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A systematic review on high-frequency spinal cord stimulation therapy for neuropathic pain

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Abstract:

Neuropathic pain is a complex, chronic pain caused by damage to the nervous system, affecting 6.9% to 10% of the population globally. In contemporary society, the therapeutic efficacy of high-frequency spinal cord stimulation (HF10) at 10 kHz has been confirmed by multiple studies and clinical tests, especially in alleviating pain associated with complex regional pain syndrome (CRPS), diabetes-related neuropathy and Peripheral nerve damage. HF10 therapy not only significantly reduces pain, but also avoids the paresthesia caused by traditional SCS during the treatment process. According to a SENZA study, 88% of participants reported greater than 50% pain reduction after one year, and HF10 excelled at improving daily activities and quality of life. In addition, HF10 treatment has fewer side effects and good long-term effects and is free of paresthesia, making it significantly cost-effective. These findings highlight the potential of HF10 as an innovative treatment in the management of chronic neuropathic pain, providing new hope for patients.

Key words: 10kHz SCS, neuropathic pain, adverse impact.

1. Introduction

Neuropathic pain is a type of chronic pain caused by damage to the nervous system. It differs from pain usually caused by human tissue damage (such as burns, or trauma). Neuropathic pain is caused by abnormal activity of the peripheral nervous system or the central nervous system, so it is often difficult to relieve with conventional painkillers and opioids [1]. People with neuropathic pain usually experience persistent burning, tingling, or electric shock-like pain. Neuropathic pain could be intermittent, it can also be continuous and may be accompanied by allodynia or hyperalgesia.

Neuropathic pain is caused by many factors:

(1) Peripheral nerve damage is usually caused by trauma or surgery.

(2) Diabetic neuropathy: patients who have poor blood sugar control, which leads toneuropathic pain [2].

(3) Cancer-related neuropathy: cancer and its treatment (such as radiation therapy, and chemotherapy) may injure nerves and cause pain.

(4) Complex Regional Pain Syndrome (CRPS), usually caused by trauma or surgery.

Neuropathic pain affects a large number of people worldwide. Studies estimate that the global prevalence of neuropathic pain is 6.9% to 10% [3], which means that hundreds of millions of people around the world may suffer from varying degrees of neuropathic pain. According to one study, approximately 20% to 25% of patients with diabetes will develop diabetic neuropathy, and approximately 50% of these patients may experience significant neuropathic pain [4].

Fundamental theory is proposed by Ronald Melzack and Patrick Wall in 1965 [5]. The theory telling us the spinal cord has a mechanism that allows pain signals to be transmitted to the brain for processing in order to reduce the intensity of the pain at the spinal cord.

It was first experimentally used on a patient in 1967 and significantly reduced his lung pain after two days. SCS has become the standard treatment for pain since the 1980s.

However, before the advent of high-frequency SCS, it was common to cause paresthesia in the painful area, which some patients may find uncomfortable or paresthesia. To align the paresthesia feeling with the sore spot, the patient needs to provide vocal feedback during the treatment. On the other hand, paresthesia is not produced by high-frequency SCS at 10 kHz, hence the epidural used in this treatment can be placed exclusively using anatomical landmarks [6].

According to the SENZA Study (a randomized controlled trial of 10kHz high-frequency SCS), 10kHz SCS has a significant effect on relieving refractory chronic back and lower limb pain. Trial results show that after one year of treatment, up to 88% of patients reported pain relief of more than 50% and no sensory stimulation [7]. In comparison, only about 60% of patients treated with traditional SCS achieved similar relief.

10kHz SCS can not only effectively reduce pain when patients are at rest but also provide pain relief during dynamic activities (such as walking, bending, etc.). Studies have shown that patients who received 10kHz SCS therapy experienced considerable pain alleviating in daily life activities and were able to perform a wider range of body movements [8].

2. The type of pain for treatment

2.1 Back and Leg Pain

An article published on 2017 May 1 illustrates that, unlike conventional paresthesia-based SCS, 10kHz therapy does not require the patient to feel paresthesia, nor does it call for paresthesia mapping during lead implant or post-operative programming [9].

This multicenter trial included patients who have low back or leg pain who had previously received an HF10 treatment device implanted for up to 2 years. Patients scored their level of discomfort both before and after HF10 treatment. The spinal cord stimulation program for each patient was temporarily changed to a paresthesia-inducing, low frequency (LF; 60 Hz), wide pulse width (~470 mus). Patients marked all areas where they had LF paresthesia and the locations of their persistent, intractable pain on a human body diagram with the modified software active. Finally, the association between the pain relief and paresthesia overlap was examined.

