

ORIGINAL RESEARCH

Effectiveness of a multimodal analgesia protocol in the perioperative period of knee replacement surgery in men

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Abstract

This study aimed to explore the efficacy of a multimodal analgesic regimen during the perioperative period for male patients undergoing knee replacement surgery. A total of 80 male patients scheduled for elective knee replacement surgery in our hospital's orthopedic department from March 2022 to March 2023 were selected through digital randomization. They were equally divided into a control group (received a conventional analgesic protocol) and an observation group (treated with a multimodal analgesic protocol that included patient-controlled analgesia (PCA), ultrasound-guided nerve block and physical analgesia). Parameters such as postoperative celecoxib capsule dosage, Visual Analog Scale (VAS) scores at 6, 12, 24 and 72 hours after surgery, levels of neurotransmitters and stress markers at the time of surgery, 24 hours post-surgery, and 72 hours post-surgery, sleep quality scores, the timing of first ambulation, and the overall incidence of adverse reactions were compared between the groups. After intervention, the observation group showed a statistically significant reduction in the dosage of celecoxib capsules compared to the control group ($p < 0.05$). VAS scores in the observation group were significantly lower than those in the control group at all measured time points. Furthermore, levels of substance P (SP), beta-endorphin (β -EP), 5-hydroxytryptamine (5-HT), cortisol (Cor), C-reactive protein (CRP) and white blood cell (WBC) counts in the observation group were significantly lower than those in the control group at 24- and 72-hours post-surgery. The incidence of adverse reactions was also significantly lower in the observation group ($p < 0.05$). We conclude that implementing a multimodal analgesic protocol in the perioperative period could significantly reduce pain, regulate neurotransmitter and stress levels, and enhance sleep quality in the early postoperative phase of male patients undergoing knee replacement surgery.

Keywords

Multimodal analgesia; Men; Artificial knee replacement surgery; Pain; Stress response; Postoperative rehabilitation

1. Introduction

Total knee arthroplasty (TKA) ranks among the most effective interventions for managing pain in patients with end-stage degenerative knee disease [1]. Projections from 2005 to 2030 indicate a significant increase in demand for primary TKA in the United States, with an estimated growth of 673% to 3.48 million procedures annually by 2030 [2]. Due to the invasive nature of TKA, which includes intraoperative osteotomies and prosthesis implantation, this surgery is recognized as one of the most painful orthopedic procedures [3, 4]. Inadequate pain control can impede early postoperative rehabilitation, adversely affecting recovery by compromising diet, sleep and mood [5], and may lead to complications associated with immobilization, such as venous thrombosis, due to reduced

mobility from postoperative pain [6]. Consequently, optimizing analgesia to enhance recovery and patient satisfaction has become a critical concern for anesthesiologists and surgeons. Recent years have seen the development of multimodal analgesia, a strategy that integrates various analgesic methods to enhance pain relief, and its application in post-TKA pain management [7]. This approach includes the preoperative administration of analgesics to prevent pain, minimize stress responses, amplify analgesic efficacy, and decrease both postoperative analgesic requirements and the risk of complications [8]. Effective pain management is pivotal for the prognosis following knee replacement [9]. Despite the reported success of multimodal analgesic protocols in various surgical contexts [10], the specific efficacy of these protocols in TKA among male patients still requires in-depth research and discussion.

2. Information and methods

2.1 General information

A cohort of 80 male patients scheduled for artificial knee replacement surgery at the Department of Orthopedics, West China Hospital of Sichuan University, from March 2022 to March 2023, was enrolled and allocated into two groups through digital randomization: 40 participants in the control group and 40 in the observation group. The observation group received a multimodal pre-analgesia protocol comprising patient-controlled analgesia (PCA), ultrasound-guided nerve block, and physical analgesia, whereas the control group was subjected to a conventional analgesic protocol.

Participants were eligible for inclusion in the study if they were aged 18 years or older, classified as American Society of Anesthesiologists (ASA) grade I to II, diagnosed with unilateral knee joint disease, met the criteria for artificial total knee replacement surgery with an elective approach for minimally invasive surgery, and provided informed consent from themselves and their families. Exclusion criteria comprised individuals with impaired consciousness or mental disorders, those suffering from severe organ failure or advanced tumors, and cases involving open fractures.

