https://doi.org/10.24884/2078-5658-2025-22-6-32-38

Сравнение комбинации ибупрофена и парацетамола с кеторолаком и парацетамолом у пациенток, перенесших гинекологические операции: анализ уровня боли, показателей свертываемости крови и уровня интерлейкина-6

M. K. MAARIF[1], A. T. MUSBA[1, 2], M. D. DATU[1, 3], S. GAUS[1, 2], N. S. WIRAWAN[1, 3], A. ADIL[1, 2]*

[1] Кафедра анестезиологии, интенсивной терапии и обезболивания, медицинский факультет, Университет Хасануддина, Макассар, Индонезия

[2] Отделение анестезиологии, интенсивной терапии и обезболивания, медицинский факультет, больница общего профиля имени доктора Вахидина Судирохусодо, Макассар, Индонезия

[3] Отделение анестезиологии, интенсивной терапии и обезболивания, медицинский факультет, Университетская больница Хасануддина, Макассар, Индонезия

Поступила в редакцию 23.07.2025 г.; дата рецензирования 05.10.2025 г.

РЕЗЮМЕ

Введение. Послеоперационное обезболивание в гинекологической хирургии остается серьезной проблемой, поскольку многие пациентки испытывают боль от умеренной до сильной, несмотря на стандартные методы обезболивания. Использование определенных анальгетиков повышает риск осложнений, таких как кровотечение и длительное восстановление, что подчеркивает необходимость поиска оптимального метода обезболивания.

Цель – сравнить эффективность двух комбинированных схем обезболивания: ибупрофен-парацетамол и кеторолак-парацетамол путем сопоставления уровня болевого синдрома, показателей свертываемости крови и уровня IL-6.

Материалы и методы. Проведено двойное слепое рандомизированное исследование с участием 40 пациенток, перенесших гинекологическую операцию. 1-я группа получала внутривенно ибупрофен (400 мг) + парацетамол (1000 мг); во 2-й группе внутривенно вводили кеторолак (30 мг) + парацетамол (1000 мг). Уровень боли, время свертывания крови, время кровотечения и уровень IL-6 оценивали через 6, 24 и 48 часов после операции.

Результаты. Показатели боли и время свертывания крови статистически значимо не отличались между группами. Во 2-й группе наблюдалось значительное повышение уровня времени кровотечения через 24 и 48 часов ($p < 0,05$), в то время как в 1-й группе уровень IL-6 был значительно ниже через 24 часа ($p < 0,05$).

Вывод. Обе схемы лечения были одинаково эффективны в борьбе с болью. Однако комбинация «кеторолак-парацетамол» значительно продлевала время кровотечения, тогда как «ибупрофен-парацетамол» была более эффективна в уменьшении воспаления за счет снижения уровня IL-6. Эти различия следует учитывать, особенно у пациентов с риском кровотечения.

Ключевые слова: обезболивание, мультимодальный анальгетик, профиль коагуляции, интерлейкин-6, ибупрофен, кеторолак, парацетамол, гинекологическая хирургия

Для цитирования: Maarif M. K., Musba A. T., Datu M. D., Gaus S., Wirawan N. S., Adil A. Сравнение комбинации ибупрофена и парацетамола с кеторолаком и парацетамолом у пациенток, перенесших гинекологические операции: анализ уровня боли, показателей свертываемости крови и уровня интерлейкина-6// Вестник анестезиологии и реаниматологии. – 2025. – Т. 22, № 6. – С. 32–38. https://doi.org/10.24884/2078-5658-2025-22-6-32-38.

Comparison of Ibuprofen and Paracetamol combination with Ketorolac and Paracetamol combination in patients undergoing gynecologic surgery: a review of pain level, coagulation profile, and interleukin-6 levels

M. K. MAARIF[1], A. T. MUSBA[1, 2], M. D. DATU[1, 3], S. GAUS[1, 2], N. S. WIRAWAN[1, 3], A. ADIL[1, 2]*

[1] Department of Anesthesiology, Intensive Care and Pain Management, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia

[2] Department of Anesthesiology, Intensive Care and Pain Management, Faculty of Medicine, Dr. Wahidin Sudirohusodo General Hospital, Makassar, Indonesia

[3] Department of Anesthesiology, Intensive Care and Pain Management, Faculty of Medicine, Hasanuddin University Hospital, Makassar, Indonesia.

