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Effects Of Intravenous Lidocaine Infusions On Postoperative Opioid Consumption In Adults Undergoing Laparoscopic Abdominal Surgery

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Abstract

Lidocaine is a local anesthetic that is often administered to surgical patients undergoing anesthesia. While it was originally utilized as an intravenous antiarrhythmic or for local infiltration, it is now frequently used for the proven opioid-sparing and anti-inflammatory effects during surgeries (Beaussier et al., 2018). A common complaint of postoperative patients is pain, and the administration of intravenous lidocaine can potentially decrease patients' perception of pain after surgical procedures (Lee & Schraag, 2022).

Opioids are commonly administered to patients to help control their pain immediately after surgical procedures. Though opioids are the typically chosen treatment for acute surgical pain, they can have significant side effects. As stated by Wei et al. (2019), opioid administration can lead to reduced gastric motility, postoperative nausea and vomiting, and increased length of hospital stay. These adverse effects can be minimized by using intravenous lidocaine as a part of multimodal anesthesia for pain management by decreasing opioid consumption. This study examines the effects of intravenous lidocaine on postoperative opioid use in patients undergoing laparoscopic abdominal surgery. Overall, intravenous lidocaine is proven to reduce postoperative pain scores and decrease perioperative opioid use.

Key words: Intravenous Lidocaine, Opioid consumption, Postoperative pain, Abdominal

Effects of Intravenous Lidocaine Infusions on Postoperative Opioid Consumption in Adults

Undergoing Laparoscopic Abdominal Surgery

With concern surrounding opioid use across the nation, the addition of non-opioid analgesia has become important in providing safe and effective care to patients undergoing general surgery. Lidocaine, a local anesthetic, has been rising in popularity among anesthesia providers as a perioperative analgesic adjunct when administered systemically during the perioperative time. There have been many studies that demonstrate the effectiveness of continuous perioperative intravenous lidocaine infusions. These studies demonstrate a decrease in postoperative pain and opioid consumption in various types of surgical procedures, such as open abdominal and neuro-spine procedures. However, little has been published regarding lidocaine infusions utilized during laparoscopic abdominal procedures (Awal et al., 2022).

In addition to decreasing opioid use and postoperative pain scores, there is also a potential for reducing postoperative nausea and vomiting and improving postoperative gastric motility. Reducing the stated adverse effects of opioid administration can enhance patient's postoperative recovery and decrease the amount of time spent in the hospital after laparoscopic abdominal surgeries (Lee & Shraag, 2022). The purpose of this literature review is to compare and analyze recently published studies that measure perioperative opioid consumption of patients undergoing laparoscopic abdominal procedures who receive continuous intravenous lidocaine infusions compared to those who receive a continuous placebo infusion of normal saline. It is hypothesized that the use of systemic lidocaine will aid in decreasing postoperative pain and perioperative opioid consumption.

Background

Perioperative Opioid Use

  In recent years, there has been a push for anesthesia providers to incorporate non-opioid analgesic adjuncts into their anesthesia care. By utilizing multimodal methods to provide pain control to patients undergoing surgical procedures, anesthesia providers can decrease the amount of opioids used during an anesthetic. Examples of opioid medications commonly utilized in the perioperative period include fentanyl, morphine, hydromorphone, and oxycodone. Opioid epidemic aside, there are several other reasons to minimize the use of opioids both during and after surgical procedures as well. While opioids provide rapid, reliable, and effective analgesia during the perioperative time, there are many adverse side effects to consider when administering these medications to patients (Koepke et al., 2018). In addition to the side effects listed above, others include constipation, itching, altered mental status, respiratory depression, and urinary retention. Each of these adverse effects of opioids is not only dissatisfying to patients, but can also lead to an unnecessarily increased length of stay in the hospital after a surgical procedure (Keopke et al., 2018).

  By decreasing opioid use both during and after surgical procedures in patients undergoing laparoscopic abdominal surgeries, these opioid related side effects can be minimized, leading to better patient satisfaction and earlier discharge from the hospital (Keopke et al., 2018). Some non-opioid adjuncts that could be utilized in this setting include magnesium, non-steroidal anti-inflammatory medications, Tylenol. One other possible way to achieve this desired outcome is to incorporate continuous intravenous lidocaine into the perioperative period, as will be discussed in this review of recently published literature.

Lidocaine Pharmacology

Lidocaine was initially synthesized as Xylocaine in 1942 and approved for clinical use in Sweden in 1948 (Lee & Schraag, 2022). It has been listed as an essential medicine by the World Health Organization as a local anesthetic and also as a medication for the management of ventricular tachyarrhythmias (Lee & Shraang, 2022). As defined by Nagelhout & Sass (2018), when administered in the vicinity of a peripheral nerve, lidocaine, which is an amide local anesthetic, reversibly binds to voltage gated sodium channels during their open or inactivated states, blocking the propagation of an action potential of the nerve cells.

Although the exact mechanism of action of intravenous lidocaine as an adjunct analgesic is not well known, Foo et al. (2021) explains that lidocaine possesses anti-nociceptive, anti-hyperalgesic, and anti-inflammatory properties, which may help to explain why infusions of lidocaine during the perioperative time can provide a patient with prolonged analgesic effects both during and after a surgical procedure. Foo et al. (2021) goes on to explain that when administered intravenously at a therapeutic dose, ranging between 1.5-3mg/kg/hr, lidocaine blocks Muscarinic (M1 and M3) receptors, as well as N-methyl-D-aspartate (NMDA) receptors. Ghimire et al. (2020) also confirms that it is not well understood exactly how lidocaine contributes to analgesia when administered intravenously, but there are some suggestions of mechanism of action of intravenous lidocaine, such as increasing acetylcholine at the spinal cord level and activating nicotinic receptors, as well as by activating inhibitory glycine receptors, which therefore inhibits spinal neurons excitatory response (Ghimire et al., 2020). Umana et al. (2018) further explains this by stating that the activation of nicotinic receptors can provide

similar analgesic effectiveness to opioid medications, specifically in the descending modulatory pain pathway and periaqueductal gray.

