Pain

Does Autonomic Neuropathy Influence Spinal Cord Stimulation Therapy Success in Diabetic Patients with Critical Lower Limb Ischemia?

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BACKGROUND
Spinal cord stimulation (SCS) improves microcirculatory blood flow and relieves diabetic neuropathic and ischemic pain, reducing the amputation rate in patients with peripheral arterial occlusive disease (PAOD). The purpose of this study was to evaluate whether the presence of autonomic neuropathy in diabetic patients with PAOD influences the success of SCS therapy.

METHODS
Sixty consecutive diabetic patients (15 with early and 13 with definite and/or combined autonomic neuropathy) with an ankle/brachial systolic pressure index (ABI) less than 0.20 ± 0.08, underwent spinal cord stimulation after failed conservative or surgical treatment. The neuropathic status of the patients was evaluated before implantation and pedal TcpO2 measurements on the dorsum of the foot were performed.

RESULTS
Limb salvage and pain relief >75%, evaluated with the visual analogue scale, were achieved in 35 patients, whereas in 12 a partial success with pain relief >50% and limb salvage for at least 6 months were obtained. In 13 patients the method failed and the ischemic limbs were amputated. Among the 28 diabetic patients with autonomic neuropathy the treatment failed or resulted in only partial success in 25, whereas in all 32 patients without neuropathy limb salvage and pain relief >75% were achieved (p < 0.0001). Partial success in 10 patients with early neuropathy and in two with definite was achieved (p = 0.008), whereas in 11 patients with definite neuropathy and in two with early the method failed (p < 0.001). The stage of the neuropathy was inversely related to the success of SCS therapy, independent of the stage of the disease. The method’s success was related to the presence of adequate paraesthesias and warm feeling in the painful area with size reduction of the trophic lesions.

CONCLUSIONS
Diabetic patients with peripheral arterial occlusive disease presenting with intractable pain may be successfully treated with spinal cord stimulation unless they have associated severe autonomic neuropathy. © 2000 by Elsevier Science Inc.

KEY WORDS
Spinal cord stimulation, diabetes, neuropathy, lower limb ischemia, transcutaneous oxygen tension.

Spinal cord stimulation (SCS) has been suggested to improve microcirculatory blood flow, to relieve ischemic pain and reduce the amputation rate in patients with severe peripheral arterial occlusive disease (PAOD) [3,16,17,22,24,31]. Vascular reconstruction is the treatment of choice for patients with severe PAOD classified as Fontaine’s stages III (chronic ischemic rest pain) and IV (ischemic pain with ulcers and/or dry gangrene) [1,3,22]. Advances in endovascular treatment and vascular surgery have resulted in increased limb salvage rates. Despite this undeniable progress, the number of patients with non-reconstructable lesions remains high [15,16]. Ideal treatment in these stages allows the patient to retain his limb with no or tolerable pain and to regain a satisfactory level of independence. SCS was used initially (two decades ago) in clinical practice to manage patients with chronic intractable pain or to improve motor function in patients with partial spinal cord lesions [2,3,20,26]. Several authors observed marked improvement in lower limb blood flow in a group of patients who were being treated with spinal cord stimula-
tion for pain related to multiple sclerosis. Based on these observations SCS has attracted greater interest in the treatment of ischemic rest pain and neuropathic diabetic pain [3,21,22,24,34]. Some authors have reported significant pain relief and healing of ischemic ulcers in both diabetics and other patients with end-stage vascular disease who are receiving SCS [9,34,24–26]. Recently, Jacobs et al. [21,22] found that the number of capillaries perfused and the red blood cell velocity were significantly increased by SCS. Several noninvasive (Doppler, rheography, plethysmography, thermography, transcutaneous oxygen tension) and minimally invasive (201TI muscle scintigraphy, xenon133 clearance) techniques have been applied in the effort to quantify the SCS effect on blood flow [8,9,14,19,23,30,35]. However, in diabetic patients with severe lower limb ischemia, in whom autonomic neuropathy is often present, the efficacy of SCS has not, to our knowledge, been investigated before. The purpose of this study was to investigate whether the presence of autonomic neuropathy in PAOD diabetic patients with ischemic pain influences the success of SCS therapy.

