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The Impact of Preemptive Analgesia Combined with Multimodal Analgesia on Perioperative Pain and Postoperative Fracture Healing in Elderly Patients with Hip Fractures

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Abstract: *Objective:* To investigate the impact of preemptive analgesia combined with multimodal analgesia on perioperative pain and postoperative fracture healing in elderly patients with hip fractures. *Methods:* A total of 202 patients who underwent total hip arthroplasty from January 2024 to December 2024 were selected and divided into two groups based on different analgesic methods: a control group receiving routine postoperative multimodal analgesia and a study group receiving preemptive analgesia combined with multimodal analgesia, each with 101 cases. The analgesic effects were compared between the two groups. *Results:* The pain scores of the study group at all postoperative time points were significantly lower than those of the control group ($P < 0.05$); the number of patient-controlled intravenous analgesia pumps and the frequency of rescue analgesia in the study group were significantly lower than those in the control group ($P < 0.05$); the levels of stress response indicators in the study group were significantly lower than those in the control group after surgery ($P < 0.05$); the fracture healing time in the study group was significantly shorter than that in the control group ($P < 0.05$). *Conclusion:* The application of preemptive analgesia combined with multimodal analgesia in elderly patients with hip fractures can provide superior perioperative analgesic effects, effectively reduce surgical stress responses, promote early functional rehabilitation, and have a positive effect on postoperative fracture healing.

Keywords: Hip fracture; Preemptive analgesia; Multimodal analgesia; Pain; Fracture healing

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1. Introduction

Geriatric hip fractures are a common orthopedic emergency. Patients with such fractures often experience severe perioperative pain due to their advanced age, multiple underlying medical conditions, and decreased pain thresholds. This pain can trigger stress responses such as elevated blood pressure and increased heart rate, exacerbating the burden on cerebral blood vessels and adversely affecting fracture healing and prognosis [1]. While

traditional single-agent analgesic regimens can alleviate some pain, they are limited by inadequate analgesic efficacy and numerous adverse reactions, making it difficult to meet clinical needs [2]. Multimodal analgesia, which involves the combined use of analgesic drugs and techniques with different mechanisms of action, aims to achieve synergistic analgesia while reducing the dosage and side effects of individual drugs and has become one of the core principles of modern perioperative management. The core concept of preemptive analgesia is to implement effective analgesic interventions before the onset of noxious stimuli to prevent peripheral and central sensitization, thereby alleviating acute pain and preventing its transition to chronic pain. It is now widely used in clinical surgical analgesia [3]. Based on this, the present study explores the effects of preemptive analgesia combined with multimodal analgesia on perioperative pain and postoperative fracture healing in elderly patients with hip fractures, aiming to provide evidence for clinical analgesia.

2. Materials and methods

2.1. General information

A total of 202 patients who underwent total hip arthroplasty from January 2024 to December 2024 were selected and divided into a control group and a study group based on different analgesic methods, with 101 patients in each group. The general information of the two groups was comparable ($P > 0.05$), as shown in **Table 1**.

Table 1. Comparison of general information between the two groups

Group	*n*	Gender (%)		Age (years)	BMI (kg/m^2)	Type of fracture		ASA classification	
		Male	Female			Femoral neck fracture	Intertrochanteric fracture of the femur	Grade II	Grade III
Control	101	56 (55.45)	45 (44.55)	73.34 ± 6.32	23.66 ± 3.51	53 (52.48)	48 (47.52)	65 (64.36)	36 (35.64)
Study	101	57 (56.44)	44 (43.56)	73.12 ± 6.61	23.75 ± 3.62	51 (50.50)	50 (49.50)	63 (62.38)	38 (37.62)
Statistic (χ^2/t)		0.020		0.242	0.179	0.079		0.085	
P-value		0.887		0.809	0.858	0.778		0.770	

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) Age > 65 years; (2) Diagnosed with femoral neck fracture or intertrochanteric fracture of the femur via X-ray or CT, and scheduled for surgical treatment; (3) American Society of Anesthesiologists (ASA) classification grade II–III; (4) Informed consent obtained from the patient or their family members.

Exclusion criteria: (1) Pathological fractures or open fractures; (2) Patients with severe cognitive impairment or mental illness that prevents cooperation in pain assessment; (3) History of long-term opioid abuse or addiction to analgesic drugs; (4) Allergies to anesthesia/analgesic drugs used in the study; (5) Infection at the puncture site or severe abnormalities in blood coagulation function.

