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Improvement in pain by using lidocaine combined with esketamine in elderly patients receiving local anaesthesia for percutaneous kyphoplasty: a randomized controlled study

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Abstract

Background Elderly patients often experience severe pain during percutaneous kyphoplasty under local anaesthesia. The aim of this work was to evaluate the effect of lidocaine combined with esketamine on pain improvement in elderly patients receiving local anaesthesia via percutaneous kyphoplasty.

Methods This prospective, randomized comparative trial was conducted on 66 elderly patients, aged 60–80 years, with an American Society of Anaesthesiologists (ASA) grade of I-III, I–III and a BMI of 18.5–25 kg/m^2, who underwent single-level lumbar percutaneous kyphoplasty under local anaesthesia. Patients were divided into two equal groups (33 per group). Group LE received 200 mg of 1% lidocaine and 25 mg of esketamine (total volume of 20 ml), and Group L received 200 mg of 1% lidocaine (total volume of 20 ml). Patient characteristics, surgery, VAS scores, MAP, HR, MOAA/S scores, patient satisfaction and related adverse reactions were compared for the groups. The VAS scores during and after surgery were considered the primary outcome.

Results There were statistically significant differences in the VAS score between the two groups at the following time points: channel establishment by the puncture needle, balloon dilation, bone cement injection and postoperative period ($P < 0.05$). The VAS score decreased in the LE group, but the MAP and HR were more stable, and the difference was statistically significant ($P < 0.05$). The difference in the MOAA/S score between the two groups was statistically significant ($P < 0.05$), and the MOAA/S score in the LE group decreased. The patient satisfaction level in the LE group was 100% and 48.48% in the L group ($P < 0.05$). There were no related complications or adverse reactions in either group.

Conclusion The application of lidocaine combined with esketamine in local episcopal percutaneous vertebral kyphoplasty in elderly patients not only provides an effective analgesic effect but also improves surgical safety and patient comfort, which has important clinical value in promoting the optimization of surgical anaesthesia management in elderly patients.

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Trial registration The study was registered at Chictr.org.cn with the number ChiCTR2400083466 on 06/12/2023.
Keywords Esketamine, Adjuvants, Local anaesthesia, Old age, Percutaneous kyphoplasty

Percutaneous kyphoplasty (PKP) is an interventional surgery primarily used to treat pain caused by vertebral fractures in elderly patients with osteoporosis [1]. However, elderly patients often experience severe pain during percutaneous vertebral augmentation under local anaesthesia, which leads to a negative experience [2]. Additionally, pain and anxiety can enhance the sympathetic nervous system and endocrine activities, which is detrimental to the delicate physiological functions of elderly patients [3]. Therefore, optimizing anaesthesia methods in clinical practice for elderly patients undergoing PKP is an urgent issue for anaesthesiologists.

Currently, three anaesthesia methods are available for PKP: general anaesthesia, local anaesthesia with monitored intravenous sedation and analgesia, and local anaesthesia alone. General anaesthesia may present certain drawbacks for elderly patients undergoing PKP. Due to frequent circulatory, respiratory, nervous, and endocrine system comorbidities in elderly patients, these patients may have poor tolerance to general anaesthesia [4]. Tracheal intubation and general anaesthesia can easily lead to respiratory complications, and intraoperative neurological symptoms may not be promptly detected [5, 6]. There are also limitations to using local anaesthesia with monitored intravenous sedation and analgesia for elderly patients undergoing PKP. For example, the intravenous administration of sufentanil carries the risk of respiratory depression for patients. Additionally, the frequent use of a C-arm machine for fluoroscopy during the procedure further hinders management of the patient's airway by an anaesthesiologist. Despite the disadvantage of significant intraoperative pain in local anaesthesia, its advantages include faster postoperative recovery and the ability to promptly detect abnormalities in lower limb nerve function during the procedure. Hence, local anaesthesia remains a commonly used protocol at present [7]. Our research aims to determine if the combination of appropriate adjuncts with local anaesthetics alleviate intraoperative pain in elderly patients undergoing PKP.

