

Comparison of The Effects of Fentanyl versus Ketamine on The Quality of Recovery Post General Anesthesia with QoR-40 Scoring in Laparotomy Surgery

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ABSTRACT

Background: Evaluating recovery after general anesthesia is vital to assess the success of anesthesia procedures. The quality of recovery-40 (QoR-40) questionnaire comprehensively measures post-anesthesia recovery. Poor postoperative pain management can lead to complications and chronic pain. Researchers studied ketamine because of its potential to enhance standard analgesics, improve pain control, and promote better recovery outcomes.

Methods: This double-blind, randomized controlled trial involved 42 patients undergoing laparotomy at Haji General Hospital, Medan. Participants were randomized into two groups: one receiving fentanyl at 0.7 µg/kg body weight (BW) and the other receiving ketamine at 0.2 mg/kg BW. Consecutive sampling was used for participant selection, including patients who met specific inclusion and exclusion criteria. The QoR-40 questionnaire, validated in Indonesian, was administered postoperatively to assess recovery across five dimensions: comfort, feelings, support, independence, and pain.

Results: The results of the study showed that the total QoR-40 score for fentanyl use had an average of 172.4762 ± 3.81601 , while in the group using ketamine, the average score was 174.7619 ± 3.37498 , which had a significant difference between the fentanyl group and the ketamine group with $p < 0.05$.

Conclusion: Ketamine provides a superior quality of recovery compared to fentanyl, as evidenced by higher comfort and total QoR-40 scores. These findings support ketamine's use as an effective alternative in anesthetic protocols for laparotomy procedures, promoting better recovery and reducing dependence on opioids.

Keywords: fentanyl; general anesthesia; ketamine; laparotomy; postoperative recovery; QoR-40

INTRODUCTION

The Ministry of Health reported that among all surgical procedures, 32% are laparotomies, with postoperative pain being a common issue following these surgeries. A study at Saiful Anwar Hospital in East Java revealed that 78% of post-laparotomy patients experience mild to moderate pain, while only 22% are pain-free. Suboptimal management of postoperative pain increases the risk of prolonged opioid use, dependency, and chronic postsurgical pain. Persistent pain has been observed in 10–50% of patients undergoing procedures like hernia repair, breast surgery, and thoracic surgery, often leading to higher morbidity, delayed functional recovery, and reduced quality of life.^{1,2}

Opioids remain a primary choice for pain management during general anesthesia and postoperative recovery. Among them, fentanyl is favored for its rapid analgesic effect, attributed to its fat solubility, which enhances its ability to cross the blood-brain barrier. This property allows fentanyl to provide quicker relief from severe postoperative pain compared to morphine. However, opioid use is associated with several adverse effects, including postoperative nausea, vomiting, dizziness, hypoxia, constipation, urinary retention, delirium, and respiratory depression. These complications can extend hospital stays, increase medical costs, and heighten the risk of severe outcomes or mortality.^{1,2}

The Quality of Recovery-40 (QoR-40) questionnaire, developed in Australia in 2000, is a tool designed to comprehensively assess recovery after general anesthesia. It evaluates not only clinical outcomes but also factors affecting patient satisfaction with anesthesia care. The Indonesian version of the QoR-40 questionnaire, validated

by the Anesthesiology Department of the Universitas Indonesia at Dr. Cipto Mangunkusumo Hospital, demonstrated strong validity with an Aiken V coefficient exceeding 0.5. As such, it is a reliable tool for evaluating postoperative recovery quality in Indonesia.^{3,4}

METHOD

This study employs a categorical comparative analytical experimental method with a double-blind randomized controlled trial design (RCT). The objective of this study is to analyze the comparison of the effects of fentanyl and ketamine on the quality of recovery post-general anesthesia in patients undergoing laparotomy, assessed using QoR-40 at Haji General Hospital, Medan.

QoR-40 score is a measure of quality of recovery after surgery or anesthesia, ranging from 40-100. A higher score indicates a better quality of recovery. The research subjects were selected using the consecutive sampling technique. Consecutive sampling is a subject selection technique where all subjects who arrive and meet the inclusion and exclusion criteria are included in the study until the required number of subjects is reached.

