Correlation between abdominal wall stimulation and spinal cord stimulator tip location : a nonrandomized clinical trial

Correlation between abdominal wall stimulation and spinal cord stimulator tip location (CAWSAN): a non-randomized clinical trial

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AWS, abdominal wall stimulation

Abstract

Objectives

This study aimed to investigate the correlation between the vertebral level of paddle placement and abdominal wall stimulation (AWS) after Differential Target Multiplexed™ spinal cord stimulation (DTM™ SCS) in order to improve the safety and effectiveness of SCS for chronic pain patients, particularly those with low back pain (LBP).

Materials and Methods

The CAWSAN study was a non-randomized clinical trial that included 24 patients with DTM™ SCS for persistent spinal pain syndrome (PSPS) type 2 (trial ID: NCT05565469). The intervention involved increasing stimulation amplitude to a maximum tolerable value and obtaining NRS scores for AWS. The primary outcome measure was the association between AWS, the neurostimulator tip and conus medullaris location, while the secondary outcome was the pre-post interventional difference in proportion of patients experiencing AWS. Patient demographics and post-operative imaging were assessed. Statistical analyses involved descriptive statistics, a descriptive logistic regression, and a McNemar test.

Results

The results of the study showed that 7 (29%) of the 24 patients experienced AWS either previously or during interventional stimulation. However, there was no significant correlation found between AWS and the location of the neurostimulator tip or conus medullaris, and there was no difference in the pre-post interventional proportion of patients experiencing AWS.

Conclusions

The study concludes that a relatively high proportion of patients who received DTM™ SCS for PSPS type 2 experienced or previously experienced AWS. There was no significant correlation found between the location of the neurostimulator tip and the occurrence of AWS. This suggests that AWS may not be solely dependent on the stimulation itself and emphasizes the need to consider other factors. Nonetheless, this study provides important insights into the occurrence of AWS in patients receiving SCS for PSPS type 2 and highlights the need for further research in this area.

Keywords

Neuromodulation, spinal cord stimulation, abdominal wall stimulation, complications

Introduction

Low back pain (LBP) is the number one cause of years lived with disability and is highly prevalent in the neurosurgical setting. Chronic LBP, which lasts for more than 12 weeks, can be particularly challenging to manage and often requires a multidisciplinary approach. However, for some patients LBP persists even after conventional therapies (PSPS type 1) and back surgeries (PSPS type 2). As the prevalence of these conditions continues to rise, so does the need for effective treatments that can improve quality of life for affected individuals.

For these patients, spinal cord stimulation (SCS) can help reduce their symptoms and increase the quality of life. Despite its high prevalence, treating LBP with traditional SCS can be challenging [5, 6, 7]. This is because LBP often involves complex, multi-factorial pain mechanisms that can be difficult to target with conventional SCS methods. The development of new SCS devices like Differential Target Multiplexed™ spinal cord stimulation (DTM™ SCS) has the potential to improve the treatment of LBP and other chronic pain conditions.

The Differential Target Multiplexed™ spinal cord stimulation (DTM™ SCS, Medtronic®) uses multiplexed electrical pulses that can differ in amplitudes, pulse widths, charge balancing, and frequencies (Fig 1). This innovative approach to SCS has the potential to improve pain relief outcomes and minimize adverse effects associated with traditional SCS methods [8].

While the literature describes complications during and after surgery, there is little known about the side-effects that can present during SCS [9]. Only two case-reports and one case-series focus on gastrointestinal (GI) symptoms during SCS [10, 11, 12]. The patients in these studies presented with diverse symptoms, including increased parasympathetic tone, diarrhea, vomiting, increased GI motility, constipation, abdominal pain, and distention [11]. Reducing the stimulation settings below paresthesia threshold resulted in reduced GI symptoms for one patient [10]. In the case-series, immediate postoperative abdominal pain was identified in 7 out of 86 cases of epidural SCS implantation. Thoracic radiculopathy was suggested as the most likely cause of immediate postoperative abdominal pain after SCS placement. Small, transient epidural hematomas were hypothesized to explain the thoracic radiculopathy [12].

Although some complications associated with SCS have been reported in the literature, there is a limited understanding of the long-term adverse effects, particularly for abdominal wall stimulation. While a small number of case-reports and case-series have described GI symptoms during SCS, the reported symptoms have been diverse, and the incidence is unclear.

