Neuromodulation techniques, complications, and troubleshooting

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Abstract

Spinal cord stimulation has become one of the mainstays of chronic treatment for patients in pain units. It is a safe, effective, and reversible technique, although the rate of complications is approximately 30%-40%. The most common complication, despite technological breakthroughs and advances in equipment, continues to be electrode migration, which currently occurs in approximately 13% of cases. The most serious complication is related to neurologic problems after infections in the epidural space. A review of technique-related complications is performed, classifying them into mechanical and biological complications, including the strategies to avoid them, mainly through careful patient selection, correct surgical technique, and good selection of the programmed electrical parameters.

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Neurostimulation

Introduction

Over the past few decades, spinal cord stimulation (SCS) has become one of the main treatments in the therapeutic arsenal at pain treatment units. New systems have been developed, neurostimulation indications have been extended, although the main indications continue to be neuropathic pain and pain of vascular ischemic origin (stages III and IV peripheral vascular disease using the Leriche-Fontaine classification), and new electrode implantation techniques have been developed for new locations in the nervous system, such as subcutaneous implantation. This has all led to a significant advance for health care professionals specializing in pain treatment, although a satisfactory outcome of the technique continues to be based on the same factors: good patient selection, which appears to be one of the main factors to reduce complications, especially long-term complications, good surgical technique and, lastly good management of the electrical parameters at the time of programming.

In all these cases, there are 2 types of techniques that may be used: a percutaneous technique and a "surgical" technique, which requires performance of a laminectomy to enable the insertion of the electrodes. In the former, the electrodes are inserted percutaneously, whereas in the latter, a laminectomy is performed to enable placement of the electrodes. In both cases, there is no difference in the second part of the technique: placing the generator and connecting the electrodes. The implantation technique can be considered a safe, reversible, and effective technique for pain relief and improvement of the patients’ performance and quality of life. Both techniques have been shown to be effective in all these aspects.

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Despite being considered a safe and reversible technique, the documented rate of complications requiring surgical review is 30%-40%, with good patient selection currently being the most important factor for obtaining an optimal final outcome.\textsuperscript{7-11}

Complications can be classified as hardware-related complications and biological complications. The former are more common than the latter, mainly those derived from problems with the electrodes, such as migration, which currently continues to be the most common complication.\textsuperscript{12} On other occasions, complications can be classified as preoperative, intraoperative, and postoperative (Tables 1 and 2). Most complications are neither serious nor life threatening for the patient and resolve on removal of the system.\textsuperscript{8} The most serious complication reported to date is paralysis occurring after infection at the electrode site,\textsuperscript{13} although cervical spinal cord compression syndrome has also been reported owing to compression by the system implanted at the cervical level.\textsuperscript{14} The objective of this article is to discuss the complications derived from the implantation of electrodes, classified as mechanical complications and biological complications, and to provide some guidance for their treatment.

**Mechanical complications**

As mentioned in the introduction of the article, although mechanical complications are numerically the most important, it is important to bear in mind that patient selection appears to be essential for the treatment to work well, not only in the short term, but, more importantly, in the long term.

Before proposing this treatment in a patient, the following should be assessed: the type of pathology of the patient, with neuropathic pain being the gold standard as an indication for the technique, whether conventional treatment has not been effective, and whether the patient has any major psychiatric condition or any issues of secondary gain or litigation, and also that the patient has no problems of drug or alcohol addiction.\textsuperscript{14-17}

**Electrode breakage and migration**

Electrode migration continues to be the most common complication (Figure 1) of this technique, with an incidence varying between 13.7% and 23%,\textsuperscript{8,18} although these figures may even decrease to 6.4%, if we consider migration only when surgical treatment is required to correct it.

Electrode migration has evidently decreased with improvements in equipment. The development of different anchorage systems and the types of electrodes used, either cylindrical or paddle electrodes, also have an influence on this type of complication, with migration being more common with the former than with the later, with an incidence of 6.4% for cylindrical electrodes vs 3% for paddle electrodes.\textsuperscript{19} As expected, the rate of electrode replacement after their migration has decreased with the first monopolar electrodes (45%) in comparison with quadrripolar leads (11%), owing to the possibility of recapturing paresthesia or of reprogramming the patient with new programming systems.\textsuperscript{20,21}

Electrode migration is seen in those cases that require a surgical intervention to replace the electrode owing to loss of paresthesia at the site of pain, which cannot be recaptured by reprogramming the system. Multiple causes are given, which may explain why migration occurs in a system implanted and anchored in the muscle fascia. Longitudinal migration appears to be due to lack of experience of the implanting physician in suturing the anchor, inadequate anchorage, excessive pressure on the anchor with no prior attachment of the electrode to the anchor, attachment to fatty tissue causing it to break free, trauma, or excessive patient movement.\textsuperscript{22}