The mean age in the control group was 75.02 ± 4.30 years, and in the observation group, it was 75.13 ± 4.26 years. Statistical analysis revealed no significant difference in the

baseline data between the two patient groups ($p > 0.05$).

2.2 Research methods

2.2.1 Research methods of the control group

In the control group, conventional nursing approaches were employed, which included several strategies aimed at managing postoperative pain. First, pain education was provided, offering patients comprehensive information about the potential sensations of pain following the surgery to improve their understanding and ability to manage pain. Secondly, music therapy was utilized, exploiting the pleasurable and calming effects of music to create a relaxing environment that can help lessen postoperative pain. The third strategy involved the attention diversion method, where patients were guided to shift their focus from pain to engaging or enjoyable activities, aiding in the reduction of their pain perception. Lastly, pharmacological analgesia was administered based on the individual's pain intensity and medical requirements, ensuring the patient received sufficient pain relief after surgery through the rational use of pain medications.

2.2.2 Research methods of the observation group (Fig. 1)

The observation group received a multimodal analgesic nursing intervention, detailed as follows:

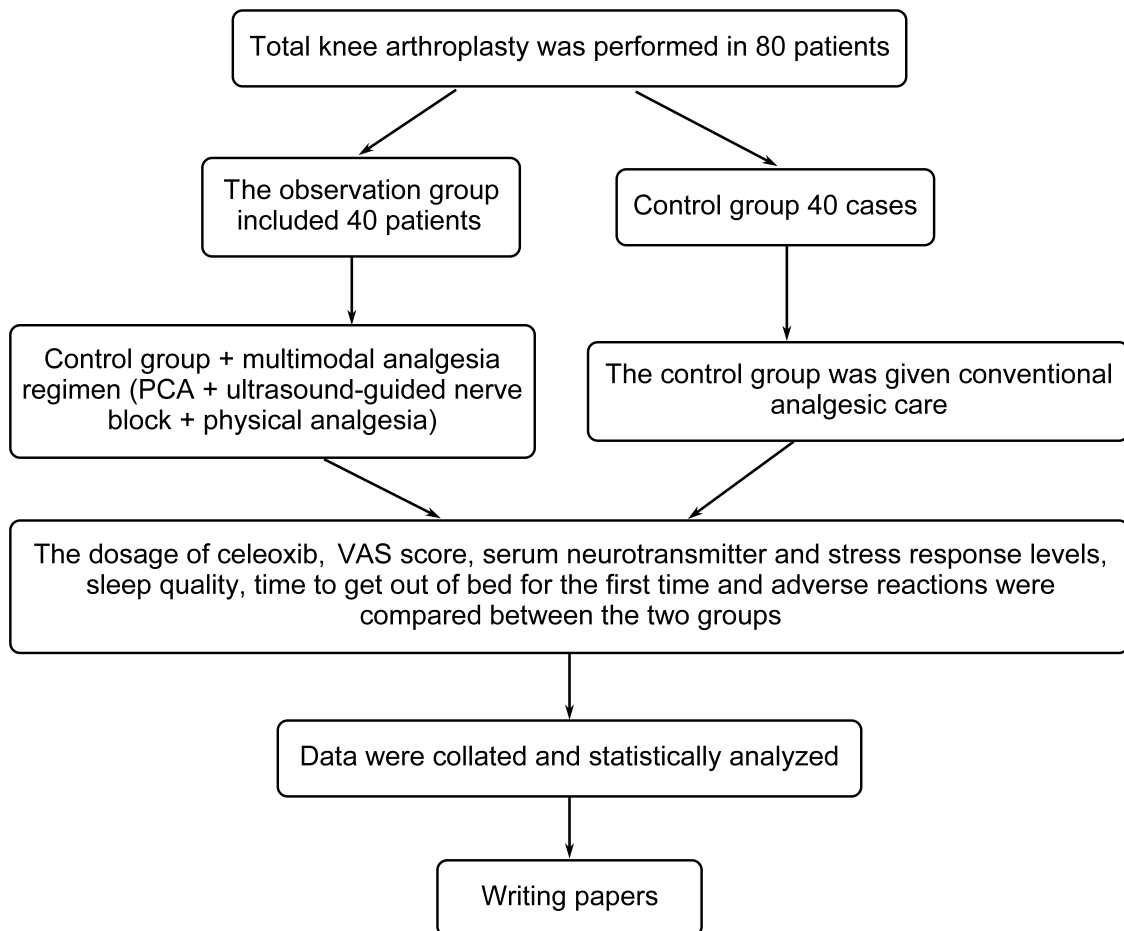


FIGURE 1. Technology roadmap Annotate. PCA: patient-controlled analgesia; VAS: Visual Analog Scale.

Preoperative preparation (over-the-counter analgesia):

(a) Patient Education: Nurses actively communicated with patients and their families 1 to 2 days before surgery, emphasizing the importance of pain management and setting expectations for postoperative pain and analgesic methods. This included the expectation of postoperative pain and the feasibility of analgesic methods.

(b) Emotional support: Nurses provided emotional support by addressing patients' concerns, offering comfort, and alleviating preoperative stress.

(c) Preoperative Analgesic Drugs: Based on medical prescriptions, preoperative analgesics were administered to minimize discomfort before surgery.

Postoperative management (analgesic drug care):

(a) Epidural analgesia pump: The anesthetic regimen for the epidural analgesic pump was tailored to complement the anesthetic drugs utilized during the patient's surgery. This pump, typically used for a continuous duration of 48 hours post-surgery, is important in maintaining consistent and effective pain management throughout the early recovery phase.

(b) Medication adjustment: Analgesic dosages were tailored to the patient's pain levels and needs, with adjustments made as necessary. Intravenous infusion of non-steroidal anti-inflammatory medications was utilized to enhance analgesia when required.