Patients and Methods

In a prospective controlled study, 60 consecutive insulin dependent (type I) diabetic patients, 35 men, 25 women (28 with autonomic neuropathy), mean age 60 years (range 46–75) with ischemic pain and nonreconstructible PAOD of the lower limbs were selected by an independent vascular surgeon from the outpatients attending our Institution. The median duration of their diabetes was 22 years (range 15–40). The indications for SCS were based on clinical and laboratory tests. Patients underwent a full history and examination, which included the assessment of neuropathic symptoms and deficit scores. Exclusion criteria included nonmeasurable ankle pressure due to noncompressible, extensively calcified arteries in diabetics, ulcer beyond the aponeurosis, treatment with anticoagulants, neuropathic pain in the upper limbs, presence of peripheral neuropathies from causes other than diabetes, life expectancy less than 18 months due to concomitant diseases, and inability to obtain selective angiography. Other exclusion criteria were a significant heart failure, severe pulmonary or renal insufficiency, unstable angina, non cooperative patient, spinal disease, limb gangrene with osteomyelitis and wet gangrene with lesions larger than 3 cm², and excess alcohol consumption. To benefit from SCS therapy the patient had to be able to understand the principles of the treatment. The stimulation produces paraesthesias, which the patient had to be willing to accept.

The inclusion criteria included a discrimination line of ankle/brachial blood pressure index (ABF) of $0.20 \pm 0.08$ and toe systolic blood pressure of $\leq 30$ mm Hg. and persistent ischemic pain at rest for at least 2 weeks requiring major analgesia. The selection criteria include thorough vascular evaluation, failure of previous attempts at conservative and surgical therapy, and adequate professional equipment, experience, and follow-up facilities. Intra-arterial subtraction or intraoperative selective arteriograms were obtained from all patients and showed occluded femoral and tibial vessels or unsuitable vessels for a bypass procedure or angioplasty. The intensity of symptoms, particularly the ischemic pain, was severe in all cases. The duration of vascular history ranged from 6 months to more than 6 years. Before implantation all patients had received conservative treatment (pentoxifylline, antiplatelet agents, defibrotide, buflomedil), including management of risk factors, pain therapy (tricyclic antidepressants, nonsteroid anti-inflammatory, or dihydrocodeine plus paracetamol) and surgical foot care. Nonreconstructible cases were defined as those without a suitable artery available for reconstructive surgery as demonstrated by good quality selective angiography, delineating the anatomy of the large vessels throughout the limb and the foot. Furthermore, if only ankle or foot arteries were available to bypass but the autogenous venous conduit is absent, or if there were contraindications (including lack of consent) to the surgical treatment, the patient was also regarded as nonreconstructable.

Twenty Fontaine’s stage III patients (7 with neuropathy) with ischemic rest pain of at least two months’ duration, 20 stage IV patients (nine with neuropathy) with ulcers $<3$ cm², and 20 (12 with neuropathy) with trophic lesions $>3$ cm² with dry gangrene of one or two toes, were treated with SCS and included in the present study. All patients gave informed consent to participate in the study.

Assessment of Autonomic Neuropathy

Autonomic neuropathy was evaluated using the cardiovascular autonomic neuropathy tests described by Ewing and Clarke [13]. These tests give a practical guide that we consider reliable, reproducible, simple and noninvasive. The total time required was about 20 minutes and the equipment needed includes a sphygmomanometer, an electrocardiograph, an aneroid manometer, a handgrip dynamometer, plus couch and chair. The flow plan for
performing tests of cardiovascular autonomic function was the following: 1) Tests reflecting cardiac parasympathetic damage: a) Heart-rate response to Valsalva maneuver (patient position: sitting); b) Heart rate (R-R interval) variation during deep breathing (sitting); c) Immediate heart-rate response to standing (lying 5–10 minutes to standing). 2) Tests reflecting cardiac sympathetic damage: a) Blood-pressure response to standing (lying 5–10 minutes to standing) and b) Blood-pressure response to sustained handgrip (sitting).

