

# Comparison of a single intravenous infusion of alfentanil or sufentanil combined with target-controlled infusion of propofol for daytime hysteroscopy: a randomized clinical trial

Xiaofeng Lei\*, Tinghuan Zhang\* and Xuezu Huang 

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## Abstract

**Background:** The administration of either alfentanil or sufentanil as a single injection, combined with target-controlled infusion (TCI) of propofol, represents a frequently employed anesthetic regimen for daytime hysteroscopy.

**Objectives:** This study was designed to evaluate and compare the safety and efficacy of alfentanil and sufentanil in the context of daytime hysteroscopy.

**Design:** A total of 160 patients, scheduled for daytime hysteroscopy, were randomly allocated into two groups: Group A and Group S respectively received alfentanil 10 µg/kg or sufentanil 0.15 µg/kg as a single intravenous injection. Both groups were given propofol with TCI for sedation.

**Methods:** Monitoring of vital signs was conducted from pre-anesthesia through to 2 h postoperatively. The primary outcome measured was hypoxemia, defined as SpO<sub>2</sub> levels below 92% for a duration of 30 s, which necessitated manual positive pressure ventilation. Secondary outcomes included various perioperative complications, such as postoperative nausea and vomiting (PONV) occurring 2 h after surgery, as well as hemodynamic indicators, NRS scores for pain, and other anesthesia-related data. This comprehensive dataset was meticulously documented and subsequently analyzed for comparative purposes.

**Results:** The analyses revealed that Group A had a significantly lower incidence of hypoxemia ( $p=0.002$ ) and PONV ( $p=0.021$ ). Additionally, group A demonstrated overall more stable blood pressure and heart rate, as well as higher SpO<sub>2</sub> levels.

**Conclusion:** For daytime hysteroscopy, alfentanil at a dose of 10 µg/kg is safer than sufentanil at a dose of 0.15 µg/kg when combined with propofol TCI.

**Trial registration:** This study was registered with the Chinese Clinical Trial Registry (The URL of registration is <https://www.chictr.org.cn/showproj.html?proj=177784>; registration number: ChiCTR2200063939). The date of first registration was September 21, 2022.

Correspondence to:

**Xuezu Huang**  
Department of  
Anesthesiology, Women  
and Children's Hospital of  
Chongqing Medical  
University (Chongqing  
Health Center for  
Women and Children),  
120 Longshan Road,  
Yubei District, Chongqing  
401147, China  
[huang\\_xuezu@126.com](mailto:huang_xuezu@126.com)

**Xiaofeng Lei**  
Department of  
Anesthesiology, Women  
and Children's Hospital  
of Chongqing Medical  
University (Chongqing  
Health Center for Women  
and Children), Chongqing,  
China

**Tinghuan Zhang**  
Department of  
Anesthesiology, Chongqing  
Rongchang Health Center  
for Women and Children,  
Chongqing, China

\*These authors are  
co-first authors as their  
contributions to this article  
are equal.

## Plain language summary

### Alfentanil combined with propofol is safer and more suitable for daytime hysteroscopy

Why was the study done? Hysteroscopy is a procedure to look inside the uterus, and managing pain and safety is crucial. The study was conducted to compare the safety and effectiveness of two pain relief medications, alfentanil and sufentanil, used during daytime hysteroscopy. What did the researchers do? We included 160 patients scheduled for daytime hysteroscopy. And we divided these patients into two groups: Group A: Received a

single injection of 10 µg/kg of alfentanil. Group S: Received a single injection of 0.15 µg/kg of sufentanil. Both groups were also given propofol, a sedative, during the procedure. What did the researchers find? Group A (alfentanil): Fewer patients experienced low oxygen levels (hypoxemia) and postoperative nausea and vomiting. They also had more stable blood pressure and heart rate. Group S (sufentanil): More patients experienced hypoxemia and postoperative nausea and vomiting. What do the findings mean? The findings suggest that alfentanil at 10 µg/kg is safer and just as effective for pain relief during daytime hysteroscopy compared to sufentanil at 0.15 µg/kg. It leads to fewer breathing problems and other side effects, making it a better option for patients undergoing this procedure.

