Journal for Re Attach Therapy and Developmental Diversities
eISSN: 2589-7799
2023 August; 6 (10s): 125-135

Comparison Between Ibuprofen and Paracetamol as Preemptive Analgesia during Laparotomy in General Anesthesia

Annisa Juwita*, Christrijogo Sumartono, and Belindo Wirabuana

Specialist Doctor Education Program 1, Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, Universitas Airlangga Surabaya, Indonesia

***E-mail**: annisajuwita@yahoo.com

Received: 24- June -2023
Revised: 23- July -2023
Accepted: 04- August -2023

Abstract

Introduction: Preemptive analgesia has the potential to be more effective than the same analgesic therapy given after surgery because of its protective effect on the nociceptive system. The purpose of this study was to analyze the comparison of ibuprofen and paracetamol as preemptive analgesia in patients undergoing laparotomy under general anesthesia at the Integrated Surgery Center (GBPT), Dr. Soetomo Hospital Surabaya.

Objectives: This study aims to compare the effectiveness of ibuprofen and paracetamol as preemptive analgesia in patients undergoing laparotomy surgery at Dr. Soetomo Hospital Surabaya. The research seeks to evaluate and compare the postoperative pain scores at 2 hours, 6 hours, and 24 hours between patients administered ibuprofen and those given paracetamol as preemptive analgesia. Additionally, the study aims to assess the need for additional opioids during and after surgery in patients receiving ibuprofen versus paracetamol as preemptive analgesia. Furthermore, the research will examine any potential differences in blood pressure, breathing frequency, heart rate frequency, and qNOX between patients administered ibuprofen and those given paracetamol as preemptive analgesia during the laparotomy surgery.

Methods: Analytical study, quasy experimental, prospective. A total of 30 patients with PS ASA 1-3 aged 18-60 years who underwent laparotomy were recruited in this study. In this study, strict monitoring was carried out using the qNOX device to maintain the depth of the anesthetic stage so that the anesthetic drug given was not excessive. Monitoring of blood pressure, respiratory rate, pulse, qNOX in patients given ibuprofen compared to paracetamol as preemptive analgesia during and post operatively. In addition, it was seen the addition of fentanyl during and post operatively.

Results: There were no significant differences in blood pressure, respiratory rate, pulse, qNOX in patients given ibuprofen compared to paracetamol as preemptive analgesia, there were no significant differences in the need for opioids during and postoperatively in patients given ibuprofen compared to paracetamol as preemptive analgesia. In the inter-variable test, a significant relationship was found between the addition of fentanyl and systolic blood pressure in paracetamol group ($r=0,56$ p value = 0.027, p value <0.05).

Conclusions: There were no significant differences in blood pressure, both systolic and diastolic, respiratory rate, pulse, qNOX in patients given ibuprofen compared to paracetamol as preemptive analgesia, there were no significant differences in the need for opioids during and postoperatively in patients given ibuprofen compared to paracetamol as preemptive analgesia.

Keywords: preemptive analgesia, paracetamol, ibuprofen, laparotomy.

1. Introduction

Preemptive analgesia involves administering analgesia before surgical incision to reduce central sensitization caused by incisional injury and inflammation. It is continued during the surgical procedure to minimize nociceptive transmission from the surgery. Therapies used for preemptive analgesia include NSAIDs, peripheral nerve blocks, and anti NMDA receptors (Stoelting & Hillier, 2012).

Surgical stress during a surgery is a complex process involving neuroendocrine, inflammatory stress, and hypoxic stress. Inflammatory stress can lead to catabolism, endothelial dysfunction, fatigue, and gastrointestinal dysfunction. Hypoxic stress, due to vasodilation and extravasation, is associated with increased oxygen demand,

which can lead to hypoxemia and hypoperfusion. In elective laparotomy surgery, various methods can be used to reduce perioperative surgical stress, such as minimally invasive surgery, neuraxial blockade using epidural or peripheral blockade with local anesthesia, NSAIDs (Non-Steroidal Anti-inflammatory Drugs), and glucocorticoids. Neuraxial blockade has been shown to reduce surgical stress, postoperative ileus, respiratory complications, and pain scale in elective laparotomy cases. However, not all cases are suitable for neuraxial blockade, particularly in situations involving sepsis, coagulopathy disorders, limited facilities, or lack of expertise (Foss & Kehlet, 2020).

Studies conducted by Koh et al. (2015) have shown that more than 80% of postoperative patients experience moderate pain, and 31-37% experience severe pain. A survey by Apfelbaum et al. reported that 80% of patients experience acute postoperative pain, with 86% of them experiencing moderate to severe pain. Inadequate pain management after surgery can have negative impacts, causing patient discomfort, increased risk of myocardial ischemia, delayed wound healing, decreased immunity, complications due to poor respiratory function, and an elevated risk of thromboembolism due to prolonged immobilization.

Preemptive analgesia holds potential for better effectiveness compared to the same analgesic therapy given after surgery due to its protective effect on the nociceptive system (Simone et al., 2013). In August 2022, there were 751 cases of patients undergoing surgery under general anesthesia at RSUD Dr. Soetomo Surabaya. Out of those, 21 cases involved laparotomy surgery in patients aged 18-65 years, with 16 cases receiving paracetamol as postoperative therapy and 4 cases receiving ibuprofen as postoperative therapy.

