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Original Article

Preemptive hydromorphone analgesia reduces postoperative delirium and stress response in laparoscopic cholecystectomy patients

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Abstract: Objective: To evaluate the effects of preemptive hydromorphone analgesia on postoperative delirium and stress response in patients undergoing laparoscopic cholecystectomy. Methods: A retrospective cohort study was conducted, including 167 patients who underwent laparoscopic cholecystectomy at Xi'an Central Hospital between June 2021 and November 2023. Patients were categorized into an observation group (n=87) receiving preemptive hydromorphone hydrochloride analgesia and a control group (n=80) without preemptive analgesia. Postoperative pain was assessed using the Visual Analogue Scale (VAS), and stress response was evaluated by measuring epinephrine, norepinephrine, and dopamine levels. The incidence of postoperative delirium was recorded. Logistic regression analysis was performed to identify risk factors for postoperative delirium. Results: The VAS score at 30 minutes postoperative was significantly lower in the observation group than that in the control group (P<0.001). Similarly, postoperative levels of epinephrine, norepinephrine, and dopamine were significantly reduced in the observation group (all P<0.001). The incidence of postoperative delirium was also significantly lower in the observation group (P<0.05). Multivariate logistic regression analysis identified higher doses of propofol (P<0.001; odds ratio =3.102, 95% confidence interval: 1.144-9.777) and remifentanil (P=0.001; odds ratio =2.376, 95% confidence interval: 1.469-4.290) as independent risk factors for postoperative delirium, indicating a significant increase in delirium risk with higher drug doses. Conclusion: Preemptive hydromorphone analgesia significantly alleviates postoperative pain, reduces stress responses, and lowers the incidence of postoperative delirium in patients undergoing laparoscopic cholecystectomy. Compared to conventional analgesia strategies, hydromorphone provides superior pain control and a favorable safety profile.

Keywords: Hydromorphone hydrochloride, preemptive analgesia, laparoscopic cholecystectomy, postoperative delirium, stress response

Introduction

Laparoscopic cholecystectomy (LC) is a widely performed minimally invasive surgical procedure, valued for its minimal trauma, rapid recovery, and short hospital stays [1]. However, postoperative pain and stress responses remain critical challenges impacting patient recovery quality [2]. Postoperative pain not only causes discomfort but also induces physiological responses, such as elevated blood pressure, increased heart rate, and immunosuppression, which may heighten the risk of postoperative complications [3, 4]. Thus, effective management of postoperative pain and stress responses has become a key area of research in anesthesiology.

In recent years, preemptive analgesia (PA) has garnered significant attention as an essential strategy for postoperative pain control [5]. PA is grounded in the concepts of "central sensitization" and "hyperalgesia", suggesting that administering analgesics before surgical stimuli can block or attenuate pain signal transmission, preventing excessive central nervous system excitation [6-8]. This proactive approach aims to reduce the intensity and duration of

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postoperative pain by inhibiting nociceptive-induced neural activity, ultimately improving recovery outcomes [9]. PA encompasses not only preoperative analgesic administration but also multimodal pain management during and immediately after surgery to ensure effective, continuous analgesia [10]. Increasing clinical evidence supports PA's efficacy in reducing postoperative pain, minimizing opioid consumption, and lowering postoperative complication rates [11].

Among analgesics, opioids are central to PA strategies due to their potent analgesic effects. Hydromorphone hydrochloride, a semi-synthetic opioid, activates μ-opioid receptors in the central nervous system, providing robust pain relief [12]. Compared to traditional opioids such as morphine, hydromorphone offers several advantages, including rapid onset, superior analgesic potency, straightforward metabolism, and renal safety, making it a favorable option in postoperative pain management [13]. When administered preoperatively or intraoperatively, its rapid onset not only improves postoperative pain control but also mitigates intraoperative stress responses [14].