Received 23.07.2025; review date 05.10.2025

ABSTRACT

Introduction. Postoperative pain management in gynecological surgery remains a significant challenge, with many patients experiencing moderate-to-severe pain despite standard analgesic interventions. The risk of complications, such as bleeding and prolonged recovery, is heightened by the use of certain analgesics, emphasizing the need for optimal pain management strategies.

The objective was to compare the efficacy of two multimodal analgesic regimens: Ibuprofen– Paracetamol and Ketorolac- Paracetamol on pain, coagulation and IL-6 levels.

Materials and methods. A double-blind randomized trial was conducted with 40 patients who underwent gynecological surgery. Group 1 received IV Ibuprofen (400 mg) + Paracetamol (1000 mg); Group 2 received IV Ketorolac (30 mg) + Paracetamol (1000 mg). Pain (NRS), clotting time (CT), bleeding time (BT), and IL-6 were assessed at 6, 24, and 48 hours postoperatively.

Results. Pain scores and CT did not differ significantly between the groups. The Ketorolac group showed a significant increase in BT at 24 and 48 hours ($p < 0.05$), while the Ibuprofen group had significantly lower IL-6 levels at 24 hours ($p < 0.05$).

Conclusion. Both regimens were equally effective in pain control. However, Ketorolac- Paracetamol significantly prolonged the bleeding time, whereas Ibuprofen-Paracetamol was more effective in reducing inflammation by lowering IL-6 levels. These differences should be considered, especially in patients at risk of bleeding.

Keywords: pain management, multimodal analgesic, coagulation profile, Interleukin-6, Ibuprofen, Ketorolac, Paracetamol, gynecological surgery

For citation: Maarif M. K., Musba A. T., Datu M. D., Gaus S., Wirawan N. S., Adil A. Comparison of Ibuprofen and Paracetamol combination with Ketorolac and Paracetamol combination in patients undergoing gynecologic surgery: a review of pain level, coagulation profile, and interleukin-6 levels. *Messenger of Anesthesiology and Resuscitation*, 2025, Vol. 22, № 6, P. 32–38. (In Russ.). https://doi.org/10.24884/2078-5658-2025-22-6-32-38.

* *Для корреспонденции:*
Muhammad Khaerul Maarif
E-mail: khaerulmaarif19@yahoo.com

* *Correspondence*:
Muhammad Khaerul Maarif
E-mail: khaerulmaarif19@yahoo.com

Introduction

Gynecological surgery is a common procedure that frequently results in postoperative pain of varying intensity, ranging from moderate to severe [4]. Inadequate perioperative pain management can lead to several morbidities, including hemodynamic instability, prolonged recovery time, immunosuppression, and an increased risk of developing chronic pain [16]. Postoperative pain following gynecological procedures may arise from various surgical approaches, including laparotomy and laparoscopy [15]. Although laparoscopy is considered a minimally invasive technique, postoperative pain remains a significant concern that warrants appropriate management.

Postoperative pain involves a combination of nociceptive, inflammatory, and neuropathic components resulting from tissue injury and the inflammatory response to surgical trauma [7]. Therefore, a multimodal analgesic approach that combines multiple drugs with different mechanisms of action is strongly recommended to achieve optimal pain control while minimizing the adverse effects associated with high doses of a single agent [16].

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and Paracetamol (Acetaminophen) are central components in multimodal postoperative analgesia. Ibuprofen is a non-selective cyclooxygenase (COX) inhibitor that reduces the production of prostaglandins, which are involved in pain and inflammation. Ketorolac is a more potent NSAID with strong analgesic effects and is frequently administered intravenously for the management of severe postoperative pain [13]. Paracetamol, although its mechanism of action is not fully understood, is believed to act centrally to exert analgesic and antipyretic effects [14].

Despite their effectiveness, NSAIDs are associated with potential side effects, particularly affecting the coagulation and gastrointestinal systems. All NSAIDs can inhibit platelet aggregation to varying degrees, with Ketorolac being associated with a higher risk of bleeding due to its greater potency [8]. Postoperative coagulation disturbances may lead to serious hemorrhagic complications, especially in surgeries with significant bleeding potential, such as gynecological procedures.

Moreover, the postoperative inflammatory response – mediated by pro-inflammatory cytokines such as Interleukin-6 (IL-6) – is also of concern. IL-6 is released in response to tissue injury and correlates with pain intensity and the overall postoperative stress response [1, 12]. NSAIDs are known to modulate this inflammatory cascade. Comparing the effects of different analgesic combinations on IL-6 levels can provide insights into their capacity to attenuate systemic inflammation.