Similarly, Awal et al. (2022) explains that the mechanism of action of intravenous lidocaine is difficult to define, but the most prominent systemic effect of this medication is related to its central anti-hyperalgesic effects. Awal et al. (2022) goes on to explain that mechano-insensitive nociceptors, which are activated during surgery by chemicals released by the body's stress response, lead to hyperalgesia and central sensitization to pain. These nociceptors are known to be sensitive to lidocaine. Therefore, when lidocaine is administered intravenously during the perioperative time, it can decrease the expected central sensitization to pain and minimize the degree of hyperalgesia. This seems to be exceptionally beneficial when the lidocaine infusion is initiated prior to surgical incision and initiation of the pain pathway response. With the potential for many benefits, specifically decreasing the hyperalgesia associated with surgical procedures, the use of intravenous lidocaine has been increasing in popularity, and both improves patient's recovery and also decreases opioid use in the postoperative period (Awal et al., 2022).

Laparoscopic Surgery

Laparoscopic surgery is a minimally invasive surgical technique when compared to open procedures. In laparoscopic procedures, the surgeon utilizes multiple smaller incisions and inserts instruments, which are called trocars, into the abdomen to assist with visualization and surgical manipulation. The surgeon then insufflates the abdomen with carbon dioxide (CO_2) and utilizes cameras on the trocars to visualize the surgical field (Sharp et al., 2022). Laparoscopic surgery for abdominal procedures has been increasing in popularity for a multitude of reasons. Li et al. (2018) describes laparoscopic cholecystectomy as an advantage over an open

cholecystectomy because of the smaller surgical scars, a decreased postoperative length of stay in the hospital, and a quicker recovery overall.

Though laparoscopic surgeries are generally thought to be associated with lesser pain than open procedures, Li et al. (2018) states that reported postoperative pain ranges from moderate to intense in approximately 50-70% of patients who underwent laparoscopic cholecystectomy, which ultimately has the potential to delay recovery and increases the risks for postoperative complications. Furthermore, according to Moslemi et al. (2018), up to 80% of patients require additional analgesia for postoperative pain following laparoscopic procedures, which most often consists of opioid medications. The following literature review explores the benefits of intravenous lidocaine in decreasing opioid use and postoperative pain specifically for abdominal laparoscopic procedures.

Literature Review

Methods

A literature search was completed using CINAHL, EMBASE, PubMed, Scopus, and Google Scholar. This search was limited to Randomized Controlled Trials, Meta-Analysis, and Systemic Reviews published between the years of 2017-2022. Keywords used in this search were "Intravenous Lidocaine," "Opioid consumption," "Postoperative pain," "Abdominal," and "Laparoscopic." Any study that did not include laparoscopic abdominal surgery and did not measure postoperative pain and opioid consumption as an outcome was excluded. A total of 23 studies were reviewed and 16 studies were selected for this literature review. Studies omitted from this review were either conducted greater than 5 years ago or did not focus strictly on laparoscopic procedures.

Procedures in the studies included in this literature review include gynecological laparoscopic procedures, laparoscopic hernia procedures, laparoscopic colorectal procedures, and laparoscopic cholecystectomies. Only one study focused on robotic assisted laparoscopic surgery. Similarly, meta-analysis of previously studied RCTs published within the past five years describing the effects of perioperative intravenous lidocaine infusions and the effect on patient's pain level were also included in this literature review.

Each of the studies included in this literature review used lidocaine infusions in the study group and compared the results to a placebo group that received normal saline. For example, two trials in the past five years focused on decreasing opioid consumption specifically following laparoscopic cholecystectomy procedures by initiating a lidocaine infusion during the perioperative period. Both studies were double blinded and randomized, and used normal saline as a placebo to intravenous lidocaine (Saleh et al., 2018; Song et al., 2017). Similarly, RCTs conducted by Awal et al. (2022) and Moslemi et al. (2018) compared lidocaine infusions to normal saline placebo infusions but focused strictly on laparoscopic gynecological procedures. Most other RCTs and Meta-Analysis compared lidocaine to normal saline as a placebo, with the exception of two studies. The systemic review by Moslemi et al. (2018) compared intravenous lidocaine to either a placebo group or to a group who received epidural anesthesia, and the randomized controlled trial by Andjelković et al. (2018) included a lidocaine group, a normal saline control group, and a group receiving dexmedetomidine. Only one study, conducted by Herzog et al. (2020) examined the effect of perioperative intravenous lidocaine infusions on decreasing postoperative opioid use during robotic assisted laparoscopic surgery.

Patient Selection

ASA classification is used to describe a patient's medical comorbidities and determine risks relating to anesthesia. The American Society of Anesthesiologists describes the ASA classes as the following; ASA I describes a healthy patient, II describes mild comorbidities that are well controlled, III describes severe systemic disease that may be poorly controlled, IV describes comorbidities that are threatening to a patient's life, such as cardiac ischemia or septic shock, V describes an unhealthy patient who would otherwise not survive without the proposed procedure, and VI describes brain death and organ donation. ("ASA Physical Status," 2020).

Patient selection in each of the studies included in this literature review differed slightly depending on the type of procedure or inclusion criteria determined by the individual authors. For example, two randomized controlled trials completed by Awal et al. (2022) and Moslemi et al. (2018) included only female patients undergoing laparoscopic gynecological procedures. Awal et al. (2018) included patients of the ASA Physical Status classification of I. Alternatively, Moslemi et al. (2018) included patients of the ASA Physical Status classification of I and II. Both studies utilized patients in a similar age range. Other literature, such as the meta-analysis conducted by Ji et al. (2021), included patients with ASA classification between I and III, and focused specifically on patients who were receiving scheduled laparoscopic colorectal cancer resection. Similarly, the single-blind randomized controlled trial by Andjelković et al. (2018) consisted of patients with ASA classes between I and III, but focused on elective laparoscopic intestine resection, with no mention of colorectal cancer. There were no studies that included patients with an ASA class of IV or greater, and no studies included any cases that were done emergently.

Intravenous Lidocaine Dose and Duration

Though each of the studies included in this literature review utilized a similar dosing regimen for the intravenous lidocaine infusion rate, there were slight differences in both the initial bolus dose and in the weight-based infusion dosing between the various trials. A study published by Ghimire et al. (2020) focused on intraoperative intravenous lidocaine administered to patients undergoing laparoscopic inguinal hernia repair. Just prior to induction, the patients in the study group received a 1.5mg/kg intravenous lidocaine bolus followed by a lidocaine infusion administered at a rate of 2mg/kg/hr. The lidocaine infusion was turned off at the time of extubation at the end of the procedure. The control group received an equivalent volume of normal saline as a placebo (Ghimire et al., 2020). Similarly, studies by Awal et al. (2022), Liu et al. (2022), Durrani et al. (2022), and Song et al. (2017) provided the same bolus dose of 1.5mg/kg and then a continuous infusion dose of 2mg/kg/hr. Again, the lidocaine infusion was discontinued just after procedure end in each of these cases. These studies all administered the placebo to the control group in a similar manner with an equal volume and duration of bolus and infusion.

