Administration of flurbiprofen axetil and dezocine for the postoperative analgesia in patients with non-small cell lung cancer: A randomized, controlled study

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Abstract. Flurbiprofen axetil or dezocine monotherapy has been applied for analgesia of postoperative non-small cell lung cancer (NSCLC); however, their combination is rarely investigated. Consequently, the present study aimed to explore the effect of flurbiprofen axetil plus dezocine on postoperative pain, surgical outcomes and its safety profile in patients with NSCLC. A total of 150 patients with resectable NSCLC were enrolled and randomized into three groups: i) The flurbiprofen axetil plus dezocine group (n=50), ii) the flurbiprofen axetil group (n=51) and iii) the dezocine group (n=49). A total of 50 mg flurbiprofen axetil, 5 mg of dezocine or their combination were administered intravenously 3 h prior to surgery and subsequently every 12 h until day 3 (D3) following surgery. The postoperative pain was lower in the flurbiprofen axetil plus dezocine group compared with that of the flurbiprofen axetil group at 6 h (P=0.008), 12 h (P=0.003), day 1 (D1) (P=0.013), day 2 (D2) (P=0.036) and D3 (P=0.010); in addition, it was lower in the flurbiprofen axetil plus dezocine group compared with that of the dezocine group at 6 h (P=0.010), 12 h (P=0.012) and D1 (P=0.020). Patient-controlled analgesia consumption was also lower in the flurbiprofen axetil plus dezocine group compared with that of the flurbiprofen axetil (P=0.010) and dezocine (P=0.002) groups. Furthermore, the length of hospital stay was lower in the flurbiprofen axetil plus dezocine group compared with that of the flurbiprofen axetil (P=0.008) and dezocine (P=0.048) groups, while other surgical outcomes and adverse events were similar among these three groups. Moreover, the expression of tumor necrosis factor-α was lower in the flurbiprofen axetil plus dezocine group compared with that of the dezocine group at 12 h (P<0.001), D1 (P<0.001) and D3 (P=0.033). The data indicated that flurbiprofen axetil and dezocine combination was superior to monotherapy for postoperative analgesia in patients with resectable NSCLC.

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Introduction

Non-small cell lung cancer (NSCLC) accounts for ≥85% of primary lung cancer cases and has shown increasing incidence and mortality rates globally (1,2). The surgical resection is still regarded as the cornerstone of the curative option for early-stage patients with NSCLC (3,4). However, postoperative pain, which is a commonly reported complication following surgery, induces psychological distress and reduces the satisfaction of patients with resectable NSCLC (5,6). Moreover, poorly controlled postoperative pain may transition into chronic and persistent pain, which also serves as a critical issue for clinicians (7,8). Therefore, the development of a novel analgesic strategy is urgently required for patients with NSCLC to improve their postoperative pain management.

Flurbiprofen axetil, a non-steroidal anti-inflammatory drug (NSAID), relieves pain via induction of an inhibitory effect on inflammatory cytokines and subsequent inflammation-mediated nociceptor sensation (9-11). Previous studies have revealed that flurbiprofen axetil plays a critical role in postoperative analgesia for patients with cancer, such as those who undergo radical thyroidectomy, open chest radical surgery, or laparoscopic radical surgery of gynecological cancers (12-14). Moreover, dezocine, a synthetic mixed agonist/antagonist opioid plays a critical role in postoperative pain management of patients with cancer and has demonstrated promising analgesic effects (15-17). Flurbiprofen axetil and dezocine exhibit certain analgesic effects on postoperative pain management in patients with cancer via different mechanisms; therefore, it was hypothesized that flurbiprofen axetil plus dezocine may further improve the analgesic effect compared with monotherapy in patients with NSCLC; however, a limited number of studies have examined this hypothesis.

Therefore, the present randomized, controlled study recruited 150 patients with resectable NSCLC, aiming to

explore the effect of flurbiprofen axetil plus dezocine on post-operative pain relief, surgical outcome, patient satisfaction and expression of inflammatory cytokines in patients with NSCLC.

Materials and methods

Patients. The present study consecutively enrolled 150 patients with resectable NSCLC between August 2021 and November 2022. The enrollment criteria for the patients were as follows: (i) Pathologically diagnosed with NSCLC; (ii) planned to receive surgical resection; (iii) aged between 18 and 80 years old; (iv) American Society of Anesthesiologists grade of I-II and (v) capable of understanding the study protocol and willing to comply. The exclusion criteria were as follows: (i) Severe organ dysfunction; (ii) known allergies to the drugs used in the present study; (iii) history of smoking, alcohol abuse, opioid abuse, or other drug abuse; and (iv) pregnancy or lactation. The present study was approved by the Ethics Committee of Handan Central Hospital (approval no. 2021030035; Handan, China). Each patient signed an informed consent form.

