1 Comparison of the Effect of Intraoperative 1 mg/kg/h and 2 mg/kg/h IV Lidocaine

Infusion on Postoperative Pain and Nausea-Vomiting in Laparoscopic Gastric

3 Bypass Surgery

- Objective: To relieve postoperative pain and nausea and vomiting, various drugs and methods, including intraoperative IV lidocaine infusion in different surgeries. However, the exact same dose has not yet been determined. The purpose of this study was to evaluate and compare the effect of intraoperative 1 mg/kg/h and 2 mg/kg/h IV lidocaine infusion on
- 8 postoperative pain and nausea-vomiting in laparoscopic gastric bypass surgery.
- 9 Methods: This clinical trial study was performed on patients undergoing laparoscopic
- gastric bypass surgery in Rasoul-e-Akram Hospital, Iran. Patients were randomly assigned into two groups (I ma/kg/h lidocaine) and (2 mg/kg/h lidocaine). Postoperative pain and
- 11 into two groups (1 mg/kg/h lidocaine) and (2 mg/kg/h lidocaine). Postoperative pain and
- 12 nausea and vomiting were evaluated at times 0, 30 min, 1 h, 6 h, 12 h and 24 h after surgery.
- 13 Data was analyzed using statistical tests and SPSS 22.
- 14 **Results**: There was no significant difference in the effect of intraoperative 1 mg/kg/h and 2
- 15 mg/kg/h IV lidocaine infusion on static and dynamic pain and nausea-vomiting, agitation,
- 16 systolic BP, diastolic BP, pulse rate and postoperative administration of pethidine in
- 17 *laparoscopic gastric bypass* (P>0.05).
- 18 Conclusion: Based on results of this study, administration of low dose lidocaine (1 mg/kg/h)
- 19 can be considered as an appropriate dose of IV lidocaine infusion in order to control
- 20 postoperative pain and nausea and vomiting in laparoscopic gastric bypass surgery.
- 21 **Keywords**: lidocaine, pain, nausea-vomiting, gastric bypass

22 **1. Introduction**

- 23 In post-operative time, it is important to control and reduce postoperative pain and nausea-
- vomiting (1). Different drugs and methods are used to relieve postoperative pain and nausea
- and vomiting in different surgeries (2). One of these methods, which has been studied on
- 26 numerous occasions, is intraoperative intravenous (IV) lidocaine infusion undergone in a
- wide range of surgical procedures such as laparotomy, laparoscopy, gynecological surgery,
- 28 orthopedics, etc., and has a positive effect in most cases in reducing postoperative pain and
- 29 nausea-vomiting (3). Considering the pharmacological effects of IV lidocaine, which has
- 30 both anti-inflammatory and analgesic effects (protein receptor inhibitor G and NMDA),
- 31 lidocaine has been used to relieve postoperative pain (4). According to numerous studies on
- various surgical procedures, intraoperative IV lidocaine infusion has been shown to reduce
- postoperative pain and nausea and vomiting (5-14). Although the exact same dosage is still
- unknown, the conducted studies have used 1-2 mg/kg/h dosages. In a double-blind clinical
- trial on 41 patients undergoing microdiscectomy in two groups receiving 1.5 mg/kg/h lidocaine
- 36 infusion and normal saline infusion as placebo, Kim et al (2014) concluded that fentanyl

37 administration and postoperative pain intensity were significantly lower in the lidocaine 38 group except 48 hours after surgery. Total fentanyl administration, hospital stay and 39 satisfaction were significantly lower in lidocaine group than placebo group. Finally, 40 intraoperative systemic infusion of lidocaine reduces pain level during microdiscectomy 41 surgery (6). According to the studies, this study tends to evaluate and compare the effect of 42 intraoperative 1 mg/kg/h and 2 mg/kg/h IV lidocaine infusion on postoperative pain and 43 nausea-vomiting in laparoscopic gastric bypass to determine a more suitable and effective 44 dosage.