**Keywords:** alfentanil, ambulatory surgical procedures, hypoxia, hysteroscopy, sufentanil

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### Introduction

Daytime hysteroscopy is an invasive procedure, that frequently produces patient discomfort and pain, which are foremost clinical concerns.<sup>1</sup> Procedural sedation, omitting endotracheal intubation, is gaining popularity for achieving painless hysteroscopy.<sup>2</sup> The standard anesthesia involves the administration of the sedative propofol, delivered via target-controlled infusion (TCI), along with a single intravenous infusion of an opioid such as alfentanil or sufentanil for pain management. Upon binding to opioid receptors, opioids induce a conformational change that forms a G protein-opioid receptor complex. This complex inhibits adenylate cyclase, increases K<sup>+</sup> efflux, and decreases Ca<sup>2+</sup> influx, ultimately diminishing the transmission of pain signals.<sup>3</sup> While sufentanil is notably effective for pain relief, it is associated with adverse effects, including coughing,<sup>4</sup> respiratory depression,<sup>5</sup> postoperative nausea and vomiting (PONV),<sup>6</sup> hemodynamic instability, and an overall elevation of potential for adverse reactions. In contrast, alfentanil exerted a milder influence on respiratory system compliance, resulting in fewer instances of respiratory depression and a diminished risk of regurgitation and aspiration.<sup>7</sup> Alfentanil appears to be more advantageous than sufentanil in this aspect. Nonetheless, alfentanil exhibits a less potent analgesic effect and has a shorter duration of action. The differences between the two opioids may be attributed to alfentanil's relatively lower binding affinity for δ-opioid receptors and µ-opioid receptors, as well as its shorter half-life.<sup>8</sup> In comparison to sufentanil, whether it can effectively alleviate visceral pain arising from cervical

traction and uterine distension during hysteroscopy while maintaining stable anesthesia throughout the procedure without exacerbating postoperative pain remains to be unequivocally established in relevant trials. Therefore, we carried out a single-center, prospective, randomized study employing alfentanil and sufentanil in conjunction with propofol TCI for daytime hysteroscopic surgery. The objective was to evaluate and compare the analgesic efficacy, hemodynamic stability, and complication rates associated with these two opioid medications.

### Materials and methods

#### *Ethical approval*

The study has received ethical approval from the Medical Ethics Committee of Chongqing Health Center for Women and Children (Registration number: 2022-055) and was duly registered with the Chinese Clinical Trial Registry ([www.chictr.org.cn](http://www.chictr.org.cn); registration number: ChiCTR2200063939). The date of first registration was September 21, 2022. The reporting of this study conforms to the CONSORT statement.<sup>9</sup> All participants have provided written informed consent, and the protocols strictly adhered to the principles of the Helsinki Declaration.

#### *Sample size calculation*

We estimated the occurrence of hypoxemia as the primary outcome. Previous studies have found that the probability of alfentanil causing

hypoxemia is 10%–18%,<sup>10</sup> and that of sufentanil is 43.9%.<sup>11</sup> Based on our pilot study, we anticipated incidence rates of 10% and 30% for the 10 µg/kg of alfentanil and 0.15 µg/kg of sufentanil respectively. We set a significance level ( $\alpha$ ) of 0.1 and a power of 90%. Using Power Analysis and Sample Size (PASS) software, version 2024 (NCSS, LLC, Kaysville, UT, USA), we calculated a sample size of 67 for each group. Factoring in a 15% dropout rate, we required at least 80 patients per group, totaling a minimum of 160 participants.

### *Selection of patients*

Inclusion criteria were: patients scheduled for daytime hysteroscopy aged 18–60 years; and an American Society of Anesthesiologists (ASA) physical status of I or II. Patients meeting any of the following criteria were excluded from the study: allergies to sedative or opioid drugs, alcoholism, other drug addictions, pathological obesity, obstructive sleep apnea syndrome, a history of PONV, or dizziness. The withdrawal requirements included: a patient's refusal to continue the study protocol, and the expansion of the surgical scope to laparoscopy. Between October 2022 and April 2023, a total of 160 patients were enrolled who underwent daytime hysteroscopy at the Chongqing Health Center for Women and Children (Women and Children's Hospital of Chongqing Medical University).

### *Randomization, allocation, and concealment:*

We used a computer-generated list for random assignment into two groups, maintaining allocation concealment with sealed opaque envelopes that were only opened upon the patient's arrival in the surgery room. The opioids were prepared by independent researchers who were not involved in the treatment or in evaluating the outcomes based on group assignments. Opioid dosing was based on patient weight: alfentanil at 10 µg/kg and sufentanil at 0.15 µg/kg, both diluted to 10 mL with saline. Administer slowly via intravenous push over a period of 15 s. Blinding of research personnel was maintained throughout the observation period.

