




Intravenous Lidocaine for Acute Pain: A Single-Institution Retrospective Study

Kyle De Oliveira¹ · Naveen Eipe¹ 

Published online: 9 July 2020
© The Author(s) 2020

Abstract

Background In the perioperative period, intravenous lidocaine has been used as an opioid-sparing systemic analgesic with additional anti-inflammatory and anti-hyperalgesic properties.

Objective The aim of this retrospective study was to review the utilization, efficacy, and safety of intravenous lidocaine on our Acute Pain Service (APS) and identify surgical and patient populations where this intervention was found to be useful.

Patients and Methods This retrospective study was designed to assess acute pain management in patients who received an intravenous lidocaine infusion between February 2013 and December 2017. Data collected included demographics, surgery type, infusion duration, pain scores, analgesic consumption, and adverse effects. Pain scores included rest and active pain scores and were analyzed by surgical model and subgroups. Clinically important differences (CIDs) in pain were determined by changes in pain score difference of ≥ 2 (11-point scale) or $\geq 30\%$ reduction in pain intensity. A patient was considered to have a true CID if a CID was observed with rest and/or active pain scores at both first to second (4–24 h) and first to final time point (4 h to infusion end) comparisons.

Results In total, 544 patients received intravenous lidocaine during this period, and 394 were included in the final analysis. The average (\pm standard deviation) duration of infusion was 68.60 ± 49.52 h. Surgical specialties included gastrointestinal surgery (41%), orthopedics (28%), neurosurgery (15%), vascular surgery (10%), and others (6%). Overall, 56.1% of the study population experienced a CID, with reduced pain scores at rest and/or with activity. CIDs were also observed in patients with chronic pain (53.5%) and when intravenous lidocaine was used as a rescue technique (69.6%). Within the rescue cohort, opioid-dependent and opioid-naïve patients experienced 23.0% and 45.6% reductions, respectively, in their 8-h intravenous opioid consumption. In total, 37 patients in the study experienced transient signs of mild local anesthetic toxicity, which resolved with infusion titration (conservative) management. One serious adverse event required intervention, and the patient was successfully resuscitated.

Conclusions This retrospective study at a single institution with an APS policy for intravenous lidocaine in the postoperative period identifies benefits of intravenous lidocaine in certain surgical and patient populations. The findings need to be confirmed with further research.

Presented by Dr. Kyle De Oliveira as a poster at the Euroanaesthesia meeting, June 2019, Vienna.

✉ Naveen Eipe
neipe@toh.ca

¹ Department of Anesthesiology and Pain Medicine, The Ottawa Hospital, University of Ottawa, 1053 Carling Avenue, B309, Ottawa, ON K1Y 4E9, Canada

Key Points

Intravenous lidocaine reduces pain and analgesic requirements for patients undergoing gastrointestinal, spine, trauma, and vascular surgery.

Intravenous lidocaine is also an effective rescue analgesic intervention in the acute postoperative period.

Greater reductions in postoperative intravenous opioid use were observed in opioid-naïve than in opioid-dependent patients.

1 Introduction

Despite advances in multimodal analgesia and the implementation of standardized protocols, the management of postoperative pain continues to be challenging in some patients undergoing certain surgical procedures [1]. Inadequately treated pain increases morbidity, impacts patient satisfaction, and delays discharge. Additionally, poorly controlled pain has the potential to lead to both persistent pain and chronic opioid use after surgery [1–3]. All these are probably more frequently seen with traditional opioid-centric pain management strategies.

Within the perioperative period, intravenous lidocaine was introduced as an opioid-sparing systemic analgesic with additional anti-inflammatory and anti-hyperalgesic properties [4]. A recent systematic review of 68 randomized controlled trials included a wide variety of surgical models, with the investigators concluding that the acute pain benefits of perioperative intravenous lidocaine remained uncertain [5]. Previous level I evidence confirmed that intravenous lidocaine reduced pain scores and both the consumption of opioid analgesics and their side effects in the postoperative period [6–8]. These benefits have been best described in gastrointestinal surgery, both open and laparoscopic procedures, where intravenous lidocaine promotes early oral intake, improves mobilization, reduces time to bowel recovery, and facilitates early discharge [9–11]. These are some of the important goals of enhanced recovery after surgery (ERAS) protocols [6, 7, 12–14].