Ibuprofen is a propionic acid derivative NSAID with anti-inflammatory, antipyretic, and analgesic properties. It exists in oral and intravenous forms and is useful for treating mild, moderate, and severe pain when combined with opioids. Ibuprofen works by inhibiting cyclooxygenase 1 and cyclooxygenase 2. A study by Le et al. (2016) found that ibuprofen, used as preemptive analgesia, was able to reduce the stress cortisol response ($P < 0.0001$) in patients undergoing cholecystectomy surgery.

Another study conducted by Unal et al. (2015) stated that there was no significant difference in the addition of fentanyl in patients given preemptive analgesia with paracetamol and ibuprofen in open nephrectomy surgery. Paracetamol, also known as acetaminophen, is used as an analgesic and antipyretic and shares similarities with NSAIDs. A study by Hassan (2014) showed that cesarean section patients who were given paracetamol as preemptive analgesia could reduce the amount of opioid consumption during and after surgery ($P < 0.005$). Moreover, a study by Vittayakittipong & Areewattana (2022) indicated that the use of paracetamol as preemptive analgesia decreased the amount of opioid consumption during surgery.

Although overseas research comparing ibuprofen and paracetamol already exists, there is no specific data discussing laparotomy surgery. Based on the above data, there has been no study conducted in Surabaya comparing the effectiveness of ibuprofen and paracetamol as preemptive analgesia for postoperative pain and opioid requirements during laparotomy surgery under general anesthesia at Integrated Surgery Center (GBPT), Dr. Soetomo Hospital Surabaya.

2. Objectives

Based on the aforementioned background, this research aims to compare the effectiveness of ibuprofen and paracetamol as preemptive analgesia in patients undergoing laparotomy surgery under general anesthesia at Integrated Surgery Center (GBPT), Dr. Soetomo Hospital Surabaya. The study seeks to evaluate and compare the postoperative pain scores at 2 hours, 6 hours, and 24 hours between patients administered ibuprofen and those given paracetamol as preemptive analgesia. Additionally, the research aims to assess the need for additional opioids during and after surgery in patients receiving ibuprofen versus paracetamol as preemptive analgesia. Furthermore, the study will examine any potential differences in blood pressure, breathing frequency, heart rate frequency, and qNOX between patients administered ibuprofen and those given paracetamol as preemptive analgesia during the laparotomy surgery.

3. Methods

This study employed an analytic, quasi-experimental, and prospective design. The sample was divided into two groups: the ibuprofen group and the paracetamol group, and the administration of medication was determined through a Randomized Control Trial (RCT) in a single-blind manner. Both groups received the same treatment

during induction, maintenance of anesthesia, and in the postoperative period. Assessments were made for blood pressure, pulse rate, breathing frequency, qNOX, MAP (mean arterial pressure), and pain scores using the Wong Baker Pain Scale at 2 hours, 6 hours, and 24 hours postoperatively in the recovery room. Additionally, the use of additional fentanyl during surgery was recorded.

Sample selection followed specific inclusion and exclusion criteria. The calculated sample size for each group was 15 patients, satisfying the inclusion criteria of age between 18-60 years, PS ASA I-III, elective or planned surgery with low to moderate postoperative pain expected, undergoing general anesthesia technique, and providing informed consent to participate.

Exclusion criteria were set for patients with comorbid hypertension, tachycardia, severe cardiac, liver or renal impairment, allergy to ibuprofen and paracetamol, and those with a difficult airway to intubate, intubated more than twice. Pain assessment was performed by a highly competent assessor with experience in intubation.

The independent variable in this study was Preemptive Analgesia, represented by either Paracetamol or Ibuprofen administration. The dependent variables included pain scores using the Wong Baker Pain Scale, the number of rescue analgesia use, blood pressure, pulse rate, and qNOX.

Data were collected using a dedicated data collection sheet (LPD) provided in the appendix. The collected data underwent processing through computer software (SPSS 22) and were tested for normality using the Kolmogorov-Smirnov test. Depending on the data distribution, either the Spearman correlation statistical test or the Mann Whitney U Test was employed for analysis.

4. Results

Systole and Diastole Blood Pressure Test Analysis

The analysis of systolic and diastolic blood pressure during surgery in the paracetamol and ibuprofen groups involved a comparative test using the T-test when the data followed a normal distribution, and the Mann-Whitney test when the data did not meet normality assumptions. The normality of the data was assessed using the Shapiro-Wilk test since the data size in both the paracetamol and ibuprofen groups was less than 30.

The results of the normality test using Shapiro-Wilk indicated that the p-values for both systolic and diastolic blood pressure in the paracetamol and ibuprofen groups were greater than 0.05. This suggests that the distribution of systolic and diastolic blood pressure data in both groups is considered normally distributed. As all groups met the normality assumption, the comparison test for systolic and diastolic blood pressure in the paracetamol and ibuprofen groups employed parametric methods, specifically the T-test.