Randomization. The patients were randomized into the flurbiprofen axetil plus dezocine, flurbiprofen axetil and dezocine groups at a ratio of 1:1:1 based on computer-generated random number allocation following enrollment. To maintain concealment of the assignment, randomly generated group names were printed and placed in individually sealed opaque envelopes with consecutive numbers. The envelopes were opened only when the patient was deemed eligible for inclusion.

Intervention. All included patients received surgical resection. To relieve surgical pain, analgesic treatment was performed. In the flurbiprofen axetil plus dezocine group, flurbiprofen axetil (Beijing Tide Pharmaceutical Co., Ltd.) was administered at a dose of 50 mg intravenously at 3 h prior to surgery (-3 h) and a dose of 50 mg subsequently every 12 h following surgery until day 3 (D3); dezocine (Nanjing Yoko Pharmaceutical Co., Ltd.) was administered at a dose of 5 mg intravenously at -3 h and subsequently a dose of 5 mg every 12 h following surgery until D3. In the flurbiprofen axetil group, flurbiprofen axetil was administered at a dose of 50 mg intravenously at -3 h and at a dose of 50 mg subsequently every 12 h following surgery until D3. In the dezocine group, dezocine was administered at a dose of 5 mg intravenously at -3 h and subsequently at a dose of 5 mg every 12 h following surgery until D3. In addition, all patients were initiated on treatment for patient-controlled analgesia (PCA) following surgery until D3. PCA treatment comprised a 200 ml mixture including 200 μg sufentanil, 15 mg tropisetron and 200 μg dexmedetomidine. The background input quantity of PCA was 1 ml/h; the lock time was 15 min and the single dosage was 1 ml.

Assessment. The primary outcome was the pain score, which was assessed with a 10 cm visual analog scale (VAS) at 6 and 12 h, day 1 (D1), day 2 (D2), D3 and day 7 (D7) following surgery. The secondary outcomes were PCA consumption, patient satisfaction score, tumor necrosis factor-α (TNF-α) levels and drug adverse events. Patient satisfaction was scored from 0 to 10 points at D1, D3 and D7, and a higher score indicated higher levels of patient satisfaction. For the evaluation of TNF-α levels, the peripheral blood samples of patients were collected at 12 h, D1, D3 and D7. Subsequently, serum was isolated and TNF-α levels were detected by ELISA using a Human TNF-α ELISA Kit (cat. no. PT518; Beyotime Institute of Biotechnology) as per the instructions provided by the manufacturer. The drug adverse events were recorded in detail for assessment.

Statistics. SPSS Statistics software (version 22.0; IBM Corp.) was used for statistical analyses. The sample size was estimated on the basis of the hypothesis that the pain scores in the flurbiprofen axetil plus dezocine, flurbiprofen axetil and dezocine groups were 3.0, 4.0, and 4.0, respectively, with standard deviations <1.5 (13). With a power of 0.90 and a significance level of 0.05, using one-way analysis of variance (ANOVA), the minimum sample size was 44 in each group and adjusted to 47 considering a dropout rate of 5%. Comparison analyses among groups were completed using ANOVA, the χ^2 or the Kruskal-Wallis H rank sum tests, followed by post-hoc comparisons using the least significant difference test, Bonferroni's test or Dunn's multiple comparisons test. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Study flow. Initially, 169 patients with resectable NSCLC were invited; among them, 19 patients were excluded (Fig. 1). Subsequently, the remaining 150 patients were randomly divided into the flurbiprofen axetil plus dezocine (n=50), flurbiprofen axetil (n=51) and dezocine (n=49) groups at a 1:1:1 ratio. In the flurbiprofen axetil plus dezocine group, patients received 50 mg flurbiprofen axetil plus 5 mg dezocine intravenously 3 h prior to surgery and subsequently every 12 h for 3 days; moreover, PCA was applied for 3 days. In the flurbiprofen axetil group, the patients received intravenous flurbiprofen axetil and PCA treatment for 3 days. In the dezocine group, the patients received intravenous dezocine and PCA treatment for 3 days. Subsequently, pain VAS score, patient satisfaction and TNF-α levels were recorded at different time points. In addition, PCA consumption and adverse events were recorded in all patients. All patients were included in the final analysis based on the intention-to-treat principle (Fig. 1).