2. Materials and Methods

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This study was a randomized clinical trial. The studied population included elective patients who were candidate for laparoscopic gastric bypass referred to Rasoul-e-Akram Hospital since June 2014 to March 2015. Sampling method was convenient sampling. Sample size was determined using Cohen table with 80% statistical power, 0.05 alpha and 0.9 accuracy (21 subjects in each group). This study was a randomized clinical trial. Block randomization was done in quadrilateral blocks. This study was performed on 42 elective patients who were candidate for laparoscopic gastric bypass referred to Rasoul-e-Akram Hospital since June 2014 to March 2015. After obtaining consent and qualifying patients for inclusion and exclusion, 41 patients were assigned into 2 groups of 21 patients (A and B) in 4 blocks. After entering the operating room, standardized monitoring (ECG-POM-NIBP-Etco2) and insertion of two 20G IV catheters and 3 cc/kg crystalloid serum infusion were performed for all patients. Then, 3 mcg/kg fentanyl based on TBW and 20 mcg/kg midazolam based on TBW were administered as premedication for all patients. For induction, all patients received 5 mg/kg thiopental sodium based on TBW followed by 0.2 mg/kg atracurium based on IBW and 1.5 mcg/kg bolus lidocaine based on IBW for general anesthesia. After intubation of the patients, all of them received 1.2 mac isoflurane followed by 0.03 mg/kg atracurium every 30 minutes and 50 mcg fentanyl every 40 minutes as maintenance. From the beginning of surgery, group A received 1 mg/kg/h IV lidocaine infusion and group B received 2 mg/kg/h IV lidocaine infusion by the pump until the end of surgery for a maximum of 4 hours. After the end of surgery and discontinuation of all drugs, patients were placed in reserve by 0.04 mg/kg nisosigine and 0.02 mg/kg atropine and extubation was done; patients were transferred to PACU (recovery). The time to enter recovery was set at t=0; for 24 h, patients were monitored for pain based on numerical rating score (0-10), static and dynamic nausea-

- 69 vomiting, blood pressure (BP), heart rate and agitation in predicted times in the recovery or
- surgery wards.
- Finally, data was analyzed by SPSS software version 22. In the analytical step, Kolmogorov-
- 72 Sminov test was used for determining normality of quantitative values. Then, independent T-
- 73 test or Mann-Whitney U-test were used for comparing the quantitative variables of two
- 74 groups A and B. Chi-square test (Z) was used to compare the qualitative variables. Repeated
- 75 measure ANOVA or Friedman test was used to check and compare the changes.

3. Results

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- 77 In this study, 42 patients who were referred to surgery ward of the Rasoul-e-Akram Hospital
- in 2016 and underwent laparoscopic elective gastric bypass were enrolled in the study. In
- group A, 21 patients (50%) received intraoperative 1 mg/kg/h IV lidocaine infusion; in group
- 80 B, 21 patients (50%) received intraoperative 2 mg/kg/h IV lidocaine infusion.
- The patients aged 18-49 years (36.15 ± 6.88) ; 18 patients (42.9%) were male and 24 patients
- 82 (57.1%) were female. BMI was $38-46 \text{ Kg/m}^2$ (42.23±2.22 Kg/m²). Ten patients (23.8%)
- were in Class ASA 1, 25 patients (59.5%) were in Class ASA 2 and 7 patients (16.7%) were
- in Class ASA 3.
- 85 According to the patients, 16 people (38.1%) had a history of hypertension. None of the
- patients had a history of heart disease. Four patients (9.5%) had a history of diabetes, 9
- patients (21.4%) had a history of fatty liver disease, and 8 (19%) had a history of other
- 88 diseases.