The RCT focusing on robotic laparoscopic colorectal surgeries that was published by Herzog et al. (2020) also described the administration of a bolus of intravenous lidocaine prior to starting the infusion. While the bolus dose of lidocaine was the same as the previously mentioned studies at 1.5mg/kg, the continuous infusion was administered at 1.5mg/kg/hr. The bolus dose of lidocaine was administered prior to induction of anesthesia. However, the infusion of intravenous lidocaine was maintained for two hours after the surgery was completed (Herzog et al., 2020). Similarly, a trial completed by Sharma et al. (2022) utilized the administration of a 1.5mg/kg bolus of lidocaine during induction of anesthesia, followed by a continuous infusion of

1.5mg/kg/hr given throughout the duration of the procedure. This study, however, discontinued the lidocaine infusion only one hour after the completion of surgery as opposed to two hours in the previously mentioned study. Both trials administered normal saline placebo in an equal volume to the randomly selected control group.

Other trials included in this literature review differed in the fact that they only utilized a continuous infusion and did not administer a lidocaine or placebo bolus prior to the start of the infusion. Saleh et al. (2018) conducted their research with this method, where they completed induction of anesthesia without a bolus of lidocaine or normal saline, then began the continuous infusion of intravenous lidocaine at a rate of 2mg/kg/hr after induction but prior to the start of the surgical procedure. There is no mention of exactly when the lidocaine infusion was turned off in this study (Saleh et al., 2018).

Another anomaly regarding dosing occurred in the trial by Andjelković et al. (2018), where there were three randomly selected groups. The patients in this study received either intravenous lidocaine, intravenous dexmedetomidine, or an infusion of a normal saline placebo. The lidocaine group in this study received no lidocaine bolus, and the continuous infusion was administered at 1.5mg/kg/hr. The dexmedetomidine group received a continuous infusion at a rate of 0.5mcg/kg/hr, and the normal saline group received a similar volume of normal saline placebo. Andjelković et al. (2018) states that all intraoperative continuous infusions were turned off at the conclusion of the surgical procedure.

The systemic reviews of RCTs included in this literature review contained a variety of dosing and methods of administering perioperative continuous lidocaine. One meta-analysis by MacFater et al. (2017) compared three separate RCTs that each studied intravenous lidocaine compared to a placebo. One of these RCTs utilized a 1.5mg/kg lidocaine bolus with a continuous

infusion of intravenous lidocaine that was stopped at the end of surgery. A second study did not

administer a bolus of lidocaine and administered an intravenous lidocaine infusion at 2mg/min if

the patient was over 70kg, and 1mg/min if the patient was under 70kg, which was turned off at

the return of bowel function, though the study does not define the specific criteria measured to

assess bowel function (MacFater et al., 2017). The third study that MacFater et al. (2017)

included in the meta-analysis utilized a 1.5mg/kg bolus with a 2mg/min intraoperative lidocaine

infusion that was titrated down to 1.33 mg/min at surgery end and maintained during recovery

and for another 24 hours postoperatively. Each of the studies included in the meta-analysis by

MacFater et al. (2017) used normal saline as the placebo bolus and infusion. Other meta-

analysis, such as those completed by Li et al. (2018), Rollins et al. (2020), Zhao et al. (2018),

and Wei et al. (2020) described studies where lidocaine bolus dosing ranged from no bolus to

1.5mg/kg, followed by continuous lidocaine infusions at a variety of rates, anywhere from

1mg/kg/hr to 3mg/kg/hr, with the most common dose being 2mg/kg/hr.

Intraoperative Anesthetic Management

Each of the studies included in this literature review described the use of an intravenous

lidocaine infusion compared to a normal saline placebo. The studies each measured the opioid

sparing effect of lidocaine following various laparoscopic abdominal surgeries. Though each

study examined the use of lidocaine during general anesthesia, there were some minor

differences in anesthetic management. In each study, anesthesia was administered in the same

basic method to each patient, following specific guidelines for when to administer adjunct pain

medications. However, each study differed slightly in the specific medications or guidelines that

were used.

In the study by Ghimire et al. (2020), induction of general anesthesia was achieved with weight-based fentanyl, propofol, and vecuronium. Every patient received 1 gram of intravenous paracetamol, and each incision site was infiltrated with 2mL of 0.25% bupivacaine. Patients involved in the study, regardless of their assigned study group, received 0.5mcg/kg of intravenous fentanyl as supplemental pain medication intraoperatively if the mean arterial pressure (MAP) and heart rate increased by 20% above their baseline.

Patients enrolled in the trial by Sharma et al. (2022) received almost identical anesthetic interventions as the patients enrolled in the Ghimire et al. (2020) study. Slightly different than the previously mentioned studies, the RCT by Awal et al. (2022) achieved induction of anesthesia with weight-based fentanyl, propofol, and rocuronium. Anesthesia was maintained with appropriately dosed Nitrous Oxide and Isoflurane for each patient. Every patient, both in the study group and control group, received 0.5mcg/kg of fentanyl every hour during the procedure as appropriate, regardless of vital sign changes, and every patient received 30mg of ketorolac prior to emergence.

Liu et al. (2022) achieved induction of anesthesia with weight-based propofol, sufentanil, and rocuronium. Every patient also received a transversus abdominal plane (TAP) block on the side of surgery at the start of the procedure, which contained 20mL of 0.375% ropivacaine. Intraoperatively patients received both remifentanil infusions titrated between 0.1-0.5mcg/kg/min and a propofol infusion between 4-6mg/kg/hr to maintain an adequate depth of anesthesia. Similar to the study by Ghimire et al. (2020), whenever the patient's heart rate or blood pressure deviated greater than 20% higher than baseline, an adjunct pain medication was administered, and in this trial by Liu et al. (2022), the medication of choice was 5mcg of sufentanil. Additionally, 30 minutes prior to the conclusion of surgery, another dose of 5mcg of

sufentanil was administered to each patient in preparation of the remifentanil infusion being discontinued. Likewise, Herzog et al. (2020) induced anesthesia with sufentanil, propofol, and rocuronium, however, instead of a remifentanil infusion, sufentanil was administered at the discretion of the anesthetist with the goal of maintaining stable circulation and a bispectral index between 40-60, with no mention of consistent dosing used.