In 2009, the acute pain service (APS) of this tertiary-level university hospital implemented a policy that allowed for use of intravenous lidocaine within its well-established postoperative multimodal analgesia protocols. That protocol, the indications, procedures, and monitoring for intravenous lidocaine has been described in detail elsewhere [15]. Since the implementation of that policy, the use of intravenous

lidocaine has extended beyond gastrointestinal surgery and been incorporated into other APS protocols and patient care pathways. Intravenous lidocaine has been used in patients who have undergone elective and emergency surgeries, including neurosurgery, spine, orthopedics, trauma, vascular, and other procedures. Intravenous lidocaine has also been used as a rescue analgesic for the treatment of acute pain crises in the early postoperative period, especially in patients with a history of chronic pain, opioid tolerance, and substance abuse [15].

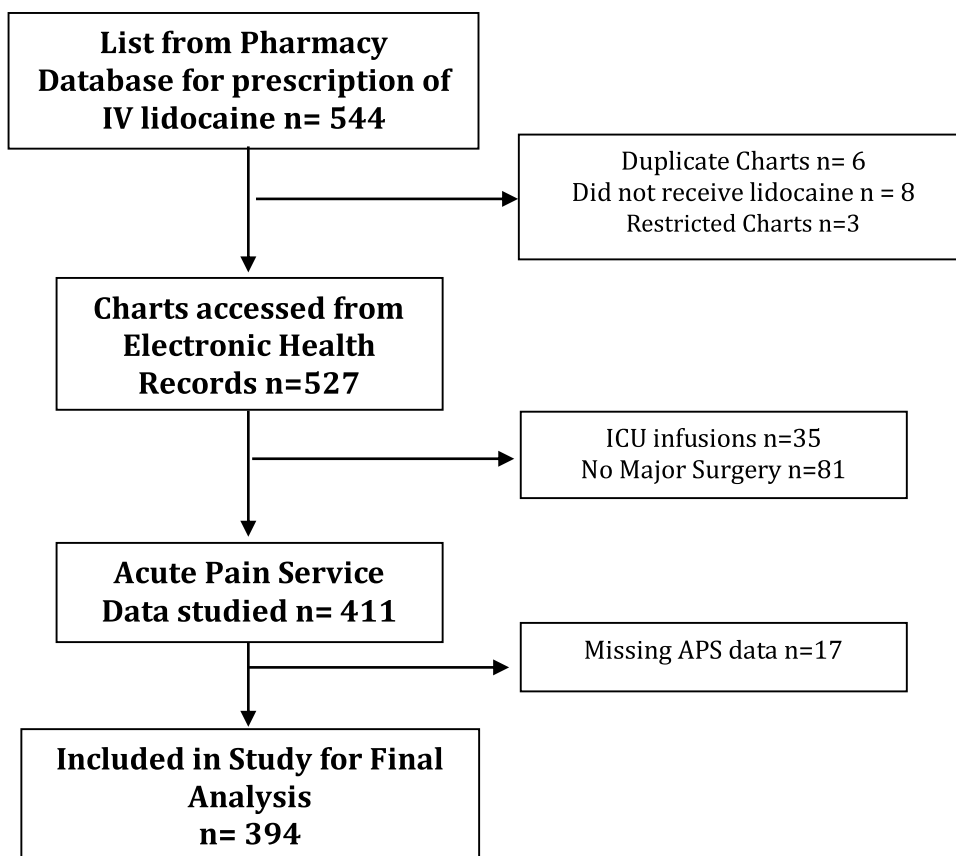
Given the paucity of the literature and the inconsistency of reported benefits for the use of intravenous lidocaine in general surgical populations, this review of a single institution's experience of intravenous lidocaine for acute pain was proposed. The aims of this retrospective study were to review the utilization, efficacy, and safety of intravenous lidocaine for postoperative pain and identify surgical models and patient subgroups where this intervention was found useful in order to guide further investigation and research.