In our clinic in Belgium, some patients seem to experience abdominal wall stimulation (AWS) after DTM™ SCS implantation. This phenomenon is rarely reported and requires further investigation to determine its underlying causes and potential clinical implications. In this prospective interventional study, we aim to investigate whether abdominal wall stimulation after DTM™ SCS placement is correlated with the vertebral level of paddle placement. By gaining a better understanding of this phenomenon, we hope to improve the safety and effectiveness of SCS for patients with chronic pain.

Materials and Methods

Study design

The CAWSAN study is a non-randomized clinical trial. The TREND guidelines were used for reporting the results [13].

AWS, abdominal wall stimulation

The clinical trial was registered on clinicaltrials.gov (ID: NCT05565469) and approved by the local ethics committee of the Jessa Hospital Belgium (registration number B2432022000021). The study was conducted in accordance with the Declaration of Helsinki. Written consent was obtained from all participants.

Participants

Patients with DTM™ SCS at the thoracic level for persistent spinal pain syndrome (PSPS) type 2, previously known as failed back surgery syndrome, were eligible for the study. Patients were excluded if they (1) were younger than 18 years of age, (2) could not understand the Dutch language, (3) were unable or not willing to participate.
The electronic patient record was used to identify eligible patients. Patients were contacted by the physician or nurse and invited to provide study information.

Intervention

During a general consultation, patients were asked if they previously experienced AWS after the placement of the SCS with a numerical rating scale (NRS). Hereafter, patients were seated, and the amplitude of the stimulation of the tip electrodes were increased to a maximum tolerable value. A new NRS score was obtained after the stimulation. After 5 minutes, the settings were reset to previous values. An NRS score of 0 corresponds with the absence of abdominal wall stimulation and a score of 10 with heavy abdominal wall stimulation.

Objective

The primary objective was to evaluate the relationship between the projection of the neurostimulator tip on imaging and the presence of AWS.

Outcome Measures

The primary outcome of this study was to assess the association between experiencing AWS, the neurostimulator tip and conus medullaris location. The secondary outcome of this study was to assess the difference in proportion of patients experiencing AWS before and after interventional stimulation.

Data collection

Patients were measured in height and weight during the general consultation. Using the electronic patient record, the location of the neurostimulator tip was obtained from postoperative imaging and verified by a radiologist. The analyzed images included X-rays and thoracic CT-scans. The type of implanted electrode was also obtained. Furthermore, demographic information such as age and gender were obtained.

Statistical analysis

Due to limited data in literature, no sample size could be calculated. Therefore, descriptive analyses were used to present group characteristics. A binary logistic regression model was used for descriptive purposes to assess the association between the presence of AWS, neurostimulator tip and conus medullaris location in adjusted and unadjusted odds ratios. A McNemar test was used to evaluate the difference in proportion of patients experiencing AWS before and after the interventional stimulation. A two-sided $p<0.05$ was considered a significant effect. All statistical analyses are conducted with IBM SPSS Statistics v29.0.

Results

Patient characteristics

Patient selection and exclusion is presented in a TREND flow diagram (Fig 1). Since DTM™ SCS is a relative new technique, all patients with DTM™ SCS in our clinic were assessed for eligibility (n = 34). A total of 24 patients were ultimately included in the study. Patient demographics were summarized in table 1.

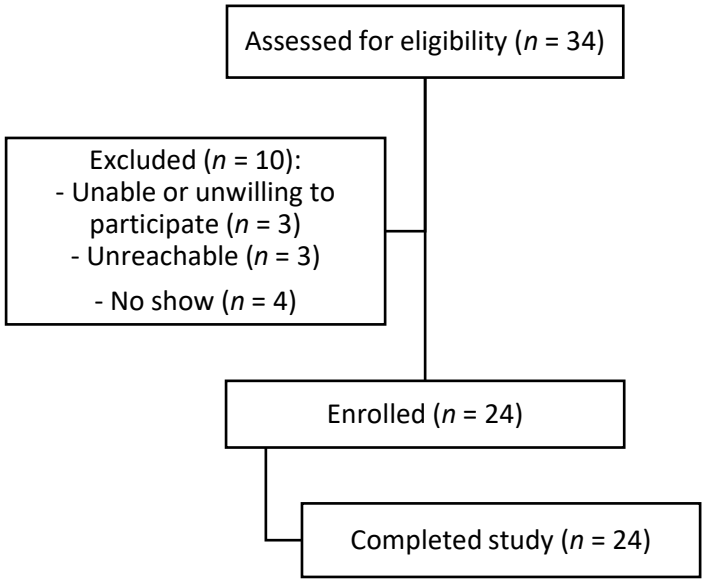


Figure 1: TREND flow diagram presenting patient selection, exclusion, and participation.