Song et al. (2017) administered weight-based midazolam, fentanyl, propofol, and cis-atracurium for induction of anesthesia. Intraoperatively, the patients included in this study also received remifentanil infusions that were titrated to maintain heart rate and blood pressure within 20% of the patient's normal values. In this study, however, there is no mention of adjunct pain medication administered prior to the remifentanil infusion being turned off. The study by Andjelković et al. (2018) achieved induction of anesthesia using similar techniques as previously mentioned, including weight based propofol, fentanyl, and rocuronium. Intraoperatively, the patients in this study were being monitored with an analgesia nociception index (ANI) which is used for pain measurement, and fentanyl 2mcg/kg was administered any time that value dropped under 50. Each patient received 1 gram of paracetamol intraoperatively.

Both meta-analysis by Zhao et al. (2018) and Li et al. (2018) discussed many RCTs that utilized patient-controlled analgesia, and one that utilized intravenous opioid bolus dosing for postoperative pain management, but neither study differentiated between the type of opioid or the dose used. Wei et al. (2020) simply lists the analgesic that was given postoperatively in each of the RCTs included in the meta-analysis. For these studies, morphine was most commonly administered, followed by meperidine, piritramide, sufentanil, and fentanyl (Wei et al., 2020).

Postoperative Analgesia Management

Each of the studies included in this literature review utilized additional postoperative pain management depending on patient's reported pain, and measured the difference in opioid consumption in patients who received continuous intravenous lidocaine compared to those who received a placebo infusion of normal saline. Each of the studies included in this literature review utilized either the numeric pain rating scale (NRS) or the visual analog scale (VAS) for postoperative pain scores, both of which similarly encourage the patient to rate their pain on a scale from 0 to 10, with 10 being the most pain and 0 being no pain.

In the study by Ghimire et al. (2020), at the end of the procedure, 30mg of intravenous ketorolac was administered to every patient, followed by another 30mg of ketorolac every 8 hours. In the post anesthesia care unit (PACU), patients were asked their pain scores on the NRS scale and received 1mg of morphine every 5 minutes until that score decreased to below a 3. After 2 hours, the patients were transferred to the ward, where they received 50mg of intravenous tramadol every 10 minutes to maintain an NRS score less than 3. A maximum dose of 300mg of tramadol was given (Ghimire et al., 2020).

The study by Sharma et al. (2022) was managed very similarly, except for the dosing of intravenous ketorolac. Postoperatively, when reported VAS scores exceeded 3, these patients received 0.5mcg/kg of intravenous fentanyl in the PACU, and 25mg of tramadol on the ward (Sharma et al., 2022). Alternatively, in the study conducted by Awal et al. (2022), patient's postoperative pain was assessed via the NRS pain scale, and 1.5mg of intravenous morphine was given to patients every five minutes until their pain score dropped below a 4 out of 10 (Awal et al., 2022). In contrast, Liu et al. (2022) utilized sufentanil as a postoperative analgesic. In this

RCT, 5mcg of sufentanil was administered after extubation in 10-minute intervals until a VAS

score less than 3 was achieved (Liu et al., 2022).

Postoperatively in the study by Herzog et al. (2020), the patients received patient

controlled intravenous morphine 0.04mg/kg with a lockout of 7 minutes with no basal rate. The

study by Herzog et al. (2020) mentions that paracetamol and NSAID medications were

administered postoperatively as determined by surgeon discretion, however, no consistent dosing

or guidelines were mentioned regarding postoperative medication administration.

The trial by Song et al. (2017) utilized a patient controlled intravenous analgesia (PCIA)

in the postoperative period, in which the patient would receive a 20mcg fentanyl bolus when they

pressed the delivery button. The PCIA had a lockout time of 10 minutes and did not have a basal

rate. Similar to the previous studies mentioned, Andjelković et al. (2018) utilized a PCIA in the

postoperative setting, where piritramide was delivered by patient control as needed every 30

minutes. However, unlike the other studies that mentioned PCIA use, the study by Andjelković

et al. (2018) provided a continuous rate of piritramide at 0.5mg/hr. In addition to the patient-

controlled analgesics, patients were also given additional 3mg of piritramide for breakthrough

pain scores of higher than 3, as well as 1 gram of paracetamol every 6 hours, and metamizole

30mg/kg every 12 hours.

In the RCT by Moslemi et al. (2018), after the procedure was completed and the patient

was recovering in PACU, meperidine 0.5mg/kg was administered to each patient who expressed

a pain score higher than 4. Likewise, the study by Durrani et al. (2022) also does not provide

significant information regarding induction or maintenance of anesthesia, but similarly treated

patient's pain scores that were rated higher than 4 on the NRS scale with 2mg of nalbuphine

during the postoperative time.

Pain Scores and Analgesic Requirements

Although each trial had slightly different methods and used varying analgesic techniques in addition to the lidocaine study group versus the normal saline control group, the combined result of the studies in this literature review described an overall decrease in pain scores and opioid use in the perioperative period. There was only one exception: the study by Herzog et al. (2020) did not show a significant difference between the control and study groups regarding either reported pain scores or perioperative opioid consumption.

Ghimire et al. (2020) studied the pain scores and opioid consumption in patients undergoing totally extraperitoneal laparoscopic inguinal hernioplasty, with the overall conclusion that using perioperative lidocaine infusions does decrease opioid use, among other beneficial findings such as increased patient satisfaction. This RCT determined that the lidocaine study group received less fentanyl intraoperatively (median of 0 mcg) than the control group (median of 20 mcg) (P = <0.001). The time between surgery completion and first pain perception was an average of 30 minutes in the patients who received lidocaine as opposed to the control group, whose first pain perception was an average of 10 minutes (P <0.001). At 24 hours after the surgical procedure was completed, the amount of morphine equivalents received by each patient measured much lower in the group who received lidocaine (0-1 mg of morphine) than the group who received intravenous saline placebo (0-4 mg of morphine) with a P value of 0.003. Ghimire et al. (2020) goes on to state that in addition to intravenous opioid requirements being decreased in the lidocaine group patients, they also required a decreased median dose of tramadol during their stay in the surgical unit, with the median dose required being 0-0 in the lidocaine group and 0-50 mg in the control group (P= <0.001). Other outcomes observed in this study include increased postoperative nausea and vomiting in the control group, increased satisfaction in the

lidocaine group, and similar postoperative sedation levels between the two groups (Ghimire et al., 2020).