2 Methods

This single-center retrospective quality assurance study was approved (OHREB#: 20180265-01H) and conducted at The Ottawa Hospital. We intended to identify all inpatients who received an intravenous lidocaine infusion for acute pain over a 10-year period January 2008 to December 2017. These patients were identified using the pharmacy electronic medication records for intravenous lidocaine administration during the defined time period. Individual patient medical record numbers associated with each lidocaine order were then given a unique study identification number. Patient information and all study data were stored on an approved and appropriately encrypted file on a password-protected virtual hard drive within the hospital system.

In February 2013, the APS implemented a specialized online acute pain management software program (Cissec© ACUPAM). From here onwards, more detailed information was available, including pain scores, analgesic consumption, and adverse effects related to the intravenous lidocaine infusions. Prior to February 2013, all APS data were recorded on paper charts that were scanned and uploaded to the electronic health record system. Because of this transition from paper chart to electronic records, data prior to 2013 were not included in the final study outcome analysis even though an intravenous lidocaine protocol was established at this institution in 2009. Figure 1 describes the identification, inclusion, and final numbers included in the analysis.

Fig. 1 STROBE flow chart for study participants. *APS* acute pain service, *ICU* intensive care unit, *IV* intravenous



2.1 Study Exclusions

From the pharmacy list of patients for whom intravenous lidocaine was dispensed, electronic health records were accessed for details of their acute pain management. Patients were excluded if they had received a lidocaine infusion while in the intensive care unit, if no major surgery was performed, and if no pain scores or concomitant analgesic usage was recorded. Data collected included demographics, surgery type, infusion duration, pain scores, analgesic consumption, and adverse effects.

2.2 Primary Outcomes

The primary outcomes were postoperative pain scores at rest and with activity following the initiation of intravenous lidocaine infusion, typically at 1 mg/kg/h (range 0.5–2) for postoperative analgesia. Pain scores at 4 h, 24 h, and infusion end were analyzed based on surgical model and subgroups. Clinically important differences (CIDs) in pain were determined by a raw pain score difference of ≥ 2 on a numeric rating scale of 0–10 or by a $\geq 30\%$ change in pain intensity [16, 17]. Absolute pain scores were calculated for each individual patient between rest pain and active pain scores from first to second time points and from first to final time points.

A patient was considered to have a true CID if a CID was observed with rest and/or active pain scores at both first to second (4–24 h) and first to final time point (4 h to infusion end) comparisons. A patient who received a lidocaine infusion for <24 h was considered to have a true CID if a CID was observed with rest and/or active pain scores between first time point (4 h) and infusion end.

CIDs in pain were aggregated for each surgery type, surgical subgroup, and patient population (e.g., chronic pain). Patients who received intravenous lidocaine as a rescue regimen were identified and analyzed separately.

2.3 Postoperative Analgesic Consumption Analysis

Analgesic (i.e., intravenous opioid) consumption was calculated solely from our rescue cohort to allow us to determine average opioid consumption before and after the introduction of lidocaine infusion commencement. Only patients who were concomitantly prescribed an intravenous hydromorphone or hydromorphone-ketamine patient-controlled analgesia (PCA) prior to rescue lidocaine infusion commencement were analyzed in this regard.

Total intravenous opioid consumption was calculated by obtaining the amount of intravenous opioid consumed during the 8-h period immediately preceding lidocaine intervention

and during the 8-h period immediately following the same intervention for each individual patient. Intravenous opioid consumption was recorded at 8 h before and after lidocaine intervention, as these were the most consistently reported time points at which intravenous opioid consumption was recorded on our APS. Patients were excluded if intravenous opioid consumption was not recorded at both 8 h before and after lidocaine intervention.

The total amount of intravenous opioid consumed post-lidocaine intervention over an 8-h period was divided by the total amount of intravenous opioid consumed pre-lidocaine intervention to obtain the relevant percentage change in average opioid consumption for the rescue cohort that met inclusion criteria. Opioid-naïve and opioid-dependent patients were then analyzed separately from the rescue cohort to determine average opioid consumption and percentage change between the two subgroups following rescue lidocaine intervention.