Hierarchical analgesic nursing:

(a) Pain assessment: Visual Analog Scale (VAS) was used for regular assessment of patients' postoperative pain at 3–6 hours intervals. Following each evaluation, three successive measurements were conducted within 30 min, and the average of these scores was documented to ensure accurate pain assessment.

(b) Analgesic strategy: Strategies were devised based on VAS scores, with non-pharmacological methods prioritized for scores below 3. For scores of 3 to 6, a combination of non-pharmacologic and moderate pharmacologic analgesia was used, and for scores above 6, pharmacologic analgesia was recommended.

Non-pharmacological analgesia:

(a) Music therapy: The pleasurable effects of music were used to create a serene environment for patients to improve psychological comfort and promote a sense of well-being.

(b) Emotional support: Nurses provided emotional support to patients to enhance their psychological resilience and help them in managing the stress associated with post-surgical recovery.

(c) Family affectionate support: Family support was provided to enhance the patient's confidence in the treatment process, effectively reducing sensations of pain and establishing a conducive atmosphere for recovery.

(d) Early activity and muscle relaxation method: Patients were encouraged to initiate early rehabilitation activities and muscle training to maintain joint mobility and prevent venous thrombosis. Meditation and relaxation techniques were also taught to reduce stress and tension.

Pain recording and management:

(a) Patient self-assessment: Patients were advised to perform self-assessments at 1 to 2-hour intervals for a more

accurate understanding of their condition. Additionally, keeping a pain diary was encouraged, wherein they documented the intensity, location, timing and other relevant aspects of their pain. This diary serves as a vital tool for the nursing staff to comprehend the patient's pain status comprehensively, facilitating timely adjustments to the treatment plan tailored to meet the patient's specific needs.

(b) Regular assessment: Nurses regularly reviewed the patient's pain diaries and discussed any changes in their pain experiences. Utilizing the insights gained from the diaries, the nursing team made adjustments to medication dosages and non-pharmacological analgesic approaches or offered additional support to ensure effective pain management for each patient.

Regular review and adjustment:

(a) Adjustment of the care plan: The patient's care plan was continuously evaluated and refined. As the patient recovered and exhibited varying responses to pain management, the nursing team dynamically adapted the analgesic protocol, tailoring it to address the unique needs and circumstances of the patient.