Based on the results of the normality test using Shapiro Wilk, it was found that for systole and diastole blood pressure in the paracetamol and ibuprofen groups, the p value was all> 0.05, so it can be interpreted that the distribution of systole and diastole blood pressure data in the paracetamol and ibuprofen groups was declared normally distributed. Because all groups are normal, the comparison test for systole and diastole blood pressure in the paracetamol and ibuprofen groups uses parametric methods with the test used is the T test. For detailed results of the comparative test of systolic and diastolic blood pressure in the paracetamol and ibuprofen groups during surgery, refer to Table 1.

Table 1. Comparative test of systole and diastole in the paracetamol and ibuprofen groups during surgery

	Group		
Blood Pressure	**Paracetamol (n=15)**	**Ibuprofen (n=15)**	**p values**
Systole			
Mean ± SD	117,33 ± 5,12	115 ± 6,09	0,266*
Diastole			
Mean ± SD	66,33 ± 4,24	67,93 ± 4,73	0,337*

The results of the systolic blood pressure comparison test indicated that the mean systolic blood pressure for the paracetamol group was 117,33 ± 5,12, while for the ibuprofen group, it was 115 ± 6,09. Based on these results, it appeared that systolic blood pressure during surgery in patients using paracetamol tended to be higher than in

those using ibuprofen. However, when conducting statistical tests using the T-test, the obtained p-value was 0,266, which is greater than 0,05. This indicates that the difference in systolic blood pressure during surgery between patients using paracetamol and ibuprofen was not considered statistically significant.

Regarding the diastolic blood pressure comparison test results presented in Table 1, the mean diastolic blood pressure for the paracetamol group was 66,33 ± 4,24 whereas for the ibuprofen group, it was 67,93 ± 4,73. Based on these findings, it was observed that diastolic blood pressure during surgery in patients using paracetamol tended to be lower than in those using ibuprofen. However, upon conducting statistical tests using the T-test, the resulting p-value was 0,337 which is greater than 0,05. As a result, the difference in diastolic blood pressure during surgery between patients using paracetamol and ibuprofen was not considered statistically significant

Breath Test Analysis

The comparison of breath tests during surgery between the paracetamol and ibuprofen groups was conducted using the T-test when the data was normally distributed, and the Mann-Whitney test when the data was not normally distributed. The normality of the data was assessed using the Shapiro-Wilk test since the amount of data in both the paracetamol and ibuprofen groups was less than 30.

The results of the normality test using Shapiro-Wilk showed that the p-value for breath data in both the paracetamol and ibuprofen groups was less than 0,05. This indicates that the distribution of breath data in both groups was not normal. Since both groups were declared non-normal, the comparison test for breath in the paracetamol and ibuprofen groups used a non-parametric method, specifically the Mann-Whitney test.

Based on the results of the Breath comparison test, the mean and standard deviation for the paracetamol group were 18,87 ± 0,83 while for the ibuprofen group, it was 18,73 ± 0,80. These results suggest that breathing during surgery in patients using paracetamol tended to be higher than in those using ibuprofen. However, when conducting statistical tests using the Mann-Whitney test, the obtained p-value was 0,657 which is greater than 0,05. Therefore, the difference in breathing during surgery between patients using paracetamol and ibuprofen was not considered statistically significant. Table 2 presents the results of the comparative test of breath delta in the paracetamol and ibuprofen groups.

Table 2. Comparative test of breath delta in the paracetamol and ibuprofen groups

	Group		
Pulse	**Paracetamol (n=15)**	**Ibuprofen (n=15)**	**p values**
Mean ± SD	13,87	17,13	0,249*

* declared significantly different if the p value <0,05

The mean delta breath for the paracetamol group was 13,87 which was lower than the mean delta breath for the ibuprofen group, which was 17,13. The calculated p-value was 0,249. Based on this p-value, it can be concluded that there is no significant difference between the delta breath of patients using paracetamol and those using ibuprofen during the surgery.

Pulse Test Analysis

The comparison of pulse rates during surgery between the paracetamol and ibuprofen groups was performed using the T-test when the data was normally distributed. However, for data that was not normally distributed, the Mann-Whitney test was used. The normality test applied was the Shapiro-Wilk test, as the data size in both the paracetamol and ibuprofen groups was less than 30.

The results of the Shapiro-Wilk normality test indicated that the p-value for pulse rates in both the paracetamol and ibuprofen groups was less than 0,05. This finding suggests that the distribution of pulse rate data in both groups was not normal. As a result, non-parametric methods, specifically the Mann-Whitney test, were employed for the comparison of pulse rates between the two groups.

Based on the results of the pulse comparison test, the mean and standard deviation for the paracetamol group were 87,20 ± 8,20 while for the ibuprofen group, it was 89,27 ± 5,91. These findings indicate that the pulse rate during surgery in patients using paracetamol tended to be lower than in those using ibuprofen. However, when conducting statistical tests using the Mann-Whitney test, the obtained p-value was 0,692, which is greater than 0,05. Hence, the difference in pulse rate during surgery between patients using paracetamol and ibuprofen was not considered

statistically significant. Table 3 presents the results of the comparative test of pulse rates in the paracetamol and ibuprofen groups.