This complication is easy to recognize. The patient loses paresthesia at the stimulated site and it is not possible to recapture it with reprogramming. It is important to bear in mind that with this type of complication, the patient’s paresthesia continues, although the location of the paresthesia would not be at the initially programmed site. Possible migration is confirmed by x-ray, compared with the patient’s previous x-ray. The methods to reduce this type of complication include paying special attention when attaching the electrode, checking for the presence of any loops in the anchorage site and also in the generator implantation site, using the anchorage devices provided by the different

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**Table 1 – Mechanical and biological complications.**

<table>
<thead>
<tr>
<th>Mechanical</th>
<th>Biological</th>
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<tbody>
<tr>
<td>Electrode fracture</td>
<td>Infection</td>
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<tr>
<td>Electrode migration</td>
<td>Allergy</td>
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<tr>
<td>Battery failure</td>
<td>Seroma</td>
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<tr>
<td>Disconnection of the connections or electrodes</td>
<td>Epidural fibrosis</td>
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<td></td>
<td>Epidural hematoma</td>
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<td></td>
<td>Dural puncture</td>
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<td>Nerve injury</td>
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<td>Spinal cord injury</td>
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<td>Nerve compression</td>
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<td>Stimulation changes</td>
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**Table 2 – Time period-dependent complications.**

<table>
<thead>
<tr>
<th>Preoperative</th>
<th>Intraoperative</th>
<th>Postoperative</th>
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<tbody>
<tr>
<td>Patient selection</td>
<td>Pain</td>
<td>Immediate</td>
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<tr>
<td></td>
<td>Lack of collaboration</td>
<td>Superficial bleeding</td>
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<td></td>
<td>Technical difficulty</td>
<td>Epidural bleeding</td>
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<tr>
<td></td>
<td>Coverage failure</td>
<td>Superficial infection</td>
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<td></td>
<td></td>
<td>Headache</td>
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<td></td>
<td>CSF fistula</td>
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<td>Late</td>
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<td></td>
<td>Hardware</td>
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<td>Battery failure</td>
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<td></td>
<td></td>
<td>Electrode fracture</td>
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<td>Loss of connections</td>
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<td>Electrode migration</td>
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<td>Biological</td>
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<td>Seroma</td>
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<td></td>
<td>Epidural hematoma</td>
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<tr>
<td></td>
<td></td>
<td>Paralysis</td>
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commercial suppliers, and anchoring following their indications, avoiding the use of excessive tension in the suture allowing for migration of the electrode through the anchorage. There appear to be 2 factors that may be most important to avoid migration. The first is the location of implantation, when implantation is done at a spinal site, as is the case with implantation at the upper thoracic level, where the spinal cord is most immobile, and the second is the experience of the implanting physician.

Electrode fractures and disconnections (Figure 2) are also common mechanical complications, ranging from 6%-9% of cases. In this case, a difference should be made between macrofracture and microfracture. In the first case, reprogramming is not possible and the patient presents with sudden loss of stimulation. In the case of microfracture, it is occasionally possible to reprogram the patient, avoiding the use of the poles close to or involved in the microfracture. The diagnosis in this case is based on the loss of paresthesia. Sometimes it can be visualized in an x-ray, although most commonly the fracture cannot be seen in the x-ray. If this type of complication is suspected, measurement of the impedance of the system can be of great help, with values being much higher than normal owing to the presence of an open circuit in the system because of the fracture or disconnection.

Battery failure
Battery failure is considered to be the least common in this category, with an estimated incidence of 1.7%. Battery failure is considered to occur when the battery needs to be replaced earlier than expected. Battery failures, which are different from the mere running down of the battery, reported in the literature tend to be related to the occurrence of a short circuit owing to loss of insulation of the electrodes as they enter the generator.

Currently, with the implantation of rechargeable systems, other types of battery-related complications have appeared, such as problems with recharging because of the depth of the generator or malfunctioning of the external recharging system and lack of communication between the recharging system and the generator because of the excessive depth of the system or the lack of understanding and management of these more complex systems by some patients. All of this means that the patient has to undergo surgery again and the physician has to review the system so as to replace it, review the whole system, and the causes of failure identified.
it, or change it for a more simple system that causes fewer problems or complications for the patient.