- In terms of the history of previous drugs, 5 patients (11.9%) took cigarette, 4 patients (9.5%)
- 90 took loratadine, 3 (7.1%) took metoral, 4 (9.5%) took metformin, 2 (4.8%) took
- 91 levothyroxine, 1 (2.4%) took loratadine and levothyroxine, 4 (9.5%) took loratadine and
- 92 metformin, 1 (2.4%) took atenolol and levothyroxine, 2 (4.8%) took metformin and
- 93 glibenclamide, 2 (4.8%) took metformin and metoral, and 1 (2.4%) took loratadine and
- 94 metformin and hydroxin. Descriptive characteristics and comparison of age and gender of
- patients undergoing elective laparoscopic gastric bypass in two groups A and B are
- 96 summarized in Table 1.

Table 1: Descriptive characteristics and comparison of age and gender of patients undergoing elective laparoscopic gastric bypass in two groups A and B

| Characteristic | Gro | P-Value | |
|-------------------------|------------|-----------|---------|
| Characteristic | A | В | r-value |
| Age (year) Mean ± SD | 34.48±5.34 | 37.9±7.96 | 0.11 |
| Gender | | | 1 |

| Male | 9 (42.9%) | 9 (42.9%) | |
|---------------|------------|------------|--|
| Female | 12 (57.1%) | 12 (57.1%) | |

99 According to Table 1, there is no significant difference in age and gender of patients

undergoing elective laparoscopic gastric bypass between two groups A and B (P>0.05).

3.1. Determining and Comparing Pain in Two Groups A and B Based on Numerical Rating

Score at Times 0, 30 min, 1 h, 6 h, 12 h and 24 h after Laparoscopic Gastric Bypass

In order to compare the pain level in 2 groups A and B based on numerical rating score at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass, the Mann-Whitney U-test was used. Friedman test was used for comparison at times 0, 30 min, 1 h, 6 h, 12 h and 24 h after laparoscopic gastric bypass in each of the two groups A and B (separately). Descriptive features and comparison of pain levels are summarized in Table 2.

Table 2: descriptive features and comparison of pain level in two groups A and B based on numerical rating score at times 0, 30 min, 1 h, 6 h, 12 h and 24 h after laparoscopic gastric bypass

| Time | Group | | Test statistic | p-value |
|------------------|--------------------------|--------------------------|----------------|---------|
| 1 iiie | A (mean \pm SD) | $B (mean \pm SD)$ | Test statistic | p-value |
| 0 | 1.67 ± 1.01 | 1.71 ± 0.78 | 0.014 | 0.989 |
| 30 min | 2.67 ± 0.73 | 2.67 ± 0.65 | 0.139 | 0.889 |
| 1 h | 3.29 ± 0.84 | 3.19 ± 0.98 | 0.346 | 0.729 |
| <mark>6 h</mark> | 5.71 ± 0.9 | 5.57 ± 1.2 | 0.898 | 0.369 |
| 12 h | 4.86 ± 0.96 | 4.71 ± 0.95 | 0.404 | 0.687 |
| 24 h | 3.95 ± 1.39 | 3.81 ± 1.03 | 0.199 | 0.842 |
| | $P < 0.001, X^2 = 94.18$ | $P < 0.001, X^2 = 88.29$ | - | |

Based on the results of Table 2, there was no significant difference between pain levels of patients in 2 groups A and B based on numerical rating score at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass (P>0.05). There was a significant difference between pain levels of patients based on numerical rating score at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass in group A (P<0.001, X^2 =94.18). There was a significant difference between pain levels of patients based on numerical rating score at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass in group B (P<0.001, X^2 =88.29).

3.2. Determining and Comparing Static Nausea-Vomiting in Two Groups A and B at Times 0, 30 min, 1 h, 6 h, 12 h and 24 h after Laparoscopic Gastric Bypass

In order to compare static nausea-vomiting levels in 2 groups A and B after laparoscopic gastric bypass, Z-test was used. Friedman test was used for comparison at times 0, 30 min, 1 h, 6 h, 12 h and 24 h after laparoscopic gastric bypass in each of the two groups A and B (separately). Frequency values and nausea-vomiting comparison are summarized in Table 3.