(b) Teamwork: The medical team, including anesthesiologists, surgeons, and pain management specialists, conducted regular consultations to develop and adjust treatment plans, ensuring optimal pain management for patients.

(c) Ongoing patient education: Patients and their families received ongoing information and guidance on pain control, enhancing their understanding of treatment progress and the significance of pain management. This approach improved patient engagement in the treatment process.

2.3 Observation indexes

Observation indices for this study included:

2.3.1 Dosage of celecoxib capsules

This involved comparing the postoperative dosage of celecoxib capsules administered to patients in both groups to assess the effectiveness and efficiency of pain management strategies.

2.3.2 Resting pain scores

We compared the resting pain scores of patients in both groups at specific intervals post-surgery (6, 12, 24 and 72 hours) using VAS, which is a 10-cm line with endpoints representing no pain and severe pain, where higher scores denote more severe pain.

2.3.3 Neurotransmitter and stress response levels

We evaluated changes in levels of neurotransmitters (Substance P (SP), Beta-Endorphin (β -EP), 5-Hydroxytryptamine (5-HT)) and stress responses (Cortisol (Cor), C-reactive protein (CRP), White Blood Cell count (WBC)) between the two patient groups at 24 and 72 hours postoperatively, highlighting the physiological impact of pain management strategies.

2.3.4 Sleep quality and first time getting out of bed

Sleep quality was assessed one week postoperatively using the Pittsburgh Sleep Quality Index, with scores ranging from 0 to 21, where higher scores indicate poorer sleep quality.

Additionally, the time until patients first get out of bed post-surgery is compared between groups, indicating the recovery pace.

2.3.5 Total incidence of postoperative complications

Here, we compared the duration of hospital stays and the incidence of specific postoperative complications (lower limb interosseous vein thrombosis, abdominal distension, defecation dysfunction) between the two groups, assessing the overall safety and effectiveness of the pain management protocols employed.

2.4 Statistical analysis

Data analysis was conducted using the SPSS v25.0 (IBM SPSS Statistics, IBM Corporation, Armonk, NY, USA). Measurement data following normal distribution are presented as mean \pm standard deviation ($\bar{x} \pm s$), while non-normally distributed data are presented as medians (M) with the 25th and 75th percentiles (P25, P75). Comparisons between the two groups were performed using the *t*-test for normally distributed data and the Mann-Whitney U-test for non-normally distributed data. To analyze differences across multiple time points within the groups, repeated-measures Analysis of Variance (ANOVA) was utilized. Categorical data were represented as frequencies (percentages) and analyzed using the Chi-square (χ^2) test. Rank data comparisons were made using the rank-sum test. A *p*-value of less than 0.05 was considered to indicate a statistically significant difference.

3. Results

3.1 Comparison of postoperative celecoxib capsule dose between the two groups

The dosage of celecoxib capsules administered postoperatively differed significantly between the two groups. In the control group, the dose was 200 mg, ranging from 0 to 400 mg, which was notably lower than the 400 mg dose, ranging from 0 to 800 mg, given to the observation group. This difference in dosage was statistically significant, as evidenced by the Mann-Whitney U test result ($U = 453.674, p < 0.001$).

3.2 Comparison of VAS scores between the two groups at different times during the postoperative period

Regarding the comparison of VAS scores at various postoperative times, significant differences were observed between the two groups. The analysis considered group differences, time points, and their interaction, with all showing statistically significant variances ($p < 0.05$), as detailed in Table 1. This finding suggests that the pain experiences of patients in the observation group and the control group varied significantly over time during the postoperative period.

3.3 Comparison of neurotransmitter levels and stress response indexes at different times after surgery between the two groups of patients

The analysis of neurotransmitter and stress level indicators between the two groups over various postoperative timepoints demonstrated statistically significant differences ($p < 0.05$), as presented in Table 2, underscoring the impact of the interventions on physiological stress and pain management outcomes.

3.4 Comparison of sleep quality scores and first-time out-of-bed activities between the two groups of patients

The observation group reported a lower sleep quality score compared to the control group, indicating better sleep quality. Additionally, the time taken for patients in the observation group to get out of bed for the first time post-surgery was significantly shorter than that of the control group, with the difference being statistically significant ($p < 0.05$, Table 3).

