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# [Intervention Review]

# Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery in adults

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# ABSTRACT

# Background

The management of postoperative pain and recovery is still unsatisfactory in a number of cases in clinical practice. Opioids used for postoperative analgesia are frequently associated with adverse effects, including nausea and constipation, preventing smooth postoperative recovery. Not all patients are suitable for, and benefit from, epidural analgesia that is used to improve postoperative recovery. The non-opioid, lidocaine, was investigated in several studies for its use in multimodal management strategies to reduce postoperative pain and enhance recovery. This review was published in 2015 and updated in January 2017.

# Objectives

To assess the effects (benefits and risks) of perioperative intravenous (IV) lidocaine infusion compared to placebo/no treatment or compared to epidural analgesia on postoperative pain and recovery in adults undergoing various surgical procedures.

# Search methods

We searched CENTRAL, MEDLINE, Embase, CINAHL, and reference lists of articles in January 2017. We searched one trial registry contacted researchers in the field, and handsearched journals and congress proceedings. We updated this search in February 2018, but have not yet incorporated these results into the review.

# **Selection criteria**

We included randomized controlled trials comparing the effect of continuous perioperative IV lidocaine infusion either with placebo, or no treatment, or with thoracic epidural analgesia (TEA) in adults undergoing elective or urgent surgery under general anaesthesia. The IV lidocaine infusion must have been started intraoperatively, prior to incision, and continued at least until the end of surgery.

# Data collection and analysis

We used Cochrane's standard methodological procedures. Our primary outcomes were: pain score at rest; gastrointestinal recovery and adverse events. Secondary outcomes included: postoperative nausea and postoperative opioid consumption. We used GRADE to assess the quality of evidence for each outcome.

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#### **Main results**

We included 23 new trials in the update. In total, the review included 68 trials (4525 randomized participants). Two trials compared IV lidocaine with TEA. In all remaining trials, placebo or no treatment was used as a comparator. Trials involved participants undergoing open abdominal (22), laparoscopic abdominal (20), or various other surgical procedures (26). The application scheme of systemic lidocaine strongly varies between the studies related to both dose (1 mg/kg/h to 5 mg/kg/h) and termination of the infusion (from the end of surgery until several days after).

The risk of bias was low with respect to selection bias (random sequence generation), performance bias, attrition bias, and detection bias in more than 50% of the included studies. For allocation concealment and selective reporting, the quality assessment yielded low risk of bias for only approximately 20% of the included studies.

#### IV Lidocaine compared to placebo or no treatment

We are uncertain whether IV lidocaine improves postoperative pain compared to placebo or no treatment at early time points (1 to 4 hours) (standardized mean difference (SMD) -0.50, 95% confidence interval (CI) -0.72 to -0.28; 29 studies, 1656 participants; very low-quality evidence) after surgery. Due to variation in the standard deviation (SD) in the studies, this would equate to an average pain reduction of between 0.37 cm and 2.48 cm on a 0 to 10 cm visual analogue scale . Assuming approximately 1 cm on a 0 to 10 cm pain scale is clinically meaningful, we ruled out a clinically relevant reduction in pain with lidocaine at intermediate (24 hours) (SMD -0.14, 95% CI -0.25 to -0.04; 33 studies, 1847 participants; moderate-quality evidence), and at late time points (48 hours) (SMD -0.11, 95% CI -0.25 to 0.04; 24 studies, 1404 participants; moderate-quality evidence). Due to variation in the SD in the studies, this would equate to an average pain reduction of between 0.10 cm to 0.48 cm at 24 hours and 0.08 cm to 0.42 cm at 48 hours. In contrast to the original review in 2015, we did not find any significant subgroup differences for different surgical procedures.

We are uncertain whether lidocaine reduces the risk of ileus (risk ratio (RR) 0.37, 95% CI 0.15 to 0.87; 4 studies, 273 participants), time to first defaecation/bowel movement (mean difference (MD) –7.92 hours, 95% CI –12.71 to –3.13; 12 studies, 684 participants), risk of postoperative nausea (overall, i.e. 0 up to 72 hours) (RR 0.78, 95% CI 0.67 to 0.91; 35 studies, 1903 participants), and opioid consumption (overall) (MD –4.52 mg morphine equivalents, 95% CI –6.25 to –2.79; 40 studies, 2201 participants); quality of evidence was very low for all these outcomes.

The effect of IV lidocaine on adverse effects compared to placebo treatment is uncertain, as only a small number of studies systematically analysed the occurrence of adverse effects (very low-quality evidence).