Postoperative delirium, a common and reversible complication characterized by acute changes in consciousness, typically occurs in the early postoperative period [15]. It adversely affects recovery, prolongs hospital stays, and is associated with increased mortality. Evidence links postoperative delirium to various factors, with pain and stress responses serving as major triggers [16]. Consequently, effective analgesic strategies for pain control could potentially reduce the incidence of delirium. While hydromorphone exhibits excellent analgesic properties, its use carries risks of adverse effects, including nausea, vomiting, respiratory depression, and postoperative delirium [17]. Delirium, as a central nervous system complication, may be associated with opioid administration. Hence, balancing hydromorphone's analgesic efficacy with its potential risks through appropriate dosage and timing is crucial.

This study aims to evaluate the impact of preemptive hydromorphone hydrochloride analgesia on postoperative delirium and stress responses in LC patients. By comparing conventional anesthesia protocols with those incorporating PA, this research seeks to assess the effectiveness of hydromorphone in pain control, its potential to reduce postoperative complications, and its overall safety and efficacy, thereby providing evidence for its clinical application.

Methods and materials

Study design

This retrospective cohort study evaluated the effects of PA with hydromorphone hydrochloride on postoperative delirium (POD) and stress responses in patients undergoing LC. The study was approved by the Xi'an Central Hospital Ethics Committee and adhered to the ethical principles of the Declaration of Helsinki.

Patient selection

A total of 167 patients who underwent LC at Xi'an Central Hospital between June 2021 and November 2023 were included. Patients were assigned to either the observation group (n=87), receiving PA with hydromorphone, or the control group (n=80), receiving a conventional analgesia regimen.

Inclusion and exclusion criteria

Inclusion criteria: Patients aged 18 years or older, undergoing LC, with normal cognitive function and no hearing or vision impairments. Only patients classified as ASA I or II were included.

Exclusion criteria: Patients were excluded if they received local anesthesia, had incomplete clinical data, or used anti-delirium or delirium-inducing drugs. Exclusion also applied to those with preoperative delirium, coma, ASA classification III or above, or severe hepatic or renal dysfunction.

Anesthesia protocols

Patients were grouped based on the anesthesia protocol used in clinical practice rather than predetermined by the researchers. All patients underwent standard preoperative anesthesia evaluation and adhered to preoperative fasting protocols (8 hours for food, 6 hours for liquids).

Anesthesia induction and maintenance: Induction involved intravenous administration of

fentanyl (2 μg/kg), propofol (1.5 mg/kg), and cisatracurium (0.2 mg/kg), followed by endotracheal intubation for controlled mechanical ventilation. Maintenance utilized sevoflurane inhalation (1.0 MAC), continuous intravenous infusion of remifentanil (0.1-0.2 μg/kg/min) and propofol (4-10 mg/kg/h). All anesthetic agents were discontinued 5 minutes before surgery ended.

Postoperative management: Residual muscle relaxants were reversed using atropine sulfate and neostigmine methylsulfate. Tropisetron hydrochloride was administered to prevent postoperative nausea and vomiting. After regaining spontaneous respiration and full consciousness, patients were extubated and transferred to the post-anesthesia care unit (PACU) for observation.

Analgesia protocol: Patients in the observation group received intravenous hydromorphone hydrochloride (15 μg/kg, diluted to 10 ml with normal saline) as a PA measure, administered 10 minutes before the skin incision. Patients in the control group did not receive PA.

Data extraction

Data were extracted from the hospital's electronic medical record system.

Preoperative data: General patient information, including age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) classification [18], and medical history (hypertension, diabetes, smoking, alcohol use), was collected. Additional demographic data such as education level, residence, ethnicity, marital status, and occupation were also recorded to compare baseline characteristics between groups and ensure comparability.

Intraoperative data: Key intraoperative metrics included surgery duration, anesthesia time, mean arterial pressure (MAP), and heart rate (HR) measured preoperatively, at the end of surgery, and 30 minutes postoperatively. Total doses of propofol and remifentanil were recorded to evaluate the impact of analgesia regimens on intraoperative and postoperative stress responses and pain management.