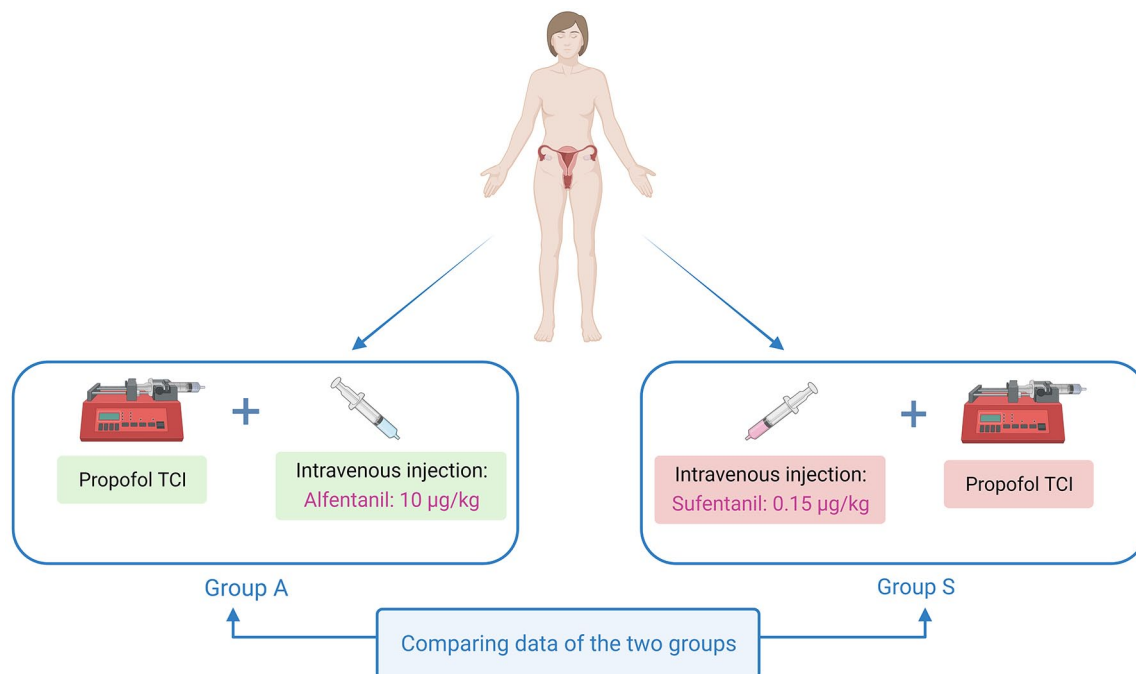
### *Study outcomes*

The primary outcome of this study was hypoxemia ( $\text{SpO}_2 < 92\%$  persists for 30 seconds despite

oxygen supplementation, necessitating manual positive pressure ventilation). The secondary outcomes involved other perioperative adverse events, hemodynamic indicators, pain scores, awakening time, and propofol dosage.

### *Study protocol*

Patients have observed an 8-h fasting period for solid foods and a 2-h restriction on clear liquid intake before the surgical procedure, with the exclusion of preoperative medications. After entering the operating room, patients were positioned in the lithotomy posture, and intravenous access was initiated. Hemodynamic parameters, encompassing electrocardiography, heart rate (HR), non-invasive blood pressure (NIBP; including systolic blood pressure (SBP) and diastolic blood pressure (DBP)), and oxygen saturation ( $\text{SpO}_2$ ), were continuously monitored until 2 h after surgery. Oxygen was administered through a simple facial mask and the oxygen flow rate was 5 L/min. Patients were randomly allocated to one of two drug groups. A TCI pump (Beijing SLGO Medical Technology Co., Ltd., model: CP-730TCI, Beijing, China) administered propofol (AstraZeneca UK Limited, batch number: H20130504, Caponago, Italy) using the Marsh model with a target plasma drug concentration of 2.5 µg/mL. Following the loss of consciousness, in accordance with the patient's group assignment, single intravenous opioid analgesics were administered as follows: Group A was given alfentanil (Nhw Pharmaceutical Co., Ltd., batch number: H20213853, Jiangsu China) at a dose of 10 µg/kg, and Group S was given sufentanil (Renfu Pharmaceutical Co., Ltd., batch number: H20054171, Yichang, China) at 0.15 µg/kg. In the event of body movement during the procedure, a single intravenous bolus of 20–30 mg of propofol was administered. If there was retroglossal collapse, an oral airway was inserted. If hypoxemia was observed ( $\text{SpO}_2 < 92\%$  persists for 30 s despite oxygen supplementation, necessitating manual positive pressure ventilation), positive pressure mask ventilation was instituted until recovery. If the HR dropped below 50 beats/min, atropine sulfate (Southwest Pharmaceutical Co., Ltd., batch number: H50020044, Chongqing, China) at a dose of 0.2–0.5 mg was administered, and if SBP decreased by more than 30% from the preoperative value, ephedrine hydrochloride (Chengdu Betta Pharmaceutical Co., Ltd., batch



**Figure 1.** Graphical abstract.

number: H32021530, Chengdu China) was injected at a dose of 3–6 mg. The study followed the standardized research protocol (see Figure 1).