2.3. Methods

Both groups of patients received intraspinal anesthesia combined with ultrasound-guided nerve block. The study group utilized preemptive analgesia combined with multimodal analgesia: Preemptive analgesia involved intravenous injection of 0.2 mg of hydromorphone and 50 mg of flurbiprofen axetil 30 minutes before surgery.

Postoperative analgesia involved a patient-controlled intravenous analgesia (PCIA) pump with a formulation consisting of 40 mg of nalbuphine, 200 mg of flurbiprofen axetil, diluted with normal saline to a total volume of 100 ml. The parameters were set as follows: background dose of 1 ml/h, single-press dose of 2 ml, and a lockout time of 15 minutes. Additionally, patients received daily intravenous injections of 50 mg of flurbiprofen axetil for three consecutive days after surgery. The control group received conventional postoperative analgesia: a postoperative PCIA pump with a formulation consisting of 100 mg of sufentanil diluted to 100 ml with normal saline. The parameters were set as follows: a background infusion rate of 1 ml/hour, a bolus dose of 2 ml per press, and a lockout interval of 15 minutes. If necessary, intravenous butorphanol 1 mg was administered for rescue analgesia.

2.4. Observation indicators

2.4.1. Perioperative pain

Assessed using the Visual Analog Scale (VAS) at 1 hour before surgery and at 6, 12, 24, 48, and 72 hours after surgery, with scores ranging from 0 to 10. The score is positively correlated with the degree of pain.

2.4.2. Postoperative analgesia monitoring

The number of PCIA pumps and the frequency of rescue analgesia within 48 hours postoperatively were recorded. Rescue medication was administered when the VAS score was ≥ 4.

2.4.3. Stress response indicators

Peripheral venous blood samples were collected before and 24 hours after surgery to measure serum cortisol (Cor) and interleukin-6 (IL-6) levels using the ELISA method.

2.4.4. Fracture healing time

The time taken to reach clinical healing criteria was recorded, which included the absence of local tenderness, longitudinal percussion pain, and abnormal movement, as well as the time when X-rays showed blurred fracture lines and continuous callus formation.

2.5. Statistical methods

Measurement data and count data were respectively expressed as mean ± standard deviation (SD) and *n* (%), and analyzed using statistical software (SPSS 24.0) with *t*-tests and chi-square (χ^2) tests. A *P*-value less than 0.05 was considered statistically significant.

3. Results

3.1. Perioperative pain

There was no significant difference in VAS scores between the two groups 1 hour before surgery ($P > 0.05$). However, at 6, 12, 24, 48, and 72 hours postoperatively, the VAS scores in the study group were significantly lower than those in the control group ($P < 0.05$). See **Table 2**.

Table 2. Perioperative pain (mean ± SD, points)

Group	*n*	Pre-op (1h)	Post-op 6h	Post-op 12h	Post-op 24h	Post-op 48h	Post-op 72h
Control group	101	6.73 ± 1.23	3.74 ± 1.01	3.56 ± 0.84	3.02 ± 0.77	2.76 ± 0.65	2.34 ± 0.56
Study group	101	6.74 ± 1.21	2.23 ± 0.67	2.15 ± 0.34	1.83 ± 0.63	1.63 ± 0.45	1.32 ± 0.23
t-value		0.058	12.521	15.637	12.021	14.365	16.933
P-value		0.954	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

3.2. Number of PCIA pumps and rescue analgesia episodes

The number of PCIA pumps and rescue analgesia frequency in the study group were significantly lower than those in the control group ($P < 0.05$). See **Table 3**.

Table 3. Number of PCIA pumps and rescue analgesia frequency (mean ± SD, times)

Group	*n*	Total PCIA attempts	Effective PCIA attempts	Rescue analgesic doses
Control group	101	25.45 ± 4.43	20.23 ± 3.35	1.84 ± 0.65
Study group	101	12.57 ± 3.24	8.34 ± 2.13	0.36 ± 0.14
t-value		23.585	30.100	22.370
P-value		< 0.001	< 0.001	< 0.001

3.3. Stress response indicators

At 24 hours postoperatively, the levels of Cor and IL-6 in the study group were significantly lower than those in the control group ($P < 0.05$). See **Table 4**.