RESULTS

The average age of patients in the fentanyl group was 49.43 ± 8.9 years, with a median weight of 66.14 ± 8.2 kg and an average height of 163.80 ± 5.65 cm. The Mean Arterial Pressure (MAP) was 96.7 ± 7.9 mmHg, and the average pulse rate was 87.4 ± 8.9 beats per minute. Males were more prevalent in this group, accounting for 57.1% (12 subjects), compared to 42.9% (9 subjects) for females. In terms of ASA physical status, 33.3% (7 subjects) were classified as ASA PS 1, while 66.7% (14

subjects) fell under ASA PS 2. Notably, no patients in the fentanyl group required rescue analgesia.

In the ketamine group, the average age was slightly lower at 48.3 ± 10.04 years, with a median weight of 67.80 ± 6.9 kg and an average height of 166.85 ± 5.30 cm. The MAP was 86.01 ± 13.1 mmHg, and the average pulse rate was 80.09 ± 8.4 beats per minute. Gender distribution in this group showed a slightly higher percentage of females at 52.4% (11 subjects), compared to males at 47.6% (10 subjects). For ASA physical status, 23.8% (5 subjects) were ASA PS 1, while 76.2% (16 subjects) were ASA PS 2. Like the fentanyl group, no rescue analgesia was required in the ketamine group. (Table 1)

When comparing the comfort aspect, the fentanyl group scored an average of 50.48 ± 2.94 , whereas the ketamine group had a higher average score of 52.43 ± 2.13 . This difference was statistically significant, with $p < 0.05$

(Table 2). These results indicate that ketamine may provide superior comfort compared to fentanyl during recovery.

In the feelings aspect, the fentanyl group had an average score of 40.05 ± 1.28 , while the ketamine group scored 40.48 ± 2.13 . This difference was not statistically significant ($p > 0.05$). For the support aspect, the fentanyl group had an average score of 33.57 ± 1.08 , compared to 33.43 ± 1.08 in the ketamine group, with no significant difference observed ($p > 0.05$). In the independence aspect, the fentanyl group scored an average of 17.71 ± 1.31 , while the ketamine group scored 17.67 ± 1.28 , showing no significant difference ($p > 0.05$). In the pain aspect, the fentanyl group scored 30.67 ± 2.11 on average, compared to 30.76 ± 2.02 in the ketamine group, with no significant difference ($p > 0.05$). However, the total QoR-40 score revealed a significant difference, with the fentanyl group scoring 172.48 ± 3.82 and the ketamine group scoring 174.76 ± 3.37 .

Table 1. Patient characteristics

Variable	Fentanyl Mean \pm SD	Ketamine Mean \pm SD
Age (years)	49.43 ± 8.9	48.3 ± 10.04
Weight (kg)	66.14 ± 8.2	67.80 ± 6.9
Height (cm)	163.80 ± 5.65	166.85 ± 5.30
MAP (mmHg)	96.7 ± 7.9	86.01 ± 13.1
Heart rate (bpm)	87.4 ± 8.9	80.09 ± 8.4
Gender		
Male (%)	12 (57.1%)	10 (47.6%)
Female (%)	9 (42.9%)	11 (52.4%)
PS ASA		
PS ASA 1 (%)	7 (33.3%)	5 (23.8%)
PS ASA 2 (%)	14 (66.7%)	16 (76.2%)
Rescue Analgesia	0 (0%)	0 (0%)

Table 2. QoR-40 comparison between fentanyl and ketamine

Agent	QoR-40
Fentanyl	172.4762 ± 3.81601
Ketamine	174.7619 ± 3.37498
p-value	0.046

DISCUSSION

The main function of ketamine, a phencyclidine derivative, is to block N-methyl-D-aspartate (NMDA) receptors noncompetitively. Because of its special qualities, it is frequently utilized in psychiatry, pain treatment, and anesthesia. The medication has a wide volume of distribution, is lipid-soluble, and quickly passes the blood-brain barrier. Cytochrome P450 enzymes mostly break it down into active metabolites like norketamine, which have a brief half-life of two to four hours and are eliminated through the urine and bile.⁵