3.5 Comparison of the total incidence of postoperative complications between the two groups of patients

The total incidence of postoperative complications in the observation group was found to be significantly lower than in the control group, as detailed in Table 4 ($p < 0.05$).

4. Discussion

4.1 Multimodal analgesic protocol can reduce patients' postoperative pain level

The findings of this study reveal significant differences in VAS scores across groups, over time and in their interactions at various post-surgical intervals ($p < 0.05$). Notably, the dosage of celecoxib capsules in the observation group was less than that in the control group, suggesting that a multimodal analgesic approach not only enhances pain management, thereby reducing patients' pain levels, but also decreases the necessity for non-steroidal anti-inflammatory drugs, limiting their potential adverse effects [11]. The initial assessment is important for developing a personalized analgesic plan, ensuring each patient receives a bespoke pain management strategy. This approach aims to alleviate pain effectively while also curtailing the risk of opioid dependency by judiciously increasing the use of celecoxib [12]. Patient-controlled analgesia (PCA) systems offer timely pain relief within a safe margin, empowering patients to manage their pain more actively. This autonomy in pain management helps lessen pain perception and diminishes the need for supplementary analgesics [13]. Gao *et al.*'s [14] findings aligned with our present study, demonstrating that ultrasound-guided nerve block techniques can pinpoint and block nerves more precisely. This precision reduces the amount of local anesthetic required and significantly alleviates postoperative pain, underscoring the efficacy of this study's results. Overall, the combined effect of various drugs within a multimodal analgesic regimen culminates in superior pain control.

TABLE 1. Comparison of VAS scores at different moments after surgery between the two groups ($\bar{x} \pm s$).

Group	Number of cases	6 h after surgery	12 h after surgery	24 h after surgery	48 h after surgery
Observation group	40	5.32 ± 0.69	3.60 ± 0.93	2.87 ± 0.56	2.87 ± 0.56
Control group	40	5.53 ± 0.91	4.68 ± 1.16	4.14 ± 1.18	3.68 ± 0.94
F_{time}, P_{time}		126.67	<0.001		
$F_{interaction}, P_{interaction}$		13.41	<0.001		
$F_{withingroup}, P_{withingroup}$		495.88	<0.001		

Note: The VAS scores at 6-, 12-, 24- and 48-hours post-surgery showed an inverse relationship with time, decreasing as the postoperative period progressed. The observation group exhibited significantly lower VAS scores than the control group at all measured time points, indicating more effective pain management. Statistical analysis revealed significant differences in VAS scores across time, between groups, and in their interaction, demonstrating the efficacy of the multimodal analgesic approach.

TABLE 2. Comparison of neurotransmitter and stress levels after surgery between the two groups ($\bar{x} \pm s$).

Group	Number of cases	Neurotransmitter levels			Indicators of stress levels		
		P material (ng/L)	β -EP (ng/L)	5-HT (nmol/L)	Cor (nmol/L)	CRP (mg/L)	WBC ($\times 10^9/L$)
Observation group							
Immediately after surgery	40	24.35 ± 4.07	18.21 ± 1.74	144.10 ± 13.78	235.50 ± 20.09	1.96 ± 0.50	7.23 ± 1.58
24 h after surgery		64.07 ± 2.79	43.19 ± 2.08	355.23 ± 27.22	528.07 ± 29.77	2.45 ± 0.75	6.42 ± 1.67
72 h after surgery		47.55 ± 5.93	37.05 ± 2.37	214.15 ± 18.06	376.15 ± 29.37	2.41 ± 0.85	7.16 ± 1.06
Control group							
Immediately after surgery	40	22.66 ± 3.45	18.28 ± 1.72	169.34 ± 20.41	246.53 ± 13.94	1.91 ± 0.41	8.17 ± 2.07
24 h after surgery		87.07 ± 1.94	63.35 ± 2.17	498.07 ± 29.76	709.20 ± 44.49	5.70 ± 1.02	11.02 ± 1.16
72 h after surgery		66.52 ± 6.38	57.20 ± 7.37	383.85 ± 22.22	528.07 ± 29.77	2.71 ± 0.54	7.71 ± 0.70
F_{time}, P_{time}		5464.27, <0.001	6617.56, <0.001	3545.32, <0.001	4891.07, <0.001	207.40, <0.001	23.57, <0.001
$F_{interaction}, P_{interaction}$		316.79, <0.001	561.31, <0.001	363.03, <0.001	282.41, <0.001	124.19, <0.001	59.51, <0.001
$F_{withingroup}, P_{withingroup}$		924.71, <0.001	820.94, <0.001	1579.83, <0.001	550.69, <0.001	136.79, <0.001	110.13, <0.001