Given the importance of achieving effective pain control with a favorable safety profile, this study aimed to compare the efficacy and safety of two commonly used analgesic combinations – Ibuprofen-Paracetamol and Ketorolac-Paracetamol – in patients undergoing gynecological surgery. This comparison focused on postoperative pain intensity, changes in coagulation parameters (clotting time – CT, bleeding time – BT), and serum Interleukin-6 levels.

Materials and Methods

A double-blind, randomized clinical trial was conducted between December 2024 and March 2025 at Dr. Wahidin Sudirohusodo General Hospital and its affiliated network hospitals. The study design was approved by the Research Ethic Committee of Hasanuddin University (No.: 1010/UN4.6.4.5.31/PP36/2024).

Eligible patients were patients aged 18–65 years undergoing gynecologic surgery and had an American Society of Anesthesiologists (ASA) physical status I–II. Patients with a history of asthma, hypertension, cardiovascular disease, epilepsy, or use of antiepileptic drugs; chronic pain or psychiatric disorders; diabetes mellitus; kidney failure; liver disorders; alcohol use or previous opioid/neuropathic analgesic/anti-inflammatory drug use; currently undergoing chemotherapy; neurological, immunological, or hematological disorders; and allergies to study materials were excluded from this study. Furthermore, patients who experienced major bleeding or blood transfusion during surgery (> 40% of MABL), withdrawal from the study, and conversion to general anesthesia during surgery were excluded from this study. After obtaining informed consent, the samples were divided into two groups: Group 1 (Ibuprofen + Paracetamol) and Group 2 (Ketorolac + Paracetamol).

Table 1. **Characteristics of research subjects, Mean ± SD**

Characteristics	Group P1 (n = 20)	Group P2 (n = 20)	p
Age (year)	40.3 ± 7.39	41.5 ± 10.29	0.674[a]
Body weight (kg)	64.1 ± 8.54	61.55 ± 5.67	0.273[a]
Height (m)	154.3 ± 4.41	155.8 ± 2.95	0.183[b]
Body Mass Index (kg/m^2)	26.98 ± 4.18	25.35 ± 2.66	0.157[b]
Operation duration (minutes)	133.5 ± 32.97	111.0 ± 33.86	0.102[b]
Bleeding (mL)	305.0 ± 122.36	302.5 ± 106.96	0.925[b]

N o t e: [a] – Independent sample t test; [b] – Mann–Whitney test; $p < 0.05$ is significant.

Table 2. **Comparison of NRS at rest and NRS during movement between groups, Mean ± SD**

Time	Group P1 (n = 20)	Group P2 (n = 20)	p
NRS at rest			
6 hours post-surgery	2.6 ± 0.5	2.95 ± 0.76	0.183
12 hours post-surgery	1.6 ± 0.5	2.1 ± 0.97	0.134
24 hours post-surgery	1.25 ± 0.44	1.6 ± 0.59	0.091
48 hours post-surgery	0 ± 0	0.1 ± 0.31	0.602
NRS upon movement			
6 hours post-surgery	3.6 ± 0.5	3.55 ± 0.51	0.752
12 hours post-surgery	3.0 ± 0.86	2.70 ± 0.72	0.349
24 hours post-surgery	2.35 ± 0.49	2.45 ± 0.51	0.524
48 hours post-surgery	1.1 ± 0.31	1.0 ± 0	0.152

N o t e: Mann – Whitney test, p <0.05 is significant.

After informed consent was obtained and the inclusion criteria were met, the patients were randomly assigned to the treatment groups using block randomization with a block size of four, generated by a computer-based random number generator. Group allocations were placed in sealed, opaque envelopes and opened by a nurse who was not involved in the data collection or patient evaluation.

Both the anesthesiologist responsible for postoperative pain management and the researcher collecting data were blinded to the group allocation (double-blind). Patients were also unaware of the medications they received (double-blind).

After surgery was completed and the patient had recovered from anesthesia in the Post-Anesthesia Care Unit (PACU), the assigned analgesic regimen was administered 1 hour postoperatively according to group allocation. Group 1 (Ibuprofen-Paracetamol) received Ibuprofen 400 mg diluted in 100 mL of 0.9% NaCl plus 10 mL of placebo every 8 hours and Paracetamol 1000 mg intravenously every 6 hours. Group 2 (Ketorolac-Paracetamol) received Ketorolac 30 mg diluted in 10 mL of 0.9% NaCl plus 100 mL of placebo every 8 hours and Paracetamol 1000 mg intravenously every 6 hours. Medications were administered for the first 24 hours postoperatively.