Ketamine is an N-methyl-D-aspartate receptor antagonist that has sedative and analgesic effects. It not only acts quickly but also minimizes the chances of respiratory depression. It has been widely shown that ketamine, as an adjunct to local anaesthesia, can enhance the analgesic effect [8, 9].

Esketamine is the dextrorotatory isomer of ketamine and has a lower application dosage, stronger sedative and analgesic effects, a shorter recovery period, and fewer adverse reactions [10]. It does not cause mental symptoms and can help patients maintain good postoperative mood [11, 12]. It is commonly used in general anaesthesia, but there are few reports on its use as an adjunct to local anaesthesia. Considering the enhanced analgesic effect of ketamine when used as an adjunct to local anaesthesia, we hypothesize that it can enhance patients' analgesic effect when used as an adjunct to local anaesthesia. Therefore, this study aimed to evaluate whether lidocaine combined with esketamine improved pain to a greater extent than lidocaine alone in elderly patients who underwent PKP. The secondary outcomes included sedation, cardiovascular influence, and patient satisfaction with intraoperative pain management.

Methods

Research subjects

This was a single-centre, prospective, randomized controlled study. This study was approved by the Ethics Committee of Li Huili Hospital of Ningbo Medical Center (approval number: KY2023SL226-01), which is registered in the Chinese Clinical Trial Registry (http://www.chictr.org.cn, ChiCTR2400083466) on 06/12/2023, and all patients signed informed consent forms. Sixty-six patients from the Department of Orthopaedics of Li Huili Hospital of Ningbo Medical Center who planned to undergo single-level lumbar percutaneous kyphoplasty under local anaesthesia from September 2023 to March 2024 were enrolled. The random envelope method was used to allocate the patients, and a double-blind design was adopted. The envelope was opaque and marked with the enrolment number on the outside and the group printed on the inside. The envelope was opened by a third party according to the order of patient visits, the intervention measures in the envelope were applied according to the patient group, and the intervention measures were unknown to both the patients and the researchers. Patients were divided into 2 groups according to the local anaesthetic configuration: the lidocaine combined with esketamine group (LE group, 33 patients) and the lidocaine group (L group, 33 patients).

The inclusion criteria were as follows: (1) single-level lumbar percutaneous kyphoplasty; (2) aged 60–80 years; (3) American Society of Anaesthesiologists (ASA) grade I–III; and (4) body mass index (BMI) 18.5–25 kg/m^2.

The exclusion and withdrawal criteria for patients were as follows: ① hypersensitivity to lidocaine; ② inability to complete local anaesthesia surgery after evaluation by the surgeon; ③ severe intellectual disability, inability to complete the collection of relevant indicators; ④ use of oral analgesics in the past week; ⑤ esketamine allergy and mental disorders; ⑥ spontaneous withdrawal from

surgery; ⑦ allergic reactions after anaesthesia; 8 intraoperative modifications of general anaesthesia; and ⑨ changes in operation methods and other methods. The study termination criterion was serious adverse events that occurred during the operation, such as massive bleeding, cardiovascular and cerebrovascular events, hallucinations, and psychomania.

Anaesthesia and operation

Allocation of local anaesthetics

Lidocaine combined with esketamine group (LE group): Local anaesthetic was administered with 200 mg of 1% lidocaine and 25 mg of esketamine (total volume of 20 ml) (esketamine, batch No. 230214BL, Jiangsu Hengri Pharmaceutical Co., Ltd.).

Lidocaine group (L group): Local anaesthetic was administered with 200 mg of 1% lidocaine (total volume of 20 ml).

2.2 Each patient was briefly informed of the preoperative protocols and was evaluated according to a visual analogue scale (VAS score (0: no pain; less than 3 points: slight pain, the patient can tolerate; 4 to 6 points: patients with pain and poor sleep can still tolerate pain; score 7–10: patients have intense pain that is unbearable). These scales report pain scores, as well as adverse reactions such as nausea and vomiting, decreased skin sensation, or numbness in the lower extremities. The patients routinely fasted for 8 h before the operation. The peripheral veins were opened prior to the operation. Blood pressure, electrocardiogram results and oxygen saturation were monitored while the patients were in the prone position, and oxygen was administered by a nasal catheter at a rate of 2–3 L/min. All local anaesthesia and surgical procedures were performed by the same team of highly experienced and skilled surgeons; local anaesthetics were administered by the same nurse.