In the study involving gynecological laparoscopic surgery by Awal et al. (2022), NRS pain scores upon arrival to the PACU were much lower in the group that received lidocaine compared to the control group. In addition to the decreased pain scores, both the morphine requirements in the PACU and the amount of rescue analgesics required over the following 24 hours were much lower in the lidocaine group. According to Awal et al. (2022), 22 patients in the lidocaine group needed no morphine at all in the PACU compared to 6 patients in the control group, with a P value of 0.00. One patient in the lidocaine group required one dose of morphine, compared to 15 patients in the control group (P=0.00). Furthermore, 0 patients who received lidocaine required 2 doses of morphine, while 5 control group patients required a second dose (P=0.015), and no lidocaine group patients received 3 or more doses of morphine during recovery while 1 patient in the saline group required a third dose (P=0.176). Overall, the group of patients who received lidocaine intraoperatively in the study by Awal et al. (2022) had a significantly lower mean pain score, as exemplified in table 1 below. In this study, the lidocaine group consisted of 23 patients and the control group consisted of 27 patients, and Awal et al. (2022) considered significance if the P value was less than 0.05. Other findings included decreased levels of postoperative nausea and vomiting, but an increased level of sedation upon arrival to PACU in the lidocaine group, also noted in Table 1 below.

Table 1

Outcomes from Lidocaine Group and Control Group

Parameter	Group L	Group NS	P
NRS pain score on arrival in PACU [Median (IQR)]	0 (0-2)	4 (4-5)	<0.001
Ramsay Sedation Score on arrival in PACU [mean±SD]	2.22±0.85	1.63±0.63	0.004
No requirement of morphine in PACU (number of patients)	22 (96%)	6 (22%)	<0.005
Nausea & vomiting requiring antiemetics (number of patients)	2 (9%)	11 (41%)	0.005
Time to achieve PADSS score ≥9 (mins) [mean±SD]	30.65±12.37	80.00±20.38	<0.001
NRS pain score at 24 h [Median (IQR)]	1 (0-1)	3 (2-3)	<0.001
No requirement of rescue analgesia over 24 h (number of patients)	22 (96%)	6 (22%)	<0.005
Quality of Recovery [Median (IQR)]	197 (196-199)	178 (175-181)	<0.001
Emotional State [Median (IQR)]	45 (44-45)	41 (40-42.5)	<0.001
Physical Comfort [Median (IQR)]	59 (58-60)	52 (49-53.5)	<0.001
Psychological Support [Median (IQR)]	35 (35-35)	33 (32-33)	<0.001
Physical Independence [Median (IQR)]	25 (25-25)	23 (21.5-23)	<0.001
Pain [Median (IQR)]	35 (34-35)	31 (30-32)	<0.001

NRS - Numeric Rating Scale; PACU - Post anesthesia care unit; PADSS - Post anesthesia discharge scoring system; QoR - Quality of recovery

Note. This table was produced by Awal et al (2022) and compares primary and secondary findings between group L (lidocaine group) and group NS (control group).

The other study that focused on laparoscopic gynecological procedures conducted by Moslemi et al. (2018) had similar results. This RCT consisted of 60 female patients who were assigned to either the lidocaine group or normal saline control group. VAS pain scores were decreased in the group of patients who received lidocaine infusions, with a P value of 0.02, however, the lidocaine and control group both displayed a similar downward trend slope regarding pain intensity over the length of one day, with VAS scores in the control group being slightly higher than the lidocaine group at each hourly interval (P = 0.022). The study by Moslemi et al. (2018) also determined that patients in the lidocaine group were 3.8 times less likely to require postoperative analgesics than the control group. Ultimately, the mean total analgesic dose of postoperative meperidine differed significantly, with the lidocaine group receiving an average of 1.3mg and the control group receiving an average of 38.2mg (P=<0.01) (Moslemi et al., 2018).

In the trial conducted by Song et al. (2017) that studied patients undergoing laparoscopic cholecystectomy, patients who received intraoperative lidocaine infusions showed a decrease in

pain and opioid consumption. This study measured pain scores using the VAS scale at 2, 6, and

24 hours postoperatively. Mean VAS scores were lower in the lidocaine group at both 2 and 6

hours, with scores being 3.01 ± 0.65 at 2 hours and 3.38 ± 0.42 at 6 hours postoperatively, while

the normal saline placebo group had pain scores at 4.27 ± 0.58 at 2 hours and 4.22 ± 0.67 at 6

hours postoperative (P=0.01). Song et al. (2017) did not, however, find any significant

differences in VAS pain scores at 24 hours postoperatively. Overall, the group that received

intravenous lidocaine had a total mean fentanyl requirement dose of 98.27 ± 16.33 mcg versus

the placebo group who had a mean fentanyl requirement dose of 187.49 ± 19.76 mcg (P = 0.005).

The first dose of analgesic required in PACU was later following surgery in the lidocaine group

than the control group, at 126 ± 21 minutes versus only 56 ± 13 minutes respectively (P= 0.01).

Other outcomes included an accelerated return of bowel function in the lidocaine group, and a

slight decrease in postoperative nausea and vomiting in the lidocaine group (Song et al., 2017).

      Sharma et al. (2022) studied patients undergoing laparoscopic intraperitoneal onlay mesh

repair and had similar data collection guidelines as Song et al. (2017), as they also measured

VAS pain scores and fentanyl consumption at hourly intervals of 0, 2, 4, 8, 12, and 24 hours

postoperatively. Sharma et al. (2022) determined that the lidocaine group had overall lower VAS

pain scores at each hourly interval, and while the control group had a comparatively higher

average VAS pain score at each measured interval, both groups displayed a gradual decline in

postoperative pain over the first 24 hours. As exemplified in Figure 1 below, though the

lidocaine group had overall lower VAS pain scores, after the 4-hour time interval, VAS pain

scores were relatively close between the two groups.