Postoperative data: Postoperative data included: Stress-related hormone levels (epinephrine (E), norepinephrine (NE), and dopamine (DA)) measured at 10 minutes before surgery (T1) and 30 minutes postoperatively (T3). Visual Analogue Scale (VAS) scores [19] and Ramsay sedation scores [20] at 30 minutes, 6 hours, and 12 hours postoperatively. Extubation time and time to spontaneous respiration recovery. Postoperative complications such as nausea, vomiting, respiratory depression, hypotension, pruritus, and POD.

Data verification

Data extraction was conducted by two independent researchers, each responsible for different patient records. Cross-verification was performed to ensure accuracy, and any discrepancies were resolved by a third researcher to achieve consensus.

Outcome measurements

Primary outcomes: Incidence of postoperative delirium (POD): POD was diagnosed based on the DSM-5 criteria by experienced neurologists. Delirium events occurring within five postoperative days were recorded. Logistic regression analysis was conducted to identify independent risk factors for POD.

Postoperative stress response: Stress responses were assessed by measuring hormone levels E, NE, and DA at T1 and T3. The effects of analgesia regimens on these markers were compared between groups.

Secondary outcome measures: Intraoperative physiological parameter changes: Heart rate (HR) and mean arterial pressure (MAP) were recorded at three time points: 10 minutes before surgery (T1), at the end of surgery (T2), and 30 minutes postoperatively (T3). These parameters were compared between the control and observation groups to evaluate the impact of the analgesia regimen on intraoperative conditions.

Postoperative pain and sedation scores: Postoperative pain intensity was assessed using the VAS, while sedation levels were evaluated with the Ramsay sedation scale. Measurements were taken at 30 minutes (T3), 6 hours (T4), and 24 hours (T5) postoperatively to track the effectiveness of postoperative analgesia.

Table 1. Comparison of baseline characteristics

Factor	Control Group (n=80)	Observation Group (n=87)	t/χ^2 Value	*P* Value
Age	49.61±5.44	50.83±5.10	1.485	0.139
Sex (Male/Female)	35/45	34/53	0.375	0.540
BMI (kg/m^2)	23.17±1.55	23.00±1.52	-0.679	0.498
ASA Classification (I/II)	37/43	42/45	0.069	0.793
History of Hypertension (Yes/No)	6/74	9/78	0.413	0.521
History of Diabetes (Yes/No)	7/73	10/77	0.343	0.557
Smoking History (Yes/No)	28/52	34/53	0.297	0.586
Alcohol Use History (Yes/No)	6/74	4/83	0.624	0.430
Education Level (≥ High School/< High School)	38/42	38/49	0.245	0.620
Residence (Urban/Rural)	43/37	52/35	0.616	0.433
Ethnicity (Han/Other)	76/4	84/3	0.250	0.617
Marital Status (Married/Other)	72/8	76/11	0.289	0.591
Occupation (Employed/Retired)	64/16	74/13	0.743	0.389

Note: BMI, body mass index; ASA, American Society of Anesthesiologists Classification.

Surgery and anesthesia-related parameters: Surgery duration and the total doses of propofol and remifentanil used during the procedure were recorded. These parameters were compared between the two groups to assess the impact of the analgesia regimens on surgical efficiency and anesthetic requirements.

Extubation time and spontaneous respiration recovery time: The time taken for extubation and the recovery of spontaneous breathing were recorded as recovery indicators. Comparisons were made between the control and observation groups to determine the impact of the analgesia regimen on postoperative recovery speed.

Postoperative adverse events: The incidence of postoperative adverse events, including nausea, vomiting, respiratory depression, hypotension, pruritus, and POD, was recorded. These events were analyzed to evaluate the safety and tolerability of the different analgesia regimens.

Statistical analysis

All statistical analyses were conducted using SPSS version 26.0. Figures were generated using GraphPad Prism 9 for enhanced result visualization. Normality tests were performed for continuous variables. Normally distributed variables were expressed as mean ± standard deviation (SD) and compared between groups using the independent sample t-test. Categorical variables were analyzed using the χ^2 test or Fisher's exact test, as appropriate. Variables recorded at multiple time points were analyzed using repeated measures ANOVA, with Bonferroni post-hoc tests for specific group differences. Multivariate logistic regression analysis was performed to identify independent risk factors for POD. A *P*-value <0.05 was considered statistically significant.