3 Results

Between February 2013 and December 2017, a total of 544 patients on the APS received an intravenous lidocaine infusion. Following exclusions, 394 patients were included in the final study analysis (Fig. 1). The majority of exclusions were (1) patients who had received a lidocaine infusion in the intensive care unit while intubated and/or sedated, (2) patients who did not actually undergo major surgery during their admission to hospital but instead received intravenous lidocaine as treatment for acute pain presentation, and (3) patient records that did not have adequate pain scores or analgesic consumption recorded.

The study population consisted of 194 (49.2%) female and 200 (50.8%) male patients. Average (\pm standard deviation) infusion duration was 68.60 ± 49.52 h (2.86 ± 2.06 days). The main intravenous lidocaine indications included gastrointestinal surgery (41%), orthopedics (28%), neurosurgery (15%), vascular (10%), and others (Table 1).

Overall, 56.1% of the total study population experienced a CID and reduced analgesic consumption postoperatively. Improvements in mean pain scores, both at rest and with activity, were observed in a significant proportion of patients from various surgical specialties (Table 2). Within these surgical specialties, CIDs were observed in certain patients (chronic pain 53.5%), certain situations (lidocaine rescue 69.6%), and specific procedures (Table 3).

3.1 Intravenous Opioid Consumption

A majority (303/394 [77%]) of the study population were also concurrently prescribed an intravenous PCA pump.

Table 1 Study demographics

Characteristics	Total
Patients (<i>n</i>)	394
Age (years)	54.82 \pm 15.54 years (range 18–93)
Sex	Male 200, female 194
Duration of infusion (h)	68.60 \pm 49.52
Surgical types [<i>n</i> (%)]	Gastrointestinal (161 [41%]), orthopedic (110 [28%]), neurological (61 [15%]), vascular (39 [10%]), others (21 [6%])
Use of patient-controlled analgesia (<i>n</i> = 303)	Fentanyl (<i>n</i> = 9), hydromorphone (<i>n</i> = 111), hydromorphone + ketamine (<i>n</i> = 180), meperidine (<i>n</i> = 1), morphine (<i>n</i> = 2)

Table 1 summarizes the different types of PCA pumps prescribed.

Of the 291 records for patients who received either a hydromorphone or a hydromorphone-ketamine PCA, 73 had missing data and were excluded from the intravenous opioid consumption analysis. In total, 82 of the remaining 218 patients received intravenous lidocaine as a rescue regimen; 44% (*n* = 36) of these were on preexisting opioids before their surgery. Average intravenous opioid consumption was calculated over 8-h periods before and after rescue lidocaine infusion start (Table 4). Opioid-naïve patients experienced a 45.6% reduction (~ 2.5 mg/8 h, $p < 0.001$) and opioid-dependent patients experienced a 23.0% reduction (~ 2.23 mg/8 h, $p = 0.01$) in intravenous opioid consumption, respectively.

3.2 Adverse Effects

In total, 37 patients experienced transient signs of possible mild toxicity (Table 5). These adverse effects included agitation, blurred vision, dizziness, metallic taste, nausea, perioral numbness, rash, somnolence, tachycardia, tinnitus, tremor, and visual disturbances.

All adverse effects were associated with mild toxicity, which resolved with conservative management involving reduction of lidocaine infusion dosing (typically infusion rate decrease by 0.25–0.5 mg/kg/h) followed by reassessment and further decrease if necessary or discontinuing intravenous lidocaine infusion altogether. One serious adverse event occurred on the surgical floor: a cardiac arrest was caused by inadvertent rapid lidocaine bolus. On the patient's arrival from the recovery room, the lidocaine infusion was disconnected from the pump transiently to facilitate transfer of the patient from the stretcher to the hospital bed. This allowed the lidocaine to run freely through the intravenous line, and the patient inadvertently received approximately 2000 mg of intravenous lidocaine over 20 min. The

Table 2 Clinically important differences in pain scores and proportion of patients experiencing benefit by surgery type

