Effect of the Perioperative Intravenous Lidocaine Infusion of 1.25 mg/kgBW/H on the Bowel Sound Recovery and Pain Intensity after Laparoscopic Cholecystectomy

Syafri Kamsul Arif, Yongki Rawung, A. Muh Takdir Musba, and A. Husni Tanra

Abstract—The purpose of this research is to assess the effect of perioperative intravenous lidocaine infusion of 1.25mg/kgBW/H on the bowel sounds recovery and pain intensity after laparoscopy cholecystectomy. The research used the experimental method, i.e. 42 patients who met the inclusive criteria and who would undergo laparoscopic cholecystectomy surgery under the general anesthesia, using the randomized double blind technique, and then were divided into two groups. The Treatment Group (KL, n = 21) received perioperative intravenous lidocaine infusion of 1.25 mg/kg/H, while the control group (KN, n = 21) received the perioperative infusion of placebo of 0.9 NaCl. After the surgery, the assessments of the bowel sounds recovery time, the NRS scores at 2h, 6h, 12h, and 24h and the fentanyl requirement within 24 hours with PCA were conducted. The data were analyzed using the Chi square test, independent t-test, and Mann-Whitney test with p<0.05 to reveal the statistical significance. The research results indicated that the time of the bowel sounds recovery in KL group was 147.14 ± 24.928 minutes, faster than in KN group it was 322.86 ± 34.079 minutes (p=0.000). The postoperative NRS score at 2h and 6h in KL group was lower than the KN group with p=0.000, but there was no significant difference in the postoperative NRS score at 12h and 24h in both groups (p>0.05). The postoperative fentanyl requirement was lower in KL group (114.29 ± 31.196 mcg) compared to the KN group (258.33 ± 27.764) mcg with p=0.000. The Perioperative intravenous lidocaine infusion of 1.25 mg/kgBW/H could speed up the bowel sounds recovery and reduce the pain intensity after laparoscopic cholecystectomy.

Index Terms—Bowel Sounds Recovery, Laparoscopic Cholecystectomy, Lidocaine, Pain Intensity

I. INTRODUCTION

Acute pain after surgery and acute postoperative pain and postoperative ileus (IPO) usually occur in patients after abdominal surgery. Analgesic opioid is effective in reducing postoperative pain but can cause undesirable side effects, such as respiratory depression, nausea, vomiting, somnolence and IPO. One of drugs that has promised in providing analgesia, before, during, and after a surgical procedure is lidocaine (Grady et al., 2012).

Lidocaine has the effect of analgesia, antihyperalgesia, and anti-inflammation after intravenous administration (Deeb et al., 2013). Recent research has shown that intravenous lidocaine which is given as a single dose or as a continuous infusion is beneficial in restoring intestinal motility postoperatively and has a biochemical effect on the pain process (Grady et al., 2012). The use of intravenous lidocaine after major abdominal surgery has also shown a less morphine effect (Martin et al., 2008).

Intravenous lidocaine infusion (ILIV) has been included in the fast-track surgery protocol in which epidural placement cannot be performed or is contraindicated. Trials have used ILIV at different doses in bolus doses and continuous infusion from the beginning to the end of the administration of lidocaine infusions at different times. The completion time for ILIV administration is the most important aspect of the regimen because it has major implications for postoperative monitoring and management. Some studies stop ILIV immediately after surgery, while others continue to do it after surgery for various periods of time. Continuing ILIV to recovery rooms and surgical wards is not practical and not optimal in many institutions because of the lack of available monitoring. The lack of a final time setting for using ILIV causes uncertainty when using ILIV. Previous metaanalysis has shown a beneficial effect from ILIV, but there is no definite completion time provision of ILIV (Khan et al., 2016).

Perioperative continuous intravenous lidocaine infusion has been used as a fast-track protocol to prevent and reduce postoperative complications and accelerate postoperative recovery. The final metaanalysis conducted by Kranke et al. (2015), and also Ventham et al. (2015), showed that bolus of lidocaine 1.5 mg / kgBB / IV before surgical incision and was followed by continuous intravenous lidocaine infusion during surgery with varying doses between 1 , 5 mg / kg up to 3 mg / kg have given effect to recovery of bowel function more quickly and reduce postoperative pain and shorten the hospital stay.