Normal levels are as follows: β -EP (ng/L): 46.19 ± 1.41 pg/mL; 5-HT (nmol/L): 161.45 ± 31.3 ng/mL; Cor (nmol/L): 6.8–61.8 μ g/L; CRP (mg/L): <8 mg/L; WBC for males: $(4.0-5.5) \times 10^{12}/L$; WBC for females: $(3.5-5.0) \times 10^{12}/L$.

The neurotransmitter levels (Substance P, β -EP, 5-HT) and stress indicators (Cor, CRP, WBC) were compared between two groups of patients at various postoperative times: immediately after surgery, 24 hours post-surgery, and 72 hours post-surgery. Over time, all indicators showed continuous improvement. Specifically, the observation group demonstrated significantly better outcomes in both neurotransmitter levels and stress indicators at all measured time points compared to the control group, indicating a statistically significant difference.

β -EP: Beta-Endorphin; 5-HT: 5-Hydroxytryptamine; Cor: Cortisol; CRP: C-reactive protein; WBC: White Blood Cell.

TABLE 3. Comparison of sleep quality score and first-time out-of-bed activity between the two groups ($\bar{x} \pm s$).

Grouping	Number of cases	Sleep Quality Score	First-time out-of-bed Activity
Observation group	40	6.45 \pm 1.25	3.80 \pm 1.14
Control group	40	9.72 \pm 1.26	4.82 \pm 0.67
<i>t</i>		-11.622	-4.903
<i>p</i>		<0.001	<0.001

TABLE 4. Comparison of the total incidence in postoperative complications (n (%)).

Grouping	Number of cases	lower limb interosseous vein thrombosis	Postoperative abdominal distension, defecation dysfunction	Both	Total incidence
Observation group	40	3 (7.5%)	3 (7.5%)	1 (2.5%)	7 (17.5%)
Control group	40	6 (15.0%)	7 (17.5%)	3 (7.5%)	16 (40.0%)
χ^2					5.952
<i>p</i>					0.015

4.2 Multimodal pre-analgesic protocols can control serotonin levels and stress in patients

The multimodal analgesic regimen demonstrates enhanced effectiveness in managing patients' neurotransmitter levels and stress responses when compared to traditional PCA [15]. Our study's findings indicate that multimodal analgesia can significantly regulate serum neurotransmitter levels and diminish patients' stress responses. The regimen utilizes a comprehensive approach for pain control, incorporating local anesthetics, analgesic medications, nerve blocks and physical methods of pain relief [16], thus offering a more pronounced impact on neurotransmitter levels and stress responses. According to Ochroch *et al.* [17], the diverse drugs and techniques employed in the multimodal protocol synergistically adjust neurotransmitter levels, such as lowering inflammatory mediator release and influencing β -EP and 5-HT levels, thereby reducing sensory pain and stress responses. This approach also exerts a greater inhibitory effect on stress indicators like Cor, CRP and WBC by reducing inflammatory responses and the release of inflammatory mediators, thus effectively minimizing neurotransmitter levels and stress responses [18]. Prasad *et al.* [19] further corroborate that a multimodal analgesic regimen provides more reliable and all-encompassing pain management through an array of mechanisms, reducing pain perception and likely resulting in a more stable modulation of neurotransmitter levels and stress responses, aligning with the findings of our present investigation.