Table 3: descriptive features and comparison of static nausea-vomiting levels in two groups A and B after laparoscopic gastric bypass

| Time | Group | | Tost statistic | |
|------------------|------------------|----------------------|----------------|---------|
| 1 IIIIe | A (N, %) | B (N, %)) | Test statistic | p-value |
| 0 | 2 (9.5%) | 5 (23.8%) | 1.26 | 0.896 |
| 30 min | 4 (19%) | 3 (14.3%) | 0.4 | 0.655 |
| 1 h | 0 (0%) | 1 (4.8%) | 0.22 | 0.587 |
| <mark>6 h</mark> | 0 (0%) | 0 (0%) | 0 | 0.5 |
| 12 h | 0 (0%) | 0 (0%) | 0 | 0.5 |
| 24 h | 0 (0%) | 0 (0%) | 0 | 0.5 |
| | $P=0.01, X^2=15$ | $P=0.008, X^2=15.73$ | - | |

Based on the results of Table 3, there was no significant difference between static nauseavomiting levels of patients in 2 groups A and B at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass (P>0.05). There was a significant difference between static nausea-vomiting levels of patients at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass in group A (P=0.01, X²=15). There was a significant difference between static nausea-vomiting levels of patients at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass in group B (P=0.008, X²=15.73).

3.3. Determining and Comparing Dynamic Nausea-Vomiting in Two Groups A and B at Times 0, 30 min, 1 h, 6 h, 12 h and 24 h after Laparoscopic Gastric Bypass

In order to compare dynamic nausea-vomiting levels in 2 groups A and B after laparoscopic gastric bypass, Z-test was used. Friedman test was used for comparison at times 0, 30 min, 1 h, 6 h, 12 h and 24 h after laparoscopic gastric bypass in each of the two groups A and B (separately). Frequency values and nausea-vomiting comparison are summarized in Table 4.

Table 4: descriptive features and comparison of dynamic nausea-vomiting levels in two groups A and B after laparoscopic gastric bypass

| Times | Group | | Tost statistic | |
|------------------|-------------------|----------------------|----------------|---------|
| Time | A (N, %) | B (N, %)) | Test statistic | p-value |
| 0 | 8 (38.1%) | 6 (28.6%) | 0.65 | 0.742 |
| 30 min | 14 (66.7%) | 11 (52.4%) | 0.95 | 0.828 |
| 1 h | 5 (23.8%) | 5 (23.8%) | 0 | 0.5 |
| <mark>6 h</mark> | 0 (0%) | 0 (0%) | 0 | 0.5 |
| 12 h | 0 (0%) | 0 (0%) | 0 | 0.5 |
| 24 h | 0 (0%) | 0 (0%) | 0 | 0.5 |
| | $P=0.001, X^2=45$ | $P=0.001, X^2=33.77$ | | |

Based on the results of Table 4, there was no significant difference between dynamic nauseavomiting levels of patients in 2 groups A and B at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass (P>0.05). There was a significant difference between dynamic nausea-vomiting levels of patients at times 0, 30 min, 1 h, 6 h, 12 h, and 24 h after laparoscopic gastric bypass in group A (P=0.001, $X^2=45$). There was a significant difference

between dynamic nausea-vomiting levels of patients at times 0, 30 min, 1 h, 6 h, 12 h, and 24

h after laparoscopic gastric bypass in group B (P=0.001, $X^2=33.77$).

3.4. Determining and Comparing Agitation in Two Groups A and B at Times 0, 30 min and 1 h

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In order to compare agitation levels in 2 groups A and B after laparoscopic gastric bypass, Z-test was used. Friedman test was used for comparison at times 0, 30 min and 1 h after surgery in each of the two groups A and B (separately). Frequency values and agitation comparison are summarized in Table 5.