Table 3. Comparative test of pulse in the paracetamol and ibuprofen groups

	Group		
Pulse	**Paracetamol (n=15)**	**Ibuprofen (n=15)**	**p values**
Mean ± SD	1 ± 13,421	8,3 ± 10,307	0,104*

* declared significantly different if the p value <0,05

The pulse delta for the paracetamol group was 1 ± 13,421, while for the ibuprofen group, it was 8,3 ± 10,307. The calculated p-value was 0,104. Based on this p-value, it can be concluded that there is no significant difference in the pulse delta between patients using paracetamol and ibuprofen.

QNOX Test Analysis

The QNOX comparison test between the paracetamol and ibuprofen groups during surgery was conducted using different statistical tests based on the normality of the data. Specifically, the T-test was employed if the data was normally distributed, and the Mann-Whitney test was used if the data was not normally distributed. To determine the normality of the data, the Shapiro-Wilk test was applied since the amount of data in both the paracetamol and ibuprofen groups was less than 30.

The results of the Shapiro-Wilk normality test revealed that the p-value for QNOX in the paracetamol group was less than 0.05, indicating that the distribution of QNOX data in the paracetamol group was abnormal. On the other hand, the p-value for QNOX in the ibuprofen group was greater than 0.05, indicating that the distribution of QNOX data in the ibuprofen group was normal. Since one of the groups (paracetamol) was declared abnormal, the comparison test for QNOX between the paracetamol and ibuprofen groups utilized a non-parametric method, specifically the Mann-Whitney test. Table 4 presents the results of the comparative test of QNOX in the paracetamol and ibuprofen groups.

Table 4. Comparative test of QNOX in paracetamol and ibuprofen groups

	Group		
QNOX	**Paracetamol (n=15)**	**Ibuprofen (n=15)**	**p values**
Mean ± SD	38-40 (38)	36-40 (38)	0,305*

* declared significantly different if the p value <0,05

Based on the results of Table 4 of the QNOX comparison test, the mean and standard deviation for the paracetamol group were 38,60 ± 1,06 whereas for the ibuprofen group, it was 38,13 ± 1,25. These findings suggest that QNOX during surgery in patients using paracetamol tended to be slightly higher than in those using ibuprofen.

However, when conducting statistical tests using the Mann-Whitney test, the obtained p-value was 0.305, which is greater than 0,05. Therefore, the difference in QNOX during surgery between patients using paracetamol and ibuprofen was not considered statistically significant. It's worth noting that in this study, QNOX was used to monitor the additional dose of analgesic and sedation drugs to ensure it did not exceed the target range during surgery. The target range was set between 40 to 60, and both groups were observed every 15 minutes throughout the surgery.

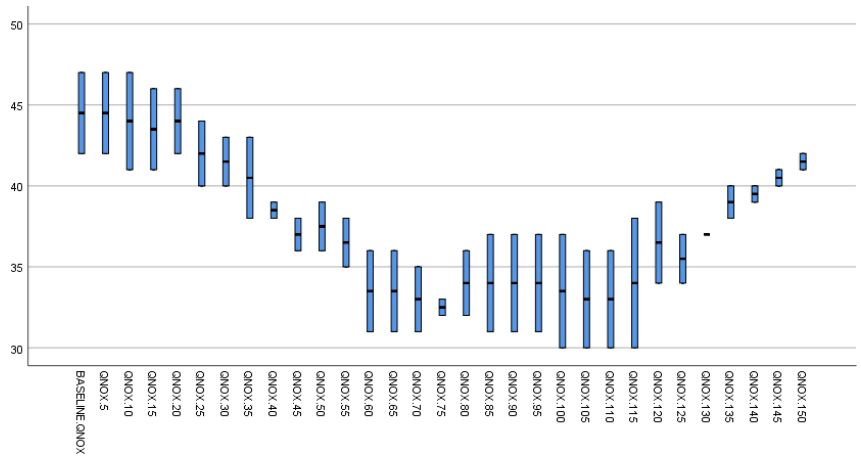

Figure 1. Intraoperative qNOX value

The qNOX values showed an increase at the 15th minute after intubation, followed by a subsequent decrease, and then an increase again towards the end of the operation.
To conduct the delta qNOX analysis test for paracetamol and ibuprofen, the normality test was performed using the Shapiro-Wilk test. This test was employed to assess the normality of the delta qNOX data in both groups, as the number of data points was less than 30.

Table 5. Comparison test of qNOX in paracetamol and ibuprofen groups

	Group		
qNOX	**Paracetamol (n=15)**	**Ibuprofen (n=15)**	**p values**
Mean ± SD	-6,20 ± 2,077	-5,73 ± 1,709	0,507*

* declared significantly different if the p value <0,05

The delta qNOX of paracetamol was 6,20 ± 2.077 and the delta qNOX of ibuprofen was -5,73 ± 1,709 with a p value of 0,507 so that there was no significant difference in the delta qNOX of paracetamol and ibuprofen.

Pain Test Analysis

Pain comparison test analysis based on WBFS scores during surgery in the paracetamol and ibuprofen groups was performed using the Mann Whitney test because the data were in ordinal form, namely in the categories of no pain, mild pain, moderate pain, severe pain and severe pain. The following table shows the results of the pain comparison test.