Results

Comparison of baseline characteristics

Baseline characteristics between the control and observation groups showed no significant differences in age (P=0.139), sex distribution (P=0.540), body mass index (BMI) (P=0.498), American Society of Anesthesiologists (ASA) classification (P=0.793), history of hypertension (P=0.521), history of diabetes (P=0.557), smoking history (P=0.586), alcohol use history (P=0.430), education level (P=0.620), residence (P=0.433), ethnicity (P=0.617), marital status (P=0.591), or occupation (P=0.389) (**Table 1**).

Comparison of HR and MAP between the two groups at T1-T3

HR and MAP were compared at T1, T2, and T3. No significant differences were observed at T1 and T2 (P>0.05). However, at T3, the observa-

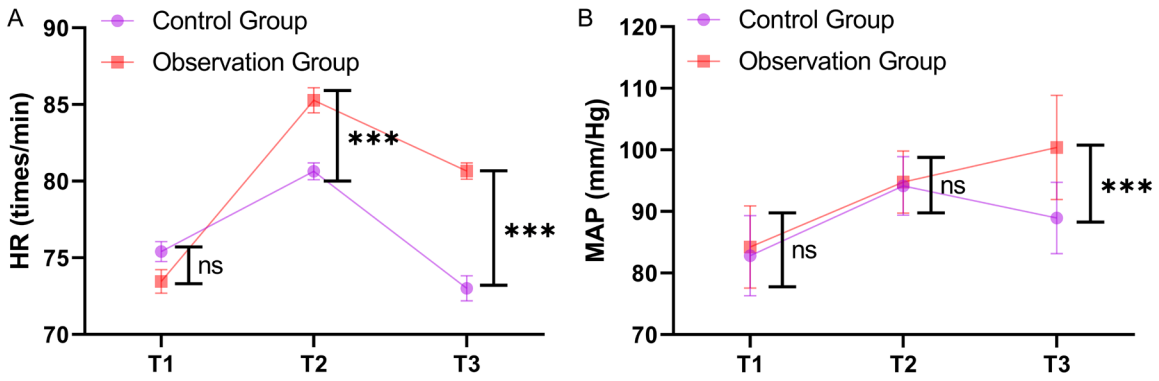

Figure 1. Comparison of HR and MAP changes between control and observation groups at different time points. A. Comparison of HR at three time points: T1, T2, and T3. B. Comparison of MAP at three time points: T1, T2, and T3. Note: ***P<0.001 indicates a significant difference between groups; ns indicates no significant difference; HR, heart rate; MAP, mean arterial pressure.

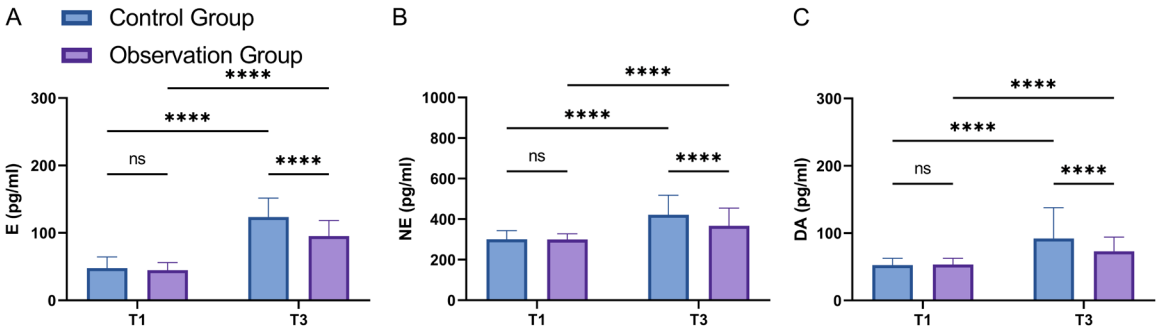

Figure 2. Comparison of E, NE, and DA levels between control and observation groups at T1 and T3. A. Comparison of E at two time points: T1 and T3. B. Comparison of NE at two time points: T1 and T3. C. Comparison of DA at two time points: T1 and T3. Note: ****P<0.001 indicates a significant difference between groups; ns indicates no significant difference; E, epinephrine; NE, norepinephrine; DA, dopamine.

tion group had a significantly lower HR compared to the control group (P<0.001, **Figure 1A**). Similarly, no significant differences were noted at T1 and T2 (P>0.05). At T3, MAP was significantly lower in the observation group (P<0.001, **Figure 1B**).

