Interventional Pain Medicine 2 (2023) 100275

Contents lists available at ScienceDirect

Interventional Pain Medicine

journal homepage: www.journals.elsevier.com/interventional-pain-medicine

Spinal Cord Stimulation (SCS) reduces Morphine Milligram Equivalents (MME) in patients using Opioid analgesics for Chronic Non-Cancer Pain

Benjamin M. Jacobs [a,*], Marcel S. Kerr [b], John P. Broadnax [a,c], Eric Anderson [a,c]

[a] Anne Burnett Marion School of Medicine at Texas Christian University, 4055 International Plaza, Fort Worth, TX, 76109, USA
[b] School of Biomedical Sciences, University of North Texas Health Science Center, 3500 Camp Bowie Boulevard, Fort Worth, TX, 76107, USA
[c] Department of Anesthesiology, Anne Burnett Marion School of Medicine at Texas Christian, 4055 International Plaza, Fort Worth, TX, 76109, USA

ARTICLE INFO

Keywords:
Morphine equivalents
Opioids
Spinal cord stimulation
Chronic pain
Pain management
Pain alternatives

ABSTRACT

Summary of background data: Chronic Pain is a prevalent condition that affects many people in the United States. Spinal Cord Stimulation (SCS) has been documented to help reduce perceived pain; however, few studies have analyzed the impact of perceived pain on opioid consumption before and after SCS.
Objectives: This retrospective cohort study aimed to evaluate the impact of spinal cord stimulation on opioid consumption after permanent SCS implant.
Methods: This IRB-approved retrospective single-center study investigated the opioid consumption of 26 adults at three different times: (1) Initial date of service-baseline- (2) SCS implant date, and (3) 6 months post-SCS implant date. Mean opioid consumption was calculated over the month prior and after to visit of (1), (2), and (3) to generate 3 separate month averages. Opioid consumptions were measured using Morphine Milligram Equivalents (MME). To determine the difference in MME consumption from baseline to permanent SCS implantation, we conducted a series of paired-sample *t*-tests.
Results: Patients' MME significantly decreased from baseline ($M = 52.63$, $SD = 45.07$) to 6-months post-SCS implantation ($M = 24.64$, $SD = 31.97$, $t(25) = 4.29$, $p < .001$). The effect of this difference was large ($d = 0.84$). Whereas patients' morphine equivalents decreased from date of SCS implantation ($M = 35.73$, $SD = 52.78$) to 6-months post-SCS implantation ($M = 24.64$, $SD = 31.97$), this difference was not significant ($t(25) = 1.66$, $p = .11$) but yielded a small effect size ($d = 0.34$).
Discussions/conclusion: In our study, patients using opioids for non-cancer pain management, SCS moderated the perception of pain neurocircuitry and noxious stimuli-manifestation, resulting in a reduced sense of pain and decreased opioid usage.

1. Introduction

Pain is an unpleasant sensory and emotional experience associated with or resembling actual or potential tissue damage. Although pain is an uncomfortable perception, its function is critical to communicate environmental information for the central nervous system (CNS) to react. Pain may be classified as acute or chronic pain. Acute pain is characterized as a short-term response that serves a biological purpose. Continuous repetition of unpleasant (nociceptive) stimuli can lead to a pathophysiological process and transition to chronic pain [1]. Chronic pain is considered a disease state [2]. In 2016, an estimated 50 million adults in the United States, or 20.4% of the population, were suffering from chronic pain [3].