Ketamine offers several advantages in managing postoperative pain and improving recovery outcomes. As an N-methyl-D-aspartate (NMDA) receptor antagonist, it plays a significant role in reducing central sensitization, which can prevent acute pain from progressing to chronic pain. Its ability to block NMDA receptors helps reduce hyperalgesia and opioid-induced tolerance, making it a valuable adjunct in multimodal pain management strategies.^{5,6}

Perioperative ketamine use has been demonstrated in clinical studies to decrease the requirement for opioid analgesics, including fentanyl, both during and after surgery. As a result, sedation and nausea associated with opioids are reduced. For instance, patients who received ketamine and fentanyl together needed less intraoperative fentanyl supplementation than those who only received fentanyl. Additionally, preemptive ketamine injection has been linked to decreased use of patient-controlled analgesia (PCA) opioids and lower postoperative pain levels.^{5,6}

Ketamine's advantages go beyond its ability to reduce pain. It is appropriate for patients who are hemodynamically unstable due to its little effect on cardiorespiratory function. Furthermore, even at follow-up intervals of up to six months, it has been demonstrated that continuous low-dose infusions after major surgeries improve overall pain control, lessen hyperalgesia, and diminish residual pain. Ketamine is a good choice for improving surgical recovery and halting the onset of chronic pain because of these qualities.^{5,6} While there are no significant changes in other characteristics, including feelings, patient support, independence, or pain, this study shows a significant difference in average comfort levels between the two groups ($p < 0.05$). There is also a notable distinction between fentanyl and ketamine based on the QoR-40 questionnaire's overall score. These findings align with the study by Pratama et al., which reported an average comfort score of 54.6 ± 1.99 in the ketamine group and 51.47 ± 1.55 in the fentanyl group. The ketamine group also showed higher average scores in feelings (41.4 ± 1.20 vs. 40.73 ± 1.10), patient support (32.2 ± 1.37 vs. 31.67 ± 1.35), independence (21.8 ± 1.21 vs. 21.73 ± 1.10), and pain (31.47 ± 1.19 vs. 31.00 ± 1.00). Furthermore, the total score was significantly higher in the ketamine group (181.07 ± 5.32) compared to the fentanyl group (176.60 ± 2.59), with a statistically significant difference ($p = 0.007$).⁷

Gao et al. found that patients in the s-ketamine group had an average QoR-40 score of 182, which was higher than the control group's score of 169. In the ketamine group, the average comfort score was 54 compared to 51 in the control group, the feelings score was 41 versus 40, the independence score was

22 versus 20, the patient support score was 34 versus 31, and the pain score was 32 versus 29. These differences were statistically significant ($p < 0.001$). Similarly, Zhang et al. reported both statistically and clinically significant differences in QoR-40 scores on the first postoperative day (POD 1), with the s-ketamine group scoring 178 (range: 168–186) compared to 168 (range: 160–178) in the control group, yielding a mean difference of 7.21 (95% CI: 5.17–9.25, $p < 0.001$). On the second postoperative day (POD 2), the difference was statistically significant but not clinically meaningful, with a mean difference of 4.81 (95% CI: 2.69–6.92, $p < 0.001$). Continuous ketamine infusion has been shown to be safe and well-tolerated for laparoscopic bariatric surgery, enhancing postoperative recovery quality and reducing pain on POD 1.⁸

Yuvaraj et al. identified a statistically significant difference in postoperative QoR-40 scores between the Opioid-Free Anesthesia (OFA) group (median: 180, IQR: 176–184) and the Opioid-Based Anesthesia (OA) group (median: 182, IQR: 178–186; $p < 0.0001$). Significant differences were observed in emotional condition scores [OFA group: median 38 (IQR: 35–42) vs. OA group: median 41 (IQR: 38–41)] and physical comfort scores [OFA group: median 52 (IQR: 50–55) vs. OA group: median 51 (IQR: 48–54)]. The OFA group also demonstrated better psychological support and physical independence scores, with minimal pain, although these differences were not statistically significant.⁹

