

Long-Term Outcome of Spinal Cord Electrical Stimulation in Patients with Refractory Chest Pain

JENS PEDER BAGGER, M.D., D.SC., FESC,* BENT SKOV JENSEN, M.D.,† GUNNAR JOHANNSEN, M.D.‡

Departments of *Cardiology, †Vascular Surgery, and ‡Anesthesia, Skejby University Hospital, Aarhus, Denmark; *Imperial College School of Medicine, Hammersmith Hospital, London, U.K.

Summary

Background and hypothesis: Treatment of patients with refractory chest pain remains a challenge. In this study, the long-term clinical effects of spinal cord electrical stimulation were evaluated in 10 consecutive male patients (mean age 53.7 years) with chronic chest pain in a prospective observational study.

Methods: After placement of the electrode in an epidural position and before implantation of the device, patients were subjected to clinical evaluation, including atrial pacing, in order to document significant antianginal effects.

Results: Spinal cord electrical stimulation abolished or improved pacing time to angina by more than 50% in seven of the patients who subsequently had the device implanted. In three of these patients, the system was ineffective after a period of 3–9 months despite paresthesia in the area of anginal pain with electrical stimulation. The effects of treatment remained satisfactory in the remaining patients (40%) after a mean follow-up of 60 (45–72) months. Thus, a long-lasting clinical response was able to be predicted in 57% of the patients.

Conclusion: Spinal cord electrical stimulation is one of the few therapeutic options in inoperable patients with refractory chest pain.

Key words: spinal cord, electrical stimulation, angina pectoris

Introduction

Spinal cord electrical stimulation (SCES) has been reported to be effective in intractable angina pectoris in patients

with and without coronary artery disease;^{1–3} however, very few reports exist on long-term results.³ Due to possible placebo effects with electrical stimulation, we decided to implant the device only after extensive preprocedural evaluation. After the electrode was placed in the epidural position we sought an optimal stimulation modus over the next days. Thereafter, anginal pain was provoked in the patients with repeated atrial pacing with and without SCES. The device was implanted only in patients with significant antianginal effects of SCES during pacing. We report on follow-up of these patients with this treatment for up to 6 years.

Material and Methods

Ten consecutive males (mean age 53.7, range 47–68 years) in New York Heart Association class III–IV due to angina pectoris were subjected to SCES in the period 1989–1993 after informed consent had been obtained. Seven had coronary artery disease (two had previous myocardial infarction, three had coronary artery bypass grafts, and one had coronary artery balloon angioplasty). One patient had coronary artery vasospasm of the left circumflex artery in addition to diffuse coronary artery disease. These patients were not considered suitable for revascularization procedures when entering this treatment. Three other patients had severe chest pain on exertion without significant coronary artery disease or extracardiac reasons for the pain. All were treated with maximal doses of antianginal medication (beta blockers, calcium antagonists, and short- and long-acting nitrates).

The spinal electrode (unipolar in the first and quadripolar in the other patients) was inserted into the midline of the epidural space caudal to the expected stimulation level by means of percutaneous technique and under local anesthesia. In one patient who had previously undergone a back operation, a small laminectomy was necessary to gain access to the epidural space. The electrode tip was placed in the mid-thoracic region in order to produce paresthesia in the area of anginal pain (Fig. 1). The electrode lead was then connected to an extension lead that was tunneled subcutaneously to the anterior subcostal area and connected to an external stimulator. During the next days, an optimal stimulation modus was obtained and, if necessary, the continuous concordance between regions of stimulation and anginal pain was secured by changing the lead position (unipolar lead) or by changing the stimulation level

J.P. Bagger was the recipient of a senior research grant by the Danish Heart Foundation.

Address for reprints:

Dr. J.P. Bagger, M.D.
Div. of Cardiology
Hammersmith Hospital
London W12 0NN, U.K.

Received: October 10, 1997

Accepted with revision: February 18, 1998

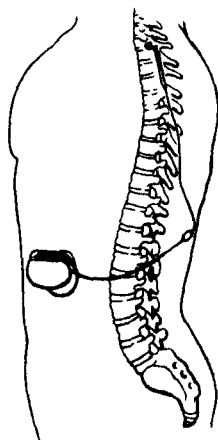


FIG. 1 Illustration of the electrode lead placed in the epidural space, the connector, and the subcutaneous extension lead connecting the pulse generator placed in the subcostal region.

when multipolar leads were employed. Prophylactic antibiotics were administered until implantation of the stimulator or removal of the lead. Optimal and tolerable stimulation amplitudes and frequencies were obtained as well. Finally, the patients were stressed by atrial pacing in the supine position after a night of fasting (Fig. 2). To prevent atrioventricular block, 0.25 mg of atropine was given intravenously just before start of pacing. Electrocardiographic lead V₅ was monitored continuously during the procedure. We aimed to pace at a rate of 150 beats/min until intolerable angina occurred or for at least 10 min. Pacing time to start of angina and maximal pacing time were registered. After an interval of 45 min, the pacing stress was repeated during SCES with the same pacing rate and pacing time in the individual patient. We have previously reported reproducible pacing time to angina pectoris and degree of cardiac ischemia with that pacing protocol.⁴ A pulse generator was implanted only if SCES abolished or delayed the occurrence of intolerable chest pain during atrial pacing by >50%.