Patient characteristics. The mean ages in the flurbiprofen axetil plus dezocine, flurbiprofen axetil and dezocine groups were as follows: 60.4±9.4 years, 59.9±10.7 years and 60.3±8.5 years, respectively (Table I). A total of 44 (88.0%) male and 6 (12.0%) female patients were present in the flurbiprofen axetil plus dezocine group; moreover, the flurbiprofen axetil group consisted of 39 (76.5%) male and 12 (23.5%) female patients; and the dezocine group comprised 39 (79.6%) male and 10 (20.4%) female patients. Following comparison, no significant differences were noted in the demographic features (including age, sex, smoking history, drinking history, marital status, employment status prior to surgery, level of education and location), chronic comorbidities (including hypertension, hyperlipidemia and diabetes), disease characteristics (including tumor differentiation, tumor size >5 cm, lymph node metastasis and tumor-node-metastasis stage), or treatment information (including surgery type, neoadjuvant

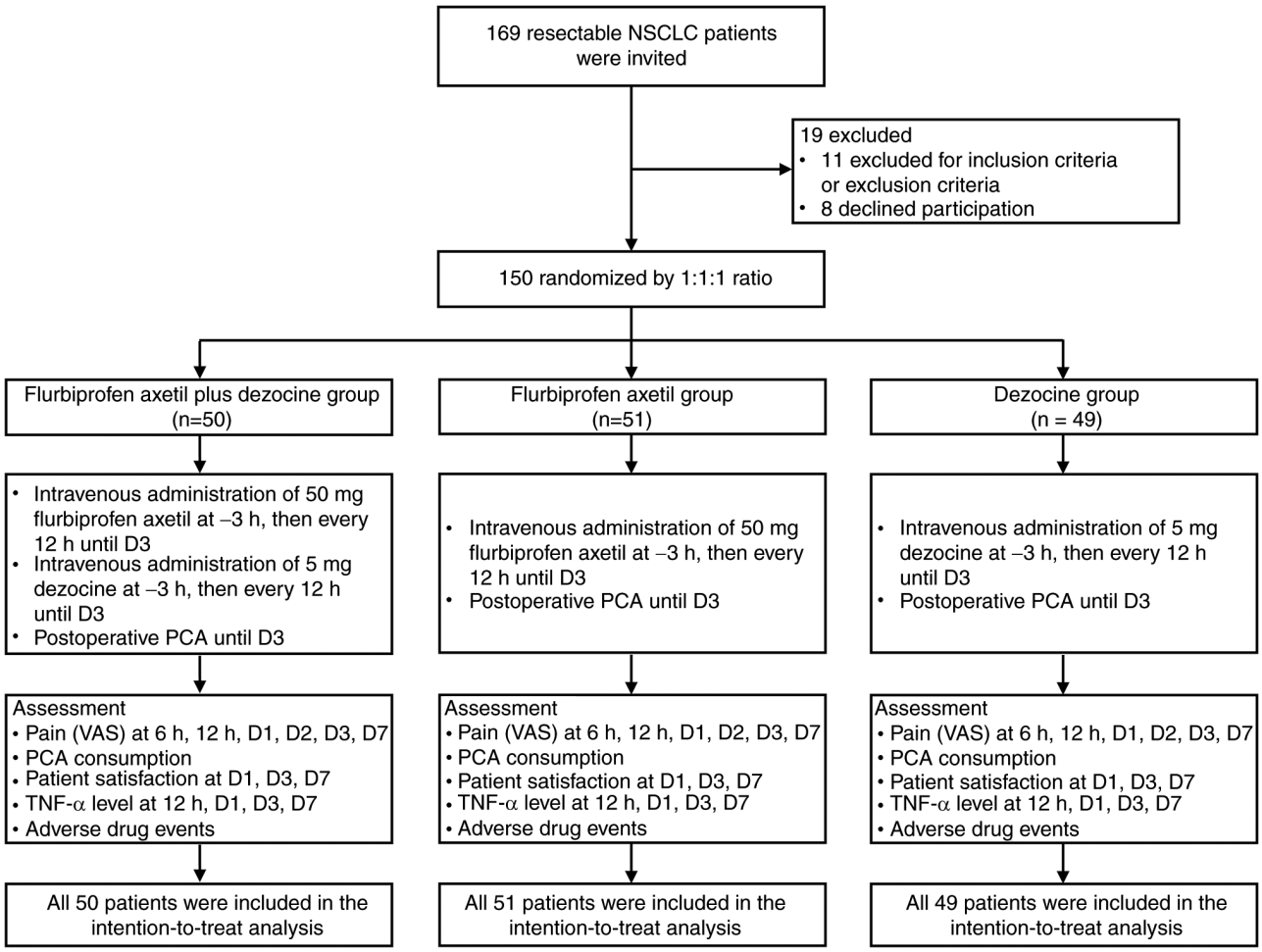


Figure 1. Study flow. NSCLC, non-small cell lung cancer; D3, day 3; -3 h, 3 hours prior to surgery; PCA, patient-controlled analgesia; VAS, visual analog scale; D1, day 1; D2, day 2; D7, day 7; TNF-α, tumor necrosis factor-α.