Orthostatic hypotension was defined as a drop of at least 20 mm Hg in systolic or diastolic blood pressure upon standing. All the subjects were carefully instructed before the test. The neuropathic score, ranging from 0 to 5, was calculated, assigning zero for normal values, one point for every abnormal test and a half point for a borderline value test. Early neuropathy was defined as parasympathetic damage, with abnormal results in one of the three tests of parasympathetic function (regardless of the tests with borderline values). Definite neuropathy was defined as two abnormal parasympathetic tests with or without abnormal sympathetic tests. The 28 patients with diabetic neuropathy had one or more complications of diabetes mellitus such as retinopathy, peripheral sensitive neuropathy and nephropathy. In 15 patients early autonomic neuropathy (1–1½ points in five patients and 2 in 10 patients) and in 13 patients definite autonomic neuropathy with or without sympathetic damage (from 2½ to 3½) were found.

TRANSCUTANEOUS OXYGEN TENSION (TCP02) PROTOCOL

TcpO2 (in mm Hg) was measured using the Microspan Combo TePO2/PcO2 monitoring system (Biochem International Inc., Milwaukee, WI, USA), to evaluate the reduction in skin circulation. The severity of PAOD was accurately determined using the TcpO2 measured by Clark’s electrode, which is known to correlate with the clinical stage of the disease and seems to be a reliable non-invasive index of tissue perfusion, useful for assessing peripheral arterial occlusive disease [8,9,14,19,23,30,35]. The electrode, attached at the dorsum of the foot, was warmed to 44°C, causing maximum vasodilatation of the underlying skin circulation and was allowed to stabilize on the skin for 15 minutes before the measurement was taken [8]. TcpO2 measurements were performed with the transducer placed at the same site, at the dorsum of the foot, before SCS device implantation 2 and 4 weeks after and with the patient in a supine position in a controlled room temperature (25°C), after a rest lasting at least 30 minutes. Systolic arterial ankle and toe pressures were measured using bi-directional Doppler ultrasonography in the posterior tibial and pedal arteries, respectively and then in the toe artery. The ABI was determined by dividing systolic ankle pressure by systolic brachial artery pressure.

CLINICAL IMPROVEMENT AND PAIN RELIEF EVALUATION

Analysis of patient pain relief and clinical improvement were evaluated before implantation, and 2 and 4 weeks after. Thereafter, patients were followed every three months for a minimum 18-month follow-up. The presence of comfortable paraesthesias instead of pain, feelings of warmth, reduction in size of the trophic lesions, increase of the pain-free walking interval under standard conditions (treadmill), and uninterrupted sleep, were evaluated. Pain relief and success rate were based on the intake of analgesic drugs (minor or narcotics) and the patient’s self-evaluation using the following visual analogue scale (VAS): (1) Success was defined as pain relief of >75% and limb salvage for at least 18 months with only minor amputation (toe). (2) Partial success was defined as limb salvage associated with pain relief between 50% and 70%, or as temporary benefit (for a minimum of 6 months). (3) Failure was defined as pain relief <50% and resulting in limb loss within the first 6 months.

IMPLANTATION TECHNIQUE

A quadripolar electrode (Pisces–Quad 3487A, Medtronic, Minneapolis, MN, USA) was placed in the epidural space between L2 and L3 or L3 and L4. The electrode was usually positioned in the midline under fluoroscopic guidance at the level T10-11 and was tested for production of comfortable paraesthesias in the painful foot or limb. The clinical effects were tested during a 2-week trial period. If the patient had significant pain relief, an implantable pulse generator (Itrel II IPG, Medtronic Inc. Minneapolis, MN, USA) was placed in an abdominal subcutaneous pocket. The setting parameters were pulse amplitude between 1.0 and 5.0 V, frequency between 40 and 120 pps and pulse width from 150 to 450 µsec. Stimulation was continuous to obtain maximum information on the clinical outcome.

