

+ paracetamol (1000 mg). Po 6, 24 a 48 hodinách po operaci jsme hodnotili numerickou škálu bolesti (NRS), dobu srážlivosti (CT), dobu krvácivosti (BT) a IL-6.

Výsledky: Skóre bolesti a CT se mezi oběma skupinami významně nelišily. Skupina s ketorolakem vykazovala významný nárůst BT po 24 a 48 hodinách ($p < 0,05$), zatímco skupina s ibuprofenem měla po 24 hodinách významně nižší hladiny IL-6 ($p < 0,05$).

Závěr: Oba režimy byly co do zvládnání bolesti stejně účinné. Ovšem kombinace ketorolak-paracetamol významně prodlužovala dobu krvácivosti, zatímco kombinace ibuprofen-paracetamol byla účinnější při redukci zánětu prostřednictvím snížení hladiny IL-6. Tyto rozdíly je třeba brát v úvahu, zejména pak u pacientek s rizikem krvácení.

Klíčová slova: léčba bolesti, koagulační profil, interleukin-6, ibuprofen, ketorolak, paracetamol, gynekologická operace.

Introduction

Gynecological surgery is a common procedure that frequently results in postoperative pain of varying intensity, ranging from moderate to severe [1]. Inadequate perioperative pain management can result in multiple complications, including hemodynamic instability, prolonged recovery, immunosuppression, and an increased risk of developing chronic pain [2]. Postoperative pain following gynecological procedures may arise from various surgical approaches, including laparotomy and laparoscopy [3]. Although laparoscopy is considered a minimally invasive technique, postoperative pain remains a significant concern that warrants proper management.

Postoperative pain involves a combination of nociceptive, inflammatory, and neuropathic components resulting from tissue injury and inflammatory response to surgical trauma [4]. Therefore, a multimodal analgesic approach combining 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 [2].

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 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 [5]. Paracetamol, although its mechanism of action is not fully understood, is believed to act centrally to exert analgesic and antipyretic effects [6].

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 [7]. Postoperative coagulation disturbances may lead to serious hemorrhagic complications, particularly in surgeries with significant bleeding potential, such as gynecological procedures.

Moreover, the postoperative inflammatory response mediated by pro-inflammatory cytokines such as 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 [8, 9]. 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 aims to compare the efficacy and safety of two commonly used analgesic combinations ibuprofen-paracetamol and ketorolac-paracetamol in patients undergoing gynecological surgery. The comparison focuses on postoperative pain intensity, changes in coagulation parameters (CT, BT), and serum IL-6 levels.

Material and Methods

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

Eligible patients were those aged 18–65 years undergoing gynecologic surgery, with American Society of Anesthesiologists (ASA) physical status I–II. Patients with significant comorbidities, prior relevant drug use, ongoing chemotherapy, or study-material allergies were excluded. 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 dropped out of this study. After providing informed consent, the subjects were divided into two groups (Group 1: ibuprofen + paracetamol; Group 2: ketorolac + paracetamol).

After informed consent was obtained and the inclusion criteria were met, patients were randomly assigned to 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 data collection or patient evaluation.

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

All patients enrolled in the study underwent surgery under spinal anesthesia in the left lateral position, with insertion at the L3–L4 interspace using a 25G Spinocan needle. The anesthetic regimen consisted of 0.5% bupivacaine 15 mg combined with fentanyl 25 µg. Surgical procedures commenced once the sensory block reached the T6 dermatome. After the surgery had been 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)