Table 1: Demographics of the 24 included spinal cord stimulation patients.

Categorical variables	N (%)
Sex	
Male	17 (71%)
Female	7 (29%)
Electrode	
Specify 5-6-5	22 (92%)
Octad 1x8	1 (4%)
Vectris 1x8	1 (4%)
Numerical variables	Mean (SD)
Age (years)	56 (9)
Height (cm)	168 (8)
Weight (kg)	78 (15)
BMI (kg/m^2)	27.71 (4.8)

Outcomes

Seven of 24 patients (29%) suffered from previous, and seven of 24 patients (29%) interventional AWS respectively (Table 2).. 13 patients in total received a different type of stimulation in the past.

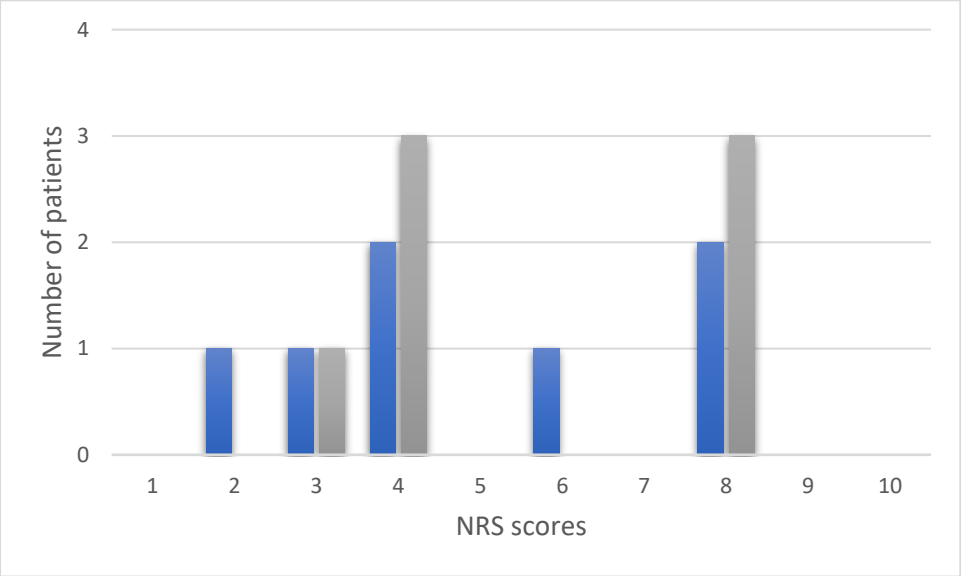
AWS, abdominal wall stimulation

However, all of these patients received DTM™ stimulation for at least 1.5 year prior to the intervention.

Out of the seven patients with previous AWS, four reported AWS during the intervention and three had a different SCS stimulation in the past. However, one of these three patients reported that AWS has always been present and one patient also reported interventional AWS. Two patients reported previous AWS, one of which had a different stimulation in the past but did not experience AWS during the intervention. Three patients reported interventional AWS, without previous AWS experience. In total, 10 patients experienced or previously experienced AWS.

Six of the seven patients who reported previous AWS mentioned in a comment when AWS specifically occurred. Two patients reported a continuous experience of AWS. Three patients reported previous AWS during moments of increased abdominal pressure, such as coughing, defecating, laughing etc. Two patients reported experiencing AWS after neurostimulator settings were changed, such as during a consultation with the pain nurse.

Figure 2: NRS scores of patients with abdominal wall stimulation before (blue) and during the intervention (grey).



AWS, abdominal wall stimulation
NRS, Numerical Rating Scale

There were a limited number of patients with the neurostimulator tip location above or below the vertebral level of T8 (supplemental table 1). Therefore, data was classified into three groups, namely neurostimulator tip above T8, at T8 and below T8. For the conus medullaris, data was classified as above L1, at L1 and below L1 (table 3). T8 was used as a reference due to manufacturer instructions of placing the neurostimulator tip at vertebral level of T8. Furthermore, T8 and L1 had the highest prevalence in our study for the neurostimulator tip and conus medullaris location, respectively. Therefore, L1 was chosen as the reference category for the conus medullaris location. The conus medullaris location could not be extracted from one patient due to heavy metal artifacts on the CT-scan and no lumbar X-ray was present.