STATISTICAL ANALYSIS

The TcpO2 data were calculated as mean values and standard deviations. Paired t-tests with appropriate correction to reduce the type-I errors and Fisher’s exact test were applied and values of $p < 0.05$ were considered statistically significant.
Clinical Results and Pain Relief After SCS Treatment. The Diabetic Patients With Therapy Success (Group A) Achieved a Pain Relief >75% and Long Term Limb Salvage, While Those With Partial Success (Group B) Achieved Pain Control >50% With or Without the Use of Minor Analgesics, and Limb Salvage for at Least 6 Months. Implanted Patients with SCS Failure (Group C) Underwent Major Amputations After Less Than 6 Months

<table>
<thead>
<tr>
<th>PATIENT CLASSIFICATION ACCORDING TO FONTAINE STAGE OF THE DISEASE:</th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.) Rest pain, (Fontaine stage III), 20 patients</td>
<td>15</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>2.) Trophic lesions &lt;3 cm², (Fontaine stage IVa), 20 patients</td>
<td>12</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>3.) Trophic lesions &gt;3 cm², (Fontaine stage IVb), 20 patients</td>
<td>8</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Overall Seriesb</td>
<td>35</td>
<td>12</td>
<td>13</td>
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</table>

aFontaine stage IVb: only patients with trophic lesions >3 cm² with dry gangrene.
bThe overall SCS therapy success and partial success rate was 78%, whereas in 22% the method failed to save the limb.

Results

All patients experienced pain relief during the test stimulation period, ranging from significant to minimal. Among the 20 patients with rest pain, limb salvage and pain relief >75% were obtained in 15. Partial success was achieved in four patients (pain relief >50% and limb salvage for at least 6 months). In one patient SCS failed to save the limb and the patient underwent major amputation within the first 6 months after implantation (Table 1). Among the 20 patients with trophic lesions <3 cm², limb salvage and pain relief >75% were obtained in 12 patients. Four patients initially had an amelioration of the ischemic pain >50% but it recurred and within a 12-month period (range 6–18) of stimulation, minor analgesic therapy was necessary. Severe ischemic pain developed in four patients (pain control <50%) within the first 6 months after implantation, leading to major amputation (Table 1). Among the 20 patients with trophic lesions >3 cm², (with dry gangrene), limb salvage and pain relief >75% were obtained in eight patients, whereas in four patients a partial success with pain relief >50% and limb salvage for at least 6 months (mean 9 months, range 6–12) was achieved. After this period the ischemic pain recurred and major amputations were unavoidable. The other eight patients initially expressed pain relief <50% but after 2 months analgesic medication (mainly major analgesics) was necessary for pain control. Within 6 months from the device implantation, all these patients underwent major amputations, because severe ischemic pain recurred (Table 1).

TcpO₂ foot values within the first 2 weeks of the test period increased from 21.4 ± 5.7 mm Hg to 31.5 ± 5.4 mm Hg (p = 0.030) in the patients with rest pain and limb salvage. In the patients with trophic lesions <3 cm² and limb salvage, TcpO₂ mean foot values showed an average improvement from 15.1 ± 6.4 to 22.0 ± 5.1 mm Hg (p = 0.030). In patients with trophic lesions >3 cm² (with dry gangrene) and limb salvage, after the 2-week test period, TcpO₂ increased from 12.1 ± 5.1 to 17.9 ± 4.7 mm Hg (p = 0.025). The increase of TcpO₂ was related to the presence of paraesthesias in the painful area instead of pain, warm feeling and increase in physical exercise during the trial period. Major changes in TcpO₂ measurements were achieved within the first 2 weeks after temporary implantation compared to the values obtained before treatment, whereas an additional minimal increase of TcpO₂ after 4 weeks was seen only in the diabetic patients with limb salvage. Changes of TcpO₂ in all amputated diabetic patients, where SCS failed to control the ischemic pain and save the limb, were not significant compared to the initial values, either at 2 or 4 weeks after device implantation (p = non-significant). No significant modifications were observed in the ABI or toe pressure values before permanent implantation (test period) and during the follow-up.

