INTRODUCTION

Total knee replacement (TKR) is one of the most common procedures conducted in the orthopedic field. From 2005 to 2030, the number of TKR operations in the United States is predicted to increase dramatically by six-fold, with about 3.5 million surgeries yearly. In most cases, TKR was done exclusively on the elderly population. Moreover, postoperative TKR pain tends to be worse compared to younger patients.

Given the high number of TKR procedures done on geriatric patients and the greater intensity of pain felt in this population, proper knowledge in managing this population is vital. In TKR surgery, inadequate analgesia inhibits early mobilization and rehabilitation and walking function, increases the risk of thromboembolism formation due to prolonged bed rest, hinders the rehabilitation process, increases hospitalization costs, and decreases the patient’s overall quality of life.

According to the “THREE-STEP Analgesic Ladder” by World Health Organization, pain management strategies are generally divided into three stages. The first stage uses non-opioid analgesic drugs such as NSAIDs or COX2-specific inhibitors with or without adjuvants; the second stage uses weak opiates with or without non-opioid analgesics and with or without adjuvants, and the third stage uses potent opiates with or without non- opiates and with or without adjuvants.

For some, the administration of multiple analgesics might be compelling due to the significant impact of inadequate pain management. In most practices, physicians prescribe excessive amounts of analgesics based on the logic “more is better than less,” especially in cases of postoperative TKR when patients go through an adaptation process towards a new implant while the surgical wound is still fresh. Other assessments may include the patient’s history, which in some instances, patients who have experienced pain sensitization will tend to request stronger dosages or even buy their painkillers. Previous studies have found that multiple analgesic combinations lead to significantly higher side effects than a single analgesic. Appropriate pain management requires an accurate analgesic prescription.

This study aims to know whether using multiple analgesics is justified by comparing the effectiveness of single and multiple analgesics in managing post-TKR pain in the Indonesian population. Speed of recovery, time to partial weight-bearing, VAS difference, and side effect incidence will be used as a parameter.

MATERIAL AND METHODS

Study design

This observational retrospective comparative study compares the post-TKR surgical outcome and the use of single, double, or triple analgesia conducted in an Orthopaedic Hospital during 2012-2021. Patients who underwent TKR in an Orthopedic Hospital between 2012-2021.
were screened for eligibility to be included in this study. Treatment of analgesia was given by the anesthesiologist who chose any drug or any other technique. Our hospital ethical board has approved this research with certificate number (No.62/EC/KEPK/FKUA/2022).

**Inclusion/exclusion criteria**

Patients included were those diagnosed with OA grade IV and treated with single/unilateral TKR under a subarachnoid spinal block. On the other hand, patients with central nervous system disease (stroke), a history of postoperative blood transfusion, a history of hospitalization in the intensive care unit, and had undergone more than one TKR in their lifetime were excluded from the research.

**Data extraction**

The patient’s medical record was used to extract demographic data, the number of analgesics used (single, double, or triple analgesia), length of stay (LOS), time to partial weight-bearing (WB), VAS, and side effects (nausea and gastric pain). In counting the number of analgesics, all analgesics (opioid and non-opioid) administered during the first third postoperative day were included. Opioids in this study used fentanyl and tramadol. Non-opioids include Amida, NSAID (Nonsteroidal Anti Inflammation Drug), Acetaminophen, and COX-2 Inhibitors.

The primary outcome of this study would be the impact of analgetic use on VAS difference, LOS, time to PWB, and VAS on days 1, 3, and 5. As a secondary outcome would be the effect of analgetic use on the incidence of side effects (gastric pain and nausea).

**Data analysis**

The tabulated data were then presented in tables. Statistical analysis compared the impact of a single, double, or triple analgesic on the VAS, LOS, time to partial weight-bearing, and complication rate. To ensure objectivity, statistical analysis was done by a non-author. Statistical analysis depended on the data’s normality as tested by Kolmogorov Smirnov. For normally distributed data, ANOVA was used.

On the contrary, not normally distributed data were tested using Kruskal Wallis. A P-value of less than 0.050 will be accepted as significant. All statistical calculation was done using the SPSS program version 23.0.

**RESULTS**

In this study, a total of 152 patients were included. Most samples were females (n = 106, 69.7%), with the patient's average age about 63.75 ± 6.31 years old. Most patients had right-sided osteoarthritis (n = 81; 53.2%), and only a few had bilateral osteoarthritis (n = 13; 8.6%). Accordingly, most TKR procedures were done on the right side of the knee (n = 88; 57.9%).

The mean Body Mass Index was 26.89 ± 4.58, which indicates that most patients were overweight. In the normality test, it was found that all parameters were not normally distributed (p = 0.043), and therefore Kruskal-Wallis test was used to determine the parameter’s significance.