Table 5: descriptive features and comparison of agitation levels in two groups A and B after laparoscopic gastric bypass

| Time | Group | | Test statistic | p-value |
|--------|---------------------|---------------------|-----------------|---------|
| 1 iiie | A (N, %) | B (N, %)) | i est statistic | p-value |
| 0 | 6 (28.6%) | 5 (23.8%) | 0.35 | 0.636 |
| 30 min | 5 (23.8%) | 6 (28.6%) | 0.35 | 0.636 |
| 1 h | 1 (4.8%) | 1 (4.8%) | 0 | 0.5 |
| | $P=0.072, X^2=5.25$ | $P=0.097, X^2=4.66$ | | - |

Based on the results of Table 5, there was no significant difference between agitation levels of patients in 2 groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass (P>0.05). There was no significant difference between agitation levels of patients at times 0, 30 min and 1 h after laparoscopic gastric bypass in group A (P=0.072, X²=5.25). There was no significant difference between agitation levels of patients at times 0, 30 min and 1 h after laparoscopic gastric bypass in group B (P=0.097, X²=4.66).

3.5. Determining and Comparing Systolic BP in Two Groups A and B at Times 0, 30 min and 1 h after Laparoscopic Gastric Bypass

In order to compare systolic BP levels in 2 groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass, independent t-test and Mann-Whitney U-test were used. Friedman test and repeated measure test were used for comparison of systolic BP levels at times 0, 30 min and 1 h after laparoscopic gastric bypass in each of the two groups A and B (separately). Descriptive features and comparison of systolic BP are summarized in Table 6.

Table 6: descriptive features and comparison of systolic BP levels in two groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass

| Time | Group | | Test statistic | n volue |
|--------|--------------------------|---------------------|-----------------|---------|
| | A (mean \pm SD) | B (mean \pm SD) | 1 est statistic | p-value |
| 0 | 141.76 ± 13.68 | 141.9 ± 14.92 | 0.032 | 0.974 |
| 30 min | 139.33 ± 13.13 | 139.43 ± 15.27 | 0.025 | 0.98 |
| 1 h | 134.05 ± 11.38 | 136.48 ± 10.42 | 0.768 | 0.477 |
| - | $P < 0.001, X^2 = 27.71$ | $P=0.012, X^2=5.59$ | - | - |

- Based on the results of Table 6, there was no significant difference between systolic BP levels of patients in 2 groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass (P>0.05). There was a significant difference between systolic BP levels of patients at times 0, 30 min and 1 h after laparoscopic gastric bypass in group A (P<0.001, X²=27.71).
- There was a significant difference between systolic BP levels of patients at times 0, 30 min and 1 h after laparoscopic gastric bypass in group B (P=0.012, X²=5.59).

3.6. Determining and Comparing Diastolic BP in Two Groups A and B at Times 0, 30 min and 1 h after Laparoscopic Gastric Bypass

In order to compare diastolic BP levels in 2 groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass, independent t-test was used. Repeated measure test was used for comparison of diastolic BP levels at times 0, 30 min and 1 h after laparoscopic gastric bypass in each of the two groups A and B (separately). Descriptive features and comparison of diastolic BP are summarized in Table 7.

Table 7: descriptive features and comparison of diastolic BP levels in two groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass

| Time | Group | | Test statistic | p-value |
|---------------|--------------------------|----------------------|----------------|---------|
| Time | A (mean \pm SD) | $B (mean \pm SD)$ | Test statistic | p-value |
| 0 | 91.24 ± 8.24 | 93.05 ± 9.71 | 0.651 | 0.519 |
| 30 min | 89.57 ± 9.3 | 91.19 ± 11.27 | 0.508 | 0.615 |
| 1 h | 86.24 ± 9.54 | 89.14 ± 7.35 | 1.18 | 0.245 |
| | $P < 0.001, X^2 = 58.94$ | $P=0.001, X^2=11.38$ | - | - |

Based on the results of Table 7, there was no significant difference between diastolic BP levels of patients in 2 groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass (P>0.05). There was a significant difference between diastolic BP levels of patients at times 0, 30 min and 1 h after laparoscopic gastric bypass in group A (P<0.001, X^2 =58.94). There was a significant difference between diastolic BP levels of patients at times 0, 30 min and 1 h after laparoscopic gastric bypass in group B (P=0.001, X^2 =11.38).