Comparison of E, NE, and DA levels between the two groups at T1 and T3

Levels of E, NE, and DA at T1 and T3 were compared between the two groups. No significant differences were found at T1 (P=0.187), but at T3, E levels were significantly lower in the observation group (P<0.001, **Figure 2A**). NE levels were similar at T1 (P=0.830) but significantly lower in the observation group at T3 (P<0.001, **Figure 2B**). For DA, there was no significant difference at T1 (P=0.632). At T3, DA levels were significantly lower in the observation group (P=0.001, **Figure 2C**).

Comparison of surgery duration, propofol, and remifentanil doses between the two groups

Surgery duration and anesthetic doses were compared. No significant differences in surgery duration were found between the groups (P=0.200, **Figure 3A**). The observation group received significantly lower doses of propofol (P<0.001, **Figure 3B**) and remifentanil (P< 0.001, **Figure 3C**) compared to the control group.

Comparison of extubation time and spontaneous respiration recovery time between the two groups

No significant differences were observed between the two groups for extubation time (P=0.076, **Figure 4A**) or spontaneous respiration recovery time (P=0.102, **Figure 4B**).

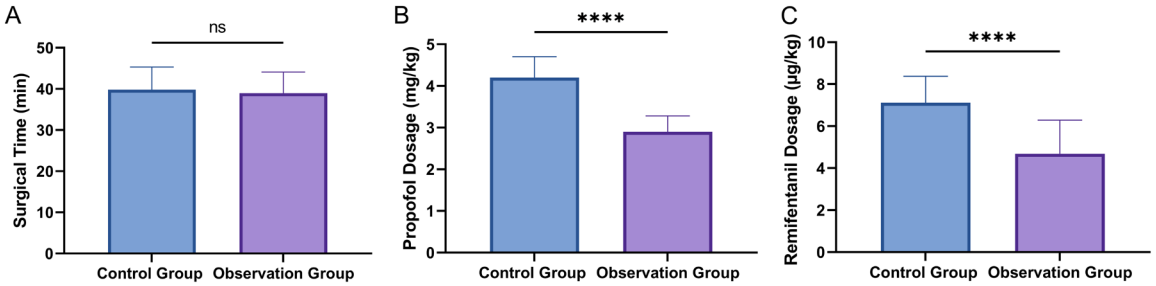

Figure 3. Comparison of surgical time, propofol dosage, and remifentanil dosage between control and observation groups. A. Comparison of surgical time. B. Comparison of propofol dosage. C. Comparison of remifentanil dosage. Note: ****P<0.001 indicates a significant difference between groups; ns indicates no significant difference.

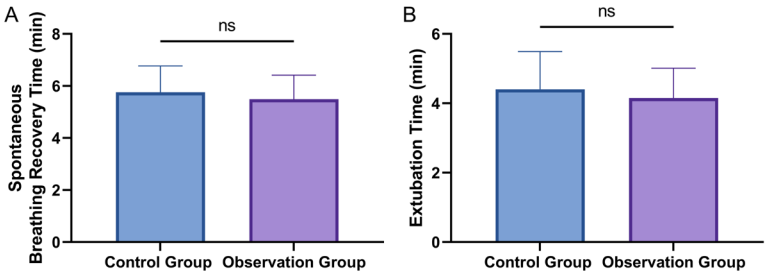

Figure 4. Comparison of extubation time and spontaneous breathing recovery time between control and observation groups. A. Comparison of spontaneous breathing recovery time. B. Comparison of extubation time. Note: ns indicates no significant difference.