If pain was not adequately controlled with the assigned regimen (NRS > 4), rescue analgesia in the form of intravenous Fentanyl at a dose of 0.5–1 mcg/kg body weight was provided. The total dose of rescue analgesia administered was recorded.

The primary endpoints were pain levels, coagulation profile, and serum interleukin-6 (IL-6) levels. Pain intensity was assessed using the numeric rating scale (NRS) at 6, 12, 24, and 48 hours postoperatively. Coagulation profile parameters, specifically clotting time (CT) and BT, were measured 2 hours before surgery (preoperative baseline) and at 24 and 48 hours postoperatively. IL-6 levels were measured 2 hours before surgery (preoperative baseline) and at 6 and 24 hours post-surgery using the Enzyme-Linked Immunosorbent Assay (ELISA) method. Blood samples were collected, and IL-6 concentration was analyzed to evaluate the inflammatory response to the surgical procedure and analgesic intervention.

Data were analyzed using the SPSS version 25.0 statistical software. The normality of the data was assessed using the Shapiro-Wilk test, with a significance level of $p > 0.05$ indicating a normal distribution. For normally distributed data ($p > 0.05$), an independent t-test was used, whereas for non-normally distributed data ($p \leqslant 0.05$), the Mann–Whitney U test and Wilcoxon test were applied to compare NRS scores, CT, BT, and IL-6 levels before and after the intervention within each group. A P value of <0.05 was considered statistically significant.

Results

This study included a total of 40 participants who were randomly divided into two groups. The baseline characteristics of the two groups (age, body weight, height, BMI, duration of surgery, and blood loss) showed no significant differences ($p > 0.05$), indicating that the groups were homogeneous. Detailed characteristics are presented in Table 1.

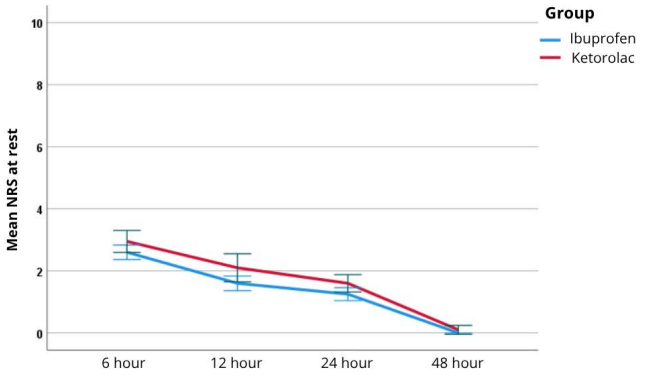

Fig. 1. Comparison of NRS at rest in both groups

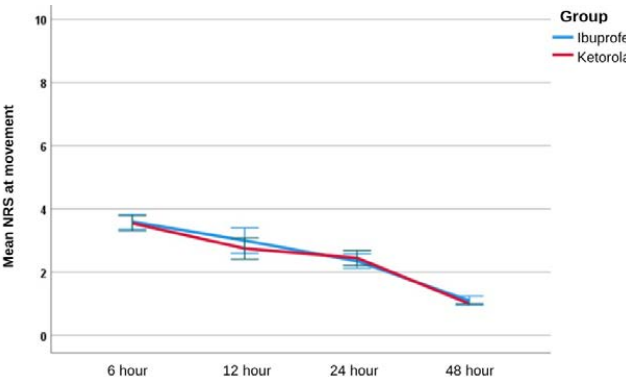

Fig. 2. Comparison of NRS during movement in both groups

***Table 3*. Comparison of CT and BT between study times, Mean ± SD**

Time	Group P1 (n = 20)	P	Group P2 (n = 20)	p
CT (minutes)[a]				
2 hours preoperative	7.67 ± 0.36	1.0	7.62 ± 0.36	0.772
24 hours post-surgery	7.67 ± 0.36		7.67 ± 0.38	
2 hours preoperative	7.67 ± 0.36	0.104	7.62 ± 0.36	0.209
48 hours post-surgery	7.72 ± 0.34		7.76 ± 0.36	
24 hours post-surgery	7.67 ± 0.36	0.104	7.67 ± 0.38	0.056
48 hours post-surgery	7.72 ± 0.34		7.76 ± 0.36	
BT (minutes)[b]				
2 hours preoperative	3.42 ± 0.2	0.317	3.36 ± 0.17	0.046
24 hours post-surgery	3.45 ± 0.24		3.46 ± 0.22	
2 hours preoperative	3.42 ± 0.2	0.074	3.36 ± 0.17	0.002
48 hours post-surgery	3.48 ± 0.22		3.60 ± 0.26	
24 hours post-surgery	3.45 ± 0.24	0.336	3.46 ± 0.22	0.044
48 hours post-surgery	3.48 ± 0.22		3.60 ± 0.26	

N o t e: [a] – Paired t-test; [b] – Wilcoxon test, p <0.05 is significant.