Local anaesthesia and operation

All patients were intramuscularly injected with 100 mg of phenobarbital sodium 30 min before surgery. After the patient entered the operating room, the patient was placed in the prone position, the surgical segment was located by a C-arm machine, and the puncture point was marked. The operative area was routinely disinfected and covered with a towel, infiltration anaesthesia was applied locally from the skin layer by layer to the periosteum surface of the outer edge of the pedicle of the affected vertebra, and 10 ml was injected on both sides. Under the guidance of the C-arm machine, the puncture needle was inserted at the puncture point, the forward and lateral perspective positions were good, the needle core was pulled out and inserted into the guide needle, and the hollow trocar was replaced along the guide needle. The C-arm machine was used to confirm that the position was satisfactory. The vertebral body was subsequently expanded and supported by an air bag, the bone cement was adjusted to the shape of toothpaste, the appropriate amount of bone cement was injected slowly into the right and left sides. At the same time, 80 mg of methylprednisolone was given intravenously, the bone cement in the vertebra was found to be full and satisfactory by fluoroscopy with a C-arm machine, the injection needle was removed, the wound was disinfected, a sterile dressing was applied, and the patient was sent to the recovery ward after the operation. The intraoperative MAP was maintained within ±20% of the baseline value, and diltiazepine or norepinephrine was given when necessary. The patient's oxygen saturation was maintained above 95% when necessary to support the jaw and mask oxygen. After the operation, the patient was sent to the ward and immobilized for 3 h. When the VAS score was greater than 3, 50 mg of flurbiprofen exate was given intravenously (12 h interval).

Observation indicators

The following VAS scores were recorded for the two groups: T1 (after prone position and before local anaesthesia), T2 (when local anaesthesia was injected), T3 (when the puncture needle was used to establish the channel), T4 (when balloon dilation was performed), T5 (when bone cement was injected), T6 (immediately after surgery), T7 (2 h after surgery), T8 (4 h after surgery) and T9 (24 h after surgery) during exercise and rest.

Changes in the MAP and HR of patients at T1, T2, T3, T4, T5 and T6 of the groups were observed.

Modified vigilance/sedation scores (MOAA/S score, 0: no response to trapezoid stimulation; 1 score: response to squeezing trapezius muscle; 2 points: response to mild stimulation or shaking; 3 points: response to repeated loud calls; 4 points: slow response to normal tone call; 5 scores: completely awake, normal response to normal tone call) and MOAA/S scores at T1, T2, T3, T4, T5, T6, T7, T8, and T9 of the two groups were recorded.

Clinical data of patients in the two groups, including age, sex, body mass index, operative stage, operative time, blood loss, amount of injected bone cement, diltiazepine dose, and dosage of flurbiprofen axidate, were recorded.

Intraoperative and postoperative adverse reactions, such as nausea, vomiting, delirium, respiratory depression, nerve numbness or anaesthesia reactions, were recorded in the two groups.

The satisfaction levels of the two groups of patients were recorded. Patient satisfaction was assessed via a standardized questionnaire that included five levels: very dissatisfied, dissatisfied, average, satisfied, and very satisfied. The questionnaire was taken immediately after surgery and was conducted by a trained investigator who ensured that the patient understood the question.

Table 1 Comparison of general data between the two groups ($n=33$ patients)

	LE group	L group	*p* value
Gender (n, female/male)	16/17	19/14	0.459
Age (years, $\bar{x}\pm s$)	70.15 ± 3.15	68.67 ± 3.06	0.057
Body mass index(kg/m^2, $\bar{x}\pm s$)	23.21 ± 1.33	22.99 ± 1.62	0.555
Operative segment (n, L1/L2/L3/L4/L5)	11/11/8/3/0	12/14/6/1/0	0.639
Operation time(min, $\bar{x}\pm s$)	22.91 ± 1.97	23.39 ± 1.98	0.323
Blood loss volume(ml, $\bar{x}\pm s$)	6.15 ± 2.60	6.30 ± 2.41	0.807
The amount of bone cement injected(ml, $\bar{x}\pm s$)	4.73 ± 1.15	4.67 ± 1.19	0.834
Diltiazepine dosage(mg, M,IQR)	0(0,5)	5(5,5)	<0.001
Dosage of flurbiprofen ester(mg, M,IQR)	0(0,0)	0(0,50)	<0.001

Note The LE group received lidocaine combined with esketamine, and the L group received lidocaine.