Comparison of VAS and Ramsay scores between the two groups at T3, T4, and T5

The observation group had significantly lower VAS scores at T3 (P<0.001, **Figure 5A**) and T4 (P<0.001). At T5, no significant difference was found (P=0.24). As for ramsay scores, no significant differences were noted between the two groups at any time point: T3 (P=0.362, **Figure 5B**), T4 (P=0.351), and T5 (P=0.398).

Comparison of adverse event incidence between the two groups

The incidence of postoperative adverse events was compared between the control and observation groups. No significant differences were observed in the incidence of nausea and vomiting (P=0.470), pruritus (P=0.583), respiratory depression (P=0.512), hypotension (P=0.952), or POD (P=0.218) (**Table 2**).

Analysis of risk factors for POD

Univariate and multivariate logistic regression analyses were conducted to identify risk factors for POD. Univariate logistic regression analysis (**Table 3**) identified that propofol dose (P<0.001, odds ratio [OR] = 6.140, 95% confidence interval [CI]: 2.848-16.048) and remifentanil dose (P<0.001, OR=3.028, 95% CI: 1.954-5.285) were significantly associated with POD. Other factors, including age, BMI, sex, ASA classification, history of hypertension, history of diabetes, smoking history, alcohol use history, education level, residence, ethnicity, marital status, occupation, surgery duration, spontaneous respiration recovery time, and extubation time, were not significantly associated with POD (P>0.05) (**Table 4**). In the multivariate logistic regression analysis (**Table 5**), propofol dose (P<0.001, OR=3.102, 95% CI: 1.144-9.777) and remifentanil dose (P=0.001, OR=2.376, 95% CI: 1.469-4.290) were identified as independent risk factors for POD.

Discussion

This study demonstrates that PA with hydromorphone hydrochloride significantly enhances postoperative recovery in patients undergoing LC. Compared to conventional analgesia regimens, the hydromorphone group exhibited superior outcomes in pain control, stress response regulation, and POD reduction.

The observation group had significantly lower VAS scores at T3 and T4, indicating effective alleviation of early postoperative pain through PA. Lower levels of stress markers (E, NE, and DA) postoperatively in the observation group suggest that hydromorphone suppresses stress responses, potentially reducing POD

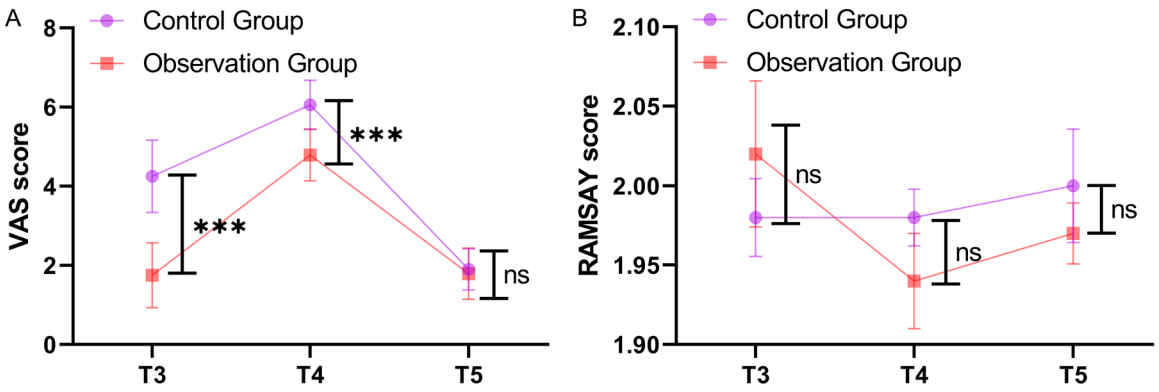

Figure 5. Comparison of VAS and RAMSAY scores between control and observation groups at T3, T4, and T5. A. Comparison of VAS at three time points: T3, T4, and T5. B. Comparison of RAMSAY at three time points: T3, T4, and T5. Note: ***P<0.001 indicates a significant difference between groups; ns indicates no significant difference; VAS, Visual Analogue Scale; RAMSAY, Ramsay Sedation Scale.