1. Pain Levels. Pain levels were assessed using the Numeric Rating Scale (NRS) at rest and during movement at 6, 12, 24, and 48 hours postoperatively. No significant differences were observed in the mean NRS scores at rest or during movement between Group 1 and Group 2 at any of the measurement time points ($p > 0.05$). The comparative results are presented in Table 2 and illustrated in Figures 1 and 2.

2. Coagulation Profile. As shown in Table 3, there were no significant differences in CT values within either Group 1 or Group 2 across the measurement time points ($p > 0.05$). For BT, Group 1 also did not exhibit significant changes. However, in Group 2, significant differences in BT values were observed between 2 hours preoperatively and 24 hours postoperatively, between 2 hours preoperatively and 48 hours postoperatively, and between 24 and 48 hours postoperatively ($p < 0.05$).

As presented in Table 4, the comparison of changes (Δ) in CT between 2 hours preoperatively and 24 hours postoperatively did not differ significantly between the two groups ($p > 0.05$). At 48 hours postoperatively, the mean CT increased by 0.05 in Group 1 and by 0.13 in Group 2; however, this difference was not statistically significant ($p > 0.05$). Regarding changes in BT, at 24 hours postoperatively, BT increased by 0.03 in Group 1 and by 0.09 in Group 2, with no significant difference between groups ($p > 0.05$).

However, the comparison of BT changes between 2 hours preoperatively and 48 hours postoperatively showed a significant difference between Groups 1 and 2 ($p < 0.05$), with mean increases of 0.05 and 0.24, respectively. No significant difference was observed in BT changes between 24 and 48 hours postoperatively in either group ($p > 0.05$).

The trends in CT and BT for both groups are illustrated in Figures 3 and 4. CT remained relatively stable in the Ibuprofen group, whereas a slight increase was observed in the Ketorolac group. BT showed minimal changes in the Ibuprofen group but increased more notably in the Ketorolac group, particularly at 48 hours postoperatively.

3. Interleukin-6 Levels. The results presented in Table 5 indicate no significant difference in the mean IL-6 levels at 2 hours preoperatively between Group 1 and Group 2 ($p > 0.05$), indicating comparable baseline IL-6 levels in both groups. However, IL-6 levels differed significantly between the two groups at 6 hours and 24 hours postoperatively ($p < 0.05$). The comparison of IL-6 levels between the groups over the study time points is illustrated in Figure 5. IL-6 levels increased from 2 hours preoperatively to 6 hours postoperatively,

***Table 4*. Comparison of CT and BT changes between groups, Mean ± SD**

Time	Group P1 (*n* = 20)	Group P2 (*n* = 20)	*p*
Delta CT (minutes)			
2 hours pre-24 hours post	0.00 ± 0.00	0.05 ± 0.13	0.429
2 hours pre-48 hours post	0.05 ± 0.13	0.13 ± 0.22	0.265
24 hours post-48 hours post	0.05 ± 0.13	0.09 ± 0.17	0.583
Delta BT (minutes)			
2 hours pre-24 hours post	0.03 ± 0.11	0.09 ± 0.21	0.201
2 hours pre-48 hours post	0.05 ± 0.15	0.24 ± 0.24	0.021
24 hours post-48 hours post	0.03 ± 0.16	0.14 ± 0.29	0.157

N o t e: Mann – Whitney test, $p < 0.05$ is significant.