The sample’s perioperative data are described in Table 1, with a progressively declining VAS daily. Crosstabulation of the number of analgesics prescribed on VAS Pre-op, LOS, Time to Partial Weight-Bearing, and postoperative VAS on day 1, day 3, and day 5 are not significantly related (p = 0.451). Detailed data are displayed in Table 2.

For the incident of adverse reaction, it was found that nausea and gastric pain significantly correlated with the number of postoperative analgesics (p = 0.011). The adverse reaction incidence seemed to increase with more analgesic prescriptions (triple analgesic vs. a single analgesic), as shown in Table 3.

**DISCUSSION**

Previous studies found that 80% of postoperative patients were treated directly using stage two of the “Three-Step Analgesic Ladder,” which uses opioids to reduce pain. Although it successfully relieves pain and results in faster postoperative improvement, it is also necessary to consider the side effects of chronic opioid use, such as opioid addiction, intoxication, and cost burden.4 Previous studies have found that multiple postoperative analgesic side effects, especially nausea and vomiting, are significantly higher than a single analgesic.4–10 As a result, it is essential for physicians to not only treat postoperative pain as a single condition but also seek and treat its underlying cause. Several studies have also found that pain relief from opioids was not always better than...
Concerning recovery, postoperative analgesics assist recovery by making early partial weight-bearing possible. Faster partial weight-bearing is beneficial in creating a better outcome for the patient. Weight-bearing will stimulate pro-angiogenesis and pro-regenerative cytokines and mediators, which ultimately help regenerate the postoperative area.\(^{15}\)

Several studies have tested the effectiveness of acetaminophen in reducing postoperative pain after total knee arthroplasty. These studies were well summarized in the systematic review and meta-analysis by Teng et al., which summarized the results of 5 studies that covered 57,072 patients. His study found several essential points: (1) The use of oral acetaminophen was as effective as the intravenous drug in reducing VAS scores in patients after total knee arthroplasty. (2) The mean reduction in VAS was the same at 24 hours and 48 hours postoperatively, and (3) The use of morphine within 24 hours was found to decrease. (4) It was also found that acetaminophen could significantly reduce LOS. [14] These findings also apply to other types of surgery. Another study focusing on the effect of intravenous acetaminophen found that administering IV acetaminophen significantly reduced LOS (reduction of 0.68 days), re-admission risk, and decreased VAS.\(^{16}\)

This study used a length of stay and time to partial weight-bearing as indicators of the patient’s recovery. The shorter the length of stay and the time to partial weight-bearing, the better the patient’s recovery. However, this study did not find a significant difference between the number of analgesics given (single, double, and triple) with VAS (p=0.991), LOS (p=0.627), and time to partial weight-bearing (p=0.543). The impact of using postoperative analgesics might be more apparent if the observation was carried out for a more extended time.

Other contributing factors that might have been overlooked in this study include the availability of social support, personality type, coping skills, or preoperative pain.

The number of postoperative analgesic modalities was also compared based on the VAS on days 1, 3, and 5. This test was conducted to test whether polypharmacy analgesic (use of more than one analgesic) combinations were better than the mono pharmacy analgesics, and it was found that there was no significant difference between the two on day 1 (p=0.991), day 3 (p=0.051), and day 5 (p=0.135). This is consistent with previous studies, which did not support using multiple postoperative analgesics unless necessary in some circumstances.\(^{14,16,19}\)

Given its comparable effect, single analgesia might be more appropriate in managing post-TKR pain unless the indication is clear for multiple analgesics. Giving higher-than-necessary analgesia might be unessential as initial pain relief. For consideration, another study found that administration of large amounts of postoperative analgesics (triple) significantly increased the risk of the side effects studied, such as nausea (p=0.011) and gastric pains (p=0.044).\(^{14,16}\)

The limitation of this study was the bias that we analyzed only the number of analgesics administered without considering the analgesic (i.e., acetaminophen vs. COX-2 Inhibitor) or the route of therapeutic (oral or injection) itself. This research is conducted cross-sectionally and only studies samples from a single center. The length of each analgesic’s use and the detail of TKR techniques were not considered.

Based on the limitations of this study, we suggest that elaboration of types, routes and length of analgesia administration be considered in future studies. Expanding concerns like previous quality of life, personality, and family support may also be advantageous. Furthermore, it would be more beneficial to elaborate on TKR techniques used in one single center than those implemented in similar healthcare facilities.

**CONCLUSION**

The effectiveness of mono pharmacy and polypharmacy analgetics is similar regarding the speed of recovery, time to partial weight-bearing, and VAS in post-TKR patients. However, multiple analgesia administration may increase the risk of side effects.

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**CONFLICT OF INTEREST**

The author reports no conflicts of interest in this work.

**AUTHOR CONTRIBUTION**

All authors contributed equally to the preparation of this manuscript.

**ETHICAL APPROVAL**

Our hospital ethical board has approved this research with certificate number (No.62/EC/KEPK/FKUA/2022).

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**REFERENCES**