Table 2. Comparison of adverse reactions between control and observation groups

Group	Nausea and Vomiting	Itching	Respiratory Depression	Hypotension	Postoperative Delirium
Control Group (n=80)	8	3	2	1	14
Observation Group (n=87)	6	2	1	1	6
χ^2 value	0.523	0.302	0.431	0.004	4.445
P value	0.470	0.583	0.512	0.952	0.035

Table 3. Variable assignment table

Factor	Type	Assignment
Age	X	<51.5=0, ≥51.5=1
BMI	X	<24.29=0, ≥24.29=1
Surgical Time	X	<44.5=0, ≥44.5=1
Propofol Dosage	X	<3.695=0, ≥3.695=1
Remifentanil Dosage	X	<7.135=0, ≥7.135=1
Spontaneous Breathing Recovery Time	X	<2.5=0, ≥2.5=1
Extubation Time	X	<5.5=0, ≥5.5=1
Treatment Plan	X	Control Group =0, Observation Group =1
Sex	X	Male =1, Female =0
ASA Classification	X	II=1, III=0
History of Hypertension	X	Yes =1, No =0
History of Diabetes	X	Yes =1, No =0
Smoking History	X	Yes =1, No =0
Alcohol Use History	X	Yes =1, No =0
Education Level	X	≥ High School =1, < High School =0
Residence	X	Urban =1, Rural =0
Ethnicity	X	Han =1, Other =0
Marital Status	X	Married =1, Other =0
Occupation	X	Employed =1, Retired =0
POD	Y	Occurred =1, Not Occurred =0

Note: BMI, body mass index; ASA, American Society of Anesthesiologists Classification; POD, postoperative delirium; Y represents the dependent variable, X represents the independent variables.

Table 4. Univariate logistic regression analysis

Factor	β	SD	*P* Value	OR	95% CI	
					Lower	Upper
Treatment Plan	-0.796	0.497	0.109	0.451	0.161	1.166
Age	0.038	0.047	0.414	1.039	0.950	1.141
BMI	-0.278	0.164	0.091	0.757	0.542	1.037
Sex	0.171	0.480	0.722	1.186	0.453	3.040
ASA Classification	0.351	0.479	0.464	1.420	0.555	3.718
History of Hypertension	0.136	0.800	0.865	1.145	0.170	4.608
History of Diabetes	-0.842	1.060	0.427	0.431	0.023	2.308
Smoking History	-0.362	0.517	0.484	0.696	0.235	1.845
Alcohol Use History	1.261	0.736	0.087	3.529	0.711	14.064
Education Level	0.205	0.477	0.668	1.227	0.476	3.163
Residence	-0.087	0.479	0.856	0.917	0.358	2.401
Ethnicity	-0.213	1.107	0.848	0.809	0.128	15.704
Marital Status	-0.368	0.680	0.588	0.692	0.203	3.191
Occupation	1.498	1.047	0.153	4.471	0.869	81.995
Surgical Time	-0.051	0.045	0.251	0.950	0.870	1.037
Propofol Dosage	1.815	0.434	<0.001	6.140	2.848	16.048
Remifentanil Dosage	1.108	0.251	<0.001	3.028	1.954	5.285
Spontaneous Breathing Recovery Time	-0.207	0.250	0.409	0.813	0.490	1.317
Extubation Time	-0.088	0.247	0.721	0.916	0.560	1.483

Note: BMI, body mass index; ASA, American Society of Anesthesiologists Classification.

Table 5. Multivariate logistic regression analysis

Factor	β	SD	*P* Value	OR	95% CI	
					Lower	Upper
Propofol Dosage	1.132	0.538	0.035	3.102	1.144	9.777
Remifentanil Dosage	0.866	0.271	0.001	2.376	1.469	4.290

incidence. These findings underscore the dual benefits of hydromorphone PA in improving pain management and mitigating postoperative central nervous system complications [21].