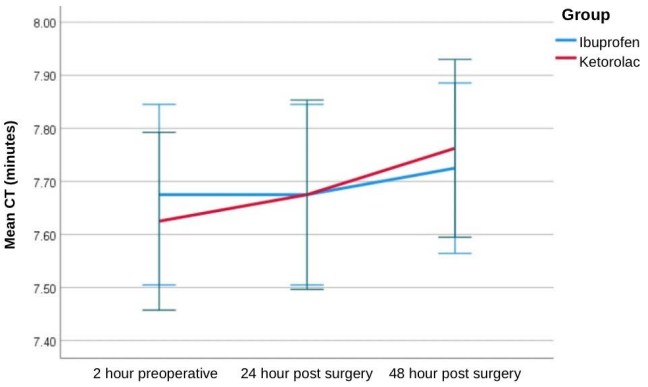

Fig. 3. CT graph in both groups

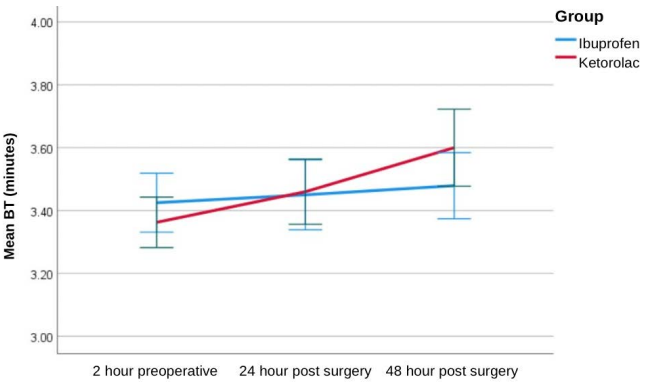

Fig. 4. BT graph in both groups

***Table 5*. Comparison of IL-6 levels between groups, Mean ± SD**

Time	IL-6 (pg/mL)		*p*
	Group P1 (*n* = 20)	Group P2 (*n* = 20)	
2 hours preoperative	28.96 ± 6.3	27.76 ± 5.47	0.522
6 hours post-surgery	46.55 ± 7.46	57.09 ± 12.72	0.003
24 hours post-surgery	35.26 ± 5.97	42.39 ± 9.4	0.007

N o t e: Mann – Whitney test, $p < 0.05$ is significant.

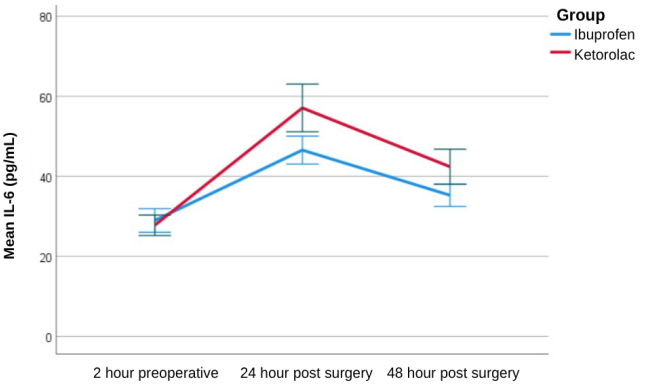

Fig. 5. IL-6 levels in both group

followed by a decline at 24 hours postoperatively in both groups.

Discussion

This study compared the analgesic efficacy, effects on coagulation profiles, and inflammatory responses of the Ibuprofen-Paracetamol combination versus the Ketorolac-Paracetamol combination in patients undergoing gynecological surgery. The findings demonstrated that both analgesic combinations – Paracetamol-Ibuprofen and Paracetamol-Ketorolac – were effective in managing postoperative gynecological pain, with no significant differences observed in Numeric Rating Scale (NRS) scores. These results are consistent with prior research by Rahim et al. (2023), which similarly reported no significant differences in pain levels between the Paracetamol-Ibuprofen and Paracetamol-Ketorolac combinations following gynecological surgery [11]. This supports the principle of multimodal analgesia, wherein drug combinations may produce synergistic effects in reducing pain and opioid consumption.

The absence of a significant difference in NRS pain scores between the two groups indicates that both Ibuprofen-Paracetamol and Ketorolac-Paracetamol combinations provide comparable analgesia in this patient population. This finding supports the concept of multimodal analgesia, where combining drugs with different mechanisms can provide effective pain relief – even though intravenous Ketorolac is typically viewed as more potent than oral Ibuprofen. The efficacy of Paracetamol as a foundational component in both regimens likely contributed to these outcomes, given

its well-established analgesic properties in postoperative pain management [16].

An important aspect of this study was the evaluation of coagulation profiles. Although both combinations provided equivalent analgesia, significant differences were observed in the coagulation profiles and IL-6 levels. The Ketorolac-Paracetamol group exhibited a significant prolongation of BT at 24 and 48 hours postoperatively. Ketorolac is known to cause prolonged bleeding time and reduced platelet aggregation [3, 5]. In contrast, Paracetamol exerts minimal effects on platelet aggregation and does not significantly prolong the bleeding time [2]. Although classified as an NSAID, Ibuprofen has been reported to have effects on platelet aggregation and coagulation that return to normal within 24 hours after the last dose [6, 9]. The increased bleeding time observed in the Ketorolac-Paracetamol group indicates a potentially higher risk of bleeding compared to the Ibuprofen-Paracetamol group, particularly in surgical procedures requiring meticulous hemostatic control.