Statistical analysis

We used PASS sample software (version 15; NCSS, LLC, Kayville, Utah, USA) to estimate the sample size. According to the pretest results, the VAS scores of the LE group and the L group were 2.50±1.30 points and 3.70±1.25 points, respectively, during the establishment of the channel by a puncture needle after local anaesthesia. The sample size of each group was 33 cases, considering a 20% shedding rate with a=0.025 (unilateral test) and 1-β=0.9. Statistical analysis was performed via SPSS software (version 21.0; IBM Corporation, New York). Normally distributed measurement data are expressed as the mean±standard deviation ($\bar{x}\pm s$), and a Group t test was used for comparisons between groups. Nonnormally distributed data are expressed as the median (M) and interquartile range (IQR), and the Mann–Whitney U test was used for intergroup comparisons. The count data are expressed as examples (%), and comparisons between groups were performed via the 2 test or Fisher's exact probability method. $P<0.05$ was considered to indicate statistical significance.

Results

Sixty-six patients were enrolled in the study. There was no significant difference in sex ratio, age, BMI, operation stage, operation time, blood loss or bone cement injection between the 2 groups ($p>0.05$). Compared with those in the L group, the intraoperative dosage of diltiepine and postoperative dosage of flurbiprofen axetil in the LE group were significantly lower ($P<0.05$). See Table 1.

There were statistically significant differences in the VAS scores between the two groups at the time of puncture needle establishment, balloon dilation, and bone cement injection; immediately after surgery; 2 h after surgery; 4 h after surgery at rest and during exercise; and 24 h after surgery at rest and during exercise ($P<0.05$). See Table 2.

Table 2 Comparison of VAS scores between the two groups ($n=33$, $\bar{x}\pm s$)

	LE group	L group	*p* value
T1 (before local anesthesia)	2.52 ± 0.57	2.52 ± 0.51	1.000
T2(during local anesthesia)	3.94 ± 0.66	3.73 ± 0.67	0.201
T3 (when using a puncture needle to create a channel)	2.82 ± 0.58	5.33 ± 0.60	<0.001
T4 (during balloon dilation)	2.45 ± 0.51	5.94 ± 0.86	<0.001
T5 (when injected with bone cement)	1.97 ± 0.73	5.27 ± 0.91	<0.001
T6 (after surgery)	0.24 ± 0.44	0.70 ± 0.68	0.002
T7 (2 h after surgery)	0.00 ± 0.00	0.18 ± 0.39	0.012
T8 (at rest 4 h after surgery)	0.00 ± 0.00	2.64 ± 0.49	<0.001
T8 (4 h exercise after surgery)	0.00 ± 0.00	2.64 ± 0.49	<0.001
T9 (at rest 24 h after surgery)	1.82 ± 0.58	3.03 ± 0.47	<0.001
T9 (24 h exercise after surgery)	1.91 ± 0.52	3.06 ± 0.43	<0.001

Note The LE group received lidocaine combined with esketamine, and the L group received lidocaine.

Table 3 Comparison of the intraoperative MAP and HR between the two groups ($n=33$, $\bar{x}\pm s$)