Different degrees of peripheral sensory neuropathy were present in patients with limb salvage and SCS therapy success and in patients in whom the method failed. The patients where the method failed to save the limb had also a worse clinical course without improvement of pain-free walking distance, healing of the trophic lesions, or thermal feeling, and analgesics were necessary more often. In contrast, the patients with SCS success had an impressive clinical course, especially the rest pain patients, with comfortable paraesthesias instead of pain in the painful area, feelings of warmth, increase in pain-free walking interval under standard conditions (treadmill), reduction in size of the trophic lesions, and overnight continuous sleep without requiring analgesics. Among the 28 diabetic patients with autonomic neuropathy the treatment failed or
resulted in only partial success in 25, whereas in all 32 patients without neuropathy, limb salvage and pain relief >75% were achieved \((p < 0.0001)\). Only in three patients (two with rest pain and one with trophic lesions <3 cm\(^2\)) with early neuropathy did SCS therapy have a long-term positive effect (Table 2). Patients with early neuropathy had a better outcome compared to those with definite \((p = 0.008)\), whereas 11 patients among the 13 where the method failed to save the limb within the first 6 months had definite (combined) neuropathy \((p < 0.001)\), (Table 2).

### Discussion

The neurophysiology of pain relief under SCS varies from simple blocking of pain transmission by a direct effect on spinothalamic tracts, segmental inhibition via coarse fiber activation, effects on the central sympathetic system, and brain stem loops to thalamocortical mechanisms [18]. The inhibitory effects of SCS on the transmission of nociceptive impulses may be exerted segmentally in the spinal cord and/or at a supraspinal level [27]. Clinical observations indicate that the mechanisms involved in the stimulation-induced relief of ischemic pain are different from those related to relief of other types of pain [28]. Indeed, nociceptive pain is more resistant to SCS and significant pain relief is almost never obtained in less than a couple of days. In contrast, neuropathic pain of peripheral origin responds well to SCS. Both components, nociceptive as well as neuropathic, are present in ischemic pain. Several authors have postulated that the principal factor in the relief of ischemic pain is the inhibition of the pain signal per se, leading to a decrease in sympathetic activity and improved skin microcirculation [20]. Another hypothesis is that SCS depresses autonomic sympathetic activity [2,28]. However, many authors have reported success even after sympathectomy [4,22]. SCS has been shown to be useful in vasosplastic disease and reflex sympathetic dystrophy [20].

Angiopathy and neuropathy is a common long-term complication of diabetes [29,33]. About 7.5% of unselected adults attending a hospital diabetic clinic have painful neuropathic symptoms, mainly in the lower limbs [7]. Pain varies from mild paresthesias in a few toes to severe unremitting pain in both legs [7,36]. Night-time exacerbation of the pain plus contact hypersensitivity to bedclothes results in loss of sleep, and pain in diabetic neuropathy can be disabling [36]. The cause of chronic sensory-motor diabetic neuropathy or indeed neuropathic pain is not known, although metabolic and microvascular systems may be involved [5,6,10,27,32]. Although the search for potential therapeutic agents to halt or reverse the neuropathic process continues [5,32], current treatment is largely aimed at relieving painful symptoms. The SCS offers a new and effective way of relieving chronic diabetic neuropathic and ischemic pain by improving exercise tolerance [3,8,15–17,21]. Some authors have shown that in patients with severe PAOD of the lower limbs SCS recruits small capillaries not ordinarily perfused, enhancing skin blood flow—improvements that may explain the beneficial clinical effects experienced by these patients [14,21]. However, their data and the use of SCS in the treatment of POAD were recently criticized, because there are no standard indications for the SCS implantation to obtain the best results. In critical limb ischemia, the aim of the SCS should be not only effective analgesia (which nowadays might be obtained with other, less expensive techniques), but also to promote the

### Table 2

**Outcome of SCS Treatment in 60 PAOD Diabetic Patients According to Neuropathic Stage of the Diabetic Disease.**

Partial Success in 10 Patients With Early Neuropathy and in Two with Definite Was Achieved \((p = 0.008)\), Whereas in 11 Patients With Definite Neuropathy and Two With Early the Method Failed \((p < 0.001)\). Among the 28 Diabetic Patients With Autonomic Neuropathy the Treatment Failed or Was Only Partially Successful in 25, Whereas Success Was Achieved in All 32 Patients Without Neuropathy \((p < 0.0001)\).\(^b\)