4.3 Multimodal analgesic protocol can improve patients' sleep quality and shorten patients' first time out of bed

This present study demonstrated superior sleep quality and earlier "first-time out-of-bed" activities among patients in the observation group compared to the control group, with statistically significant differences ($p < 0.05$), indicating that the multimodal analgesic protocol by integrating various pain management strategies, more effectively reduces postoperative

pain than conventional PCA approaches. The reduction in pain facilitates better sleep by decreasing nocturnal awakenings, thereby enhancing overall sleep quality [20]. The multimodal approach modulates neurotransmitters, such as lowering levels of β -EP, which has a positive impact on sleep, contributing to more restorative rest for patients [21]. In contrast, traditional pain management methods may rely more heavily on medications that can adversely affect sleep, including causing drowsiness or nightmares [22]. By utilizing a multimodal regimen, reliance on any single class of medication is reduced, minimizing potential side effects. Moreover, the multimodal analgesic protocol encourages early postoperative mobilization, which aids in quicker recovery, diminishes postoperative discomfort, and promotes acceptance of early ambulation activities. Early mobilization also enhances blood circulation, mitigates the risk of postoperative complications, and fosters better sleep patterns [23]. Through comprehensive pain management and the alleviation of postoperative stress and anxiety, the multimodal protocol substantially improves patients' sleep quality [24]. Consequently, the multimodal analgesic protocol offers a more holistic and effective approach to postoperative care, encompassing pain control, neurotransmitter balance, reduced medication side effects, early physical recovery, and psychological well-being, leading to an improved sleep experience for patients [25].

4.4 Multimodal analgesic protocol can reduce the incidence of postoperative adverse reactions in patients

The results of this study showed that the observation group experienced fewer adverse reactions compared to the control group, with the difference being statistically significant ($p < 0.05$). This outcome can be attributed to the multimodal analgesic protocol, which incorporates various methods such as local anesthesia, analgesic drugs, and nerve blocks [26]. Through preoperative evaluation, the multimodal analgesic protocol enables the selection of suitable drugs and techniques tailored to the patient's unique needs, thus minimizing the risk of allergic reactions or adverse responses to specific med-

ications and facilitating more personalized care [27]. The application of local analgesic methods, like nerve blocks, diminishes the systemic distribution of drugs, reducing the potential for widespread adverse effects. By integrating diverse analgesic approaches, the multimodal protocol offers more comprehensive and consistent pain management while mitigating adverse events [26]. Furthermore, it supports quicker post-surgical recovery, lessens postoperative discomfort, and encourages prompt engagement in recovery activities [28]. Early mobilization enhances blood flow and lowers the risk of postoperative thrombosis, thus decreasing the likelihood of related adverse outcomes. Additionally, the multimodal protocol significantly improves patients' psychological well-being by managing pain effectively, which in turn reduces anxiety, stress and the possibility of adverse reactions linked to psychological factors [29]. Overall, by leveraging multiple mechanisms to manage pain, the multimodal analgesic protocol effectively reduces the incidence of adverse effects, ensuring safer and more efficient pain management for patients.

5. Conclusions

In summary, this study demonstrates that the multimodal analgesic protocol offers superior pain control, more favorable neurotransmitter and stress response profiles, improved sleep quality, and enhanced early recovery metrics. Notably, patients managed with the multimodal approach experienced lower pain scores and a reduced incidence of adverse events compared to those receiving traditional pain management. Despite these promising findings, the study has several limitations that warrant consideration. The relatively small sample size might have impacted the robustness and generalizability of the results. Moreover, the single-center design introduces potential biases related to specific geographic and institutional practices, which might limit the applicability of the findings across different settings. Additionally, the focus on perioperative outcomes without an extended follow-up period restricts the ability to evaluate the long-term effects of the multimodal analgesic regimen. Future research could aim to mitigate these limitations by incorporating larger and more diverse patient populations, employing a multicenter approach, and extending the duration of follow-up. Such studies would provide a more comprehensive understanding of the benefits and potential long-term outcomes associated with multimodal analgesic protocols, thereby enhancing postoperative patient care.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

HCL, XYL and YL—designed the study and carried it out. HCL, XYL, YL, JYL, QL and XL—supervised the data collection, and analyzed the data, interpreted the data. HCL and

XYL—prepared the manuscript for publication and reviewed the draft of the manuscript. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of West China Hospital (Approval no. 2021-1699). Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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