The efficacy of hydromorphone PA likely stems from its mechanism of action. Hydromorphone activates μ-opioid receptors in the central nervous system, blocking pain signal transmission and preventing central sensitization [22]. By preemptively inhibiting central sensitization, PA reduces the intensity and duration of postoperative pain. Additionally, hydromorphone's rapid onset enables early analgesic effects during surgery, mitigating intraoperative and postoperative stress responses and reducing the excessive release of stress hormones.

Despite being an opioid, hydromorphone demonstrated a favorable safety profile in this study, with no significant differences in adverse event incidences between the hydromorphone and control groups. This suggests that the dosage and timing used were appropriate, balancing the efficacy and safety. Hydromorphone PA is an effective strategy for improving postoperative outcomes in LC patients, offering significant benefits in pain relief and stress response regulation with minimal risk of adverse effects when appropriately dosed and timed.

Our findings that hydromorphone PA significantly reduces postoperative pain and stress responses align with the findings of previous studies. For instance, Bindra et al. [23] demonstrated that using ropivacaine as PA in LC effectively reduced postoperative pain scores and decreased the need for additional analgesics. Similarly, our study found that hydromorphone PA provided substantial analgesic

effects by inhibiting postoperative pain signal transmission. However, unlike Bindra et al.'s research, our study further investigated the impact of hydromorphone on stress responses, showing significantly lower levels of E, NE, and DA, which correlated with a reduced incidence of POD. These results suggest that hydromorphone may operate via a more comprehensive mechanism, excelling in pain relief while suppressing postoperative stress responses.

Zhou et al. [24] reported similar findings for dezocine, which reduced postoperative pain and sedation scores and decreased analgesic use. However, their study did not delve into its effects on stress responses. In contrast, our findings emphasize that hydromorphone PA, through rapid analgesic action, mitigates excessive sympathetic nervous system activity and reduces stress hormone release, potentially explaining its effectiveness in reducing POD incidence. This finding aligns with the result of Yang et al. [25], who indicated that opioids in PA act through similar mechanisms.

Our results diverge from studies like Haider et al. [26], who reported higher rates of adverse effects such as nausea and vomiting with hydromorphone. In our study, no significant differences in adverse event incidence were observed between the hydromorphone PA group and the control group. This discrepancy might stem from differences in dosage and timing, suggesting that optimizing these factors in clinical practice can enhance efficacy while minimizing adverse effects. These comparisons highlight the unique advantages of hydromorphone in managing pain and stress responses, thereby reducing postoperative complications such as delirium.

POD is a common and severe postoperative complication, particularly in elderly patients, associated with increased mortality, prolonged hospital stays, and poor recovery. Its pathogenesis is multifactorial, involving age, comorbidities, surgical type, and anesthetic protocols.

Our study identified high doses of propofol and remifentanil as independent risk factors for POD. Excessive doses of these drugs may exacerbate central nervous system depression, delaying postoperative awakening and increasing the risk of delirium. This finding aligns with the results of Baek et al. [27] and Zhu et al. [28], who noted that high-dose opioids are closely linked to POD occurrence in elderly patients.

To mitigate POD risk, it is crucial to optimize propofol and remifentanil dosages, avoiding excessive or unnecessary use, especially in elderly patients. Such measures can promote smoother recovery, reduce hospital stays, and improve overall prognosis. These findings underscore the importance of carefully managing anesthetic drug dosages to minimize POD incidence.

Despite identifying significant findings, our study has limitations. First, the relatively small sample size may limit the statistical power of our results. Second, conducting the study at a single center restricts the generalizability of our findings. Lastly, we focused on specific anesthetic drug combinations and did not evaluate the effects of alternative anesthesia regimens on POD incidence. Future studies should expand the sample size, adopt multi-center designs, and explore diverse anesthesia regimens to improve the applicability and robustness of the results.

In conclusion, hydromorphone PA significantly reduces postoperative pain and stress responses in LC patients and decreases POD incidence. Compared to conventional analgesia, hydromorphone offers effective pain control and a favorable safety profile, highlighting its clinical value.

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Disclosure of conflict of interest

None.

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