Surgery type	Rest 4 h	Active 4 h	Rest end	Active end	CID ^a	Total ^b	CID ^c
Gastrointestinal	4.47 ± 2.68	6.26 ± 2.70	2.64 ± 2.21	4.29 ± 2.44	87	161	54.0
Orthopedic	5.93 ± 2.83	7.28 ± 2.76	3.94 ± 2.60	5.93 ± 2.38	59	110	53.6
Neurosurgery	6.20 ± 2.58	8.13 ± 2.21	3.90 ± 2.22	6.38 ± 2.39	32	61	51.6
Vascular	6.02 ± 3.11	7.12 ± 3.10	2.48 ± 2.65	3.85 ± 2.71	30	39	76.9

Data are presented as mean ± standard deviation unless otherwise indicated

CID clinically important difference

^aNumber of patients who experienced a CID (*n*)

^bTotal number of patients by surgery type (*N*) who experienced a CID in pain scores at rest and/or activity throughout infusion duration

^cPercentage of patients (*n/N*) who experienced a CID in pain scores at rest and/or activity throughout infusion duration

Table 3 Clinically important differences in pain scores by subgroup

Subgroup	CID (<i>n</i>)	Total (<i>N</i>)	CID % (<i>n/N</i>)
Chronic pain	100	187	53.5
Rescue	126	181	69.6
Laparotomies	66	117	56.4
Spine surgery	59	109	54.1
Trauma	27	43	62.8
Amputations	9	15	60.0
AAA	6	10	60.0
TND	5	7	71.4

CIDs as a percentage of total patients by subgroup. Spine surgery cohort includes both neurosurgical and orthopedic spine patients. Amputations refer to lower limb vascular amputation procedures

AAA abdominal aortic aneurysm repair, CID clinically important difference, TND craniotomy for trigeminal nerve decompression

presentation (altered sensorium, decreased consciousness, and hypotension) was quickly detected, and the critical care response team was called upon to attend to this. A diagnosis of local anesthetic systemic toxicity (LAST) was made, and the patient required initiation of intralipid therapy and 2 min of cardiopulmonary resuscitation (without defibrillation) before spontaneous return of circulation was achieved. The patient recovered fully without any sequelae, and their remaining hospital stay was uneventful.

Table 4 Opioid consumption prior to and following lidocaine intervention

Rescue group (<i>n</i>)	Pre-lidocaine (mg)	Post-lidocaine (mg)	Average (%) reduction
Opioid naïve (<i>n</i> = 46)	5.59 ± 4.48	3.04 ± 2.95	45.6 ± 34.2 (<i>p</i> < 0.001)
Opioid dependent (<i>n</i> = 36)	9.71 ± 8.52	7.48 ± 7.08	23.0 ± 16.9 (<i>p</i> = 0.01)
Overall (<i>n</i> = 82)	7.41 ± 6.87	5.03 ± 5.61	32.1 ± 18.3 (<i>p</i> < 0.001)

Opioid consumption in a rescue cohort of patients prescribed intravenous hydromorphone or intravenous hydromorphone-ketamine patient-controlled analgesia pumps in the postoperative period. Intravenous opioid consumption calculated as an average milligram amount over an 8-h period before and after lidocaine infusion intervention. Number (*n*) of patients indicated by patient group

4 Discussion

Acute pain management that is predominantly opioid based is well known to lead to frequent immediate and late adverse effects-sedation, respiratory depression, nausea, vomiting, hyperalgesia, and prolonged hospital stay [18–20]. Continuation of opioids after surgery can result in opioid dependence and tolerance, which are identified as risk factors for the development of chronic postsurgical pain [21]. All these implications, coupled with the increasing rate of opioid abuse and diversion, has catalyzed the shift in postoperative pain management toward non-opioid alternatives. Ongoing research is identifying patients and procedures where certain non-opioid analgesic adjuvants (ketamine, lidocaine, and dexmedetomidine, etc.) are being studied and are showing promising results [15, 22–25].