Chronic pain is a significant burden not only on the individual but also on the health care system. For the individual, chronic pain is a common reason adults pursue medical care [4], has been associated with depression and anxiety [[5,6]], and is associated with reduced perceived quality of life [7]. Some studies have even shown a connection between chronic pain and premature death [[8,9]]. From a health care system perspective, chronic pain is a major financial burden on healthcare costs [10]. Currently, opioid class medications are often included in chronic pain therapy. Despite opioids having a place in analgesia overall, there are a myriad of detrimental effects of long-term use – namely, tolerance [11], withdrawal [12], abuse [13], and addiction [[12,14,15]]. Furthermore, there is little evidence supporting effective use of opioids for chronic non-cancer pain [[16,17]]. Given the

* Corresponding author. Anne Burnett Marion School of Medicine at Texas Christian University, 4055 International Plaza, Fort Worth, TX, 76109, USA.
E-mail address: Benjamin.Jacobs@tcu.edu (B.M. Jacobs).

https://doi.org/10.1016/j.inpm.2023.100275
Received 12 June 2023; Received in revised form 31 July 2023; Accepted 8 August 2023
Available online 12 August 2023

high prevalence and systemic burden of chronic pain, and the negative consequences of opioids for long-term therapy, it is imperative to conduct research that examines safe and effective long-term analgesic alternatives for this group.

One of the most promising long-term interventions is the use of permanent spinal cord stimulators. Spinal Cord Stimulation (SCS) is a form of therapy that can be used as an alternative to prescription opioids for chronic pain [18]. SCS involves the percutaneous placement of electrodes within the epidural space of the spinal cord canal [19]. Although SCS is relatively well understood in its ability to reduce pain for patients suffering from chronic pain [20], research on whether patients' opioid prescriptions change following the implantation of SCS is limited.

The goal of this study is to grow the limited understanding on how SCS influences opioid prescription consumption and expand on the limited literature on how morphine equivalents change over time after SCS implant. Our hypothesis is that SCS analgesic effects may facilitate opioid reduction after permanent implantation.

2. Methods

2.1. Subject identification and study population

Participants were recruited from the Advanced Pain Institute of Texas in Lewisville, Texas. Data on participants were obtained via medical charts review from October 2017 to March 2022. All patients underwent SCS and were followed-up by the pain practice. The inclusion criteria were (1) Having undergone permanent spinal cord stimulator implantation; (2) Not pregnant; (3) Aged >18 years; (4) Long-term opioid consumption prior to spinal cord stimulation; and (5) Have failed other non-invasive pain treatment procedures, and are not candidates for spine surgery, or have already had unsuccessful spine surgery. Exclusion criteria were (1) Never having been placed on prescription opioid medication; (2) Having the SCS implant removed between implantation and 6 months post-op; (3) the participant being under 18 years old.

2.2. Study design

This single-center, retrospective cohort, chart-review study was exempt from further review and approved by the office of research compliance and institutional review board (IRB) at Texas Christian University.

This study was conducted between June 2022 and October 2022 and consisted of three phases: subject identification, chart review, and statistical analysis. Subjects were included if they were prescribed opioid medication for chronic non-cancer pain, underwent permanent spinal cord stimulation between December 2019 and August 2021, and met the other inclusion criteria. Opioid consumption was classified using the fields' gold standard of estimating daily opioid intake, morphine milligram equivalents (MME) [[21,22]]. Morphine equivalents were calculated at three points in time for each participant: (1) Initial date of service-Baseline-; (2) Date of permanent SCS implantation; and (3) 6 months post permanent SCS implant. For each of these three points, a 3-month average of MME usage was calculated. 3-Month averages were used for each period instead of a single, one-month value for calculations to increase the number of data points and thus, improve the accuracy of information for each participant at that phase.

For example, a participant in the study who first established care in January 2020 would have their baseline MME value consist of a three-month average from December 2019, January 2020, and February 2020. Furthermore, if this same participant underwent SCS implantation in June 2020, the months of May, June, and July 2020 would be averaged to create a three-month average for MME at date of permanent SCS implantation. Lastly, the final MME value would be calculated in our mock participant six months after implantation (e.g., December 2020). November 2020, December 2020, and January 2021 would all be used and averaged to calculate the final MME value for 6-months post operation.

Notably, the interval between a patients' baseline at initial presentation to clinic and spinal cord stimulator implantation is quite varied – as participants spent different amounts of time deciding if SCS was the right decision for them. Even with this variability between times (1) and (2), the interval between points (2) and (3) were all six months in length. A three-month average was used to calculate the MME value for each of the three points in time to acquire a more reliable measure of each patients' opioid consumption at that time in their life.