therapy and adjuvant therapy) among these three groups (all P>0.05). The detailed characteristics of the patients with NSCLC are listed in Table I.

Comparison of pain VAS score and PCA consumption. The data indicated that the pain varied among the flurbiprofen axetil plus dezocine, flurbiprofen axetil and dezocine groups at postoperative 6 h (P=0.011), 12 h (P=0.006), D1 (P=0.021) and D3 (P=0.032), whereas it did not differ among groups at D7 (P=0.635; Fig. 2A). Further post hoc comparison revealed that postoperative pain was lower in the flurbiprofen axetil plus dezocine group compared with that noted in the flurbiprofen axetil group at 6 h (P=0.008), 12 h (P=0.003), D1 (P=0.013), D2 (P=0.036) and D3 (P=0.010). Moreover, postoperative pain was also milder in the flurbiprofen axetil plus dezocine group compared with that of the dezocine group at 6 h (P=0.010), 12 h (P=0.012) and D1 (P=0.020; Fig. 2A). These data suggested that flurbiprofen axetil plus dezocine alleviated postoperative pain compared with monotherapy.

Moreover, postoperative PCA consumption was also measured to compare the analgesic effect among different interventions. Subsequently, PCA consumption was different among the flurbiprofen axetil plus dezocine, flurbiprofen axetil and dezocine groups (P=0.004; Fig. 2B). Specifically, PCA consumption was lower in the flurbiprofen axetil plus dezocine group compared with that of the flurbiprofen axetil group (91.0±14.0 ml vs. 99.6±17.3 ml, P=0.010). Moreover, PCA consumption was lower in the flurbiprofen axetil plus dezocine group compared with that of the dezocine group (91.0±14.0 ml vs. 101.3±17.8 ml, P=0.002), while no significant difference was noted between the flurbiprofen axetil and the dezocine groups (99.6±17.3 ml vs. 101.3±17.8 ml, P=0.590; Fig. 2B). These data indicated that flurbiprofen axetil plus dezocine decreased postoperative PCA consumption compared with monotherapy.

Comparison of patient satisfaction. Patient satisfaction differed among the flurbiprofen axetil plus dezocine, flurbiprofen axetil and dezocine groups at D3 (P=0.015), while it did not vary among groups at D1 (P=0.067) or at D7 (P=0.159; Fig. 3). Additional post hoc comparisons indicated that patient satisfaction was elevated in the flurbiprofen axetil plus dezocine group compared with that of the flurbiprofen axetil group at D3 (P=0.009); patient satisfactions were enhanced in the flurbiprofen axetil plus dezocine group compared with the dezocine group at D1 (P=0.023) and at D3 (P=0.017; Fig. 3). These data revealed that flurbiprofen axetil plus dezocine enhanced patient satisfaction compared with monotherapy to some extent.

Comparison of the levels of inflammatory cytokines. TNF-α is one of the key inflammatory cytokines and its levels were

Table I. Characteristics of patients with non-small cell lung cancer.