#### IV Lidocaine compared to TEA

The effects of IV lidocaine compared with TEA are unclear (pain at 24 hours (MD 1.51, 95% CI –0.29 to 3.32; 2 studies, 102 participants), pain at 48 hours (MD 0.98, 95% CI –1.19 to 3.16; 2 studies, 102 participants), time to first bowel movement (MD –1.66, 95% CI –10.88 to 7.56; 2 studies, 102 participants); all very low-quality evidence). The risk for ileus and for postoperative nausea (overall) is also unclear, as only one small trial assessed these outcomes (very low-quality evidence). No trial assessed the outcomes, 'pain at early time points' and 'opioid consumption (overall)'. The effect of IV lidocaine on adverse effects compared to TEA is uncertain (very low-quality evidence).

#### **Authors' conclusions**

We are uncertain whether IV perioperative lidocaine, when compared to placebo or no treatment, has a beneficial impact on pain scores in the early postoperative phase, and on gastrointestinal recovery, postoperative nausea, and opioid consumption. The quality of evidence was limited due to inconsistency, imprecision, and study quality. Lidocaine probably has no clinically relevant effect on pain scores later than 24 hours. Few studies have systematically assessed the incidence of adverse effects. There is a lack of evidence about the effects of IV lidocaine compared with epidural anaesthesia in terms of the optimal dose and timing (including the duration) of the administration. We identified three ongoing studies, and 18 studies are awaiting classification; the results of the review may change when these studies are published and included in the review.

# PLAIN LANGUAGE SUMMARY

# Intravenous infusion of lidocaine starting at the time of surgery for reduction of pain and improvement of recovery after surgery

#### Background

The most common problems immediately following surgery under general anaesthesia are pain, nausea and vomiting, delirium and slow or no movement of food through the digestive system. Opioid medications given to reduce postoperative pain may also be associated with nausea and constipation, also preventing a smooth recovery. It is of interest for patients and clinicians to reduce or prevent these complications leading to an early recovery so that patients can leave hospital earlier. One option for pain relief after surgery is epidural analgesia, where an opioid or local anaesthetic such as lidocaine is injected into the space surrounding the spinal cord. Not all patients may be suited to epidural analgesia, and so additional options such as intravenous non-opioid analgesic medications that enable a rapid recovery are required. The aim of this review was to assess the benefits and risks of intravenous infusion of lidocaine in patients undergoing various surgical procedures. Lidocaine is a medication used to numb tissue in a specific area.

#### Study characteristics

This review was published in 2015, and updated in 2017. We found 68 randomized controlled studies (RCTs), (clinical studies where people are randomly put into one of two or more treatment groups), with results from a total of 4525 participants. RCTs are used because they provide the most reliable evidence.

Intravenous lidocaine was compared with placebo or standard care in 66 of the studies, and with thoracic (chest area of spine) epidural analgesia in two studies. (A placebo is an inactive substance or procedure given to a participant in a medical trial to compare its effects with those of a real drug or other intervention). Lidocaine infusion was started during the surgery, before the first cut, and continued to at least the end of surgery. The included studies were moderately well conducted.

#### **Key results**

We are uncertain whether lidocaine infusion reduces pain, one to four hours after surgery when compared to placebo or usual care (29 studies, over 1600 participants). There was probably no difference in pain at 24 hours (33 studies, 1847 participants) and at 48 hours (24 studies, 1404 participants) between participants in the lidocaine and the placebo group. We are uncertain whether lidocaine infusion improves recovery of bowel function, with a reduction in the time to first defaecation or bowel movements (12 studies, 684 participants), and reduced risk of stopping the passage of food in the gut (4 studies, 273 participants). We are also uncertain whether lidocaine reduces postoperative nausea (35 studies, 1903 participants), and the requirement for opioids for pain relief (40 studies, 2201 participants). Only a limited number of studies systematically analysed adverse effects of intravenous lidocaine infusion. The side effects of intravenous lidocaine were unclear.

In the two studies that investigated intravenous lidocaine compared to epidural analgesia (102 participants), the effect on pain at 24 and 48 hours, and on the time to first bowel movement, remains unclear. The effect of lidocaine on the risk of stopping the passage of food in the gut and for postoperative nausea is also unclear, as only one small trial assessed these outcomes. Neither study investigated the effect on pain immediately after surgery, or on opioid consumption. Both studies looked at adverse effects associated with lidocaine, but the effect is uncertain.

#### **Quality of the evidence**

We rated the quality of evidence for most outcomes as very low. This was because of inconsistent findings across studies and the fact that the evidence came from small studies that were of moderate design quality or a limited number of studies. The quality of the evidence for minimal or no effect on pain at 24 and 48 hours was moderate quality. The studies involved a variety of surgical procedures. The dose of lidocaine used, and how long it was delivered for after the end of surgery, also varied between studies.