverse effects
Hautvast RW et al[22] (N = 19)	Decreased ($P = .001$)	Decreased ($P = .02$)	Not available	Decreased ($P = .001$)	No serious adverse effects
Greco S et al[23] (N = 23)	Decreased ($P < .01$)	Not available	Not available	Not available	Not available
Di Pede F et al[24] (N = 104)	Decreased (≥ 50% in 73%)	Not available	Improved (≥ 1 in 80%; > 2 in 42%)	Not available	No serious adverse effects
Lapenna E et al[25]* (N = 51)	Decreased (> 50% in 88.2%)	Not available	Improved to 2 in 88.2% ($P < .0001$)	Not available	No serious adverse effects

ECG, electrocardiogram. *Lapenna discloses a financial relationship with Medtronic (Minneapolis, MN).

tract.[3,20,22,36,37] Resistance to the use of SCS remains entrenched, mainly due to a concern that the mechanism inhibits only impulse transmission of nociceptive information, thus removing warning signals of myocardial ischemia. However, in clinical trials, pain due to an acute coronary syndrome has not been blocked and will continue to cause typical symptoms despite stimulation.[38] SCS has also been shown to decrease sympathetic tone and improve myocardial blood flow.[39-42] Anti-anginal effects are associated with reduced ischemia, increased coronary flow velocity, decreased myocardial oxygen consumption, and improved circulation to regions with impaired blood flow.

Conclusion

Based on this case of intractable angina successfully treated with SCS, we suggest that this technique may be a therapeutic alternative for patients who have exhausted all available treatments, or who have an increased risk of surgical complications and no prognostic benefit from conventional interventions. With this method of treatment, our patient had a satisfactory effect with a decrease in anginal attacks and consumption of short-acting nitrates. The procedure for placement of the SCS device is relatively easy and safe, and is usually done in an outpatient setting. Use of the device is uncomplicated and effective. However, close, careful follow-up is necessary to ensure proper management by the patient and/or caregiver.

Main Points

- Approximately 5% to 15% of patients with angina meet the criteria for refractory angina.
- Ranolazine is not currently used as a first-line treatment, pending elucidation of the complete clinical implications of its potential to prolong the QT interval, but it is recommended when standard-of-care anti-anginal drugs fail.
- Enhanced external counterpulsation may be a suitable alternative for patients in whom conventional drug therapy and invasive treatments are contraindicated.
- Spinal cord stimulation (SCS) has been used for almost 40 years in the treatment of chronic pain conditions, including failed back syndrome, phantom limb pain, complex regional pain syndrome, peripheral neuropathies, radiculitis, postherpetic neuralgia, and pelvic and rectal pain.
- In patients with intractable angina, SCS improves the quality of life, has anti-ischemic properties, and is a safe adjuvant treatment. It should be considered in the therapeutic algorithm for this group of patients.

In patients with intractable angina, SCS improves the quality of life, has anti-ischemic properties, and is a safe adjuvant treatment. It should be considered in the therapeutic algorithm for this group of patients. The future of this procedure depends on its acceptance by cardiologists in the United States who are involved in the treatment of patients with refractory angina. Trials with SCS are currently underway and should help us determine the role of this technique in the management of intractable angina before it is widely accepted by the medical community. ■

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