Furthermore, this study also examined the effects on serum IL-6 levels, an important inflammatory marker. The Ibuprofen-Paracetamol group demonstrated a more significant reduction in serum IL-6 levels at 6 and 24 hours postoperatively compared to the Ketorolac-Paracetamol group. IL-6 is a pro-inflammatory cytokine released in response to tissue injury and surgical stress [10], and it correlates with systemic inflammatory response and pain intensity [18]. The greater suppression of IL-6 by the Ibuprofen-Paracetamol combination may reflect the stronger anti-inflammatory effects of Ibuprofen compared to Ketorolac. This suggests that Ibuprofen may be more effective in modulating the systemic inflammatory response following surgery. Such a mechanism could contribute to improved patient recovery, although further investigations are warranted.

The strengths of this study include a double-blind randomized clinical trial design, which helps minimize bias. Objective measurements, such as coagulation parameters and IL-6 levels, further enhanced data robustness. However, several limitations of this study should be noted. The limitation of this study is the follow-up period, restricted to 48 hours postoperatively. This short observation window limits the ability to assess the potential long-term adverse effects associated with the administration of Ibuprofen-Paracetamol and Ketorolac-Paracetamol combinations. Therefore, further studies with extended follow-up are necessary to comprehensively evaluate the safety profiles of these analgesic regimens.

The findings of this study support that the combination of Ibuprofen-Paracetamol offers analgesic efficacy equivalent to that of Ketorolac-Paracetamol in gynecological patients, with a more favorable coagulation profile. This suggests that Ibuprofen-Paracetamol may represent a safer analgesic option, particularly for patients at risk of bleeding or those undergoing procedures with a high potential for hemorrhage. In addition, it also has a better anti-inflammatory effect.

Future research should include longer follow-up durations to evaluate the long-term impact on morbidity related to bleeding and chronic pain. Broader investigations of inflammatory markers and more comprehensive assessments of platelet function would also provide deeper insights into the mechanisms of action of these drug combinations. In addition, studies assessing the cost-effectiveness and patient satisfaction of both regimens are highly valuable.

Conclusion

The combinations of Ibuprofen-Paracetamol and Ketorolac-Paracetamol demonstrated comparable efficacy in managing postoperative pain in gynecological patients. Ibuprofen-Paracetamol combination did not significantly affect coagulation profiles (CT and BT), whereas the Ketorolac-Paracetamol combination significantly influenced coagulation profiles, specifically BT, at 24- and 48-hours post-surgery. Ibuprofen-Paracetamol combination resulted in lower IL-6 levels at 6 and 24 hours postoperatively compared to the Ketorolac-Paracetamol combination, showing that more effective in suppressing the inflammatory response. The selection of an analgesic regimen should carefully balance pain control efficacy, coagulation safety profile, and the need to modulate the inflammatory response on an individual patient basis.

Conflict of Interests. The authors state that they have no conflict of interests.

Contribution of the authors. All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, and final approval of the version to be published, and agreed to be accountable for all aspects of the work.

REFERENCES

1. Aletaha D., Kerschbaumer A., Kastrati K. et al. Consensus statement on blocking interleukin-6 receptor and interleukin-6 in inflammatory conditions: an update. *Ann Rheum Dis*, 2023, vol. 82, no. 6, pp. 773–787. https://doi.org/10.1136/ard-2022-222784.
2. Botting R. M. Mechanism of action of acetaminophen: is there a cyclooxygenase 3? *Clin Infect Dis*, 2000, vol. 31. Suppl 5, S202–210. https://doi.org/10.1086/317520.
3. Douraiswami B., Dilip P. K., Harish B. N. et al. C-reactive protein and interleukin-6 levels in the early detection of infection after open fractures. *J Orthop Surg (Hong Kong)*, 2012, vol. 20, no. 3, pp. 381–385. https://doi.org/10.1177/230949901202000325.
4. Erekson E. A., Yip S. O., Ciarleglio M. M. et al. Postoperative complications after gynecologic surgery. *Obstetrics and Gynecology*, 2011, vol. 118, no. 4, pp. 785–793. https://doi.org/10.1097/AOG.0b013e31822dac5d.