There was no difference in the proportion of patients experiencing AWS before or during the stimulation (p=1.00) using the McNemar test.

Table 3: Patients with previous and interventional abdominal wall stimulation and their neurostimulator tip and conus medullaris locations.

	Combined AWS (N=24)			
Tip location	Yes (%)	No (%)	Unadjusted OR (95% C.I.)	Adjusted OR (95% C.I.)
Above T8	2 (20.0)	6 (42.9)	0.33 (0.05 – 2.26)	0.38 (0.05 – 2.76)
At T8	7 (70.0)	7 (50.0)	Reference	Reference
Below T8	1 (10.0)	1 (7.1)	1.00 (0.05 – 19.36)	0.00
Conus medullaris				
Above L1	2 (20.0)	5 (35.7)	0.56 (0.08 – 4.14)	0.62 (0.07 – 5.17)
At L1	5 (50.0)	7 (50.0)	Reference	Reference
Below L1	2 (20.0)	2 (14.3)	1.40 (0.14 – 13.57)	1.18 (0.11 – 12.28)

AWS, abdominal wall stimulation;OR, odds ratio; C.I. confidence interval

Discussion

An interesting finding in our study is that out of the 24 patients who received SCS for PSPS type 2, 10 patients in total experienced or previously experienced AWS, which is a relatively high proportion (42%). This is in contrast to a previous randomized controlled trial of the DTM™ SCS device, which involved 67 patients and reported no instances of AWS or abdominal pain [8]. In a study conducted by D'Souza et al., they investigated the adverse events related to 10kHz SCS over a 5-year period [14]. Their analysis showed that unwanted stimulation was reported as a patient complaint in 17 cases, accounting for 10.4% of the total cases. However, the specific location of this unwanted stimulation was not specified in their study. Another RCT by Rigouard et al. using Specify 5-6-5 electrodes but different Medtronic SCS devices, found only one patient (0.9%) experiencing abdominal pain.
The discrepancy between the occurrence of AWS in our study and other studies may be due to a number of factors. One possible explanation is that AWS may be underreported in previous studies, as it is a relatively rare occurrence and may not always be recognized or reported by patients. Most studies describe abdominal pain as an adverse event, while abdominal stimulation might not always be painful. This could contribute to underreported data. Another potential factor is the variability in patient population and device settings between studies, which may contribute to differences in the occurrence of AWS. The shape and size of the electrode contact could also play a role in the occurrence of AWS, as it may affect the distribution of electrical current and the areas of the spinal cord that are stimulated. Different waveforms and the speed at which the amplitude increases could also play a role. A sinusoidal waveform might not as easily cause AWS compared to square waveforms as used in DTM™ SCS (Fig 2). The speed at which the patient increased the current might also play a role.
Additionally, differences in the location of the neurostimulator tip relative to dermatomes and nerves may also play a role in the occurrence of AWS.

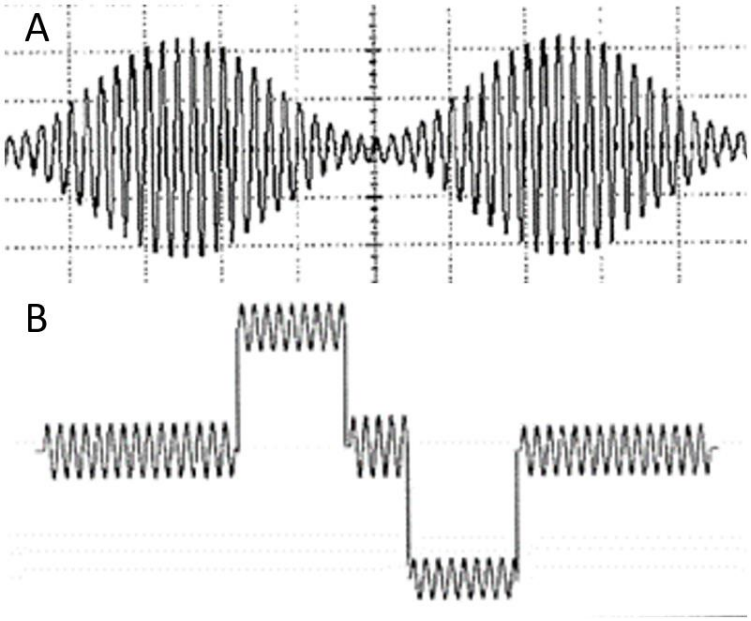


Figure 2: (A) A sinusoidal wave form has less possibility of causing AWS. (B) Square waveforms are more likely to cause AWS due to the rapidly changing nature of the waveform.