Table 6. Comparative test of pain in the paracetamol and ibuprofen groups

	Group		
Pain	**Paracetamol (n=15)**	**Ibuprofen (n=15)**	**p values**
2 hours of pain			
No pain	9 (60,0%)	11 (73,3%)	
Mild Pain	6 (40,0%)	4 (26,7%)	
			0,446*
6 hours of pain			
No pain	3 (20,0%)	2 (13,3%)	
Mild Pain	12 (80,0%)	13 (86,7%)	
			0,630*
24 hours of pain			
No pain	3 (20,0%)	3 (20,0%)	
Mild Pain	12 (80,0%)	12 (80,0%)	
			1,000*

* declared significantly different if the p value <0,05

Based on the results of Table 6, the pain comparison test at 2 hours showed that in the paracetamol group, 9 (60,0%) participants reported no pain, and 6 (40,0%) reported mild pain. There were no cases of moderate, severe, or very painful experiences, representing 0 (0%) occurrences. In the ibuprofen group, 11 (73,3%) participants reported no pain, and 4 (26,7%) reported mild pain. Similar to the paracetamol group, there were no cases of moderate, severe, or very painful experiences, which accounted for 0 (0%) occurrences. Based on these results, it appears that the paracetamol group tended to have more mild pain when compared to the ibuprofen group. However, the statistical test using the Mann-Whitney test yielded a p-value of 0,446 where the value is greater than 0,05. This means that the difference in pain at 2 hours between patients using paracetamol and ibuprofen is not considered statistically significant.

Moving to the pain comparison test at 6 hours, the paracetamol group showed 3 (20,0%) participants with no pain and 12 (80,0%) with mild pain. There were no cases of moderate, severe, or very painful experiences. In the ibuprofen group, 2 (13,3%) participants reported no pain, and 13 (86,7%) reported mild pain. Similar to previous results, there were no cases of moderate, severe, or very painful experiences, which accounted for 0 (0%) occurrences. Based on these findings, the paracetamol group seemed to have a smaller incidence of mild pain when compared to the ibuprofen group. However, the statistical test using the Mann-Whitney test yielded a p-value of 0,630 where the value is greater than 0,05. Therefore, the difference in pain at 6 hours between patients using paracetamol and ibuprofen is also not considered statistically significant.

Finally, the pain comparison test at 24 hours for both the paracetamol and ibuprofen groups yielded similar results. The occurrence of no pain was 3 (20,0%), while mild pain was reported by 12 (80,0%) participants. There were no cases of moderate pain in either group. The statistical test using the Mann-Whitney test yielded a p-value of 1,000 where the value is greater than 0,05. This indicates that there is no significant difference in pain at 24 hours between patients using paracetamol and ibuprofen.

Analysis of Fentanyl Addition Test

The comparative test analysis of fentanyl addition during surgery in the paracetamol and ibuprofen groups was conducted, employing different statistical tests depending on the normality of the data. The T-test was used when the data was normally distributed, while the Mann-Whitney test was employed for non-normally distributed data. To assess normality, the Shapiro-Wilk test was utilized due to the limited size of data in both the paracetamol and ibuprofen groups (less than 30 data points). The results of the normality test and the comparison test for fentanyl addition are presented in the following table.

The Shapiro-Wilk normality test revealed that the p-value for fentanyl addition in both the paracetamol and ibuprofen groups was less than 0,05. This indicates that the distribution of data for fentanyl addition in both groups was deemed to be abnormally distributed. As a result, a non-parametric method, specifically the Mann-Whitney test, was employed for the comparison of fentanyl addition between the two groups.

Table 7. Comparative test of fentanyl addition in paracetamol and ibuprofen groups

	Group		
Fentanyl Addition	**Paracetamol (n=15)**	**Ibuprofen (n=15)**	**p values**
Median (Range)	25-100 (50)	50-100 (50)	0,790*

* declared significantly different if the p value <0,05

Based on the results presented in Table 7, the comparison test for the addition of fentanyl during surgery showed that for the paracetamol group, the mean and standard deviation were 60,00 ± 18,42, while for the ibuprofen group, it was 60,00 ± 18,42. These findings indicate that the addition of fentanyl during surgery in patients using paracetamol and ibuprofen tended to be the same or not different. Furthermore, statistical tests were conducted using the Mann-Whitney test, and the obtained p-value was 0,790 where the value is greater than 0,05. As a result, the addition of fentanyl during surgery between patients using paracetamol and ibuprofen is declared not significantly different or not significantly different.

Relationship Analysis of Fentanyl Addition Test on Systolic Blood Pressure, Diastolic, Pulse, Breath, qNOX
Analysis of the relationship between the addition of fentanyl to systolic, diastolic, pulse, breath, qNOX blood pressure using Spearman's bivariate comparison test was carried out because the data were not normally distributed.

Table 8. Normality test of fentanyl addition in paracetamol and ibuprofen groups on systolic, diastolic, pulse, breath, qNOX

Relationship Test to Fentanyl	p paracetamol / r	p ibuprofen / r
Systolic Test	0,027 / 0,56	0,261 / 0,31
Diastolic Test	0,618 / 0,56	0,361 / 0,254
Pulse	0,689 / 0,113	0,736 / 0,071
Breath	0,094 / 0,448	0,803 / -0,273
qNOX	0,154 / 0,385	0,325 / -0,336

The relationship test results showed that in the paracetamol group, there was a significant relationship between the addition of fentanyl and systolic blood pressure ($p < 0,05$, $r = 0,56$), indicating a moderate positive correlation. However, no significant relationship was observed in the other groups, as indicated by p-values greater than 0,05. In summary, the addition of fentanyl during surgery had a meaningful impact on systolic blood pressure in the paracetamol group but not in the other groups.

