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ARTICLE

Pulse article: opioid prescription for pain after spinal cord damage (SCD), differences from recommended guidelines, and a proposed algorithm for the use of opioids for pain after SCD

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Abstract

Study design Online questionnaire of spinal cord injury (SCI) physicians.

Objectives The objective of this study is to characterize the approach to opioid prescription for persons with spinal cord damage (SCD).

Setting An international online questionnaire.

Methods A survey was posted online and circulated among international societies within the field of SCI medicine from August to November 2018.

Results One hundred and twenty-three physicians responded to the survey. Of these, 107 (92%) managed pain for persons with SCD. Most (82%) felt that opioid prescription was appropriate for uncontrolled acute pain, but fewer (67%) felt it was appropriate for chronic pain. Of those who felt opioids had a role in the treatment of neuropathic pain, 46% did not think there should be a specific upper limit of opioid dose. The majority (85%) would continue prescribing high doses (250 morphine milligram equivalent (MME) doses/day) if that dose were effective. Tramadol was the most common opioid prescribed first line.

Conclusion Most physicians who responded to this survey prescribe opioids for intractable pain after SCD. A significant proportion of respondents believed that there should not be a specific upper limit of opioid dose prescribed if the drug is tolerated; this does not align with current recommendations. Most physicians do not feel influenced in their prescribing habits by regulatory bodies. If physicians decide to taper an opioid that is being tolerated well, it is most commonly related to a fear of the patient developing an opioid-use disorder. The authors propose an algorithm that may help align practice patterns with current recommended practice guidelines.

Introduction

Four out of every five people with spinal cord damage (SCD) report pain is an ongoing problem [1]. In more than half of individuals with ongoing pain, the pain interferes with activities of daily living and work [1]. This high prevalence of disabling pain is present in persons who receive care at SCD centers throughout the world [2, 3] and illustrates that the treatments available, both pharmacological and non-pharmacological, are not all that effective. As such, clinicians sometimes resort to the use of opioids for the treatment of pain after SCD as is done for other types of intractable pain. However, similar to that in other causes of non-cancer chronic pain, the evidence for opioid effectiveness in the treatment of pain after SCD is sparse [4, 5]. Nevertheless, over one quarter of persons with SCD who have been treated in spinal cord injury (SCI) specialty

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centers take opioids on an ongoing basis to treat chronic pain [6].

The United States in 2019 remains in the midst of an opioid overdose epidemic, which has been exacerbated by the prescription of opioids for pain over the past two decades. In the United States, the rate of drug overdose deaths tripled between 1999 and 2014 [7]. Drug overdose is now the leading cause of unintentional death in the United States, with unintentional death being the third leading cause of death overall after cancer and heart disease [8]. There are also signs of emerging opioid epidemics in other countries such as Canada and Australia [9]. In 2015, Canada had the highest rate of per capita of opioid consumption in the world, at more than 800 morphine milligram equivalent (MME) per capita, with the United States just behind at nearly 700 MME per capita, Germany at over 600 MME per capita, and Australia having a rate less than 300 MME per capita [10].

Because of the increased awareness of the problem of opioid overdose in the context of limited clinical effectiveness for chronic pain, many countries have developed prescribing guidelines for opioids. Representative guidelines include those developed in the United States by the Centers for Disease Control and Prevention (CDC) [11], in Canada by the National Pain Centre [12], in Germany by the German Pain Society [13], in Great Britain by the Faculty of Pain Medicine of the Royal College of Anaesthetists [14], in Australia by the Royal Australian College of General Practitioners [15], and in South Africa by a group of physicians whose guideline was endorsed by multiple professional societies [16]. It is notable in all guidelines that there are recommendations for restricting the maximum prescribed daily dose of opioids prescribed. The recommended upper limit is 90 of MME per day in the Canadian guideline from 2017, with a recommendation to taper the dose for those on higher doses [12], 90 MME in both the South African guideline from 2014 [16], and the US CDC guideline from 2016 with a recommendation not to exceed 50 MME per day without careful justification [11]. The recommended upper limit is 100 MME per day in the Australian guideline from 2017 [15], 120 MME per day in the German guideline from 2014 [13], and 120 MME per day in the British guideline from 2017 [14].

Persons with SCD are prescribed opioids for longer durations and at higher MME doses than persons without SCD who are also prescribed opioids [17]. Persons with SCD are also at increased risk for overdose death as compared with their matched controls due to conditions related to their SCD. These conditions include respiratory insufficiency related to the SCD, sleep disordered breathing, and polypharmacy from other respiratory depressant medications [18].