5. Fithri D., Wijaya D., Arifin H. Perbedaan nilai agregasi trombosit akibat pengaruh penggunaan analgesia ketorolak dan ibuprofen intravena pascaoperasi di RSUP haji adam malik medan. *Jurnal Anestesi Perioperatif*, 2017, vol. 5, no. 3, pp. 141–146. https://doi.org/10.1581/jap.v5n3.1166.

6. Goldenberg N. A., Jacobson L., Manco-Johnson M. J. Brief communication: duration of platelet dysfunction after a 7-day course of Ibuprofen. *Ann Intern Med*, 2005, vol. 142, no. 7, pp. 506–509. https://doi.org/10.7326/0003-4819-142-7-200504050-00009.

7. Horn R., Hendrix J. M., Kramer J. Postoperative Pain Control. In: StatPearls. StatPearls Publishing.; 2025. URL: https://pubmed.ncbi.nlm.nih.gov/31335018/ (accessed: 10.11.25).

8. Mahmoodi A. N., Patel P., Kim P. Y. et al. Ketorolac. In: StatPearls. StatPearls Publishing; 2025.

9. Martini W. Z., Deguzman R., Rodriguez C. M. et al. Effect of Ibuprofen dose on platelet aggregation and coagulation in blood samples from pigs. *Mil Med*, 2015, vol. 180, 3 Suppl, pp. 80–85. https://doi.org/10.7205/MILMED-D-14-00395.

10. Park A., Anderson D., Battaglino R. A. et al. Ibuprofen use is associated with reduced C-reactive protein and interleukin-6 levels in chronic spinal cord injury. *J Spinal Cord Med*, 2022, vol. 45, no. 1, pp. 117–125. URL: https://www.tandfonline.com/doi/full/10.1080/10790268.2020.1773029 (accessed: 10.11.25).

11. Rahim Muh. R., Musba A. M. T., Palinrungi A. S. et al. Perbandingan antara kombinasi ibuprofen dan parasetamol dengan ketorolak dan parasetamol intravena terhadap derajat nyeri dan rasio neutrofil limfosit pasca-functional endoscopic sinus surgery. *Jurnal Anestesi Perioperatif*, 2024, vol. 12, no. 3, pp. 161–8. https://doi.org/10.15851/jap.v12n3.3889.

12. Rose-John S. Local and systemic effects of interleukin-6 (IL-6) in inflammation and cancer. *FEBS Lett*, 2022, vol. 596, no. 5, pp. 557–566. https://doi.org/10.1002/1873-3468.14220.

13. Singh P., Rastogi S., Bansal M. et al. A prospective study to assess the levels of interleukin-6 following administration of Diclofenac, Ketorolac and Tramadol after surgical removal of lower third molars. *J Maxillofac Oral Surg*, 2015, vol. 14, no. 2, pp. 219–225. https://doi.org/10.1007/s12663-013-0609-1

14. Sun F., Zhang Y., Li Q. Therapeutic mechanisms of ibuprofen, prednisone and betamethasone in osteoarthritis. *Mol Med Rep,* 2017, vol. 15, no. 2, pp. 981–7. https://doi.org/10.3892/mmr.2016.6068.

15. Supermaniam S. Laparoscopic Surgery in Gynaecology. In: Laparoscopic Surgery in Gynaecology and Common Diseases in Women. 1st ed. Melaka, Malaysia: Adequate Wonder; 2016.

16. Wick E. C., Grant M. C., Wu C. L. Postoperativemultimodal analgesia pain management with nonopioid analgesics and techniques a review. *JAMA Surg*, 2017, vol. 152, no. 7, pp. 691–697. https://doi.org/10.1001/jamasurg.2017.0898.

17. Wittes J. Sample size calculations for randomized controlled trials. *Epidemiol Rev,* 2002, vol. 24, no. 1, pp. 39–53. https://doi.org/10.1093/epirev/24.1.39.

18. Younus L. A. The potential impact of Ibuprofen on level of IL-6. *Maaen Journal for Medical Sciences*, 2024, vol. 3, no. 1. https://doi.org/10.55810/2789-9136.1038.

INFORMATION ABOUT AUTHOR:

Muhammad Khaerul Maarif
Department of Anesthesiology, Intensive Care and Pain Management, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia. Jalan Perintis Kemerdekaan Km.10, Tamalanrea Indah, Tamalanrea, Makassar, Indonesia.
E-mail: khaerulmaarif19@yahoo.com