5. Discussion

Analysis of Study Subject Characteristics
A total of 30 patients who met the inclusion and exclusion criteria were observed in this study. The selected surgeries included stoma closure, umbilical hernia repair, herniotomy hernioplasty, sigmoidostomy, and laparotomy myomectomy, which are expected to result in low to moderate postoperative pain.
From the general data of the sample characteristics, it was observed that gender, age, weight, height, Body Mass Index (BMI), length of surgery, type of surgery, and PS ASA all had a p-value > 0,05. Therefore, there was no statistically significant difference between the two groups (ibuprofen and paracetamol). This indicates that the samples in both groups can be considered homogeneous or equivalent.
In this study, the majority of patients were female in both the paracetamol and ibuprofen groups. The average age in the paracetamol group was higher than in the ibuprofen group, and the average body weight in the paracetamol group was also higher. Conversely, the average height in the ibuprofen group was higher than in the paracetamol group.
In Systolic Blood Pressure Comparison, the mean systolic blood pressure during surgery was 117,33 ± 5,12 for the paracetamol group and 115 ± 6,09 for the ibuprofen group. Based on these results, systolic blood pressure during surgery in patients using paracetamol tended to be slightly higher than in those using ibuprofen. However, the statistical test using the T-test resulted in a p-value of 0,266, indicating that the difference in systolic blood pressure during surgery between patients using paracetamol and ibuprofen was not statistically significant.
In Diastolic Blood Pressure Comparison, the mean diastolic blood pressure during surgery was 66,33 ± 4,24 for the paracetamol group and 67,93 ± 4,73 for the ibuprofen group. Based on these results, diastolic blood pressure during surgery in patients using paracetamol tended to be slightly lower than in those using ibuprofen. However, the statistical test using the T-test resulted in a p-value of 0,337 indicating that the difference in diastolic blood pressure during surgery between patients using paracetamol and ibuprofen was not statistically significant.
In Pulse Comparison, the mean pulse rate during surgery was 87,20 ± 8,20 for the paracetamol group and 89,27 ± 5,91 for the ibuprofen group. Based on these results, the pulse rate during surgery in patients using paracetamol tended to be slightly lower than in those using ibuprofen. However, the statistical test using the Mann-Whitney test yielded a p-value of 0,692 suggesting that the difference in pulse rate during surgery between patients using paracetamol and ibuprofen was not statistically significant.
In Pulse Delta Comparison, the pulse delta for paracetamol was 1 ± 13,421 while for ibuprofen, it was 8,3 ± 10,307. The p-value was 0,104 indicating that there was no significant difference in the pulse delta between

patients using paracetamol and ibuprofen. This result aligns with a previous study (Unal et al., 2015) which reported no significant difference in patients given preemptive analgesia paracetamol and ibuprofen in open nephrectomy surgery.

Breath Delta Comparison, the breath delta test results showed that the mean for paracetamol was 13,87 which was lower than the mean for ibuprofen at 17,13. The p-value obtained was 0,249 indicating that there was no significant difference between the breath delta of patients using paracetamol and ibuprofen. This observation can be attributed to all samples being controlled under general anesthesia, ensuring that patient breathing was regulated by an anesthesiologist until the operation was completed and the patient regained consciousness.

Postoperative Pain Score Analysis

This study aimed to analyze the effectiveness of ibuprofen (a Non-Steroidal Anti-Inflammatory Drug / NSAID) and paracetamol, a beneficial analgesic in postoperative pain management, known for its pain and inflammation reduction properties. NSAIDs have shown efficacy in managing mild to moderate postoperative pain. To achieve optimal results, the timing of administration is crucial, as NSAIDs require time to block prostaglandin synthesis and inhibit pain pathways. Preoperative administration as preemptive analgesia is vital for achieving a favorable postoperative effect .

The Wong-Baker Faces Pain Scale cut-off point ≥ 4 is used as a threshold pain score indicating the need for clinical intervention (Masigati & Chilonga, 2014). Pain scores range from 0 (no pain) to 10 (unbearable pain). WBFS < 4 (0: no pain and 1-3: mild pain) is well-tolerated, but it is important to consider that pain perception is influenced by various factors such as previous pain experiences, family, culture, and environment. If WBFS ≥ 4, rescue analgesics are administered, as it indicates moderate to severe pain that interferes with the patient's well-being.

Pain scores were assessed at 2 hours, 6 hours, and 24 hours postoperatively in this study. The pain comparison test at 2 hours showed that the paracetamol group had 9 (60,0%) participants reporting no pain and 6 (40,0%) reporting mild pain, with no cases of moderate, severe, or very painful experiences. In the ibuprofen group, 11 (73,3%) participants reported no pain, 4 (26,7%) reported mild pain, and there were no cases of moderate pain. Based on these results, the ibuprofen group tended to have a higher incidence of no pain compared to the paracetamol group, while the paracetamol group tended to have a higher incidence of mild pain compared to the ibuprofen group. However, the statistical test using the Mann-Whitney test resulted in a p-value of 0,446 indicating that the difference in pain at 2 hours between patients using paracetamol and ibuprofen was not statistically significant.