3.7. Determining and Comparing Heart Rate in Two Groups A and B at Times 0, 30 min and 1 h after Laparoscopic Gastric Bypass

In order to compare heart rate in 2 groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass, independent t-test and Mann-Whitney test were used. Repeated measure test and Friedman test were used for comparison of heart rate at times 0, 30 min and 1 h after laparoscopic gastric bypass in each of the two groups A and B (separately). Descriptive features and comparison of heart rate are summarized in Table 8.

Table 8: descriptive features and comparison of heart rate in two groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass

| Time | Group | | Test statistic | n volue |
|--------|-------------------------|----------------------|-----------------|---------|
| Time | A (mean \pm SD) | $B (mean \pm SD)$ | 1 est statistic | p-value |
| 0 | 93.05 ± 7.32 | 96.86 ± 6.64 | 1.76 | 0.085 |
| 30 min | 90.29 ± 6.66 | 92.86 ± 8.31 | 1.26 | 0.207 |
| 1 h | 86.43 ± 6.47 | 88 ± 7.44 | 0.9 | 0.364 |
| - | $P < 0.001, X^2 = 28.5$ | $P=0.001, X^2=67.43$ | - | - |

Based on the results of Table 8, there was no significant difference between heart rate of patients in 2 groups A and B at times 0, 30 min and 1 h after laparoscopic gastric bypass (P>0.05). There was a significant difference between heart rate of patients at times 0, 30 min and 1 h after laparoscopic gastric bypass in group A (P<0.001, X^2 =28.5). There was a significant difference between heart rate of patients at times 0, 30 min and 1 h after laparoscopic gastric bypass in group B (P=0.001, X^2 =67.43).

3.8. Determining and Comparing the First, Second and Third Pethidine Administrations in Two Groups A and B after Laparoscopic Gastric Bypass

In order to compare the first, second and third pethidine administrations in 2 groups A and B after laparoscopic gastric bypass, Z-test was used. Frequency values and comparison of the first, second and third pethidine administrations in groups A and B after laparoscopic gastric bypass are summarized in Table 9.

Table 9: descriptive features and comparison of the first, second and third pethidine administrations in two groups A and B after laparoscopic gastric bypass

| Time | Group | | Test statistic | m volue |
|-----------------|------------|------------|----------------|---------|
| | A (N, %) | B (N, %) | Test statistic | p-value |
| 1 st | 6 (28.6%) | 11 (52.3%) | 1.61 | 0.053 |
| 2 nd | 12 (57.1%) | 8 (38%) | 1.26 | 0.103 |
| 3 rd | 3 (14.3%) | 1 (4.8%) | 1.06 | 0.144 |

Based on the results of Table 9, there was no significant difference between the first, second and third pethidine administrations in 2 groups A and B after laparoscopic gastric bypass (P>0.05).

4. Discussion

According to the most important results of this study, there was no significant difference between the effect of intraoperative 1 mg/kg/h and 2 mg/kg/h IV lidocaine infusion on postoperative pain, static and dynamic nausea-vomiting, agitation, systolic BP, diastolic BP, heart rate and pethidine administration after laparoscopic gastric bypass. In both groups, intraoperative 1 mg/kg/h and 2 mg/kg/h IV lidocaine infusion significantly increased pain 6