<table>
<thead>
<tr>
<th>PATIENT CLASSIFICATION</th>
<th>EARLY NEUROPATHY</th>
<th>DEFINITE NEUROPATHY</th>
<th>WITHOUT NEUROPATHY</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>(A^a)</td>
<td>(B^a)</td>
<td>(C^a)</td>
</tr>
<tr>
<td>Rest pain</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Trophic lesions &lt;3 cm(^2)</td>
<td>1</td>
<td>4</td>
<td>—</td>
</tr>
<tr>
<td>Trophic lesions &gt;3 cm(^2)</td>
<td>—</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>3</td>
<td>10</td>
<td>2</td>
</tr>
</tbody>
</table>

\(^a\)A = success, \(B = \)partial success, \(C = \)failure.

\(^b\)Fisher’s exact test.
trophic-functional recovery of the body segment affected by an advanced ischemic process.

The results of the present study indicate the importance of evaluation of the severity of autonomic neuropathic damage in PAOD diabetic patients, before the final decision for permanent implantation, in terms of cost effectiveness and method success. Diabetic patients with autonomic neuropathy often have an additional pathology due to diabetes complications. The natural history of autonomic damage in diabetes is now clearer, with parasympathetic damage occurring early and sympathetic damage later [11,12]. Applying simple tests allows clinicians some diagnostic precision regarding the autonomic abnormalities present in 20 to 40% of the diabetic population due to diabetes complications [11–13]. The decrease of ischemic pain with SCS is probably secondary to the positive effects on microcirculation rather than vice versa. Pain relief may also result in attenuation of sympathetic activity with vasodilatation, leading to further pain relief [27].

It is documented that sympathetic nerve activity affects vasomotor tone after SCS by improving cutaneous circulation in the ischemic limb; this could be assessed by the TcpO₂ changes [14,19]. In PAOD diabetic patients with severe autonomic neuropathy, the vasomotor tone is already affected [5,6,10,33]. Indeed, in our study all 32 patients with PAOD and without neuropathy were able to avoid amputations using SCS, whereas only 3 of 28 patients with neuropathy obtained relief of their pain. The diabetic patients with neuropathy had a worse course after SCS treatment, inversely related to the degree of neuropathy (Table 2).

Assessment of TcpO₂ measurement, a non-invasive method, is reliable and suitable for accessing skin circulation and has been used to evaluate microcirculatory changes induced by SCS in many studies [9,14,19,23,28,30]. The accuracy of the method in selecting patients with severe PAOD is over 80% [8]. The TcpO₂ changes related to an increase in skin perfusion are not a result of improved arterial inflow [3,22]. SCS has no effect on tcpo₂, as demonstrated by the absence of ABI modifications after stimulation. The feeling of warmth and the paraesthesias in the painful area under SCS were related to increase of TcpO₂ due to improvement of the microcirculation. In patients who have both PAOD and neuropathy, SCS is less effective, but still may prevent or delay amputation in those without severe neuropathic damage. In this group of patients the TcpO₂ may be used as a predictor of therapeutic success. Change in TcpO₂ seems to correlate with the degree of pain relief from SCS, perhaps indicating preservation of certain autonomic mechanisms that produce peripheral vasodilatation in response to SCS. Patients in whom the method failed to save the limb had minimal TcpO₂ changes before and after SCS treatment even if some degree of pain relief was achieved.

Additionally, for pain control and autonomic neuropathy assessment, it is necessary, during the testing period, to carefully evaluate the effect on peripheral blood flow to ascertain if the warm feeling reported by the diabetic patient is related to increased skin microcirculation. This assessment should include determination of the pain-free walking interval under standard conditions (treadmill), confirmation of ulcer healing (surface measurements), and verification of improved blood flow. The stage of the disease is not important for SCS therapy success, but the degree of the damage is.