Out of the 30 samples, no additional opioids were administered postoperatively. This finding is consistent with previous studies. Barash et al. (2006) reported that preemptive ibuprofen reduces postoperative opioid consumption in cholecystectomy surgery, and Ciftci et al. (2019) found that intravenous ibuprofen reduced opioid consumption in the first 24 hours after gastrectomy surgery, particularly in the first 2 hours post-gastrectomy surgery.

The pain comparison test at 6 hours showed that the paracetamol group had 3 (20,0%) participants reporting no pain, 12 (80,0%) reporting mild pain, and no cases of moderate pain. In the ibuprofen group, 2 (13,3%) participants reported no pain, 13 (86,7%) reported mild pain, and no cases of moderate pain. Based on these results, the paracetamol group tended to have a lower incidence of mild pain compared to the ibuprofen group. However, the statistical test using the Mann-Whitney test yielded a p-value of 0,630 suggesting that the difference in pain at 6 hours between patients using paracetamol and ibuprofen was not statistically significant. The increase in mild pain scores in the ibuprofen group at 6 hours might be attributed to the time remaining for the next analgesic administration, while the duration of the previous analgesic drug was reduced.

The comparison test of pain at 24 hours for both the paracetamol and ibuprofen groups showed that 3 (20,0%) participants reported no pain, 12 (80,0%) reported mild pain, and no cases of moderate pain. The statistical test using the Mann-Whitney test yielded a p-value of 1,000 indicating that there was no significant difference in pain at 24 hours between patients using paracetamol and ibuprofen.

In the inpatient room, there still seems to be a lack of time discipline in the administration of postoperative analgesic drugs, which could potentially influence postoperative pain scores. The lowest pain scores were observed at 6 hours postoperatively, based on the average scores obtained at 2 hours, 6 hours, and 24 hours.

QNOX Analysis

QNOX was utilized in this study to assess depth and pain during surgery. The qNOX target was maintained at a value of 40-60 during surgery to ensure that the administration of sedation drugs remained within the appropriate dosage range. The qNOX comparison test showed that for the paracetamol group, the mean and standard deviation were 38,60 ± 1,06, while for the ibuprofen group, it was 38,13 ± 1,25. Based on these results, it can be inferred that QNOX values during surgery in patients using paracetamol tended to be slightly higher than in those using ibuprofen. However, the statistical test using the Mann Whitney test yielded a p-value of 0,305 which was greater than 0,05 indicating that the difference in QNOX values during surgery between patients using paracetamol and ibuprofen was not statistically significant.

QNOX monitoring was conducted after induction, and an increase in qNOX value was observed at the 15th minute after intubation, followed by a subsequent decrease and then a gradual increase again towards the end of the operation.

In the delta qNOX analysis test, the delta qNOX of paracetamol was 6,20 ± 2,077, and the delta qNOX of ibuprofen was -5,73 ± 1,709 with a p-value of 0,507. This indicates that there was no significant difference in the delta qNOX of paracetamol and ibuprofen. The obtained negative results suggest that the qNOX value during surgery is lower than when the patient is conscious. These findings are in line with studies conducted by Jensen & Finnerup (2014), which showed that qNOX reflects the degree of pain or nociception during general anesthesia. Clinical signs evaluated through qNOX can indicate whether the patient's qNOX may decrease or increase, with a rise in value suggesting the presence of pain.

Analysis of Fentanyl Addition

The comparison test for the addition of fentanyl during surgery showed that for both the paracetamol group and the ibuprofen group, the mean and standard deviation were 60,00 ± 18,42. Based on these results, the addition of fentanyl during surgery in patients using paracetamol and ibuprofen was found to be similar or not significantly different. The statistical test using the Mann Whitney test yielded a p-value of 0,790, which is greater than 0,05 indicating that there is no significant difference in the addition of fentanyl during surgery between patients using paracetamol and ibuprofen.

These findings are consistent with a study conducted by Unal et al. (2015), which also reported no significant difference in the addition of fentanyl between patients given preemptive analgesia with paracetamol and ibuprofen in open nephrectomy surgery.

Analysis of Fentanyl Addition on Systolic Blood Pressure, Diastolic, Pulse, Breath, qNOX

In this study, the relationship between the addition of fentanyl and various physiological parameters such as systolic blood pressure, diastolic blood pressure, pulse rate, breath rate, and qNOX was investigated using Spearman's bivariate comparison test, as the data were not normally distributed.

The results of the relationship test indicated a significant correlation between the addition of fentanyl and systolic blood pressure in the paracetamol group, with a p-value < 0,05 and a correlation coefficient (r) of 0,56. The strength of this correlation was classified as moderate. However, no significant relationships were found between the addition of fentanyl and diastolic blood pressure, pulse rate, breath rate, or qNOX in both the paracetamol and ibuprofen groups. This was evidenced by p-values > 0,05 for these parameters. It should be noted that the significant relationship observed between the addition of fentanyl and systolic blood pressure in the paracetamol group suggests that the administration of fentanyl during surgery may coincide with an increase in systolic blood pressure, potentially leading to tachycardia or an increase in qNOX value.