**Biological complications**

**Infection**

Infection is something that may always occur after a surgical intervention. In fact, 22% of all infections that occur are due to a surgical intervention, and almost all are due to the patients’ own flora. The most common site of postoperative infection is the implantation site. In the context of prosthetic implants, infection is defined as one occurring in the first year after implantation. Infections occurring with the implantation of a stimulation system, according to the Centers for Disease Control, have been split into superficial, which affect the subcutaneous tissue and the skin surrounding the implant; deep, which affect the musculature and the fascia; and organ-space infections (Figure 3).

Superficial infections, which are the most common, with an incidence of 4.5% according to the study by Turner et al., are those occurring around the surgical wound and within the first 30 days; whereas deep infections account for 0.1% according to the same study.

The most common infection site is the pocket in which the generator is placed in 54% of cases, followed by the electrode site in 17% of cases, and lastly at the lumbar incision site in 8% of cases. The published mean infection rate ranges from 2%-8% according to different publications, very similar to the data reported for other implants, such as pacemakers and cardiac defibrillators, in which the rate ranges between 1% and 7%.

In an interesting study conducted in oncology patients, it has been shown that the only factor that appears to have a statistically significant effect is surgical intervention time. In the study, it was observed that the infection rate was higher in patients with cancer-related pain and in those with intrathecal pumps compared with nononcologic patients and those implanted with a spinal cord stimulator. Although the result was not statistically significant, it was shown that the longer the duration of surgery, the higher the infection rate.

The prevention and adequate management of infections is vital for the patient. The main measures that should be taken to reduce the rate of complications are those indicated for any type of implantation of a medical prosthesis (Table 3). During the preoperative period, it is important to start monitoring the variables that should be controlled because of the effect they can have on the development of a subsequent infection. Monitoring should be performed in immunosuppressed, obese, and diabetic patients, who tend to be more prone to infections than the general population. It is important to monitor glucose levels and also to stop smoking before the procedure.

**Seroma**

Postoperative seroma can be defined as serosanguineous fluid collection that is deposited or created in the surgical pocket. Seromas are caused basically by friction between the 2 walls of the pocket created and mainly due to surgical trauma, and also when a dead space is created that is larger than necessary to place the prosthesis and is not closed adequately. The incidence of seroma reported in the literature is 2.5%. Clinically, the patient starts with edema and inflammation at the site of the surgical pocket, the patient does not necessarily show signs of infection, such as increased temperature or redness, although it is important to monitor the patient very closely so as to not allow the seroma to become an infection in the pocket in which it has occurred. If the seroma is of large size, the patient may have

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**Fig. 3** - Epidural abscess after implantation of epidural electrodes. (Color version of figure is available online.)
pain at the implantation site, although with the development of a seroma, this is not the most common case.

The development of postoperative seroma can be reduced with careful surgical technique and if the size of the pocket made is consistent with the generator to be implanted and by not manipulating the site excessively and avoiding the excessive use of coagulation or an electrosurgical scalpel. The recommendations for the treatment of this complication are not clearly gathered in the literature. From our point of view and from our experience, we believe that the most appropriate approach is to apply a pressure bandage without draining the seroma, as this can sometimes prolong the seroma. If on occasions this approach is insufficient, optimal aseptic technique is required to avoid superinfection of the seroma.

Pressure ulcer
Pressure ulcers on the skin are not a very common complication. In the study by Cameron et al, they occur in 0.2% of cases, although this incidence increases to nearly 7% when dealing with subcutaneous stimulation, in which case they are almost all because of pressure ulcers caused by the location of the electrodes. The cause of this complication tends to be superficial implantation of the electrodes in the case of subcutaneous stimulation or superficial implantation of the generator in the abdominal or gluteal area. This complication is more relevant in patients with little subcutaneous tissue or with the implantation of rechargeable systems that require implantation more superficially than is routinely done for nonrechargeable systems.

If the pressure ulcer occurs at the implantation site (Figure 4) or at the electrode anchorage site (Figure 5), action should be taken as quickly as possible to avoid superficial infection and infection in functionally important areas. In such cases, the most appropriate approach is to perform an urgent surgical review for signs of infection, with it being recommended to remove the complete system to avoid the development of serious infections.

Nerve injury and spinal injury
As mentioned earlier, in the review by Cameron et al, the most serious complication occurring with the implantation of this system was compression paralysis; there have been subsequently published reports of spinal cord compression with systems implanted at the cervical level, and lastly, a case of postimplantation quadriplegia has been published.

Injuries, both in the nerves and in the spinal cord, may be caused by direct puncture of the spinal cord or through compression of the spinal cord by the system.