The pulse generators were programmed to have pulse widths from 210 to 400 μ s, frequencies from 50 to 100 Hz, and amplitudes from 1.5 to 4 V. All patients were started on cycling stimulation (stimulation periods lasting s/min alternating with stimulation-free intervals) and only changed to continuous function if necessary. All parameters were initially set to the lowest effective mode to save battery power and to cause the least discomfort for the patients. The implanted pulse generators can be turned on and off with an external magnet. The patients were examined and questioned during regular clinical follow-up. They were seen initially within the first month and thereafter every 3 to 6 months in the outpatient clinic. Patients with reprogramming attempts were seen at shorter intervals. The evaluations were in accordance with the Declaration of Helsinki. The Wilcoxon test was used for paired comparisons. Values are shown as mean values and ranges in brackets.

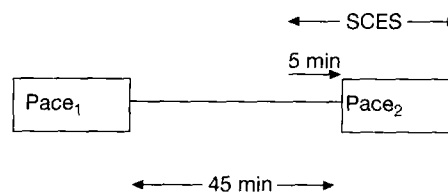


FIG. 2 The patients were paced until intolerable angina pectoris (Pace₁) occurred. After an interval of 45 min, an individually identical pacing test (Pace₂) was performed during spinal cord electrical stimulation (SCES).

Results

The patients were paced twice at a mean heart rate of 145 (122–150) beats/min and for a mean duration of 446 (150–810) s. Spinal cord electrical stimulation improved pacing time to start of angina pectoris by 78% from a mean value of 196 (45–810) s at control pacing to 348 (30–810) s during SCES ($p < 0.05$) in the 10 patients. The SCES had no effect on pacing-induced angina pectoris in three patients, but it abolished ($n = 4$) or improved pacing time to angina by 120–480 s ($n = 3$) in the remaining seven patients (of whom six had ischemic heart disease) (Fig. 3). These patients had a pulse generator implanted (Itrel I, Medtronic, $n = 1$; Itrel II, $n = 5$; or Neuromed, Siemens, $n = 1$). In this group of patients, SCES tended to improve postpacing ST-segment depression, 0.07 (0–0.03) mV at control versus 0.04 (0–0.02) mV during SCES (NS). The three patients with no effect of SCES during atrial pacing had the epidural electrode removed. None developed postoperative wound infections.

The SCES system was considered ineffective in three patients (43%) with coronary artery disease, including the patient with coronary vasospasms after a period of 3–9 months de-

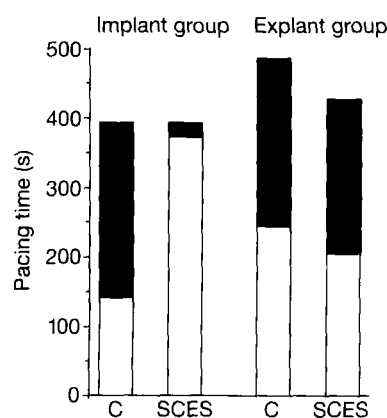


FIG. 3 Mean pacing time until start of angina (white area of bars) and from start of angina to intolerable pain (black area of bars) at control (C) and during spinal cord electrical stimulation (SCES) in seven patients who subsequently had a pulse generator implanted, and in three patients who had the electrode explanted (one of these tolerated pacing for 10 min at control vs. only 7 min during SCES).

spite paresthesia in the angina region on stimulation. After repeated reprogramming attempts (this comprised increments of pulse width, frequency, and/or amplitude to an extent that was tolerable for the patients), the system was removed on demand of the patients after a mean period of 26 (20–33) months. In the remaining four patients (57%), the treatment effect was satisfactory (improvement of 1–2 NYHA grades) after a mean follow-up of 60 (45–72) months (including the only patient who died after 48 months of treatment).

Discussion

In most studies, selection criteria for SCES treatment are based on patient symptoms.^{1–3} As considerable placebo effects are to be expected with a therapy causing constant or intermittent paresthesia in the area of chest pain, we decided to implant the device only after several days of adjustments of the system via an external stimulator and finally after documenting antianginal effects with an atrial pacing protocol.⁴ As a consequence, we did not implant the device in three patients without initial clinical benefits. Despite our strict demands of clinical effect of SCES before implantation of the generator, this treatment failed in 43% of the patients after a period of time that could be considered equivalent to a placebo effect.