Figure 1

Pain Scores Between Lidocaine Group and Placebo Group
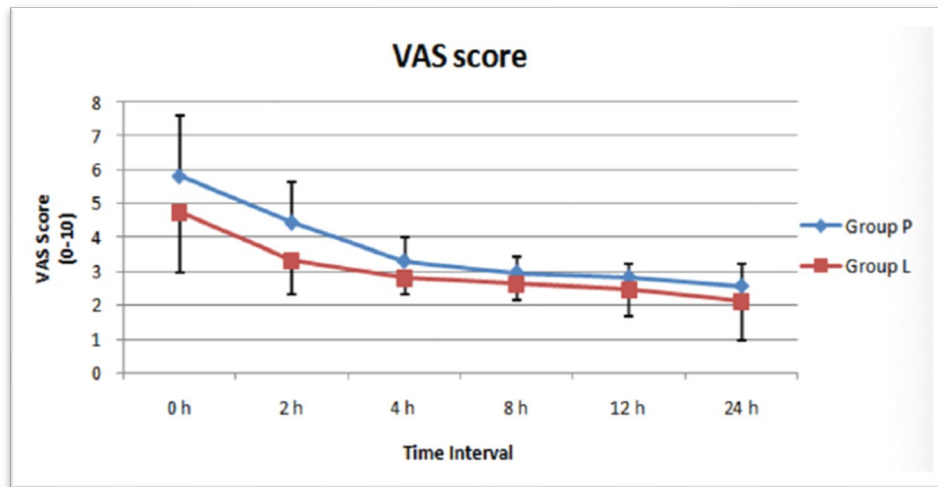
Note. This graph was produced by Sharma et al. (2018) to display the correlation between Visual Analog Scale pain scores in group L (lidocaine group) and group P (placebo group) over the course of 24 hours postoperatively.

In addition to a decrease in VAS scores at each hourly interval postoperatively, the patients in the trial by Sharma et al. (2022) who received lidocaine infusions required less intraoperative fentanyl at an average of 35.11 ± 6.51 mcg compared to the normal saline placebo group who received an average of 47.50 ± 17.32 mcg (P = 0.029). Though the lidocaine group also had a lower fentanyl requirement in the first 2 hours in PACU, the results did not show significance at 40.86 ± 16.96 mcg versus 54.82 ± 23.65 mcg with a P value of 0.072. After the patients left PACU and transitioned to tramadol for analgesic requirements, the lidocaine group again displayed an insignificant decrease in consumption of analgesics. It is important to note that no patient in the Sharma et al. (2022) trial required rescue analgesics after 12 hours post-procedure. Other significant findings from the Sharma et al. (2022) trial include increased patient satisfaction and faster bowel function recovery, measured as the mean time to first flatus, in the lidocaine group.

Another trial that measured VAS pain scores at multiple time intervals postoperatively was conducted by Saleh et al. (2018), who studied patients undergoing laparoscopic cholecystectomy. This study describes overall lower VAS pain scores after conclusion of surgery in the group who received lidocaine. At 0 hours, the lidocaine group had a median VAS score of 2 while the control group had a median VAS score of 3 (P=0.001). However, although the lidocaine group exhibited overall lower scores at hour 4, both groups had a median score of 3, with a mean VAS score of 2.77 in the lidocaine group versus 3.07 in the control group (P=0.567), making this finding insignificant. Similarly, at hour 12, the lidocaine group had a median VAS score of 3, while the control group had a median score of 3.5 (P=0.077), which is also an insignificant finding. Furthermore, at hour 16, median VAS scores in the lidocaine versus the control group were 2 and 4, respectively (P=<0.001), which is a significant finding. The study by Saleh et al. (2018) also notes that the overall dose of morphine required both intraoperatively and postoperatively was greatly decreased in the lidocaine group compared to the control group. Intraoperatively, the median dose of morphine was 4mg in the lidocaine group, while the median dose of morphine in the control group was 8mg (P=<0.001). Postoperatively, the median dose of morphine was 6mg in the lidocaine group, compared to 10mg in the control group (P=<0.001).

The study by Andjelković et al. (2018) focused on intraoperative fentanyl consumption as their primary variable, and total piritramide dose in the PACU as their second measurable variable. Overall, there was no significant difference in the dose of fentanyl given intraoperatively between the groups. Additionally, there was no difference in piritramide consumption between the groups in the PACU immediately following the conclusion on the procedure. However, Andjelković et al. (2018) did find a significant difference in piritramide

consumption between the lidocaine group and control group on both the first day postoperatively (P=0.002) and second day postoperatively (P=0.001). Overall piritramide consumption was lower in the lidocaine group compared to the control group as well (P=0.003).

In a meta-analysis by Li et al. (2018), the effect of intravenous lidocaine infusions on perioperative pain was measured in patients undergoing laparoscopic cholecystectomy. The studies that were included in this meta-analysis each measured VAS pain scores at 12, 24, and 48 hours postoperatively. At 12 hours, there was a significant decrease overall in VAS pain scores of the patients in the lidocaine groups compared to those who received a placebo (P=0.014). Similar results were presented at both 24 and 48 hours. Opioid requirements were also measured in each study included in the meta-analysis by Li et al. (2018), again reported at hours 12, 24, and 48 postoperatively. Collectively, data determined that at each of the hourly intervals, the use of continuous perioperative intravenous lidocaine infusions can reduce the requirements of rescue opioid analgesics compared to the administration of a normal saline placebo. Another meta-analysis including patients undergoing laparoscopic cholecystectomy by Zhao et al. (2018) provided similar results. Both VAS pain scores and overall opioid consumption at 12, 24, and 48 hours were decreased in the group of patients receiving intravenous lidocaine infusions compared to the patients receiving a normal saline placebo (Zhao et al., 2018).

Contrary to each of the other studies included in this literature review, the RCT conducted by Herzog et al. (2020) did not exhibit similar outcomes regarding a decrease in pain scores or opioid consumption. This study reports a median cumulative consumption of morphine equivalents of 43.3mg in the group of patients who received lidocaine compared to 41.3mg in the group of patients who received the placebo (P = 0.78). There was also no significant difference

in opioid consumption or pain score between the two groups at hour 24 or hour 48

postoperatively, as displayed in Table 2 below.

Table 2

Comparison Between Control Group and Lidocaine Group

TABLE 2 / Primary and secondary outcomes.			
Results	Control group (N = 29)	Lidocaine group (N = 29)	p-value
Cumulative opioid consumption, mg, median (IQR)[a]			
At 24 h	41.3 (25-63.8)	43.3 (35-70.6)	0.78
At 72 h	78.7 (36-125)	77 (46.6-105)	0.78
NRS, median (IQR)			
At 24 h	2 (0-3)	2 (1-3)	0.99
At 72 h	0 (0-1.5)	1 (0-2)	0.37
Antiemetic doses until 72 h, n, median (IQR)	2 (2-3)	3 (2-4)	0.21
Time to 1st flatus/defaecation, h, median (IQR)[b]	34 (26-48)	32 (24-40)	0.99
Time to discharge, days, median (IQR)	5 (4-9)	5 (4-7)	0.99
Complicated surgery, n (%)[c]	7 (24.1)	4 (13.8)	0.32

IQR = interquartile range; NRS = numerical pain score.
a) Calculated morphine equivalents according to www.medicin.dk.
b) 3 patients in each group did not have flatus/defaecation at 72 h and were not included.
c) The patients in need of any kind of reoperation, specified in the text.