	LE group	L group	*p* value
T1(before local anesthesia)	104.91 ± 6.74	102.85 ± 5.38	0.175
MAP(mmHg)	70.12 ± 5.96	67.58 ± 6.42	0.100
HR(bpm)			
T2(during local anesthesia)	113.67 ± 4.27	113.67 ± 4.60	1.000
MAP(mmHg)	76.82 ± 5.92	74.24 ± 6.09	0.086
HR(bpm)			
T3 (when using a puncture needle to create a channel)	112.70 ± 6.93	120.64 ± 7.97	<0.001
MAP(mmHg)	78.12 ± 6.77	85.36 ± 4.91	<0.001
HR(bpm)			
T4(when the balloon dilates)	110.42 ± 4.42	121.39 ± 7.46	<0.001
MAP(mmHg)	76.97 ± 5.69	89.30 ± 3.96	<0.001
HR(bpm)			
T5 (when injected with bone cement)	110.12 ± 3.80	121.00 ± 6.15	<0.001
MAP(mmHg)	73.61 ± 6.48	88.73 ± 3.40	<0.001
HR(bpm)			
T6 (after surgery)	106.33 ± 6.50	103.30 ± 4.38	0.030
MAP(mmHg)	72.91 ± 7.06	69.64 ± 7.15	0.066
HR(bpm)			

Note The LE group received lidocaine combined with esketamine, and the L group received lidocaine.

The differences in the MAP and HR between the 2 groups were statistically significant ($P<0.05$) when a puncture needle was used to establish the channel, balloon dilation was performed, and bone cement was injected. After the operation, the MAP of the LE group decreased, and the difference was statistically significant ($P<0.05$). See Table 3.

There were significant differences in the MOAA/S scores between the 2 groups during balloon dilation, after

bone cement injection, after surgery, 2 h after surgery and 4 h after surgery ($P<0.05$). See Table 4.

Patient satisfaction in the two groups was investigated after the operation. The satisfaction rate of the LE group was 100% (very dissatisfied/dissatisfied/generally/satisfied/very satisfied: 0/0/0/25/8), and the satisfaction rate of the L group was 48.48% (very dissatisfied/dissatisfied/generally/satisfied/very satisfied: 0/10/7/16/0); the difference was statistically significant ($P<0.05$).

Discussion

In this randomized clinical trial, our primary objective was to assess the impact of esketamine as an adjuvant to lidocaine in enhancing pain control during and after PKP in elderly patients. The results indicate that the incorporation of esketamine, a right-handed isomer of ketamine and an NMDA receptor antagonist, into local anaesthetic regimens leads to superior intraoperative and postoperative pain management compared with lidocaine alone. Clinically, ketamine has been shown to act as a local anaesthetic and can be administered intrathecally, epidurally, or locally through infiltration [13–15]. This finding is particularly noteworthy given the lower dosage requirement and reduced incidence of adverse effects associated with esketamine, as opposed to ketamine. Our study builds upon previous research, such as the work by Tianqi Zhu et al., which demonstrated the efficacy of 40 mg of ketamine combined with 0.375% ropivacaine (40 ml) combined with femoral nerve and sciatic nerve block for postoperative analgesia [8] and further refined the approach by optimizing the dosage for enhanced intraoperative and postoperative analgesia.

The results of this study showed that compared with the L group, the LE group achieved more satisfactory analgesic effects during the establishment of channels via a puncture needle, balloon dilation, bone cement injection, rest and exercise at 4 h after surgery, and rest and exercise at 24 h after surgery. The VAS score was less than 3 points, and no additional analgesia was required within 24 h after surgery with flurbiphenolate. These findings suggest that esketamine can produce analgesic effects, which may be related to its local effects and systemic effects after absorption. Studies have shown that esketamine acts as a local anaesthetic by blocking sodium channels in a manner similar to that of local anaesthetics. In addition, esketamine can also exert anaesthetic and analgesic effects through noncompetitive antagonism of NMDA receptors, opioid receptors, cholinergic receptors, R-aminobutyric acid and other receptors [16–18]. In our study, the same group of surgeons completed the operation, and it took approximately 5 min for the puncture needle to establish the channel after the completion of local anaesthesia, which was not enough to generate the blood drug concentration with systemic analgesia through local absorption into the systemic circulation, and the analgesic effect at this time was more likely to be its local effect. During balloon dilation and bone cement injection, patients tend to experience severe pain due to pressure changes, inflammation and anxiety caused by surgery or stimulation of nerve endings by bone cement [19, 20]. In this study, the highest pain score of Group L during balloon dilation was 7 points, which was consistent with Bao et al. [21]. In the LE group, the highest pain score was 3 points, which indicated a good analgesic effect. The vertebral body is innervated by the sinus vertebral nerves of the spinal nerves and the sympathetic fibres of the paravertebral nerves. Our surgical surgeons injected local anaesthetics into the pedicle periosteum of the affected vertebra through the skin. The L group may have experienced severe pain due to the lack of anaesthesia in the vertebra, while the possible mechanism of analgesia in the LE group was the systemic analgesic effect of esketamine through periosteum absorption, the local anti-inflammatory effect of esketamine [22], and the action of esketamine on the paraverteal nerve. The LE group in this study also achieved good analgesic effects within 24 h after surgery, without additional analgesic drugs, no adverse reactions or neurological complications, and better satisfaction.