We hypothesized that stimulation of abdominal dermatomes, including those above T8 which cover the lower ribcage and upper abdomen and those below T8 which cover the middle and lower abdomen, may lead to more patients experiencing AWS compared to T8 stimulation. However, our findings did not reveal a significant association between the location of the neurostimulator tip and the occurrence of AWS. In addition, we also evaluated the conus medullaris location in our study. This was done because we hypothesized that the position of the conus medullaris could potentially impact the occurrence of AWS in relation to the tip location level. Although the odds ratios derived from our analysis may lack precision due to the small sample size, they provide preliminary evidence of the potential association between neurostimulator tip location and the occurrence of AWS.
Furthermore, our study showed no significant difference in the proportion of patients experiencing AWS before or during the stimulation. These results highlight the importance of considering other factors such as changes in neurostimulator settings and electrodes or patient-specific characteristics that may contribute to the occurrence of AWS.

Limitations

Due to the small sample size of this study, the results need to be interpreted with care. Additionally, due to the small sample size, it was not possible to perform a robust statistical analysis. This is visible in the provided odds ratios and their intervals. However, the inclusion of odds ratios in our analysis can still provide valuable insights into the relationships under investigation. Despite their limitations, odds ratios allow for effect size estimation and can guide future research by indicating the direction and magnitude of associations, even in small samples. Likewise, it can serve as preliminary investigations to explore relationships and generate hypotheses. It is important to note that the limited number of patients in each group and the absence of a standardized definition of AWS may have affected the study's ability to detect significant associations. This study did not specify whether AWS was bi- or unilateral, rhythmic or sustained. Furthermore, not every patient received a postoperative X-ray of the neurostimulator. Therefore, other images which included CT-scans were used to evaluate the neurostimulator tip location. Lastly, selection bias could be present. Lastly, not every patient exclusively received DTM™ neurostimulation in the past. However, only one patient reported previous AWS without interventional AWS.

Future research

In light of these findings, it is evident that further research is warranted to comprehensively investigate the factors contributing to the occurrence of AWS following SCS and to explore its potential therapeutic implications. Notably, a recent study by Tanaka et al. reported successful utilization of differential target multiplexed SCS for chronic postsurgical abdominal pain, highlighting the potential of AWS to open up new therapeutic avenues [15].

Future investigations should aim to elucidate the underlying mechanisms of AWS and its relationship with SCS. One area of focus should be patient-specific characteristics, such as BMI, age, time of implantation, and other comorbidities, as these factors may influence the development of AWS. Understanding how these individual factors interact with SCS and contribute to AWS occurrence will provide valuable insights for personalized patient management. Additionally, is crucial to expand the sample size to achieve sufficient statistical power for future studies. With larger sample sizes, researchers can perform more robust statistical analyses to explore associations, control for confounding factors, and evaluate the generalizability of the findings.

Furthermore, studies should explore the role of neurostimulator settings, including parameters such as amplitude and frequency, as well as electrode type, in relation to the occurrence of AWS. Investigating these variables will help determine if there is a causal relationship between stimulation parameters and AWS, guiding the optimization of SCS protocols to mitigate the risk of AWS while maintaining therapeutic efficacy.

Importantly, future researchers should carefully differentiate between abdominal stimulation/discomfort and abdominal pain as adverse events, as both can have an impact on patients' quality of life. This differentiation will help provide a more comprehensive understanding of the range of experiences associated with AWS and inform appropriate management strategies.

Conclusion

In conclusion, our study found that a relatively high proportion of patients who received DTM™ SCS for PSPS type 2 experienced or previously experienced AWS. This is in contrast to other studies, who reported limited instances of AWS or abdominal pain. Our findings did not reveal a significant association between the location of the neurostimulator tip, conus medullaris and the occurrence of AWS. This suggests that AWS may not be solely dependent on the stimulation itself and emphasizes the need to consider other factors. Nonetheless, this study provides important insights into the occurrence of AWS in patients receiving SCS for PSPS type 2 and highlights the need for further research in this area.

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