The introduction of intravenous lidocaine on the APS at this hospital in 2009 was a major advancement that followed, and in some situations replaced, the use of continuous epidural analgesia [15]. Over the past decade, direct assessment and observation has extended the use of intravenous lidocaine from gastrointestinal surgery to other specialties. This retrospective study was designed to study the use of intravenous lidocaine for treating acute postoperative pain in a wide variety of patients, procedures, and clinical settings.

Table 5 List of adverse effects and their associated frequencies

Adverse effect	No. of events
Agitation	4
Blurred vision	1
Cardiac arrest	1
Dizziness	5
Metallic taste	6
Nausea	3
Perioral numbness	3
Rash	1
Somnolence	6
Tachycardia	1
Tinnitus	3
Tremor	3
Visual disturbance	1

4.1 Key Findings

We have reported the postoperative use of intravenous lidocaine for acute pain in a large cohort of patients in a single tertiary-level institution over a 5 year period. Though the final results are limited to the defined time period, we are able to add new information in three aspects of intravenous lidocaine in the postoperative period. First, over the past decade, we have found that—beyond gastrointestinal surgery—lidocaine reduces pain and analgesic requirements in patients undergoing spine, major trauma, and vascular surgery. Amongst these, the previously unreported surgical type in which we found analgesic benefit from intravenous lidocaine was in the vascular cohort. Despite the relatively small number of patients compared with our gastrointestinal and orthopedic/spine cohorts, the reported CID benefit in 76.9% of vascular patients requires further evaluation. The second novel aspect of intravenous lidocaine use described in this study is its role as a rescue analgesic in pain crises, which has not been previously reported. Finally, when compared with opioid-dependent patients, we found a clinically relevant and greater benefit in opioid-naïve patients. Possibly, patients with preexisting opioid use also receive ketamine and gabapentinoids as anti-hyperalgesic therapies, thereby reducing the clinical impact of intravenous lidocaine. All three of these new findings from our study need further research, clinical trials, and expert opinion.

4.2 Overall Safety

The safety of using intravenous lidocaine for postoperative acute pain continues to be of concern, especially with the limited efficacy indicated by the recent Cochrane review [5]. In our previous narrative review, we discussed the first 3 years of the protocol implementation ($n = 102$)

and reported six instances of mild toxicity [15]. The current study reports an increased utilization of intravenous lidocaine and continued safety, with mild toxicity in fewer patients. Future prospective studies in similar surgical and patient populations are required to confirm the efficacy and safety of continuing intravenous lidocaine in the postoperative period.

4.3 Limiting Factors

There are limitations to this retrospective review of the use of intravenous lidocaine on our APS. The change in patient records from hard copy charts to electronic health records in 2013 meant that data for the first 5 years were inaccessible. Beyond 2013, and similar to other retrospective reviews, there was missing data and a lack of standardization of patients, procedures, and pain management protocols. Analgesic consumption, pain scores, and side effects were extracted from patient records. Overall, the self-reporting of pain scores by patients is subjective and can differ greatly between patients, even those undergoing similar procedures [26]. The CID model to assess the clinical efficacy of postoperative intravenous lidocaine in relation to pain scores was utilized to attenuate some of these biases.

Despite these limitations, this study assessed pain scores in patients who received lidocaine infusions postoperatively as either a rescue agent or non-rescue. All study patients while on our APS receive foundational analgesia in the form of oral acetaminophen \pm nonsteroidal anti-inflammatory drugs \pm tramadol \pm gabapentinoids. A majority (73.9%) of all study patients also received a hydromorphone or hydromorphone/ketamine intravenous PCA pump. Therefore, in this type of study, it is difficult to exactly determine the single most effective analgesic intervention that improved pain postoperatively for our patient population, especially when the average intravenous lidocaine infusion duration was approximately 3 days in our study and given that postoperative pain tends to decrease with time. However, we can confidently state that oral foundational analgesia was the standard of care for all patients, so this can therefore be excluded when evaluating the single most effective analgesic intervention.