The result:

There were 61 patients in total with 28 males and 33 females, and the mean age is 55 ± 12 years. An implantable pulse generator (IPG) took on average, 19 ± 9 months to complete. Before HF10 therapy, the average predominant pain score on a 0–10 visual analog scale (VAS) was 7.8 ± 1.3; after testing, it was 2.5 ± 2.1, resulting in an average pain alleviation of 70 ± 24%. The average paresthesia coverage of pain for all patients was 21 ± 28%, and 43% of patients had no paresthesia coverage at all [9]. Fig. 1 will illustrate the point according to the data and statistical knowledge($r = 0.08$; $P = 0.56$).

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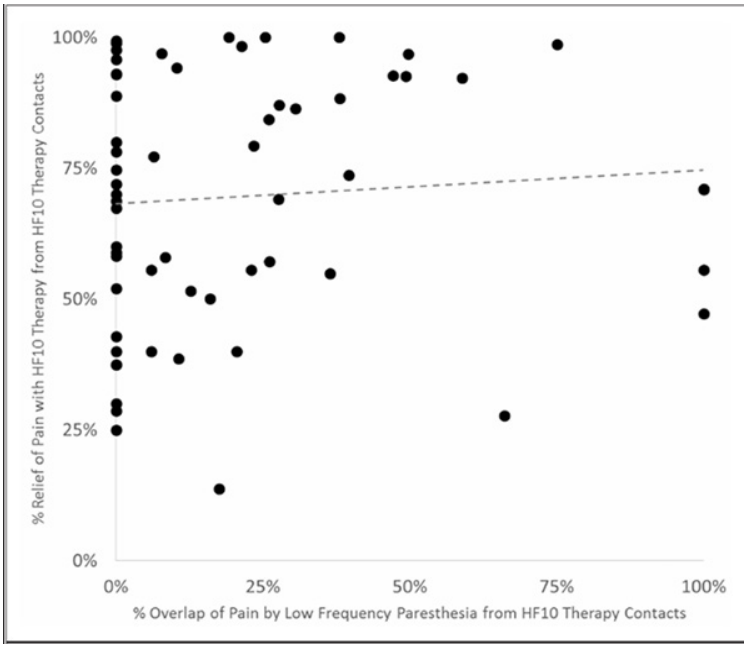

Fig. 1. The point according to the data and statistical knowledge [9]

The spread of the data points in the graph means that even if the painful area is covered by little paresthesia, patients may still get significant pain relief from HF10 therapy. This further supports the idea that HF10 therapy does not rely on paresthesia coverage, demonstrating that it can provide effective pain relief without relying on the paresthesia produced by traditional SCS treatment. That suggests that there is no relationship between high-frequency spinal cord stimulation and paresthesia [9]. ($r = 0.08$, indicating that the relationship between low-frequency paresthesia coverage and HF10 efficacy was very weak, with almost no linear correlation, $P < 0.05$ is considered statistically significant, meaning there is likely to be a significant association between the two variables. In the Fig. 2, $P = 0.56$, which is larger than 0.05, which implies that there is a negligible relationship between 10kHz SCS efficacy and low-frequency paresthesia coverage) [9].

2.2 Diabetic Neuropathy(low limb pain)

A recent study explored that 10kHz spinal cord stimulation can offer significant and long-lasting pain alleviation for patients suffering from diabetic neuropathy. At the same time, the study also estimated the positive impacts of 10kHz stimulation on glycosylated hemoglobin and weight in patients [10]. The researchers conducted 24 months of monitoring and evaluation. After 24 months, researchers found that the average amount of pain was reduced by 79.80% and the score of pain interference with sleep decreased by 65.20%. Meanwhile, researchers found that individuals with beforehand HbA1c levels greater than 7% and higher than 8% in 24 months saw reductions in glycosylated hemoglobin, at 0.5% (7%piror) and 1.1% (8%piror), respectively. Additionally, there is a substantial mean drop in weight of 3.1 kilograms among all research participants [10].

The results point to potential long-term pain alleviation as well as a proper drop of hemoglobinA1c and weight with 10kHz SCS. Fig. 2 and 3 shows the mean pain score (Visual Analog Scale, VAS; 0–10 cm scale) over time and sleep quality improvement. The Pain(sleep quality) index decreased by 65%.

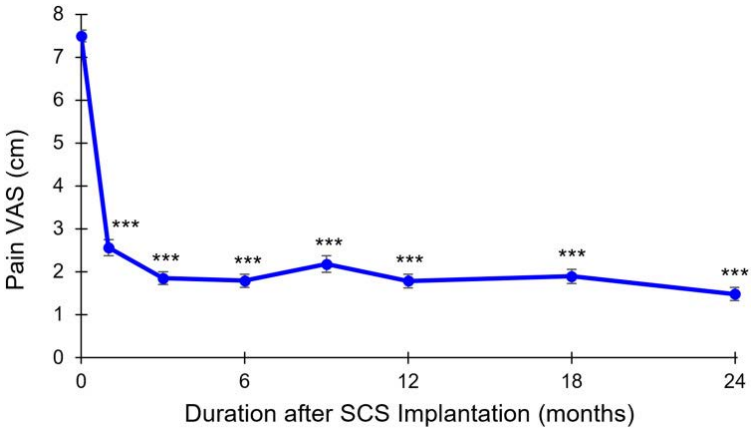

Fig. 2. Pain relief rate VS Duration after SCS [10]