6. Conclusion

Based on the results of the analysis, it can be concluded that there is no significant difference in blood pressure between patients given ibuprofen and those given paracetamol as preemptive analgesia. Similarly, there is no significant difference in breathing frequency, heart rate frequency, and qNOX between patients given ibuprofen and those given paracetamol as preemptive analgesia. Additionally, postoperative pain scores at 2 hours, 6 hours, and 24 hours in patients given ibuprofen showed no significant difference compared to those given paracetamol as preemptive analgesia. Moreover, the duration and postoperative opioid requirements in patients given ibuprofen

also exhibited no significant difference compared to paracetamol as preemptive analgesia. However, in the test between variables, there was a significant relationship between the addition of fentanyl and systolic blood pressure in the paracetamol group.

This study is not without limitations. Firstly, the monitoring for the last postoperative pain score check was only conducted at 24 hours postoperatively, whereas postoperative pain can occur up to 48 hours postoperatively. Secondly, the analysis of the relationship between the fentanyl addition test and parameters like systolic and diastolic blood pressure, pulse, breath, and qNOX could be explored in further research. Thirdly, the administration of postoperative analgesics to patients in the room was found to lack discipline in terms of timing, which could potentially affect pain scores at 6 hours and 24 hours postoperatively. The results of this study are expected to serve as a reference for future research on preemptive analgesia.

In order to provide better service, based on the results of this study, the researcher suggests further research on the relationship between preemptive analgesia and the risk of postoperative nausea and vomiting, as well as the length of treatment after surgery. Additionally, exploring other drugs for postoperative analgesic administration that are expected to more effectively reduce postoperative pain scores for up to 24 hours would be beneficial. Moreover, ensuring time discipline in administering postoperative drugs according to the schedule in the hospitalization room is recommended.

References

[1] Barash, P. G., Cullen, B. F., Stoelting, R. K., Cahalan, M. K., Stock, M. C., & Ortega, R. A. (2006). Anesthesia for neurosurgery. *Clinical Anesthesia. Philadelphia: Lippincott Williams & Wilkins*, 996–1003.

[2] Ciftci, B., Ekinci, M., Celik, E. C., Kaciroglu, A., Karakaya, M. A., Demiraran, Y., & Ozdenkaya, Y. (2019). Comparison of intravenous ibuprofen and paracetamol for postoperative pain management after laparoscopic sleeve gastrectomy. A randomized controlled study. *Obesity Surgery*, *29*, 765–770.

[3] Foss, N. B., & Kehlet, H. (2020). Challenges in optimising recovery after emergency laparotomy. *Anaesthesia*, *75*, e83–e89.

[4] Hassan, H. I. E. A. (2014). Perioperative analgesic effects of intravenous paracetamol: Preemptive versus preventive analgesia in elective cesarean section. *Anesthesia, Essays and Researches*, *8*(3), 339.

[5] Jensen, T. S., & Finnerup, N. B. (2014). Allodynia and hyperalgesia in neuropathic pain: clinical manifestations and mechanisms. *The Lancet Neurology*, *13*(9), 924–935.

[6] Koh, W., Nguyen, K. P., & Jahr, J. S. (2015). Intravenous non-opioid analgesia for peri-and postoperative pain management: a scientific review of intravenous acetaminophen and ibuprofen. *Korean Journal of Anesthesiology*, *68*(1), 3–12.

[7] Le, V., Kurnutala, L., Schiano Di Cola, J., Ahmed, K., Yarmush, J., Daniel Eloy, J., Shapiro, M., Haile, M., & Bekker, A. (2016). Premedication with intravenous ibuprofen improves recovery characteristics and stress response in adults undergoing laparoscopic cholecystectomy: a randomized controlled trial. *Pain Medicine*, *17*(6), 1163–1173.

[8] Masigati, H. G., & Chilonga, K. S. (2014). Postoperative pain management outcomes among adults treated at a tertiary hospital in Moshi, Tanzania. *Tanzania Journal of Health Research*, *16*(1).

[9] Simone, J. L., Jorge, W. A., Horliana, A. C. R. T., Canaval, T. G., & Tortamano, I. P. (2013). Comparative analysis of preemptive analgesic effect of dexamethasone and diclofenac following third molar surgery. *Brazilian Oral Research*, *27*, 266–271.

[10] Stoelting, R. K., & Hillier, S. C. (2012). *Pharmacology and physiology in anesthetic practice*. Lippincott Williams & Wilkins.

[11] Unal, S. S., Aksoy, M., Ahiskalioglu, A., Erdem, A. F., & Adanur, S. (2015). The effect of intravenous preemptive paracetamol on postoperative fentanyl consumption in patients undergoing open nephrectomy: A prospective randomized study. *Nigerian Journal of Clinical Practice*, *18*(1), 68–74.

[12] Vittayakittipong, P., & Areewattana, T. (2022). Efficacy of Preemptive Ibuprofen Combined with Paracetamol in Lower Third Molar Surgery: A Double-blind Randomized Controlled Clinical Trial. *Chiang Mai Dental Journal*, *43*(1), 57–64.