Further to this, the assessment of our rescue subgroup served as our primary indicator of the effectiveness of intravenous lidocaine infusion in improving pain scores and reducing intravenous opioid consumption in both opioid-naïve and opioid-dependent patients. We were able to assess average intravenous opioid usage per hour before and after lidocaine introduction, which provided us with sufficient basis to conclude that intravenous lidocaine in the postoperative period does indeed reduce opioid consumption. Furthermore, the reduction in intravenous opioid consumption in the rescue group also correlated with a notably high

(69.6%) percentage of rescue patients experiencing a CID in pain scores. As a result, intravenous lidocaine not only reduced intravenous opioid consumption in the postoperative period (potentially avoiding adverse effects from excess opioid consumption) but also translated into reduced pain scores for this subgroup.

Lastly, and arguably the most limiting factor to this study, was the inconsistent level of documentation recorded on our APS electronic database. During the data-acquisition phase of this study, the level of documentation ranged considerably between study patients. A large portion of the study population was excluded because of a lack of clearly recorded outcomes pertinent to our study inclusion criteria and to inadequate patient assessment in individuals receiving intravenous lidocaine in the postoperative period. In excluded patients, pain scores and intravenous opioid consumption were not adequately reported, and the occurrence of adverse effects was not clearly associated with intravenous lidocaine infusion commencement. As a result, this retrospective study analyzed a smaller study cohort than would otherwise have been included.

4.4 Future Direction

These findings have prompted changes to how we will continue to document pain assessments in patients receiving intravenous lidocaine on our APS. As this institution transitions to a completely electronic patient information system, separate mandatory fields in our daily pain assessments will be introduced to (1) determine intravenous opioid consumption postoperatively on an 8-h basis, (2) ascertain specific adverse effects relating to lidocaine infusion commencement from 4-h nursing assessments, and (3) an impact question asking patients whether they felt the introduction of intravenous lidocaine had a positive impact on their level of postoperative analgesia, in order to delineate whether a CID in analgesia has been achieved. The introduction of these mandatory fields would improve patient safety and outcomes at our institution and can also serve to achieve the same at other institutions prescribing intravenous lidocaine for postoperative analgesia. Improved documentation and monitoring with continuous APS assessment would further facilitate the attainment of the above-mentioned outcomes.

5 Conclusion

This retrospective study at a single institution with an APS policy for postoperative intravenous lidocaine infusion use indicates that intravenous lidocaine is an effective and well-tolerated analgesic intervention in certain surgical and patient populations. Additional research is necessary to

explore the surgical subgroups in which our study showed efficacy.

Acknowledgements The authors acknowledge Dr. John Penning for conceptualizing the study and Dr. Reva Ramlogan for revision of the final manuscript.

Author Contributions Drs. KDO and NE both made substantial contributions to all aspects of the work, including, and not limited to, design, data acquisition, data interpretation, data analysis, drafting, and revision of final manuscript.

Compliance with Ethical Standards

Funding This study was funded and supported by the Department of Anesthesiology and Pain Medicine, University of Ottawa, ON, Canada.

Availability of Data and Material All raw data are available upon request.

Conflicts of interest Drs. Kyle De Oliveira and Naveen Eipe have no conflicts of interest that are directly relevant to the content of this article.

Ethics Approval This study was approved (OHREB#: 20180265-01H) by the Ottawa Hospital's Research Ethics Board on April 23, 2018. The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Open Access This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc/4.0/>.

References

1. Gan TJ. Poorly controlled postoperative pain: prevalence, consequences, and prevention. *J Pain Res.* 2017;10:2287–98.
2. Sinatra R. Causes and consequences of inadequate management of acute pain. *Pain Med.* 2010;11:1859–71.
3. Eberhart LH, Morin AM, Wulf H, et al. Patient preferences for immediate postoperative recovery. *Br J Anaesth.* 2002;89:760–1.
4. Dunn LK, Durieux ME. Perioperative use of lidocaine. *Anaesthesiology.* 2017;126:729–37.
5. Weibel S, Jelting Y, Pace NL, et al. Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery in adults. *Cochrane Database Syst Rev.* 2018;6:CD009642.
6. McCarthy GC, Megalla SA, Habib AS. Impact of intravenous lidocaine infusion on postoperative analgesia and recovery from