Mulier et al. reported a higher total QoR-40 score in the OFA group compared to the OA group (89 ± 3 vs. 74 ± 6 ; $p < 0.001$). In individual components, the OFA group showed improved scores in

emotional condition (8.1 ± 0.5 vs. 7.2 ± 0.8 ; $p = 0.051$), physical comfort (10.4 ± 0.5 vs. 7.9 ± 1.0 ; $p < 0.001$), psychological support (6.7 ± 0.4 vs. 6.6 ± 0.3 ; $p = 0.62$), physical independence (4.7 ± 0.4 vs. 3.8 ± 0.6 ; $p = 0.007$), and pain (0.8 ± 0.2 vs. 0.5 ± 0.3 ; $p < 0.001$). The study concluded that the OFA group experienced better postoperative recovery quality, higher QoR-40 scores, and lower Visual Analog Scale (VAS) scores for cortisol levels the following morning.¹⁰

Ibrahim et al. found that six hours post-surgery, QoR-40 scores were higher in the OFA group compared to the Multimodal Analgesia (MMA) group (median [IQR]: 180 [173–195] vs. 185 [173–191]; $p < 0.0001$). However, this difference was no longer evident at 24 hours, where both groups had a median score of 191.¹¹

Ulbing et al. demonstrated a significant difference in QoR-40 scores at 24 hours (OFA: 166 ± 13.5 vs. OBA: 155 ± 16.5 ; $p \leq 0.001$) and 48 hours (OFA: 183 ± 9.7 vs. OBA: 173 ± 11.6 ; $p \leq 0.001$), favoring the OFA group. Their findings indicated that incorporating OFA into routine clinical practice led to reduced postoperative pain, lower opioid use, decreased incidence of Postoperative Nausea and Vomiting (PONV), and improved overall recovery outcomes.¹²

Mercanoglu et al. investigated the effects of ketamine infusion on postoperative outcomes. The KETA group received an infusion of ketamine at $10 \mu\text{g/kg/min}$ following a bolus dose of 0.5 mg/kg IV , while the control group was administered normal saline. The time to the first postoperative analgesic request was significantly longer in the KETA group compared to the control group ($P < 0.001$). Additionally, pain scores were

consistently lower in the KETA group throughout the 48-hour observation period. The control group required more intravenous patient-controlled analgesia (PCA) morphine than the KETA group ($P < 0.001$ at all monitored intervals). These findings suggest that ketamine infusion is an effective adjuvant for total intravenous anesthesia (TIVA), as it helps reduce pain and postoperative opioid requirements.¹³

Hung et al. demonstrated that ketamine and s-ketamine significantly improved Quality of Recovery (QoR) scores on postoperative day (POD) 1 and POD 2 compared to the control group (standardized mean difference [SMD]: 0.63, $P < 0.0001$ for POD 1; SMD: 0.56, $P = 0.04$ for POD 2), with no notable benefit observed on POD 3. Subgroup analysis revealed that improvements in QoR scores on POD 1 were influenced by the specific regimen used (SMD: s-ketamine 1.14; ketamine 0.01), with the emotional domain showing sustained improvement from POD 1 to POD 3, while other domains only improved on POD 1. The use of ketamine/s-ketamine was also associated with lower postoperative anxiety (SMD: 0.48, $P = 0.003$) and depression (SMD: 0.72, $P = 0.001$), as well as reduced pain severity on POD 1 and POD 2. No significant differences were noted in the risk of side effects or hospital length of stay.¹⁴

Tochi et al. compared outcomes between the Opioid-Free Anesthesia (OFA) group and the Conventional General Anesthesia (CGA) group. The OFA group exhibited significantly lower pain scores within the first 24 hours postoperatively and did not require morphine for pain relief. This group also experienced fewer hypoxemic episodes in the first six postoperative hours, required less supplemental oxygen, had

no instances of postoperative ileus, minimal Postoperative Nausea and Vomiting (PONV), and no reports of pruritus. Patients in the OFA group had a faster rehabilitation process, including earlier postoperative ambulation, and reported higher satisfaction levels with their recovery (all $P < 0.05$).¹⁵

CONCLUSION

The average QoR-40 score for assessing the quality of recovery after general anesthesia is 172.47 when using fentanyl at a dose of 0.7 mcg/kgBW. In comparison, the average QoR-40 score is 174.76 with ketamine at a dose of 0.2 mg/kgBW. Ketamine demonstrates greater effectiveness than fentanyl in terms of patient comfort, as shown by the statistically higher comfort scores on the QoR-40 questionnaire when ketamine is used.

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