Given the risks associated with the prescription of opioids to persons with SCD and the lack of convincing evidence for their effectiveness, a survey of physicians working with these patients was planned to look at their prescription of opioids. The aim of this survey was to characterize how physicians throughout the world working with patients who have SCD approach the prescribing of opioids for pain, and to compare the results to representative clinical practice guideline recommendations.

Methods

The survey was developed by Thomas Bryce with input from Marcalee Alexander and Peter New. The survey was posted online and circulated among international societies within the field of SCI medicine including the American Spinal Injury Association, the International Spinal Cord Society, and the Australian and New Zealand Spinal Cord Society. The survey was available online on REDcap from August 2018 to November 2018.

Results

A total of 128 clinicians responded to the survey, of whom 123 were physicians. Not every physician answered every survey question. The data for the five non-physicians were excluded. The majority of physicians worked more than 20 h per week in clinical practice, with only 15% working 20 h or less. Of the physicians, 92% were involved with pain management of persons with SCD as part of clinical practice duties. The physicians who managed pain were mostly from Europe (50%), 19% were from Asia, 17% from Oceania, 12% from North America, and 1% were from Africa. The vast majority of physicians who completed the survey, who managed pain, indicated a primary specialty of Physical Medicine and Rehabilitation (82%), with the remainder indicating a primary specialty of orthopedic surgery (4%), urology (3%), internal medicine (2%), neurosurgery (1%), or other (3%).

When respondents were asked about what non-opioid medications they felt would be appropriate to prescribe for the treatment of SCD-related neuropathic pain, most felt that medications of the gabapentinoid class (77%) and tricyclic antidepressants (74%) were appropriate. Fewer but still more than half of respondents felt that selective serotonin and norepinephrine inhibitors (55%) were appropriate, with other drug classes thought to be appropriate by a third or less of respondents (Fig. 1).

When respondents were asked about the treatment of any type of acute pain, defined as pain present for less than

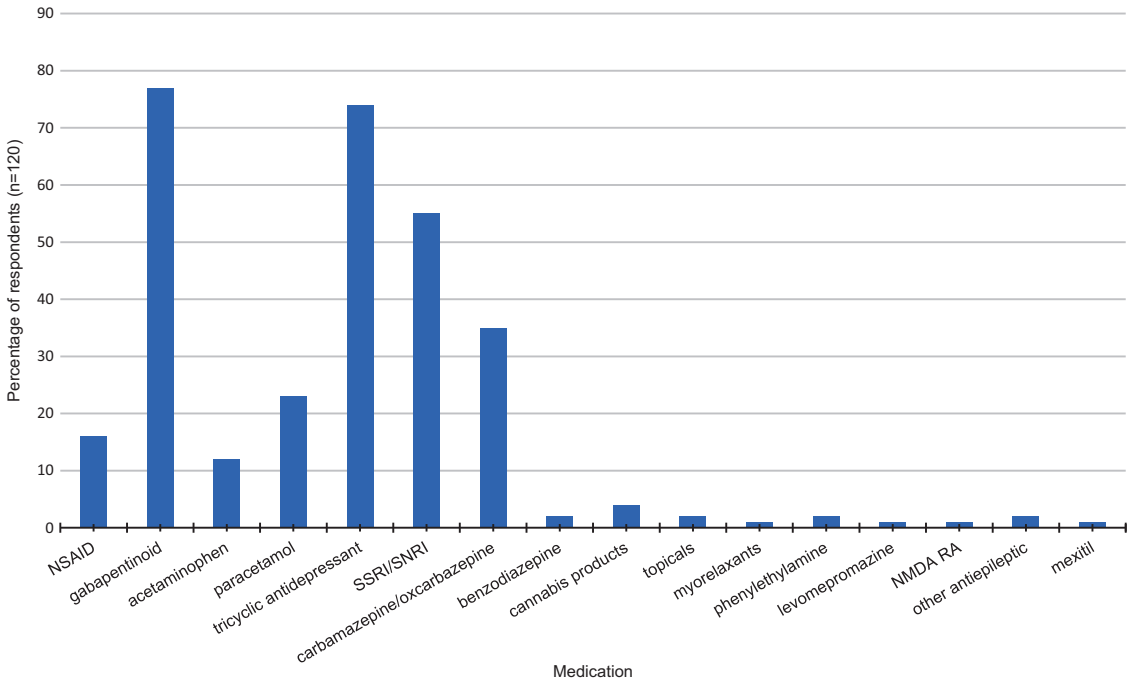

Fig. 1 Non-opioid medications felt by respondents to be appropriate to treat SCD-related neuropathic pain. Abbreviations: NMDA RA: *N*-methyl-D-aspartate receptor antagonist; NSAID: nonsteroidal anti-inflammatory drug; SNRI: serotonin and norepinephrine reuptake inhibitor; SSRI: selective serotonin reuptake inhibitor