225 hours postoperatively and significantly decreased pain 24 hours postoperatively. Moreover, 226 postoperative static and dynamic nausea-vomiting, agitation, systolic BP, diastolic BP and 227 heart rate significantly decreased 0-24 hours after the surgery. Therefore, lidocaine seems to 228 reduce postoperative pain and complications. However, high-dose and low-dose lidocaine has 229 the same significant effect in reducing pain and complications after laparoscopic gastric 230 bypass. 231 Postoperative pain not only causes physical and mental torment, but also increases the risk of 232 side effects and delayed recovery. Therefore, it is important to eliminate emotional pain and 233 stress to maintain comfortable recovery, reduce the incidence of postoperative cardiovascular 234 complications and increase sooner discharge (15). It has been previously reported that 235 preoperative IV lidocaine infusion can increase postoperative analgesic effects and accelerate 236 early recovery; intraoperative continuous infusion can effectively prevent central hyperalergy 237 through the pain pathway (16). Lidocaine has an insignificant opioid-sparing property in 238 patients undergoing various surgical procedures (17, 18). Several mechanisms have been 239 suggested to explain the insignificant opioid-sparing effect of preoperative lidocaine. First, 240 lidocaine has anti-inflammatory properties which can minimize the pain caused by surgical 241 inflammation (19, 20). Second, lidocaine also can directly block the pathways of pain 242 conducting sodium channels (21). Eventually, lidocaine can reduce the need for opioid drugs 243 or intraoperative volatile anesthetics, which may reduce the progression of postoperative pain 244 (22, 24).245 Based on literature review, this study was the first study to compare the effects of two 246 different doses of lidocaine (1 mg/kg/h vs. 2 mg/kg/h IV infusion) on postoperative pain and 247 nausea-vomiting after laparoscopic gastric bypass. However, many studies have shown that 248 different doses of lidocaine infusion reduced postoperative pain level and side effects, 249 compared with placebo and other drugs. For example, Tikuišis et al (2014) studied 64 250 patients undergoing laparoscopic colon surgery and found that pain level significantly 251 decreased 24 h after the surgery in both rest and movement in 2 mg/kg/h lidocaine group 252 compared to placebo group. Moreover, there was no significant difference between 253 postoperative complications between the two groups (5). Through a meta-analysis, Ventham 254 et al. (2015) reviewed 40 clinical trials on comparing the effect of lidocaine infusion with 255 placebo or routine postoperative laparoscopic treatments and found that lidocaine 256 intervention reduced the pain score at rest in 2, 12 and 24 hours after surgery and reduced 257 nausea and vomiting (9). Selcuk et al (2015) studied 226 patients undergoing laparoscopic 258 gynecological surgery and revealed that 1% lidocaine infusion was more effective on

- postoperative pain than placebo (12). Terkawi et al (2016) found no significant difference in
- pain scores between the two groups by follow-up of 216 patients after 2 days of abdominal
- surgery in two groups of 1 mg/kg/h IV Lidocaine infusion and epidural analgesia. In
- 262 lidocaine group, episodes of hypotension and postoperative nausea and vomiting were less
- 263 frequent than placebo group (14).
- According to previous studies some of which has been noted in the previous paragraph, on a
- 265 certain dosage, pain and nausea-vomiting were not compared between two groups of 1
- 266 mg/kg/h and 2 mg/kg/h lidocaine; positive effect of lidocaine in reducing pain and nausea-
- vomiting in most of these studies may be due to the fact that lidocaine has been compared
- with opiate and placebo. Moreover, inconsistency of this study with some studies may be due
- to differences in samples, design of studies, lidocaine doses and surgical site and procedures.
- 270 In the present study in which patients were carefully monitored for up to 24 hours after
- 271 surgery, although administration of high-dose lidocaine did not cause side effects after
- surgery, administration of low doses, as high doses, reduced pain, nausea-vomiting and
- agitation. Therefore, low doses of lidocaine (1 mg/kg/h), rather than high doses (2 mg/kg/h),
- can be used as an appropriate dose of IV lidocaine infusion to control postoperative pain and
- 275 nausea-vomiting in laparoscopic gastric bypass.

5. Conclusion

- Based on the results of this study, low doses of lidocaine (1 mg/kg/h), rather than high doses
- 278 (2 mg/kg/h), can be used as an appropriate dose of IV lidocaine infusion to control
- postoperative pain and nausea-vomiting in laparoscopic gastric bypass.

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