Characteristics	Flurbiprofen axetil plus dezocine group (n=50)	Flurbiprofen axetil group (n=51)	Dezocine group (n=49)	P-value
Demographics				
Age (years)[a], mean ± SD	60.4±9.4	59.9±10.7	60.3±8.5	0.963
Sex[b], n (%)				0.308
Male	44 (88.0)	39 (76.5)	39 (79.6)	
Female	6 (12.0)	12 (23.5)	10 (20.4)	
Smoke history[b], n (%)	28 (56.0)	24 (47.1)	22 (44.9)	0.502
Drink history[b], n (%)	22 (44.0)	19 (37.3)	27 (55.1)	0.195
Marry status[b], n (%)				0.231
Married	36 (72.0)	34 (66.7)	40 (81.6)	
Single/divorced/widowed	14 (28.0)	17 (33.3)	9 (18.4)	
Employment status before surgery[b], n (%)				0.845
Employed	22 (44.0)	21 (41.2)	23 (46.9)	
Unemployed	28 (56.0)	30 (58.8)	26 (53.1)	
Level of education[b], n (%)				0.716
Primary school or less	6 (12.0)	4 (7.8)	8 (16.3)	
High school	24 (48.0)	28 (54.9)	25 (51.0)	
Undergraduate or above	20 (40.0)	19 (37.3)	16 (32.7)	
Location[c], n (%)				0.843
Urban	44 (88.0)	46 (90.2)	45 (91.8)	
Rural	6 (12.0)	5 (9.8)	4 (8.2)	
Chronic comorbidities				
Hypertension[b], n (%)	24 (48.0)	25 (49.0)	17 (34.7)	0.277
Hyperlipidemia[b], n (%)	14 (28.0)	16 (31.4)	13 (26.5)	0.860
Diabetes[b], n (%)	8 (16.0)	11 (21.6)	5 (10.2)	0.301
Disease characteristics				
Differentiation[b], n (%)				0.263
Well	6 (12.0)	13 (25.5)	11 (22.4)	
Moderate	27 (54.0)	24 (47.1)	26 (53.1)	
Poor	17 (34.0)	14 (27.5)	12 (24.5)	
Tumor size >5 cm[b], n (%)	18 (36.0)	27 (52.9)	20 (40.8)	0.208
LYN metastasis[b], n (%)	14 (28.0)	22 (43.1)	17 (34.7)	0.280
TNM stage[b], n (%)				0.196
I	20 (40.0)	14 (27.5)	20 (40.8)	
II	16 (32.0)	16 (31.4)	15 (30.6)	
III	14 (28.0)	21 (41.2)	14 (28.6)	
Treatment information				
Surgery type[b], n (%)				0.547
Lobectomy	42 (84.0)	39 (76.5)	41 (83.7)	
Others (wedge, segmentectomy, or pneumonectomy)	8 (16.0)	12 (23.5)	8 (16.3)	
Neoadjuvant therapy[b], n (%)	13 (26.0)	23 (45.1)	16 (32.7)	0.123
Adjuvant therapy[b], n (%)	27 (54.0)	32 (62.7)	25 (51.0)	0.469

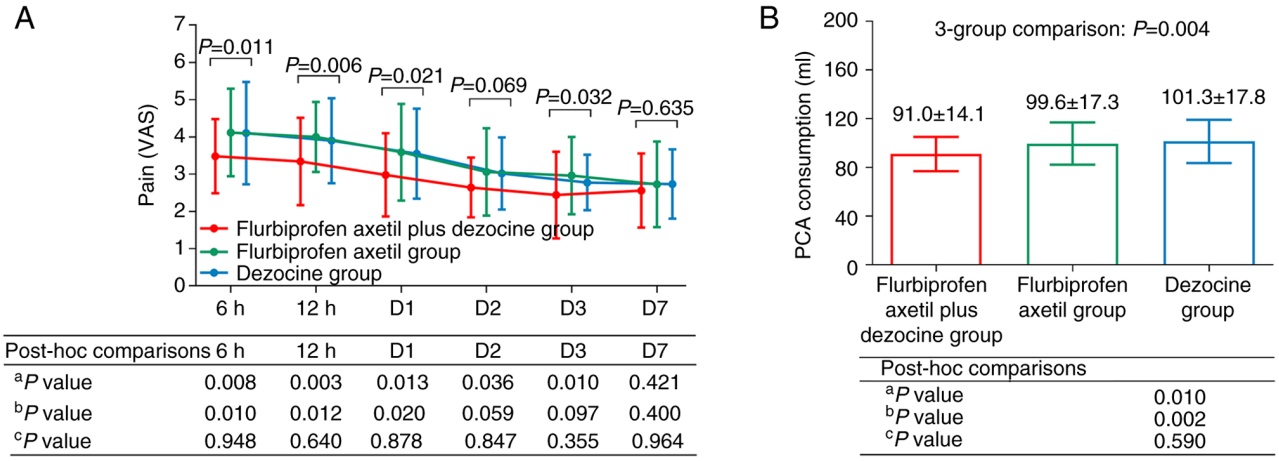
[a]One-way ANOVA test was used; [b]χ^2 test was used; and [c]Fisher's exact test was used. SD, standard deviation; LYN, lymph node; TNM, tumor-node-metastasis.

measured in the current study to assess the anti-inflammatory effect of different interventions. Subsequently, it was observed that TNF-α levels varied among the flurbiprofen axetil plus dezocine, flurbiprofen axetil and dezocine groups at 12 h (P<0.001), D1 (P=0.001) and D3 (P=0.034) whereas this result was not observed at D7 (P=0.145; Fig. 4). Specifically, TNF-α

Table II. Surgical outcomes.