Previous research by Lauwick et al. (2008), showed that administration of perioperative lidocaine infusion reduced the need for postoperative fentanyl and reduced the need for 10% desflurane during surgery in patients undergoing laparoscopic cholecystectomy. Likewise, research conducted by Yang et al. (2013), showed the efficacy of intraperitoneal and intravenous lidocaine administration in reducing post-laparoscopic pain in cholecystectomy.

Baral et al. (2010) conducted a research of 60 patients who underwent upper abdominal surgery, in which 30...
patients were given bolus of 2% lidocaine 1.5 mg / kgBW / IV followed by ILIV 1.5 mg / kgBW / hour and 30 other patients are given normal saline. The lidocaine infusion begins 30 minutes before the skin incision and is stopped 1 hour after surgery. The results showed that the pain intensity and postoperative analgesic needs were significantly lower in the lidocaine group. Deeb et al (2013), in their research revealed that perioperative intravenous lidocaine infusion for pediatric patients undergoing major abdominal surgery can reduce neuroendocrine response due to surgical stress and has resulted faster recovery of bowel function and reduced the need for postoperative opioids compared with placebo.

However, Choi et al (2012), in their research showed that intravenous administration of 1.5 mg/kgBB of lidocaine 30 minutes before a surgical incision followed by a continuous infusion of 1.5 mg/kgBW/h lidocaine during breast surgery reduced the need for sevoflurane by 5%. But there was no significant effect of intravenous lidocaine infusion on recovery of bowel function, intensity of postoperative pain, analgesic needs, and length of hospital stay.

The research by Ivan (2015), showed that the use of 1.25 mg/kgBB/syringe pump intravenous lidocaine as a treatment for postoperative laparotomy pain relief can reduce opioid use.

From the description of the background and some of the above researches, there has been no research on the effect of ILIV 1.25 mg/kgBW/hour perioperative administration on recovery of bowel sounds and the intensity of pain after laparoscopic surgery for cholecystectomy. This research intended to assess the effect of perioperative 1.25mg/kgBW/hour intravenous lidocaine infusion on recovery of bowel sounds and the intensity of pain after laparoscopic surgery for cholecystectomy.

II. MATERIAL AND METHOD
A. Location and Research Period
The research was conducted at Dr. Wahidin Sudirohusodo Hospital Makassar, Unhas Teaching Hospital and network hospitals in Makassar. The research was conducted from March 2017 until the sample was fulfilled.

B. Design and Research Variable
This research used a randomized double blind clinical trial. The research variables consisted of: independent variables (intravenous lidocaine infusion, 0.9% intravenous NaCl infusion), dependent variables (bowel noise recovery time, postoperative NRS score, postoperative fentanyl need), variable between (laparoscopic cholecystectomy surgery), and control variables (Genetics, Age, Body Mass Index, ASA PS, preoperative bowel noise frequency, pre-operative NRS score, chronic opioid use, length of operation).

C. Population and Sample
The population of this research was patients who would undergo laparoscopic cholecystectomy under general anesthesia at Dr. Wahidin Sudirohusodo Hospital Makassar, Hasanuddin University Hospital, and their network. The research samples were all affordable populations that met the inclusion criteria and agreed to participate in the research taken by the consecutive sampling method. The entire samples used were 42 study samples.