The dates of initial presentation to clinic, SCS implant date, and 6-months post-op were identified using the participants' individual medical records. To calculate morphine equivalents for each participant at different points in time, the Texas prescription monitoring program (PMP) was accessed to identify each participant's type of opioid and dosage of that medication.

2.3. Statistical analysis

To determine the difference in morphine equivalents at our three points in time for each participant, (1) Initial date of service-Baseline-; (2) Date of permanent SCS implantation; and (3) 6 months post permanent SCS implant, a series of paired *t*-tests were performed. Two different paired *t*-tests were conducted in the study: between points (1) and (3) and between points (2) and (3). The statistical software SPSS was utilized to run all analyses in our study.

3. Results

3.1. Participant characteristics and selection

The 26 consecutive, chronic pain, non-cancer patients had a mean age of 62.5 (±10.33) years at the time of SCS implant. Participant ages ranged from 42 to 80 years of age. Fifteen patients (58%) identified as female and eleven (42%) identified as male. Fourteen (54%) of participants did not have an ethnicity/race documented on their medical record, ten (38%) of the participants had "Caucasian/white" designated on their medical records and two participants (8%) had "mixed race" designated.

Three participants were excluded from our final sample because they never followed-up in our clinic after implant. Due to the lack of follow-up, the Texas PMP service was not accessed for these patients, a morphine equivalent value for 6-months post SCS was not identified, and these participants were excluded from the analysis.

3.2. Paired T-test results

The two paired *t*-tests that were performed for this study were at (1) Between initial date of presentation-Baseline- and 6-months post-SCS implant and (2) At SCS implant date to 6-months post-SCS implant.

The first *t*-test between baseline and 6-months post-SCS implant yielded significant results ($p < .001$). The mean MME at baseline was 52.63 (±45.08) with a standard error mean of 8.84. The mean MME at 6-months post-SCS implant was 24.64 (±31.97) with a standard error mean of 6.27. The Pearson correlation was 0.67 with a large effect difference ($d = 0.84$).

The second *t*-test between SCS implant date and 6-months post-SCS implant was not statistically significant but showed a trend ($p = .109$). The mean MME at SCS date of implant was 35.73 (±52.78) with a standard error mean of 10.35. The Pearson correlation was 0.59 with a small effect size ($d = 0.34$).

Other analyses investigated changes in MME usage based on gender, age, and baseline MME consumption (high/low). None of these analyses yielded statistical significance or trends.

4. Discussion

In this study, we assessed how patients' opioid consumption, as measured in morphine equivalents, changed over time from their baseline at initial presentation to clinic to their SCS implant date and through their postoperative period. The results of this study support our hypothesis that morphine equivalents would decrease after SCS implant.

The mean MME for our sample decreased over time from 52.63 at baseline to 35.73 at SCS implant date to 24.64 at 6-months post-operatively. The reduction from baseline to the 6 months-postoperative visit was significant ($p < .001$), while the reduction from SCS implant date to 6 months-postoperative visit was not ($p = .11$). From baseline to 6 months post-SCS implant, there was a greater than 50% overall reduction in morphine equivalents. In our sample, 77% of the participants had an overall reduction in MME from baseline to 6 months post-SCS implant ($n = 20$). Half of these participants ($n = 10$) reduced their morphine equivalents to zero 6 months postoperatively and were taking no medication in the opioid class. Of the remaining 6 participants, half had no change in MME over time ($n = 3$), and half interestingly had a small increase in MME ($n = 3$).

It is important to note that although the interval between SCS implant and 6 months post-SCS remained constant, the interval between initial date of service-Baseline to SCS implant date varied amongst our participants. This finding is likely due to the varying time it took participants to agree upon having SCS and deciding with their physician if it was the right treatment for them. The average amount of time between initial date of service-Baseline and SCS implant was 556.7 days (±313.73) with a range of 4 days–1093 days. Those with a short interval were likely referred for an implant while others spent months considering alternatives before getting their implant.