Outcomes	Flurbiprofen axetil plus dezocine group (n=50)	Flurbiprofen axetil group (n=51)	Dezocine group (n=49)	[a]P-value	[b]P-value	[c]P-value	[d]P-value
Postoperative complications rate[e], n (%)	21 (42.0)	17 (33.3)	17 (34.7)	0.625	>0.999	>0.999	>0.999
Chest tube duration (days)[f], median (IQR)	3.0 (2.0-3.0)	3.0 (2.0-4.0)	3.0 (2.0-4.0)	0.162	0.162	>0.999	0.710
Length of hospital stays (days)[g], median (IQR)	5.0 (4.0-7.0)	7.0 (5.0-8.0)	6.0 (5.0-8.0)	0.005	0.008	0.048	>0.999
In-hospital death rate[c], n (%)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-	-

[a]Test for 3-group comparison; [b]test for post-hoc comparison between flurbiprofen axetil plus dezocine group and flurbiprofen axetil group; [c]test for post-hoc comparison between flurbiprofen axetil plus dezocine group and dezocine group; and [d]test for post-hoc comparison between flurbiprofen axetil group and dezocine group. [e]χ^2 test followed by Bonferroni's test was used; [f]Kruskal-Wallis test followed by Dunn's multiple comparisons test was used; and [g]Fisher's exact test was used. IQR, interquartile range.



Post-hoc comparisons	6 h	12 h	D1	D2	D3	D7
[a]*P* value	0.008	0.003	0.013	0.036	0.010	0.421
[b]*P* value	0.010	0.012	0.020	0.059	0.097	0.400
[c]*P* value	0.948	0.640	0.878	0.847	0.355	0.964

Post-hoc comparisons	
[a]*P* value	0.010
[b]*P* value	0.002
[c]*P* value	0.590

Figure 2. Flurbiprofen axetil plus dezocine reduces (A) postoperative pain and (B) PCA consumption. [a]P: Comparison between the flurbiprofen axetil plus dezocine and the flurbiprofen axetil groups; [b]P: Comparison between the flurbiprofen axetil plus dezocine and the dezocine groups; and [c]P: Comparison between the flurbiprofen axetil and the dezocine groups. The one-way ANOVA followed by Tukey's multiple comparison test was used in (A) and (B). VAS, visual analog scale; PCA, patient-controlled analgesia; D1, day 1; D2, day 2; D3, day 3; D7, day 7.

levels were reduced in the flurbiprofen axetil plus dezocine group compared with those of the dezocine group at 12 h (P<0.001), D1 (P<0.001), and D3 (P=0.033) and declined in the flurbiprofen axetil group compared with those of the dezocine group at 12 h (P=0.003), while no significant difference was noted between the flurbiprofen axetil plus dezocine and the flurbiprofen axetil groups at all the time points investigated (all P>0.05; Fig. 4). These results suggested a certain anti-inflammatory effect of flurbiprofen axetil on patients with resectable NSCLC.

Comparison of surgical outcomes. Only the length of hospital stay varied among the flurbiprofen axetil plus dezocine, flurbiprofen axetil and dezocine groups (P=0.005), while other surgical outcomes, including postoperative complication rate, chest tube duration and in-hospital death rate remained similar among these three groups (all P>0.05; Table II). Further post hoc comparison indicated that the length of hospital stay was reduced in the flurbiprofen axetil plus dezocine group compared with that of the flurbiprofen axetil [median (interquartile range): 5.0 (4.0-7.0) days vs. 7.0 (5.0-8.0) days, P=0.008] and the dezocine groups [median (interquartile range): 5.0 (4.0-7.0) days vs. 6.0 (5.0-8.0) days, P=0.048; Table II].

Comparison of adverse events. No differences were noted in adverse event rates among the flurbiprofen axetil plus dezocine, flurbiprofen axetil and dezocine groups (all P>0.05; Table III). Moreover, the most commonly recorded adverse events in the flurbiprofen axetil plus dezocine group were nausea and vomiting (30.0%), constipation (14.0%), pruritus (14.0%), drowsiness (6.0%) and dizziness (4.0%).