D. Data Collection Method
The samples were divided randomly into two groups. In both groups, the patients were given the same analgesic premedication: fentanyl 2 μg/kgBB/IV. Induction using propofol 1.5-2 mg/kgBW/IV. Before intubation, atracurium 0.5 mg/kgBW/IV was given, wait for the onset of action three minutes. The treatment group was given bolus lidocaine 1.5 mg/kgBW/IV one minute before endotracheal intubation and followed by ILIV 1.25 mg/kgBW/hour syringe pump until two hours after surgery. Meanwhile, the control group was given 1.5 mg/ kgBW/IV bolus of lidocaine one minute before endotracheal intubation and followed by continuous intravenous 0.9% placebo NaCl via a syringe pump for up to 2 hours after surgery. During surgery, anesthesia maintenance was using volatile isoflurane anesthetic 1-1.5 vol% MAC, O2: Water with a ratio of 50%: 50%. After surgery the patient was extubated and transferred to the recovery room. During postoperative assessment of bowel noise recovery time, which was assessed every 30 minutes by auscultation using the Littman stethoscope in the umbilicus region until it heard the frequency of bowel sounds> 7 times/minute and then the time was recorded. Assessment of pain intensity was based on NRS scores at 2 hours, 6 hours, 12 hours, 24 hours after surgery and fentanyl needs within 24 hours after surgery.

E. Technical Data Analysis
The collected data is processed using the SPSS 17 for Windows Program. The results of processing data are displayed in the form of tables, graphs and narratives. Statistical analysis uses Chi square test for categorical variables, Independent T test for parametric numerical variables, and Mann-Whitney U test for non-parametric numerical variables. The used significance level is 5%, meaning that if p <0.05, the difference is stated to be statistically significant, with a 95% confidence interval.

III. RESULT
A randomized double blind clinical trial had been conducted to assess the effect of perioperative 1.25 mg/kgBW/hour perioperative infusion of intravenous lidocaine on the recovery of bowel sounds and the intensity of pain after laparoscopic surgery for cholecystectomy. This research was conducted at Dr. Wahidin Sudirohusodo Hospital Makassar, Unhas Teaching Hospital and network hospitals in Makassar area. The research was conducted from March 2017 until the sample was fulfilled.

The sample population was all subjects with class 1-2 ASA PS who underwent laparoscopic cholecystectomy under general anesthesia. Samples were divided into two groups: the first group received ILIV 1.25 mg/kgBW/perioperative hour (hereinafter referred to as KL group with n = 21), and the second group received 0.9% NaCl intravenous NaCl infusion (hereinafter referred to as KN group with n = 21). On gender distribution, ASA PS was given in both groups so that data could be declared statistically homogeneous (Table I).
Comparison of bowel noise recovery time of the two groups showed that there were significant differences (p <0.05) in the comparison of bowel noise recovery time of the two groups. Comparison of bowel noise recovery time of the two groups was tested using the Independent T test (Table II).

TABLE II: COMPARISON OF TIME RECOVERY OF BOTH GROUPS’ BOWEL SOUNDS

<table>
<thead>
<tr>
<th>Variable</th>
<th>Groups</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time Recovery of Bowel Sounds</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(minutes)</td>
<td>KL</td>
<td>21</td>
<td>147,14</td>
<td>24,928</td>
<td></td>
</tr>
<tr>
<td></td>
<td>KN</td>
<td>21</td>
<td>322,86</td>
<td>34,079</td>
<td></td>
</tr>
</tbody>
</table>

NRS Comparison of the two groups during break showed that KL group and KN group were significantly different at the time of observation 2 hours postoperatively and 6 hours postoperatively, whereas the observation time at 12 hours and 24 hours postoperative were not statistically different (Table III).

<table>
<thead>
<tr>
<th>NRS Break</th>
<th>KL (n=21)</th>
<th>KN (n=21)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2 hours after surgery</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>p</td>
</tr>
<tr>
<td></td>
<td>0.00</td>
<td>0.00</td>
<td>1.76</td>
<td>0.436</td>
<td>0.000*</td>
</tr>
<tr>
<td>6 hours after surgery</td>
<td>1.00</td>
<td>0.00</td>
<td>2.48</td>
<td>0.512</td>
<td>0.000*</td>
</tr>
<tr>
<td>12 hours after surgery</td>
<td>1.90</td>
<td>0.301</td>
<td>2.00</td>
<td>0.000</td>
<td>0.152</td>
</tr>
<tr>
<td>24 hours after surgery</td>
<td>1.38</td>
<td>0.498</td>
<td>1.38</td>
<td>0.498</td>
<td>1.000</td>
</tr>
</tbody>
</table>

NRS comparison of the two groups’ movements showed that KL group and KN group looked statistically different at the time of observation 2 hours and 6 hours after surgery, while the NRS moves at 12 hours and 24 hours postoperatively were not different statistically. (Table IV).