3 months, 88 physicians (82%) felt that opioids were appropriate to be considered for prescription if non-opioid interventions did not provide adequate relief. When they were asked whether there was a maximum length of time they would prescribe an opioid for non-cancer-related acute pain, over half of respondents (53%) believed that opioids should not be prescribed for more than 2 weeks, whereas over three quarters (79%) believed that opioids should not be prescribed for more than 1 month. Notably, 10% of respondents indicated that opioids should be used as long as required (without specific time limit) to control the pain (Fig. 2).

When asked specifically about the treatment of any type of chronic non-cancer pain with opioids, about two-thirds of physicians (67%) felt opioids were indicated at any time. Of those physicians who felt that there were indications for the prescription of opioids for chronic non-cancer pain, the majority (83%) felt opioids could be indicated for the treatment of neuropathic pain due to SCD. For these physicians, when given the choice of different potentially available opioids they might prescribe, the opioid chosen first line was tramadol, with nearly two-thirds of responses (65%), with other drugs selected as first line much less often: oxycodone (13%), fentanyl (7%), hydrocodone (3%), buprenorphine (3%), morphine (3%), tapentadol (3%), codeine (1%), and methadone (1%).

When physicians who felt that opioids were sometimes appropriate in the treatment of chronic non-cancer

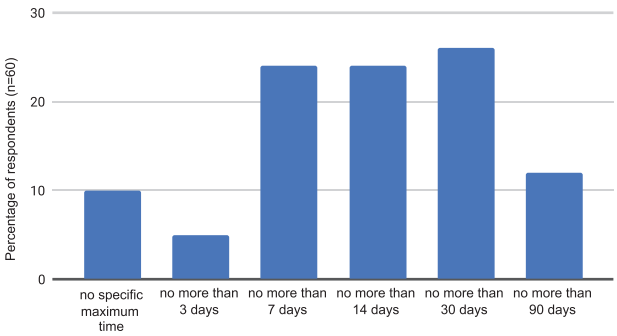

Fig. 2 Maximum time respondents believed opioids should be prescribed for non-cancer-related pain

neuropathic pain related to SCD were asked whether there was a maximum MME dosage that should be routinely prescribed for intractable pain, nearly half (46%) felt that there should be no specific limit on dose, indicating that it depends on an individual's opioid tolerance. Of those who felt that there should be a limit on how much opioid should be prescribed for use in a day, one quarter of physicians (25%) thought the maximum should be no more than 50 MME, whereas another 22% thought the maximum should be no more than 90 MME.

Respondents were presented with a hypothetical scenario in which they were treating a person with chronic SCD with neuropathic pain (not related to cancer and with no treatable cause), which was controlled on a stable dose of 250 MME

per day of an opioid. All previous attempts at dose reduction had been unsuccessful, because the pain became uncontrolled when the dose was decreased. All available treatments recommended in a recent clinical practice guideline had been tried and there were no signs of an opioid-use disorder, diversion of drug, or problematic adverse effects such as constipation or sedation. The respondents were asked whether they would continue the same effective dose of opioid. The overwhelming majority (85%) of the 60 physicians who responded said yes. Of the 9 respondents (15%) who noted they would do something different, one-third (33%) would taper off the opioid completely, just over one-fifth (22%) would taper to a maximum dose of 90 MME per day and continue to prescribe it, the same proportion (22%) would taper to a maximum dose of 50 MME per day and continue to prescribe it, 11% would refer the person to an addiction specialist, whereas the same proportion (11%) would do something different—specifically, try a gabapentinoid. The same nine respondents (15%) who indicated that they would do something different, when asked how much influence different factors had on the decision to not continue prescribing the same opioid dose, most (66%) reported that what had the maximal influence on their decision was the fear the patient would develop an opioid-use disorder. However, one-third (33%) reported that level and quality of scientific evidence regarding strong opioids being effective or ineffective for the treatment of SCD-related neuropathic pain had the maximal influence on them. The majority felt minimal to no influence of the potential perception by regulatory bodies that one could be identified as an opioid over-prescriber (89%). Also, the majority were not troubled by the regulatory burden in prescribing opioids (89%) or by the time needed to monitor for diversion or signs of an opioid-use disorder (100%).