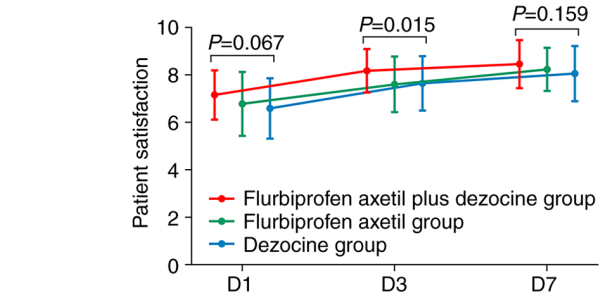
Discussion

Despite the satisfactory efficacy of morphine and other synthetic opioids in pain relief, severe adverse events have been

Table III. Adverse events.

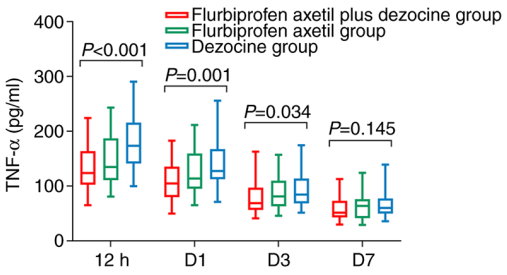
Events	Flurbiprofen axetil plus dezocine group (n=50)	Flurbiprofen axetil group (n=51)	Dezocine group (n=49)	[a]P-value
Nausea and vomiting, n (%)	15 (30.0)	13 (25.5)	17 (34.7)	0.609
Constipation, n (%)	7 (14.0)	5 (9.8)	10 (20.4)	0.326
Pruritus, n (%)	7 (14.0)	6 (11.8)	10 (20.4)	0.468
Drowsiness, n (%)	3 (6.0)	2 (3.9)	4 (8.2)	0.676
Dizziness, n (%)	2 (4.0)	2 (3.9)	3 (6.1)	0.843

[a]Test for 3-group comparison. One-way ANOVA test was used.



Post-hoc comparisons	D1	D3	D7
[a]*P* value	0.126	0.009	0.275
[b]*P* value	0.023	0.017	0.056
[c]*P* value	0.434	0.835	0.400

Figure 3. Flurbiprofen axetil plus dezocine enhances patient satisfaction. [a]P: Comparison between the flurbiprofen axetil plus dezocine and the flurbiprofen axetil groups; [b]P: Comparison between the flurbiprofen axetil plus dezocine and the dezocine groups; and [c]P: Comparison between the flurbiprofen axetil and the dezocine groups. The one-way ANOVA followed by Tukey's multiple comparison test was used. D1, day 1; D3, day 3; D7, day 7.



Post-hoc comparisons	12 h	D1	D3	D7
[a]*P* value	0.460	0.173	0.253	>0.999
[b]*P* value	<0.001	<0.001	0.033	0.124
[c]*P* value	0.003	0.168	>0.999	>0.999

Figure 4. Flurbiprofen axetil plus dezocine reduces the levels of inflammatory cytokines detected postoperatively compared with those detected following dezocine monotherapy. [a]P: Comparison between the flurbiprofen axetil plus dezocine and the flurbiprofen axetil groups; [b]P: Comparison between the flurbiprofen axetil plus dezocine and the dezocine groups; and [c]P: Comparison between the flurbiprofen axetil and the dezocine groups. The Kruskal-Wallis test followed by Dunn's multiple comparisons test was used. TNF-α, tumor necrosis factor-α; D1, day 1; D3, day 3; D7, day 7.

reported (18). One of the most serious opioid-related adverse events is pulmonary suppression, which may cause respiratory arrest and require immediate medical attention (19). Moreover, addiction to morphine and other synthetic opioids has emerged as a critical social and health issue (20). Under these circumstances, the concept of multimodality of analgesic agents has been proposed, which aims to reduce the dosage of opioids or partially replace opioids with other relatively safe medications, improve postoperative pain management and elevate patient satisfaction and quality of life (5,21,22). It is important to note that certain therapies combining multiple analgesic agents have already achieved encouraging results for postoperative pain relief among patients with cancer who have undergone surgery.

The combined therapy of flurbiprofen axetil with other analgesia yields a stronger postoperative analgesic effect than monotherapy. For example, flurbiprofen axetil plus dexmedetomidine reduces the VAS score and Bruggrmann comfort scale at 6 and 12 h following surgery compared with flurbiprofen axetil monotherapy in patients with resectable lung cancer (13). Moreover, an additional study indicated that flurbiprofen axetil plus nalbuphine decreases the pain score compared with nalbuphine monotherapy at 2, 6, and 10 h following orbital decompression (23). Furthermore, dezocine is another commonly prescribed analgesic agent in China, which has indicated effective analgesic effects in patients with liver cancer who underwent hepatectomy and in patients with postoperative breast cancer (15,16). Although both flurbiprofen axetil and dezocine show analgesic effects following single treatment, the efficacy of their combined therapy is undetermined. In the present study, flurbiprofen axetil plus dezocine exhibited a stronger analgesic effect than monotherapy, as determined by decreased postoperative VAS scores and PCA consumption in patients with NSCLC. This was due to the following reasons: Flurbiprofen axetil suppressed inflammatory cytokines, such as TNF-α in the local injury of peripheral nerves, while dezocine acted on the μ- and κ-opioid receptors in the brain; therefore, their combination may exhibit a stronger analgesic effect by two different mechanisms and further lead to reduced postoperative pain compared with monotherapy in patients with resectable NSCLC (10,24).