Note. This table was produced by Herzog et al. (2020) to display comparison between control group and lidocaine group regarding primary and secondary outcomes. P values were insignificant regarding opioid consumption and pain scores at both 24 hours and 72 hours postoperatively.

Local Anesthetic Toxicity

One of the more serious side effects of administering continuous intravenous lidocaine

infusions is local anesthetic systemic toxicity (LAST), which can occur when high doses of local

anesthetic are allowed to enter a patient's circulation. Since systemic lidocaine infusions are

administered directly into the blood vessel via an intravenous catheter, there is a higher risk for

LAST than when local anesthetic is infiltrated to surround a peripheral nerve or surgical incision.

According to Beaussier et al. (2018), symptoms of LAST can include numbness around

the mouth, ringing in the ears, blurry vision, seizures, and even cardiac arrest. However, as stated

by Foo et al. (2021), toxicity can be avoided if dosing is kept to less than 3mg/kg/hr in a healthy

patient, which was the case in the majority of studies discussed. As described by Lee & Shraag

(2022), the half-life of systemically administered lidocaine is about five to eight minutes, and at

the lower dosages discussed by the literature review, the temporary infusion of lidocaine will

likely not result in a toxicity scenario. To note, there were no reports of any symptoms of

lidocaine toxicity in any of the studies included in this literature review.

Limitations

There were some limitations to note in this literature review. First, each study had a very

limited number of participants, with most RCTs containing a total of between 55-80 patients.

Specifically, the study by Saleh et al. (2018) only enrolled a total of 60 patients for their study.

Though the study by Saleh et al. (2018) determined overall that lidocaine decreases VAS scores

and lowers perioperative opioid use, the differences in mean VAS scores at 4 hours and 12 hours

postoperatively were not significant findings. This could be due to the limited number of

participants in the study. Alternatively, one study, the RCT conducted by Liu et al. (2022), had

significantly more participants, with 166 patients participating in the trial.

A second limitation was the lack of consistency between the dose of lidocaine utilized for

a continuous infusion. Some studies, such as those by Ghimire et al. (2020), Saleh et al. (2018),

and Song et al. (2017), administered continuous intravenous lidocaine at a rate of 2mg/kg/hr,

while others, such as the trial by Sharma et al. (2022), utilized a dose of only 1.5mg/kg/hr.

Similarly, some studies included an initial bolus of lidocaine prior to starting the infusion, while

others did not administer any type of bolus dose.

A final limitation to note includes anesthetic management differences between studies.

For example, Song et al. (2017) utilized a continuous remifentanil infusion throughout the

duration of the procedure, while Ghimire et al. (2020) gave fentanyl bolus dosing based on a change in heart rate and blood pressure. It would be beneficial to further study this topic with a larger group of participants and a more consistent anesthetic plan and lidocaine dose.

Discussion

Though laparoscopic abdominal procedures provide many advantages when compared to open abdominal procedures, including decreased postoperative pain and a faster recovery time, the results of the studies reviewed above continue to demonstrate the need for additional postoperative analgesia. Although opioids have been shown to provide reliable pain relief and are widely accessible to the anesthesia provider, these medications can exhibit adverse effects in the recovery period, such as nausea, delayed gastric emptying, and prolonged hospital stay (Wei et al., 2019). According to the recent literature discussed above, a multimodal approach to perioperative analgesia, specifically utilizing a continuous infusion of intravenous lidocaine, can decrease postoperative pain and opioid requirements during laparoscopic abdominal surgeries.

Researchers, including Ghimire et al. (2020), Awal et al. (2022), and Wei et al. (2020), have discussed the advantages of using continuous intravenous lidocaine infusions during the perioperative time period of laparoscopic abdominal procedures, with a similar conclusion of decreasing postoperative pain scores and overall opioid consumption. In addition to a decrease in overall opioid use and lower postoperative pain scores, Ghimire et al. (2020) demonstrates further benefits of utilizing continuous intravenous lidocaine. Patients in the study who received lidocaine infusions demonstrated less nausea than those who received a normal saline placebo, and Ghimire et al. (2020) attributed the lower postoperative nausea incidence to the patients receiving a lower overall dose of opioid medications. The lower degree of postoperative nausea and vomiting could also be due to the lower pain scores exhibited by patients who received

lidocaine infusions, as nausea and vomiting is commonly linked to increased pain. The study also described a shorter hospital length of stay for patients receiving intravenous lidocaine, presumably due to the lower opioid medication dosages received. Wei et al. (2019) also demonstrated similar outcomes regarding postoperative nausea and vomiting (PONV) and length of stay in the hospital after surgery in addition to the decrease in postoperative pain perception and opioid consumption. As mentioned in the literature review, this was a common finding among many researchers who studied effects of continuous intravenous lidocaine infusions for laparoscopic abdominal surgeries.

Only one study included in the literature review above did not come to the conclusion that perioperative lidocaine decreases postoperative pain and opioid consumption. The results of this study by Herzog et al. (2020) showed that there was no difference in additional opioid consumption in the postoperative period when comparing patients who received normal saline and patients who received an intravenous lidocaine infusion. This study was an outlier and was also the only study to include robotically assisted laparoscopic abdominal surgeries as compared to hand-assisted laparoscopic procedures. As discussed by Herzog et al. (2020), there were only 60 patients included in the study, which may have led to the inconclusive results. As stated in the literature review, additional non-opioid pain medication administration was at the discretion of the provider caring for the patient postoperatively, and there was no strict protocol for when to administer the additional analgesic. This could have led to inconsistencies in additional opioid administration, therefore skewing results of the study.

A common concern mentioned by many researchers surrounding the administration of intraoperative lidocaine infusions is increased postoperative sedation when compared to those patients who receive only a normal saline placebo. This side effect of lidocaine was discussed in

many recent studies, and the overall conclusion showed little to no difference in postoperative

sedation between the lidocaine and normal saline test groups. For example, Ghimire et al. (2020)

utilized a specific scale to measure patient's sedation in recovery, which ranged from 0 (alert) to

4 (lack of responsiveness). Overall, the study found no difference in the sedation levels of

patients receiving intravenous lidocaine compared to normal saline at various hourly intervals in

the postoperative period. In contrast, the study by Awal et al. (2022) did find that patients who

received a continuous intravenous lidocaine infusion had a higher Ramsay sedation score than

those who received a normal saline placebo infusion (P= 0.004). However, because of the short

duration of action of systemic lidocaine, there was no clinical significance. In fact, the patients in

the lidocaine study group still had a faster discharge time compared to those who received

normal saline (Awal et al., 2022).