Respondents were subsequently presented with a second scenario in which they were treating a person with chronic SCD-related neuropathic pain (not related to cancer and with no treatable cause), which was controlled on a stable dose of 20 MME per day of an opioid and for whom all the other related conditions were the same as in the previous scenario. They were asked whether they would continue the same effective dose of opioid. The overwhelming majority (97%) of the 60 eligible respondents said yes. Of the two respondents (3%) who noted they would not continue the same dose, both responded that they would taper off the opioid completely.

Finally, when asked if cannabinoids were legally available for prescription, would the physician considering prescribing these for uncontrolled SCD-related neuropathic pain not related to cancer, the majority responded affirmatively (78% of 107 responses).

Discussion

The practice patterns related to the prescription of opioids for chronic pain in persons with SCD in this international sample of clinicians differs in several key areas from those recommended in clinical practice guidelines published in the United States [11], Canada [12], Australia [15], Great Britain [14], South Africa [16], and Germany [13]. One of these areas relates to the maximum dose of opioids that should be prescribed per day. All the guidelines state, in essence, that clinicians should use caution when prescribing opioids at any dosage and should carefully reassess evidence of individual benefits and risks when increasing dosage above a certain daily threshold. The US guideline identifies this threshold to be 50 MME per day citing evidence that holding doses below this level would "likely reduce risk among a large proportion of patients who would experience fatal overdose at higher prescribed dosages," while further noting "in general, that increasing dosages above 50 or more MME day increases overdose risk without necessarily adding benefits for pain control or function" [11]. It further recommends that when prescribing dosages above the threshold of 50 MME per day, additional precautions should be implemented, such as increasing the frequency of follow-up, and that prescribers should avoid increasing dosages to more than 90 MME per day citing incremental benefits for pain and function relative to harms as dosages approach the 90 MME per day limit [11]. The dose limit recommendation in the Canadian and South African guidelines similarly is 90 MME per day and slightly higher, at 100 MME per day, in the Australian guideline and 120 MME per day in both the German and British guidelines.

In contrast to all these guidelines, nearly half (46%) the clinicians who prescribe opioids, who completed the survey, felt that there should be no specific limit on dose, indicating that it depends on opioid tolerance how high a dose one may prescribe. This difference between clinical practice and guideline recommendations may indicate there is a lack of awareness on the part of physicians of the reasons made in the guidelines to justify limiting the maximal recommended daily dose, namely a lack of evidence for improved effectiveness with higher doses as well as emerging evidence for the much higher risk of developing an opioid overdose with higher doses.

It is very important to note that many persons with SCD are also at a greatly increased risk of overdose, for a range of reasons. Those who have a cervical or thoracic level of damage and a complete grade can have a reduction of their pulmonary reserve, and there is a high prevalence of polypharmacy, often with agents that are neurologically sedative. There is clearly a need to educate prescribers

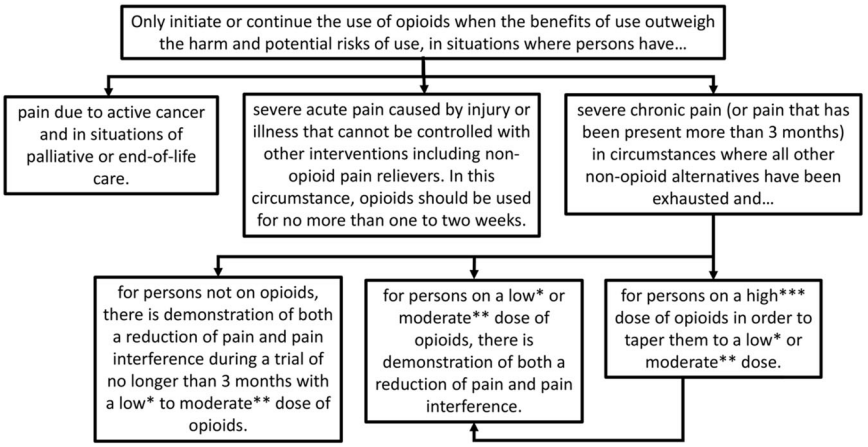

Fig. 3 Algorithm for the treatment of pain after SCI with opioids [20]. *Low dose = 20 MME per day or less. **Moderate dose = >20 MME but ≤60 MME per day. ***High dose = >60 MME per day; MME = morphine milligram equivalent

about the risks associated with higher doses of opioids, especially in the population with SCD. Most clinicians (85%) who completed the survey were willing to continue opioids indefinitely if the pain was controlled at very high doses (250 MME per day) as long as there were no signs of an opioid-use disorder, diversion of drug, or problematic adverse effects such as constipation or sedation. This practice is not consistent, e.g., with the Canadian guideline, which recommended that patients who are currently using 90 MME per day or more be tapered to the lowest effective dose, potentially including discontinuation, rather than making no change in opioid therapy [12].