Interestingly, it was observed that the differences of pain relief and PCA consumption between flurbiprofen axial plus dezocine group and dezocine group were not strongly significant. The possible reason might result from the fact that the background analgesia dose of PCA (that is 72 ml for 3 days) in all groups weakened the effect of flurbiprofen axial and additional PCA consumption. Meanwhile, it could be noted

that even though flurbiprofen axial plus dezocine group had a significantly lower consumption of PCA compared with dezocine group, it had an improved analgesic effect compared with dezocine group, indicating the superior pain relief in flurbiprofen axial plus dezocine group. In addition, the absolute difference of these two indexes between flurbiprofen axial plus dezocine group and dezocine group were calculated. The mean difference of pain VAS score of flurbiprofen axial plus dezocine group compared with dezocine group was 0.6 point, 0.6 point and 0.5 point at 6 h, 12 h and D1, respectively; the mean difference of PCA consumption of flurbiprofen axial plus dezocine group compared with dezocine group was 10 ml. Regarding pain VAS, a decrease of 1.0 point was clinically significant, while a decreased of 0.5 point was to some extent clinically significant. Regarding PCA consumption, the background was 72 ml for all groups, therefore the additional PCA consumption was 19 ml in flurbiprofen axial plus dezocine group, and 29 ml in dezocine group, which was clinically significant.

In the current study, it was demonstrated that the administration of flurbiprofen axetil plus dezocine improved postoperative patient satisfaction to a certain extent and reduced hospital stay, while it did not affect other surgical outcomes, including postoperative complication rate, chest tube duration, and in-hospital death rate compared with monotherapy in patients with resectable NSCLC. A possible explanation for this finding was that the administration of flurbiprofen axetil plus dezocine effectively reduced postoperative pain and the risk of developing psychological distress, which enhanced further patient perception and motivation for rehabilitation; therefore, flurbiprofen axetil plus dezocine enhanced patient satisfaction and reduced the hospital stay as monotherapy in patients with NSCLC (25).

Both NSAIDs and opioids are associated with several adverse events, among which gastrointestinal discomfort is the most commonly reported (9,26). For NSAIDs, their long-term usage is linked with an elevated risk of peptic ulcers and gastric bleeding (9). Moreover, opioids are related to the occurrence of constipation and bowel dysfunction (26). In the present study, adverse events were also recorded to evaluate the safety of analgesic agents; it was revealed that patients with resectable NSCLC treated with flurbiprofen axetil plus dezocine often experienced gastrointestinal discomfort, such as nausea, vomiting and constipation and nervous system impairment, such as drowsiness and dizziness. Moreover, flurbiprofen axetil plus dezocine did not increase the incidence of adverse events when administered as monotherapy, suggesting the relatively safe profile of this interventional option.

However, certain limitations are present in the current study. For example, the restricted sample size was one limitation. Moreover, the present study was a single-center study where selection bias may occur; therefore, further multicenter studies are required to validate these findings. In addition, the effect of flurbiprofen axetil plus dezocine on the recovery of long-term physical function of patients with resectable NSCLC was not determined in the current study, while future studies could address this issue. Besides, the detection of other inflammatory cytokines such as IL-6 and IL-1β could further reveal the anti-inflammatory effect of flurbiprofen axetil, which can be explored in the future studies.

In conclusion, the combination of flurbiprofen axetil and dezocine reduces postoperative pain, inflammation and hospital stay, while elevating patient satisfaction compared with monotherapy in patients with resectable NSCLC.

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Availability of data and materials

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

Authors' contributions

LZ and JH contributed to the conception of the study. XWe, ZW, YC, XWa and LM contributed to the data acquisition and drafted the manuscript. XWe, ZW, JH and LZ contributed to data analysis and revised the manuscript. XeiW and LZ confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of Handan Central Hospital (approval no. 2021030035; Handan, China). Each patient signed the informed consent form.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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