We did not perform a randomized study with the inclusion of a control group of patients with refractory angina pectoris due to the considerable need for treatment in these patients.⁵ Instead, we included the patients consecutively and performed an observational study. The control/SCES sequences in response to atrial pacing were not randomized because of the possibility of carryover effects of SCES on clinical variables. Furthermore, it would be impossible to perform identical periods of atrial pacing if pain was alleviated by SCES during the first pacing session. We have found, however, a reproducible clinical outcome with the present pacing protocol in angina patients.⁴ Also, attempts to blind this form of therapy to patients and observers are irrelevant due to paresthesia and electrocardiogram (ECG) artifacts, respectively, during the stimulation periods. Anti-ischemic effects have been reported with SCES in patients with end-stage coronary artery disease.⁵ The main mechanisms by which SCES elicits antianginal effects may be related to decreased overall sympathetic activity resulting in reduced cardiac oxygen demands⁶ or to redistribution of myocardial blood flow between nonischemic and ischemic regions.⁷ Furthermore, high-frequency stimulation transmitted to spinothalamic tract may block the effect of other incoming impulses, resulting in lessened pain perception.⁸ A predominantly analgesic effect of SCES has been considered a potential risk in patients with ischemic heart disease as it may conceal the severity of ischemic attacks. This therapy did not, however, mask pain in patients with acute myocardial infarction.⁹

Long-term intermittent urokinase infusions and transmyocardial laser revascularization are among other therapies reported in fairly large numbers of patients with refractory angina pectoris due to end-stage coronary artery disease.⁵ The

efficacy of these two approaches is thought to be based mainly on improved myocardial blood flow via the genuine vessels and by formation of collaterals, respectively.⁵ No large-scale controlled studies with SCES have been reported so far. On the other hand, patients subjected to SCES treatment have been followed for a longer period of time than patients who were treated with the other therapies. Thus, 57% of patients in the present study remained in a higher NYHA class after 60 months of SCES. Consistent with this finding, Sanderson *et al.* reported a mean improvement of one NYHA grade after 45 months of this treatment.³ The rare complications with SCES—lead displacement or fracture, wound infections, and the possibility of spinal cord infection—are no worse than episodes of bleeding during the administration of urokinase and the perioperative mortality reported with transmyocardial laser therapy.⁵ Further studies on treatment in patients with refractory end-stage ischemic heart disease seem warranted, especially since such patients are expected to increase in number.⁵ A randomized comparison of SCES with either urokinase therapy or transmyocardial laser treatment with respect to clinical efficacy and survival may be a feasible approach.

Conclusion

We found beneficial long-term clinical effects in 57% of patients with chronic chest pain selected for spinal cord electrical stimulation in this small prospective study.

References

1. Mannheimer C, Augustinsson L-E, Carlsson C-A, Manhem K, Wilhelmsson C: Epidural spinal electrical stimulation in severe angina pectoris. *Br Heart J* 1988;59:56–61
2. Eliasson T, Albertsson P, Hårdhammer P, Emanuelsson H, Augustinsson LE, Mannheimer C: Spinal cord stimulation in angina pectoris with normal coronary arteriograms. *Coron Art Dis* 1993;4:819–827
3. Sanderson JE, Ibrahim B, Waterhouse D, Palmer RBG: Spinal electrical stimulation for intractable angina: Long-term clinical outcome and safety. *Eur Heart J* 1994;15:810–814
4. Bagger JP, Nielsen TT, Thomassen A: Reproducibility of coronary haemodynamics and cardiac metabolism during pacing-induced angina pectoris. *Clin Physiol* 1985;5:359–370
5. Schoebel FC, Frazier OH, Jessurun GAJ, DeJongste MJL, Kadipasaoglu KA, Jax TW, Heintzen MP, Cooley DA, Strauer BE, Leschke M: Refractory angina pectoris in end-stage coronary artery disease: Evolving therapeutic concepts. *Am Heart J* 1997;134:587–602
6. Norrsell H, Eliasson T, Mannheimer C, Augustinsson LE, Bergh CH, Andersson B, Waagstein F, Friberg P: Effects of pacing-induced myocardial stress and spinal cord stimulation on whole body and cardiac norepinephrine spillover. *Eur Heart J* 1997;18:1890–1896
7. Hautvast RWM, Blanksma PK, deJongste MJL, Pruijm J, Van der Wall EE, Vaalburg W, Lie KI: Effect of spinal cord stimulation on myocardial blood flow assessed by positron emission tomography in patients with refractory angina pectoris. *Am J Cardiol* 1996;77:462–467
8. Melzack R, Wall PD: Pain mechanisms: A new theory. *Science* 1965;150:971–979
9. Andersen C, Hole P, Oxhøj H: Does pain relief with spinal cord stimulation for angina conceal myocardial infarction? *Br Heart J* 1994;71:419–421