- surgery a systematic review of randomized controlled trials. *Drugs*. 2010;70:1149–63.
7. Vigneault L, Turgeon AF, Côté D, et al. Perioperative intravenous lidocaine infusion for postoperative pain control: a meta-analysis of randomized controlled trials. *Can J Anaesth*. 2011;58:22–37.
 8. Koppert W, Weigand M, Neumann F, et al. Perioperative intravenous lidocaine has preventive effects on postoperative pain and morphine consumption after major abdominal surgery. *Anaesth Analg*. 2004;98:1050–5.
 9. Harvey KP, Adair JD, Isho M, et al. Can intravenous lidocaine decrease postsurgical ileus and shorten hospital stay in elective bowel surgery? A pilot study and literature review. *Am J Surg*. 2009;198:231–6.
 10. Kuo CP, Jao SW, Chen KM, et al. Comparison of the effects of thoracic epidural analgesia and i.v. infusion with lidocaine on cytokine response, postoperative pain and bowel function in patients undergoing colonic surgery. *Br J Anaesth*. 2006;97:640–6.
 11. Herroeder S, Pecher S, Schönherr ME, et al. Systemic lidocaine shortens length of hospital stay after colorectal surgery: a double-blinded, randomized, placebo-controlled trial. *Ann Surg*. 2007;246:192–200.
 12. Sun Y, Li T, Wang N, et al. Perioperative systemic lidocaine for postoperative analgesia and recovery after abdominal surgery: a meta-analysis of randomized controlled trials. *Dis Colon Rectum*. 2012;55:1183–94.
 13. Kaba A, Laurent SR, Detroz BJ, et al. Intravenous lidocaine infusion facilitates acute rehabilitation after laparoscopic colectomy. *Anaesthesiology*. 2007;106:11–8.
 14. Bryson GL, Charapov I, Krolczyk G, et al. Intravenous lidocaine does not reduce length of hospital stay following abdominal hysterectomy. *Can J Anaesth*. 2010;57:759–66.
 15. Eipe N, Gupta S, Penning J. Intravenous lidocaine for acute pain: an evidence-based clinical update. *BJA Education*. 2016;16:292–8.
 16. Farrar JT, Young JP Jr, LaMoreaux L, et al. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical rating scale. *Pain*. 2001;94:149–58.
 17. Farrar JT, Berlin JA, Strom BL. Clinically important changes in acute pain outcome measures: a validation study. *J Pain Symptom Manage*. 2003;25:406–11.
 18. Wheeler M, Oderda GM, Ashburn MA, et al. Adverse events associated with postoperative opioid analgesia: a systematic review. *J Pain*. 2002;3:159–80.
 19. Tank A, Hobbs J, Ramos E, et al. Opioid dependence and prolonged length of stay in lumbar fusion: a retrospective study utilizing the national inpatient sample 2003–2014. *Spine*. 2018;43:1739–45.
 20. Thapa P, Euasobhon P. Chronic postsurgical pain: current evidence for prevention and management. *Korean J Pain*. 2018;31:155–73.
 21. Schug SA, Bruce J. Risk stratification for the development of chronic postsurgical pain. *Pain*. 2017;2:e627.
 22. Laskowski K, Stirling A, McKay WP, et al. A systematic review of intravenous ketamine for postoperative analgesia. *Can J Anaesth*. 2011;58:911–23.
 23. Brinck EC, Tiippana E, Heesen M, et al. Perioperative intravenous ketamine for acute postoperative pain in adults. *Cochrane Database Syst Rev*. 2018;12:CD012033.
 24. Elia N, Tramèr MR. Ketamine and postoperative pain – a quantitative systematic review of randomised trials. *Pain*. 2005;113:61–70.
 25. Blandszun G, Lysakowski C, Elia N, et al. Effect of perioperative systemic α -2 agonists on postoperative morphine consumption and pain intensity systematic review and meta-analysis of randomized controlled trials. *Anaesthesiology*. 2012;116:1312–22.
 26. Giordano J, Abramson K, Boswell MV. Pain assessment: subjectivity, objectivity, and the use of neurotechnology. *Pain Phys*. 2010;13:305–15.