In this study, patients in both groups were intramuscularly injected with 100 mg phenobarbital sodium 30 min before surgery, and we found that the LE group had better intraoperative and postoperative sedation effects than the L group and was able to wake up during surgery, suggesting that esketamine was locally absorbed into the systemic circulation to produce central sedation. The difference in MOAA/S scores between the two groups occurred during balloon dilation, which could also explain why the LE group exhibited a certain degree of central analgesia at this time. No respiratory depression occurred in either group during the perioperative period.

Table 4 Comparison of MOAA/S scores between the two groups ($n=33$, $\bar{x}\pm s$)

	LE group	L group	*p* value
T1(before local anesthesia)	5.00 ± 0.00	5.00 ± 0.00	1.000
T2(during local anesthesia)	5.00 ± 0.00	5.00 ± 0.00	1.000
T3 (when using a puncture needle to create a channel)	4.24 ± 0.44	5.00 ± 0.00	1.000
T4(when the balloon dilates)	3.36 ± 0.49	5.00 ± 0.00	<0.001
T5 (when injected with bone cement)	3.30 ± 0.47	5.00 ± 0.00	<0.001
T6 (after surgery)	3.24 ± 0.44	4.48 ± 0.51	<0.001
T7 (2 h after surgery)	3.00 ± 0.00	3.91 ± 0.29	<0.001
T8 (4 h after surgery)	3.00 ± 0.00	3.97 ± 0.53	0.001
T9(24 h after surgery)	5.00 ± 0.00	5.00 ± 0.00	1.000

Note The LE group received lidocaine combined with esketamine, and the L group received lidocaine.

The results of this study revealed that the haemodynamics of the LE group were more stable than those of the L group, which may be due to better analgesia and sedation, suggesting that despite the sympathetic excitability of esketamine, 25 mg of esketamine combined with lidocaine can be safely used under local anaesthesia for PKP surgery in elderly patients.

Our study confirmed for the first time that lidocaine combined with esketamine can improve the analgesic effect of local anaesthesia in the treatment of PKP in elderly patients, which is innovative but has some limitations. Future studies should focus on monitoring local and blood concentrations of esketamine as an adjuvant while expanding the sample size to better validate the safety and efficacy of esketamine as an adjuvant in clinical use.

Conclusion

In conclusion, the application of lidocaine combined with esketamine in local episcopal kyphoplasty in elderly patients not only provides an effective analgesic effect but also improves the safety of surgery and the comfort of patients, avoiding the risks and complications caused by general anaesthesia. The results of this study have important clinical value for promoting the optimization of operation anaesthesia management in elderly patients.

Abbreviations

MAP	Mean arterial pressure
HR	Heart Rate
SpO_2	Saturation of pulse oxygen
SPSS	Statistical Package for the Social Sciences
PKP	Percutaneous kyphoplasty
VAS	Visual analogue scale
MOAA/S	Modified Observer's Assessment of Alerness/Sedation
ASA	American Society of Anesthesiologists
BMI	Body mass index

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Data availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Li Huili Hospital of Ningbo Medical Center (approval number: KY2023SL226-01).The study was registered at Chictr.org.cn with the number ChiCTR2400083466 on 06/12/2023.Written consent to participate was obtained from all participants. This study adhered to the CONSORT guidelines, and all experiments were performed in accordance with relevant guidelines and regulations(such as the Declaration of Helsinki).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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