Epidural hematoma
Epidural hematoma is a serious although fortunately uncommon complication that has an incidence less than 0.25%. The main risk factors for the development of this type of complication are male sex, age between 50 and 60 years, and the use of antiplatelet or anticoagulant drugs.

Other complications
There are other complications that do not fit into these 2 large groups of biological complications or complications due to system malfunction. In this regard, some of them, such as allergic reactions, can only be seen as sporadic cases, and are always related to the implanted material, such as silicone, platinum, or nickel allergy. In this case, the solution tends to be removal of the system.

Implant-related complications that can be listed and are not related to those mentioned previously tend to be in the area of stimulation; on the one hand, poor stimulation or variation in stimulation, which more than a complication can be seen as an occurrence inherent to stimulation, on the other hand, tolerance to SCS. Tolerance to stimulation was first described in clinical practice by Kumar et al, with an incidence of approximately 30% and was defined as the need to increase the amplitude to obtain the same benefit as at the start of therapy when the appropriate performance of the system and the correct placement of the electrodes had been checked, and it has implications for the long-term functioning of the system. The possible causes for the appearance of this complication, although it has not been possible to prove

**Table 3**

<table>
<thead>
<tr>
<th>Preoperative</th>
<th>Intraoperative</th>
<th>Postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identify risk factors</td>
<td>Cleaning of surgical field</td>
<td>Compression bandage for 24-48 hours</td>
</tr>
<tr>
<td>Improve nutritional and immunologic status</td>
<td>Adequate hemostasis</td>
<td>Keep comorbidity under check</td>
</tr>
<tr>
<td>Improve patient’s condition before surgery (glucose level and tobacco use)</td>
<td>Care with surgical manipulation</td>
<td>Monitor for signs of infection</td>
</tr>
<tr>
<td>Antibiotic prophylaxis</td>
<td>Cleaning of surgical field</td>
<td></td>
</tr>
<tr>
<td>Treatment of local or distant infections</td>
<td>Reduce surgery times</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 4 - Generator-related pressure ulcer in the abdominal area. (Color version of figure is available online.)
Mechanical complications

Programming and pump-filling mistakes
These errors can lead to pharmacologic overdosing or underdosing, with the subsequent associated potential risks. Drug administration outside the pump, in the pocket or directly on the catheter access port, can cause an overdose with respiratory depression and even death. Actually, the Food and Drug Administration has reported 8 deaths and 270 adverse outcomes requiring medical intervention between 1996 and 2010. The rate of occurrence is 1 in 10,000 cases. The best way to minimize such mistakes is a proper training of the personnel who manipulate the pumps. Some recommendations could be to check the medication (dosage and concentration), to palpate implant edges and the access port carefully and thoroughly and to aspirate residual volume.

Catheter complications
Regarding the complications of the catheters, a prospective analysis with more than 200 patients with spinal infusion demonstrated an incidence of 3.3%. Meanwhile, complications derived from the implant procedure reached 15.3%. Table 4 shows the most prevalent catheter adverse outcomes; it also explains some strategies to minimize them.

Complications derived from the electronic infusion system. The system can fail because of battery drain; to prevent this, the electronic device is provided with an alarm to notify with anteriority for its refill. It can also fail because of malfunction, and in that case, the only solution is to replace it.

There can be a failure during telemetry. The change on the orientation of the head above the pump can solve the problem. It is important to remember that multiple attempts to get a proper telemetry might alter the infusion parameters. It is recommended to make an emergency stop after 10 failed attempts. When this happens, a pump inversion can be suspected, and it may be confirmed by palpation or by radiography. If it is inverted, it can be replaced manually (with the risk of disconnection or catheter strangulation) or surgically.

If it is not turned, the implant depth must be evaluated, and if it is too deep, it has to be repositioned more superficially. If the pump fails, it has to be reimplanted.

Biological complications
A careful selection of patients and the identification of risk factors during the preoperative study are the key to success in different situations that increase the risk of complications.

Bleeding
To prevent bleeding, clinicians must follow the current guidelines recommendations, just as mentioned in the section on neurostimulators complications.

CSF fistulas
CSF fistulas develop in up to 20% of patients. In most cases, they are asymptomatic. Postpuncture headache can appear when the dura is injured with the introducer and the catheter is placed. The initial treatment is conservative and includes adequate hydration, supine recumbent position, caffeine, and...
analgesics. If headache becomes intolerable or it does not improve within the first few days, an epidural blood patch would solve the symptoms.