Comparison of fentanyl needs in 24 hours postoperatively in both groups showed that there was a significant difference (p <0.05) in the comparison of fentanyl needs within 24 hours postoperatively in both groups. For comparison of fentanyl needs within 24 hours after surgery, the two groups used the Independent T test where (p <0.05) was stated as meaningful (Table V).

IV. ANALYSIS

This research showed that the recovery time of bowel sounds in the KL group (147.14 ± 24,928) minutes, was faster than the KN group (322.86 ± 34,079) minutes with p = 0.000. Pain intensity comparisons between the two groups showed significant differences in NRS scores 2 hours and 6 hours postoperatively, where there was a decrease in pain intensity in the KL group compared to the KN group (p = 0.000), but there were no significant differences in the 12 hour NRS score and 24 postoperative hours in both groups (p> 0.05). The need for postoperative fentanyl was less in the KL group (114.29 ± 31,196) mcg compared to the KN group (258.33 ± 27,764) mcg with p = 0.000. The administration of intravenous lidocaine infusion of 1.25 mg/kg/hour per hour can accelerate recovery of bowel sounds and reduce the intensity of pain after laparoscopic surgery for cholecystectomy.

The research was conducted on 42 patients who underwent laparoscopic cholecystectomy under general anesthesia at Dr. Wahidin Sudirohusodo Hospital Makassar and its network hospitals. The sample characteristics of the two groups were included gender, ASA PS, age, BMI, frequency of preoperative bowel sounds and length of operation. For sex distribution and ASA PS were analyzed using Chi square test, while age, BMI, preoperative bowel noise frequency and duration of operation were analyzed using the Independent T test. From the results of this test, there were no significant differences (p <0.05) so that the characteristics of 42 research samples were declared homogeneous. These results are in line with the research conducted by Lauwick et al (2008), who assessed the effects of lidocaine infusion during laparoscopic surgery for cholecystectomy on fentanyl needs during surgery and after surgery in postanesthesia care unit (PACU). They concluded that there were no significant differences in the sample characteristics of the two groups. Similarly, the research of Deeb et al (2013), investigated the effect of perioperative lidocaine infusion on hormonal response, bowel function and length of hospital stay after major abdominal surgery in pediatric patients, stating that the characteristics of age, sex, height, weight, and operating time was statistically homogeneous.

Comparison of fentanyl needs in 24 hours postoperatively in both groups showed that there was a significant difference (p <0.05) in the comparison of fentanyl needs within 24 hours postoperatively in both groups. For comparison of fentanyl needs within 24 hours after surgery, the two groups used the Independent T test where (p <0.05) was stated as meaningful (Table V).

TABLE IV: COMPARISON OF BOTH GROUPS’ NRS MOVES

<table>
<thead>
<tr>
<th>NRS Moves</th>
<th>KL (n=20)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2 hours after surgery</td>
<td>Mean</td>
<td>SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.00</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 hours after surgery</td>
<td>2.00</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 hours after surgery</td>
<td>2.905</td>
<td>0.301</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 hours after surgery</td>
<td>2.286</td>
<td>0.717</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TABLE V: COMPARISON OF FENTANYL NEEDS IN 24 HOURS AFTER SURGERY FOR BOTH GROUPS

<table>
<thead>
<tr>
<th>Fentanyl Needs in 24 Hours (mcg)</th>
<th>KL</th>
<th>KN</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>21</td>
<td>21</td>
<td></td>
<td>114.29</td>
<td>31,196</td>
<td>0.000*</td>
</tr>
<tr>
<td></td>
<td>21</td>
<td>258.33</td>
<td>27,764</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
administration of perioperative lidocaine infusion reduced the need for postoperative fatigue and reduced 10% of desflurane requirements during surgery in patients undergoing LK. Whereas Choi et al (2012), in their research showed that administration of bolus lidocaine 1.5 mg/kgBW/IV 30 minutes before surgical incision followed by continuous infusion of 1.5 mg/kgBW/h lidocaine during breast surgery reduced the need for sevoflurane by 5%.