Different degrees of peripheral sensory neuropathy were found in the patients with and without autonomic neuropathy as a result of diabetes complications; however, it does not seem to be related to SCS therapy success except in rare, advanced cases. The presence of advanced sensory peripheral neuropathy affects the paresthesias that are necessary for the correct placement of the SCS electrode and might interfere with the efficacy of the method, despite the fact that severe autonomic neuropathy is improved by SCS, which affects the vasomotor tone.

In conclusion, change of TcpO₂ during the test period seems to correlate with the degree of pain relief obtainable from SCS therapy in diabetic patients, probably indicating preservation of certain autonomic mechanisms that produce peripheral vasodilatation in response to SCS. The success of SCS therapy in PAOD diabetic patients is inversely related to the stage of autonomic neuropathy. Diabetic patients with PAOD presenting with intractable pain may be successfully treated with SCS unless they have associated severe autonomic neuropathic damage; these patients will not benefit from permanent device implantation.

REFERENCES


Spinal cord stimulation (SCS) is now being used for pain control in ischemic vascular disease and intractable angina. However, SCS not only suppresses the pain, but also improves the microcirculation in the affected extremities and the myocardium; the exact mechanism of this effect is still not completely understood. In this article, Drs. Petrakis and Sciaccia review their results in the treatment of 60 diabetic patients with persistent ischemic pain in the lower extremities. Among other things, they found that the degree of associated autonomic neuropathy significantly affects the outcome of the treatment in regard to both the degree of pain relief and the percentage of patients who had to undergo amputation of the affected leg.

They also found that patients in the good outcome group (more than 75% pain relief and limb salvage for more than 18 months) had a significant increase in transcutaneous oxygen tension (TcPO$_2$) in the affected foot during the 2 weeks of trial stimulation; this phenomenon was not observed in the patients who required amputation. TcPO$_2$ reflects local microcirculation and may therefore indicate the effect of SCS on sympathetic tone in the affected extremity.

Based on these findings, the authors postulate that SCS-induced warmth and paresthesias in the painful area are related to the improvement of local microcirculation. However, the causal relationship between these two events is not absolutely clear. It is well-known that SCS produces paresthesias in distant parts of the body in patients with normal microcirculation. The development of paresthesias in painful areas is generally considered necessary for adequate pain relief, and the underlying mechanism is thought to be related to direct stimulation of non-nociceptive fibers in the dorsal columns of the spinal cord. Therefore, it could be hypothesized that suppression of pain at the spinal level results in decrease of sympathetic tone with subsequent peripheral vasodilation. Obviously, this phenomenon will be absent or less pronounced in patients with autonomic neuropathy, and therefore they will have worse outcomes with SCS.

It would be interesting to combine SCS with some kind of reversible sympathetic blockade to evaluate the degree of peripheral vasodilation in patients with impaired circulation and/or damaged autonomic nervous systems. However, until then, the findings of this study should be able to guide neurosurgeons and other pain specialists in the selection of good candidates for SCS treatment, although the fact that even in the worst group of patients, with both peripheral occlusive disease and pronounced autonomic neuropathy, some patients were helped by SCS and achieved a certain degree of pain relief should make one think twice before denying these patients therapy that could give them a small chance of symptomatic improvement.

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This article opens discussion among neurosurgeons dealing with spinal cord stimulation for the treatment of various neurological deficits. The authors of this paper demonstrated the usefulness of spinal cord stimulation to improve neuropathic pain and avoid limb amputation in patients with severe diabetes mellitus. Measurement of transcutaneous oxygen tension was shown to be a predictive index of the results before permanent implantation of the stimulating electrode. Spinal cord stimulation appears to be the treatment of choice for severely diabetic patients with peripheral arterial occlusive disease, if patient selection is carefully considered.

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I think that this is an important study in terms of providing criteria for the treatment of neuropathy and vasculopathy due to diabetes mellitus with spinal cord stimulation (SCS). SCS is an expensive treatment method even for developed countries; therefore, the criteria for patient selection and response to treatment are very important. In this study, pedal TcPO$_2$ changes were proposed as a predictive index of success during the test-stimulation period. The aim of SCS is not only to relieve the neuropathic pain but also to use the tissue protective effect of the method, as the authors stress.

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