Continuous CSF leakage and its subcutaneous accumulation might lead to the appearance of a hygroma. The management is conservative too, because they tend to resolve spontaneously. Puncture and aspiration must be avoided because of the infection risk. If the observed CSF flow is significant or the patient has neurologic symptoms, a surgical revision has to be considered.

Infections
According to the study by Fluckiger et al., the incidence of infections is approximately 0.7% per year, and it always develops during the first 3 months after the implant. The most frequent infections are in the pocket and the anchorage area. There are patient factors that can increase the risk of infections: psychologic disturbances, sleep obstructive apnea, immunosuppression, smoking, poorly controlled diabetes, coagulation disorders, and anticoagulant therapy. To minimize the risk of infection, the guideline recommendations must be followed.

Risk factors have to be controlled during the preoperative evaluation and management. Antibiotic prophylaxis is mandatory before the first skin incision (Table 5); additionally, a proper surgical asepsis has to be done. Some authors recommend solutions with antibiotics to irrigate the surgical field. Finally, clinicians should not forget the importance of a thorough follow-up of each patient during the postoperative period to detect and control any infection as soon as possible. According to the localization, the most frequent infections are on the surgical wound.

Material removal is not necessary in all cases; a close monitoring can be enough. Samples cultures must be made and empirical antibiotic treatment has to be started and then de-escalated according to the results. A surgical scrub of the wound may be needed, with posterior healing by second intention.

However, spinal infection is always an indication to remove all the material and to start intravenous administration of antibiotics. If an abscess is suspected, an image test should be done (magnetic resonance imaging [MRI] or computed tomography scan) to confirm it and evaluate a possible surgical drainage.

Neurologic injury
Neurologic injury can be a consequence of the catheter placing or secondary to an inflammatory response after the appearance of a granuloma on the catheter tip.

Granulomas are uncommon, but they are a potentially serious side effect. Their appearance was described for the first time in 1991 and the incidence is approximately 0.1%-0.5% in the implanted catheters. The etiology is unknown, but a direct relation has been seen with opioid infusion and the concentration. The most frequent opioids related to this complication are morphine and hydromorphone. The most commonly reported symptom is the decrease in pain relief (33%), followed by the emergence of new symptoms such as thoracic pain. Granulomas have been associated with medullary compressions, neurologic deficit, myelopathies, radiculopathies, etc. They can appear even after years of implant.

In 2012, the Polyanalgesic Consensus Conference published the guidelines for the treatment of granulomas. They recommend using hydromorphone instead of morphine and always at the lowest possible dose. They defend the association with clonidine. Granulomas have not been seen with the use of fentanyl or sufentanil.

Before treating the granuloma, the diagnosis should be confirmed with a computed tomography scan or an MRI, and then the possible neurologic injury and the need of spinal decompression and catheter removal should be evaluated. The pump might be left in the pocket to implant a new catheter.
If there is no neurologic harm, a conservative treatment can be made by aspirating the medication from the pump and filling it with saline. Serial MRI would show the granuloma involution, allowing to start the drug infusion again.

Pharmacologic complications

Many drugs are used for spinal infusion, and none of them is free of secondary effects. All these effects must be known and remembered when a spinal medication is prescribed (Table 6).

Because of the lack of consensus and protocols for using intrathecal medications, a group of experts was created with the aim to collect the different experiences and publish their findings regularly. According to the Polyanalgesic Consensus Conference, only morphine and ziconotide are approved by the Food and Drug Administration.63 The combination of morphine and bupivacaine is considered a first-line option to treat neuropathic pain; and hydromorphone and fentanyl for nociceptive pain. Nevertheless, these therapies have not been approved by the Food and Drug Administration.63

<table>
<thead>
<tr>
<th>Table 6 – Adverse reactions and side effects of the drugs.</th>
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<tbody>
<tr>
<td>Adverse reaction</td>
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<tr>
<td>Peripheral edema</td>
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<tr>
<td>Hormonal changes</td>
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<tr>
<td>Respiratory depression or somnolence</td>
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<tr>
<td>Granuloma</td>
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<tr>
<td>Hyperalgesia or tolerance</td>
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<tr>
<td>Immunosuppression</td>
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<tr>
<td>Psychosis, suicidal thoughts, hallucinations, or confusion</td>
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<tr>
<td>Urinary retention, weakness, and hypotension</td>
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<tr>
<td>Demyelination and necrotizing lesions</td>
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</tbody>
</table>

References

25. Kumar K, Hunter G, Demeria D. Spinal cord stimulation in treatment of chronic benign pain: challenges in treatment...
planning and present status, a 22 years experience. Neurosurgery. 2006;58:481–496.