The Deeb et al (2013) research showed that perioperative administration of intravenous lidocaine infusion in pediatric patients undergoing major abdominal surgery can reduce neuroendocrine response due to surgical stress and result faster bowel function recovery and decrease postoperative opioid requirements compared with placebo.

In this research, the values of NRS Rest and NRS Moves on 2 hours and 6 hours postoperative in the KL group were lower than the KN group and significantly different. While the values of NRS Rest and NRS Moves on 12 hours and 24 hours postoperatively in both groups, there was no difference that was statistically significant. Previous research by Lauwick et al (2008) showed that the VRS (Verbal Rating Scale) scores in the Lidocaine group and the Control group were the same in the first 24 hours postoperatively. Furthermore, the research by Cho et al (2014) also showed that there was no significant difference in the Visual Analogue Scale (VAS) score in the first 24 hours postoperatively in the treatment and control groups.

About 90% of intravenous lidocaine will experience hepatic metabolism, and has a half-life of 1.5-2 hours. The analgesic effect of lidocaine on surgical trauma is caused by blockade of nerve transmission at the site of injury, blunting the neurogenic response, and the presence of intrinsic systemic anti-inflammatory properties. The ability of lidocaine analgesia can persist even though its level in plasma decreases, in accordance with the theory of nerve conduction blocking (Stoelting, 2015). This might explain why the NRS value on 2 hours and 6 hours postoperatively in the KL group is lower than the KN group.

In this research, the need for fentanyl in the 24 hours postoperatively in the KL group was (114.29 ± 31,196) micrograms. This dose is considered small and far from toxic. This dose is in accordance with the theory of nerve conduction blocking (Stoelting, 2015). This microgram dose is considered small and far from toxic.

Postoperative pain reduction and morphine requirements, with the prevention of central hyperalgesia, have been observed in patients undergoing abdominal surgery when intravenous lidocaine (bolus 1.5 mg/kg, followed by infusion of 1.5 mg/kg/hr) was given 50 minutes before surgical incision and maintenance up to 60 minutes after skin closure, reduce the need for morphine after surgery.

In a research by Grady et al (2012), the effects of intravenous lidocaine on postoperative pain and return of bowel function were studied. The research concluded that perioperative ILIV 1.25 mg/kgBW/hour can accelerate recovery of bowel sounds after laparoscopic surgery for cholecystectomy. Provision of ILIV 1.25 mg/kgBW/hour perioperatively, can reduce the intensity of pain after laparoscopic surgery cholecystectomy. Moreover, the researchers suggest that ILIV 1.25 mg/kgBW/hour perioperative administration can be used as a general anesthetic supplement during laparoscopic cholecystectomy to speed up recovery of bowel function and reduce postoperative opioid requirements. In addition, further research is needed to assess the effect of perioperative ILIV administration on bowel function which includes the first time of flatus and the time of defecation the first time after abdominal surgery. Also, it is needed to measure the concentration of lidocaine in plasma which correlates with recovery of bowel sounds after surgery.

V. CONCLUSION AND SUGGESTION

The researchers concluded that perioperative ILIV 1.25 mg/kgBW/hour can accelerate recovery of bowel sounds after laparoscopic surgery for cholecystectomy. Provision of ILIV 1.25 mg/kgBW/hour perioperatively, can reduce the intensity of pain after laparoscopic surgery cholecystectomy. Moreover, the researchers suggest that ILIV 1.25 mg/kgBW/hour perioperative administration can be used as a general anesthetic supplement during laparoscopic cholecystectomy to speed up recovery of bowel function and reduce postoperative opioid requirements. In addition, further research is needed to assess the effect of perioperative ILIV administration on bowel function which includes the first time of flatus and the time of defecation the first time after abdominal surgery. Also, it is needed to measure the concentration of lidocaine in plasma which correlates with recovery of bowel sounds after surgery.

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