Another area that perhaps was not addressed adequately in the survey, but which was emphasized in the US guideline, is the necessity that: "before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety."

One fact that needs to be acknowledged when treating pain after SCD is that many persons with SCD have limited function due to the SCD itself, and to require that there be changes in function as a condition of opioid use may be ineffectual. Instead, other types of pain interference, such as with sleep or mood, may need to be substituted. This additional outcome of effectiveness, namely a reduction in pain interference, should be included in the decision to initiate or continue opioid prescription, rather than depending solely on reports of decreases in pain intensity. These interference items are recommended as part of the International SCI Basic Pain Data Set [19].

A third area of difference in the practice patterns of the clinicians completing the survey with the recommended US guideline relates to how long opioids should be prescribed for acute pain. The US guideline recommend that when opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. "Three days or less will often be sufficient; more than 7 days will rarely be needed" [11]. The reason the United States recommended short durations of use is because long-term opioid use usually begins with the treatment of acute pain.

In order to start to address these differences between the clinical practice of physicians who treat pain after SCD and widely available clinical practice guidelines, the authors propose an algorithm that can be used as a general guide for the prescription of opioids after SCD (Fig. 3). The algorithm, which was conceived before this survey was conducted, is based on the key principles outlined in the US guideline [11], identified primarily to reduce the risk of unintentional death due to prescription opioid overdose. Decision points within the algorithm incorporate proximate consensus guideline-recommended opioid prescription threshold doses, which are loosely correlated to the risk of opioid overdose and the development of an opioid-use disorder. In order to incorporate the increased risks of the use of opioids in special populations, such as those with SCD and pain, who may be at even higher risk of unintentional death due to prescription opioid overdose because of underlying respiratory compromise, sleep disordered breathing, and the concomitant use of other prescribed and non-prescribed sedating medications (such as are used for spasticity management), these threshold doses were weighted to the more conservative US guideline threshold doses as opposed to other older guidelines with which higher threshold doses are incorporated. The specific MME threshold dose of 60 MME (rather than 50 MME for instance) was chosen for a purely practical reason, as commercially available doses of opioids from around the world often add up to this number. Use of this number

therefore simplifies the decision-making regarding MME dosing. Finally, the algorithm takes into consideration the consensus guideline belief that pain intensity should not be the only pain outcome evaluated in the decision to continue opioid prescription. Specifically, as related to persons with SCD, the algorithm was designed to be applicable to those who have significant disability as well as pain, acknowledging that these individuals who may have limited function due to their disability may not be able to improve their function if their pain improves due to the continuance of their underlying disability, and that other measures of pain interference rather than function should be considered in these situations. This algorithm, which has yet to be validated in any population and may require further revision, may help guide practitioners in managing acute and chronic pain in patients with SCD, while reducing the risk of adverse consequences of opioid use.

Limitations of this study include the relatively small sample size and the over/under-representation of different regions of the world. It is also acknowledged that each of the different guidelines to which the results of this survey were compared were developed using different methods and were based upon different study questions. However, importantly, the guidelines all included similar common questions regarding the maximal does of opioids. This study is the first to survey clinicians regarding the prescription of opioids to people with pain following SCD.

Although this survey represents an international cross-section of treating physicians and there clearly is an international opiate focus at the present time, the fact remains that for the physicians and their patients with SCD, pain remains a significant problem. This article delves into the viewpoints of treating physicians from around the world that are working with these patients and reveals that many are willing to continue to prescribe what has been working for them despite the guidelines, or in ignorance of them. Further research with regard to the physicians' willingness to follow the algorithm is indicated, as it is would be helpful to gain more insight into the perspective of the treating physicians and not just their adherence to various clinical practice guidelines.

Conclusion

The practice patterns related to the prescription of opioids for chronic pain for persons with SCD for this international sample of clinicians differ in several key areas from those recommended in widely disseminated clinical practice guidelines. Use of an algorithm adapted for use by persons with SCD has the potential for aligning practice patterns with recommended clinical practice guidelines, although this needs further review and study.

Data archiving

Survey data are available from the corresponding author upon reasonable request.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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