The findings of this study corroborate with prior studies that found either a trend [23] or a significant difference [[[24–26]] in opioid consumption following SCS. Although our study shows a reduction in MME at 6 months compared to baseline, this reduction may or may not persist for the years to come. Some studies have shown SCS reducing MME both at the 6-month and 2-year follow-up periods [[27,28]] while others do not. Kumar and colleagues showed a reduction of opioids at the 6-month follow up for the SCS group, compared to the conservative medical management group, but no change at the 2-year follow-up [29]. The type of SCS may also influence the degree with which opioid consumption is reduced. Kapural et al. found that although opioid consumption decreased both with traditional SCS and HF10 therapy (SCS delivered at 10 kHz), HF10 therapy reduced MME more [30]. The results from our study add to the growing body of evidence supporting spinal cord stimulator implants as effective nonpharmacologic alternatives for treating chronic, non-cancer pain. This is the first study to our knowledge to track and compare patients' opioid consumption, as measured by morphine equivalents from initial clinical assessment to SCS implant date to the postoperative period. Furthermore, our study includes a unique 3-month average approach for determining MME compared to a single timepoint.

Although a majority (77%) of participants experienced an overall decrease in morphine equivalents over time after spinal cord stimulator implant, there could be a multitude of reasons why this reduction occurred irrespective of the SCS implant itself. One explanation is that participants and their physician had conversations on reducing their opioid prescription medication. Given the negative consequences of long-term opioid use, it is reasonable to consider that the physician would recommend reducing MME, thus prescribing fewer opioid-class medication and or reducing dosages and therefore resulting in a reduction in MME over time. Another explanation is that participants were prescribed less opioid class medication around the time of implant and through the postoperative period in order to assess their subjective pain without the altering effects of opioids.

Our study has several imitations given its structure and design. First, our limited sample size of 26 participants is small and the power of the study as a result is low. Second, most participants in our study did not have an ethnicity selected on their medical chart and as a result, it is hard to gauge the homogeneity or diversity of the sample. Third, our study determined morphine equivalents through the Texas PMP, which measures the amount of opioid class medication prescribed and not the amount of opioid medication taken. Although our study found a significant change in morphine equivalents over time after SCS, that change was only found by the amount of prescribed opioid class medication. It is unknown whether patients obtained opioid class medication through other avenues, or if patients were compliant with medication prescriptions, as these behaviors were not assessed in this study. Fourth, the interval between initial date of service and SCS implantation was not fixed. Patients and their physician may have altered their pain regiment prior to the SCS implant date, which could have altered the magnitude of MME reduction. Fifth, the study assessed SCS on MME for those with chronic pain; however, we did not specify the type of pain or location of pain. Sixth, our design in creating a 3-month average for MMEs may underestimate or overestimate their true opioid consumption if usage in one of the three months is moderately higher or lower than the other months. Finally, there was no formal or standardized approach to managing opioids after implantation.

5. Conclusion

The association between opioid consumption and spinal cord stimulation remains unclear, and limited studies have measured the degree to which these two factors influence each other. This study adds to the growing body of knowledge on how spinal cord stimulation may be a safe and effective long-term therapy for patients' suffering from chronic pain. Given the opioid epidemic across the United States, it is imperative that more research is conducted on how we can improve the quality of life for patients and reduce the rising number of opioid-related deaths.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Funding sources

The authors have no sources of funding to declare for this manuscript.

Authors roles

Benjamin M. Jacobs – Primary writer of the manuscript, including literature review. Marcel S. Kerr – Responsible for all statistical analyses. John P. Broadnax – Responsible for manuscript edits. Eric Anderson – Principal investigator. Responsible for supervision throughout the study and writing process.

Declaration of competing interest

Each author certifies that he or she, or a member of his or her immediate family has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Acknowledgements

We thank Dr. Ricardo Vallejo M. D, Ph.D. for reviewing and revising the manuscript.

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