Table 4. Stress response indicators (mean ± SD)

Group	*n*	Cortisol (nmol/L)		IL-6 (pg/mL)	
		Pre-op	Post-op 24h	Pre-op	Post-op 24h
Control group	101	385.65 ± 43.43	676.75 ± 68.44	15.63 ± 4.23	121.42 ± 23.23
Study group	101	384.46 ± 45.45	509.43 ± 63.23	15.66 ± 4.29	78.53 ± 18.44
t-value		0.190	18.047	0.050	14.533
P-value		0.849	< 0.001	0.960	< 0.001

3.4. Fracture healing time

The fracture healing time in the study group was 12.42 ± 2.31 weeks, significantly shorter than that in the control group, which was 15.53 ± 1.64 weeks ($P < 0.05$).

4. Discussion

Severe perioperative pain is not only the primary source of suffering for patients but can also trigger a series of pathophysiological changes, including sympathetic nervous excitation, increased heart rate, elevated blood pressure, immunosuppression, hypercoagulability, etc. These changes significantly increase the risk of complications such as cardiovascular and cerebrovascular events, pulmonary infections, thrombosis, and

postoperative delirium, seriously affecting the postoperative rehabilitation process and long-term prognosis of patients [4,5]. In recent years, increasing evidence has indicated that effective pain management not only relates to patient comfort but may also influence the final outcome of tissue repair [6]. Studies have shown that, compared with traditional analgesic modalities, preemptive analgesia combined with multimodal analgesia can create a more favorable biological environment for fracture healing through more comprehensive pain control and stress inhibition [7].

The results of this study showed that the postoperative pain scores in the study group were lower, and both the number of PCIA pumps and the number of rescue analgesic administrations were significantly lower than those in the control group. Preemptive analgesia blocks pain transmission pathways before the occurrence of noxious stimuli, preoccupies pain receptors in advance, inhibits central sensitization, and lays the foundation for postoperative analgesia. Multimodal analgesia achieves synergistic effects by combining analgesic drugs with different mechanisms of action. The combined application can provide effective perioperative analgesia. Pain is the core stressor in elderly patients with hip fractures during the perioperative period. It activates the hypothalamic-pituitary-adrenal (HPA) axis and peripheral inflammatory pathways through noxious stimuli, leading to the massive release of cortisol and IL-6 [8]. The results of this study indicate that the levels of stress response indicators in the study group after surgery were all lower. Preemptive analgesia, achieved through preoperative ultrasound-guided nerve block combined with pretreatment with hydromorphone and flurbiprofen axetil, blocks the transmission of pain signals to the central nervous system, inhibits the formation of central sensitization, and reduces stress triggers at their source. Multimodal analgesia, through the synergistic effects of opioid drugs and non-steroidal anti-inflammatory drugs, not only reduces the dosage of a single drug to minimize stress accumulation but also doubles-inhibits the excessive activation of the HPA axis by suppressing prostaglandin synthesis and κ-receptor agonistic effects, thereby reducing cortisol secretion. Simultaneously, it inhibits peripheral inflammatory cascade reactions and blocks the release of IL-6 induced by fracture trauma and pain. Fracture healing is a complex repair process influenced by various factors such as pain, stress response, and local blood circulation. Severe perioperative pain can enhance the body's stress response, increase the release of stress hormones such as cortisol and adrenaline, inhibit osteoblast activity, promote osteoclast proliferation, and delay fracture healing [9]. Meanwhile, pain can restrict early patient mobility, leading to poor local blood circulation and slow callus growth. The research findings of Wu *et al.* [10] indicate that the absence of preemptive analgesia is one of the risk factors for poor prognosis in elderly patients undergoing hip surgery. Therefore, effective analgesia has a significant impact on fracture healing and prognosis in patients. The results of this study show that the fracture healing time in the study group was significantly shorter than that in the control group. The combination of preemptive analgesia and multimodal analgesia demonstrated remarkable analgesic effects. Effective pain control alleviated the body's stress response, thereby avoiding the impact of inflammation and other factors on fracture healing. Meanwhile, effective analgesia enabled patients to engage in functional activities earlier. Functional exercises can produce beneficial mechanical stress stimulation at the fracture site, promoting callus remodeling and maturation. Through these various mechanisms, fracture healing was facilitated.

5. Conclusion

In summary, the combination of preemptive analgesia and multimodal analgesia can effectively alleviate perioperative pain, reduce stress responses, promote fracture healing, and facilitate postoperative rehabilitation in

elderly patients with hip fractures. However, this study has limitations. Firstly, it was a single-center study with a limited sample size. Secondly, the follow-up period was relatively short, which may introduce selection bias. Additionally, the optimization of different analgesic drug dosage combinations was not explored. Therefore, future research should involve multi-center, large-sample, and long-term follow-up studies to further validate the long-term efficacy and safety of this approach.

Disclosure statement

The author declares no conflict of interest.

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