Optimal Intravenous Lidocaine Infusion Dose and Duration

The studies included in this review discuss different variations of intravenous lidocaine

dose and duration. Infusion doses ranged anywhere from 1.5mg/kg/hr, as exemplified by the

study by Andjelkovic et al. (2018), up to as much as 3mg/kg/hr in the meta-analysis by Wei et al.

(2020). According to recent literature, there is not one defined dose of continuous intravenous

lidocaine that is most effective in decreasing pain scores and analgesic requirements in the

perioperative setting. Many of the studies, although they did lead to similar outcomes, utilized

slightly different continuous infusion doses, and so, as suggested by Zhao et al. (2018), there

should be further research to determine an optimal dose for perioperative lidocaine use in the

surgical setting. It is also recommended that further studies should be conducted with more

uniform anesthesia management in the perioperative period, keeping only the lidocaine dose as a

variable. This will ultimately help to determine an optimal and universal dose of intravenous lidocaine.

       Due to the differences in adjunct medications administered in the current research, it is difficult to determine the effectiveness of specific lidocaine dosing. For example, the intravenous lidocaine group in both the study by Andjelkovic et al. (2018) and the study by Sharma et al. (2022) received the same infusion rate of lidocaine at 1.5mg/kg/hr. However, the patients in the Andjelkovic et al. (2018) study received nitrous oxide, fentanyl, and piritramide doses as required perioperatively, while the patients in the study by Sharma et al. (2022) received fentanyl and tramadol in the perioperative period as required. Another study, conducted by Song et al. (2017) utilized a lidocaine infusion of 2mg/kg/hr, and administered only fentanyl as required during the perioperative period. These studies all had slightly different anesthetic management and slightly different dosing but had similar results regarding a decrease in opioid consumption in the intravenous lidocaine groups. Now that it has been published that lidocaine infusions do, in fact, decrease postoperative pain and opioid use, it would be useful to determine a more specific dose.

       An inconsistency among many of the studies recently published about perioperative continuous lidocaine infusions for laparoscopic abdominal surgeries is when to turn off the lidocaine infusion. Many of the single center randomized controlled trials, such as those conducted by Liu et al. (2022) and Awal et al. (2022), terminated the continuous lidocaine infusion (as well as the normal saline placebo infusion) at the conclusion of the surgery, around the time of skin closure. Alternatively, the study by Sharma et al. (2022) continued the lidocaine infusion and normal saline placebo infusion for 1 hour after the conclusion of the surgical procedure. Regardless of the discrepancy in the duration of the infusion in a majority of the

studies, the results still demonstrated an overall decrease in postoperative pain scores and opioid consumption.

One exception to these results, as previously mentioned, is the study by Herzog et al. (2020), in which patients received the continuous infusion of intravenous lidocaine or normal saline placebo for a total of two hours after the conclusion of the surgical procedure. Although the infusion of lidocaine was continued for a longer duration than other studies, the RCT by Herzog et al. (2020) was the only study included in this review that found no difference in postoperative pain reporting and no difference in postoperative opioid consumption when comparing patients receiving continuous lidocaine versus a saline placebo. Overall, further studies should be conducted with uniform anesthetic management, lidocaine dose, and duration of the continuous lidocaine infusion.

Further Research and Suggestions

Many of the current randomized controlled trials include a small number of study participants, most commonly enrolling under 100 total patients to divide between a study group and control group. For example, Awal et al. (2022) only utilized 55 total patients, all of which were female, as the study focused on laparoscopic gynecological procedures. Moslemi et al. (2018) similarly included only 60 total patients, again strictly female patients undergoing laparoscopically assisted gynecological surgery. Saleh et al. (2018) includes patients of both sexes, but only includes 60 total patients undergoing laparoscopic cholecystectomy. The low number of participants in these studies leaves a greater possibility that the data may be skewed one way or the other. Because each of the many studies included in this literature review, apart from just the one study by Herzog et al. (2020), have proven that continuous perioperative lidocaine administration does decrease postoperative opioid use and pain scores, it is likely that

this would not change with a higher number of participants. However, it may help to strengthen the argument and improve the data to support the current outcomes demonstrated by these studies.

Importance to the Practice of Anesthesia

Though there are multiple ways to provide anesthesia for a given case or patient situation, it is important to always strive to do what is best for the patient's health and satisfaction. Opioid medications have long been utilized for reliable analgesia during and after surgical procedures, which includes laparoscopic abdominal surgeries. However, there are known disadvantages to utilizing this class of medications that can cause dissatisfaction and delays in the patient's recovery. Although easily accessible and generally useful in decreasing the patient's postoperative pain, common side effects, which can include nausea, delayed gastric motility, and increased hospital length of stay can negatively impact patient's surgical experience.

Healthcare is constantly evolving, and the improvement of patient care is a high priority. Knowing that there are ways to incorporate multimodal analgesia that are safe and effective is very beneficial to the experience of the patient. With the majority of recent studies included in this review determining that continuous lidocaine infusions can help to decrease the use opioids, therefore reducing the incidence of those unwanted opioid-related side effects, it is clear that this is a technique that can improve the overall perioperative experience of the patient. Additionally, as mentioned earlier, with the low dose infusions of continuous lidocaine between 1.5-3mg/kg/hr, there was no evidence of Local Anesthetic Systemic Toxicity (LAST) noted, suggesting that this technique for addressing patient's perioperative pain is overall safe. Therefore, it is clear that by providing patients with this non-opioid analgesic adjunct, anesthesia providers can improve their own practice and patient outcomes overall.

Conclusion

After reviewing the benefits of decreasing opioid use in the perioperative setting, and compiling data from many recent studies, it is evident that incorporating multimodal adjuncts, such as systemic lidocaine infusions, provides better overall recovery and satisfaction in those patients undergoing laparoscopic abdominal surgeries. Utilizing continuous intravenous lidocaine infusion at doses between 1.5 and 3mg/kg/hr is a safe way to decrease postoperative pain and opioid consumption after laparoscopic surgeries. Secondary to the decrease in opioid consumption, adverse effects of opioids can be avoided, and patients can have a better perioperative experience overall.

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