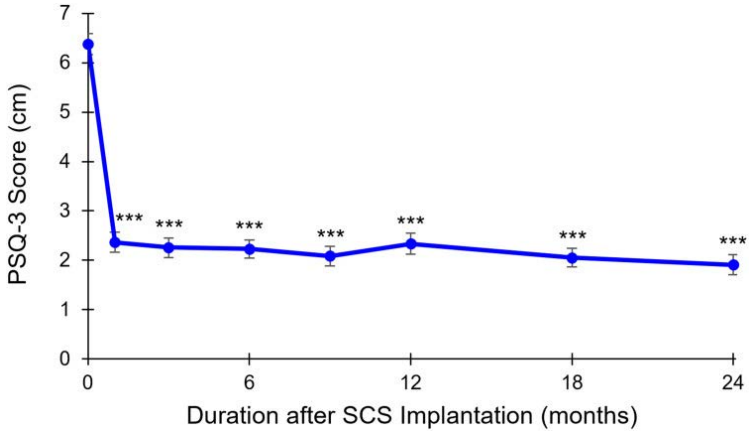

Fig. 3. Sleep quality VS Duration after SCS [11]

2.3 Complex Regional Pain Syndrome

While results are not highly consistent, high-frequency SCS has been confirmed in trials to considerably decrease pain feeling and improve the quality of life for many CRPS patients [12]. In an exploratory survey conducted in 2005, Harke et al assessed the impact of high-frequency spinal cord stimulation on performance in 29 patients with CRPS-I. Deep searing pain on the VAS dropped from 10 to 2, and allodynia on the VAS fell from 10 to 0. These results were consistent at the 3, 6, 9, and 12-month assessments following the initiation of SCS therapy [13].

Another report states that in 2012, a 17-year-old female with six years of right lower limb extremity CRPS experienced significant pain despite trying a lot of medications [14]. After an evaluation, she undergoes 10kHz spinal cord stimulation (SCS) implantation. Post-surgery, her pain decreased significantly, with VAS scores dropping from 10/10 to 4/10. Besides, the patient's CRPS severity score got better as well [14]. The patient recovered her ability to engage in daily activities and education with minimal reliance on pain medication. This case highlights the effectiveness of 10kHz SCS in treating CRPS.

3. Adverse events

10KHz SCS implantation may lead to adverse events. A study showed that 4.4% of patients encountered device-related problems, including embedded devices migration and electronics hardware failure [15]. Problems included infection (2.5%) and temporary disfunction (3.8%) in a case series with 80 patients [11,16]. Additionally, a comprehensive study found that persistent pain at the implant site and cerebrospinal fluid leaks may be linked to 10 kHz SCS. For these issues to be identified and managed, routine follow-up is necessary.

4. Cost-benefit analysis

A study from pain medicine mentions that the costs for 10kHz SCS can range from 18000 pounds to 30000 pounds for the procedure. The estimated cost includes surgical fees, anesthesia, post-procedure care, and device implantation [17]. With the following maintenance, battery replacement, and invisible cost, patients may need to pay 2000 pounds.

As for the benefit of choosing 10kHz SCS, it is considered

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to outweigh the cost. Evidence suggests that 80% of patients report at least 50% pain relief following implantation. This pain reduction improves quality of life. People can engage in social activities afterwards, and reduce their dependency on pain medications [18].

5. Conlcusion

A noteworthy development in the treatment of neuropathic pain, especially for diseases like diabetic neuropathy and complicated regional pain syndrome, is high-frequency stimulation (HF10) therapy. Studies indicate that HF10 can lead to substantial pain relief without the need for paresthesia, a common limitation of traditional spinal cord stimulation techniques. Research shows that patients experience notable reduction in pain levels, daily functioning, and overall quality of life. However, while the benefits of HF10 therapy are compelling, attention must also be given to potential adverse events associated with the procedure, necessitating ongoing monitoring and follow-up to manage these risks effectively. In a nutshell, HF10 therapy is a potentially helpful treatment for people with persistent neuropathic pain.

The future of high-frequency stimulation is about further research to optimize patient selection and treatment protocols. Recent studies emphasized the need of long-term follow-up and standardized methods to ensure stable outcomes. Additionally, people may explore the combination of HF10 with other therapeutic methods, which may enhance pain relief and improve overall patient satisfaction. Expanding clinical trials will provide deeper insights into its long-term effects and broader applications for various pain syndromes, laying the foundation for HF10 to become a standard treatment in managing neuropathic pain.

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