Response to Letter to the Editor by Soffin et al.

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Response to Letter to the Editor by Soffin et al.

To the editor of IJSS,

Dr Soffin and colleagues raised several points regarding the use of a multimodal analgesia (MMA) protocol for patients undergoing lumbar fusion in an ambulatory surgical center (ASC). Their insight into the use of a number of agents in our protocol is appreciated and will only help clarify and support the use of MMA or enhanced recovery after surgery protocols in the spine surgery community.

To Dr Soffin et al's point regarding the decision to use oxycodone controlled release for pre-emptive analgesia, we appreciate the concern of its off-label use. One of the primary goals of our MMA protocol was to minimize the use of intravenous postoperative opioids commonly administered via a patient-controlled analgesia (PCA) machine. This shift away from PCA in the ambulatory setting would allow for a significant reduction in the risk of pruritus, sedation, and postoperative nausea and vomiting, which are among the most common complications for ASC patients,[1,2] as well as the risk for significant cognitive impairment and/or respiratory depression.[3,4] In keeping with this goal, the use of oxycodone controlled release preoperatively was aimed at taking full advantage of peak preemptive analgesic effects. It may be suggested that this form of oxycodone use may place patients at higher risk for postoperative respiratory depression; however, administration at the preoperative, rather than postoperative, timepoint and application of appropriate patient selection criteria can mitigate the negative effects by maximizing overlap between the peak window of opioid effects and the period of direct clinical care. Indeed, its preoperative use is defined as "off-label", but careful dosage selection of $\leq$10 mg was made to avoid the risk of respiratory depression, which is largely in line with the recommendations by the Food and Drug Administration (FDA) (section 2.2) for approved use in opioid intolerant/naive patients.[5] Furthermore, the vast majority of medications prescribed by physicians are "off label".[6–9]

Another point that Dr Soffin and colleagues raise is the risk brought on by the use of gabapentinoids in our MMA protocol as well as its use in conjunction with oxycodone. Concern for increased risk for overdose death and respiratory failure after discharge from an ASC is not without merit, as the authors highlighted past FDA warnings and recent randomized controlled studies that may call into question its efficacy. Most important is the recent systematic review of 281 clinical trials that reported no clinical benefit to the perioperative use of gabapentinoids.[10] However, authors of the systematic review reported a high risk of bias (46%). Additionally, these same authors also reported that the similar levels of postoperative acute pain and opioid administration in both gabapentinoid and nongabapentinoid groups were based on low- to very low-quality evidence. Furthermore, even a robust review, such as this study, highlighted that the risk of respiratory depression following the use of gabapentinoids with opioids was not significantly different. Our own review of published spine literature pertaining to the use of gabapentinoids in MMA protocols has also largely suggested that its implementation can decrease overall opioid consumption while providing safe analgesia for patients.[3,11–20] It then stands to reason that our goal of implementing pregabalin was to reduce central sensitization and thereby reduce analgesic requirements. Thus far, our experience with the concomitant use of muscle relaxants (cyclobenzaprine), long-acting opioids (oxycodone controlled release), and gabapentinoids (pregabalin) among ASC spine patients continues to be positive, with few if any readmissions for severe respiratory depression following discharge from an ASC. To further curb the risk of adverse events, the protocol implements a dosage of postoperative gabapentin (75 mg) that is also in alignment with FDA recommendations (section 2.6) when used with opioids.[5] Dr Soffin and colleagues do raise a valid point regarding the role of gabapentinoids in MMA protocols in the long term and are commended for their own randomized controlled trial detailing the successful use of an enhanced recovery pathway for lumbar fusion patients. However, what is unclear is the claim that these authors have eliminated the regular use of gabapentinoids, while citing a study in which gabapentin is used in their protocol.[21] We agree that this represents an important topic for exploration, but more empirical evidence is required to draw any

meaningful conclusions and permanent adjustments to our protocol. However, the authors of this paper have carried out randomized controlled trials with 240 orthopedic surgery patients that have demonstrated efficacy with gabapentinoids.[22]

Lastly, coprescribing multiple opioid analgesics in the postoperative period has incited questioning behind its use by Dr Soffin et al. We agree that any reliance on opioid medications for pain control is not ideal, especially given associated potential for adverse events as well as the recommendations of several major pain societies to minimize their use. However, while significant advances have been made in perioperative analgesia, opioid medications remain an important aspect of effective pain control for patients undergoing major surgery. The focus of multimodal postoperative analgesia has been to significantly reduce the use of intravenous analgesics while maintaining adequate analgesia. As such, use of tramadol, which is a known weak μ-opioid receptor agonist, was implemented to minimize the use of more potent opioids (oxycodone). While our protocol does incorporate the use of some narcotic medications, their use, as described in the study of discussion,[23] is at half dosage, as recommended by the FDA,[5] and is primarily for breakthrough pain in the postoperative recovery room as well as for patients discharged on postoperative day 0. Furthermore, there is sufficient evidence that controlling acute pain after surgery can reduce chronic pain.[22] Also, it is important to note that current alternative protocols detailed in the literature may actually involve greater or less tightly controlled reliance on opioid-based analgesia. For example, the MMA protocol published by Soffin et al includes no preoperative opioid medications but involves the use of PCA with intravenous hydromorphone in addition to tramadol for postoperative pain control.[21] In fact, Soffin et al report a median postoperative opioid consumption of 62 and 57.5 oral morphine equivalents on the day of surgery,[8,21] which is nearly twice the mean value observed for patients in our cohort.

While Dr. Soffin et al raise valid concerns about the use of multiple opioid analgesics postoperatively, this aspect of our protocol has significant benefit to patients. Specifically, the use of multiple different analgesic medications allows for synergistic pain control while minimizing the dosage and associated side effects of any one medication.[4] Our practice strives to standardize our lumbar fusion "pathway" to the greatest extent possible, which has been instrumental to our success with ambulatory lumbar fusion procedures. The use of a standardized MMA protocol rather than more variable PCA for postoperative pain control allows for greater predictability and uniformity, reducing the potential for errors or complications in the postoperative period.

In summary, Dr. Soffin et al raise concerns regarding the use of individual components of our MMA protocol. However, it is our belief that, when considered in its entirety, our protocol continues to provide safe yet effective analgesia for appropriately selected patients.

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