#### Data collection

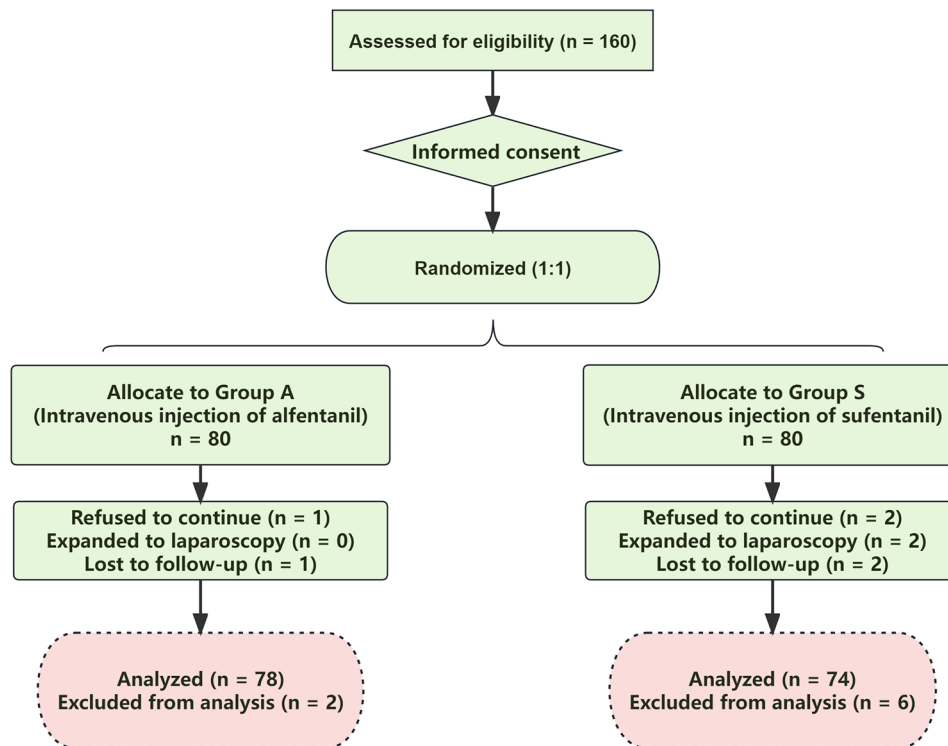
Recorded parameters encompassed demographics and hemodynamic parameters, including NIBP, HR, and SpO<sub>2</sub>, at specific time points: prior to anesthesia induction (T0), at the commencement of surgery (T1), 5 min after the start of surgery (T2), at the end of surgery (T3), and upon entry to the post-anesthesia care unit (PACU) (T4). Additional recorded data included details about the surgical procedure, its duration, patient satisfaction, propofol dosage, the duration of anesthesia recovery (from propofol discontinuation to the patient's response to their name), postoperative pain evaluation using the numerical rating scale (NRS) in the PACU and 2-h after the surgery (with 0 indicating “no pain” and 10 indicating “worst pain imaginable”),<sup>12</sup> and additional analgesia (NRS scores >3).

Recorded adverse events encompassed intra-operative body movements, bradycardia (HR < 50 bpm), hypotension/hypertension (SBP decrease/increase exceeding 30% of the preoperative value), PONV graded criteria in four grades 2h after surgery: Grade I—no nausea, Grade

II—mild nausea, mild abdominal discomfort, no vomiting, Grade III—evident nausea and vomiting, but no material expelled, Grade IV—severe vomiting, expulsion of gastric contents necessitating medication, postoperative dizziness at the 2-h post-surgery mark, pruritus, and delirium.

#### Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Science (SPSS) for Windows, version 21.0 (SPSS Inc., Chicago, IL, USA). Normality was assessed using the Shapiro-Wilk test. Quantitative data were presented as mean ± standard deviation (SD) and compared using the Student's *t* test (for data with a normal distribution), or presented as median (inter-quartile range) and compared using the Mann-Whitney *U* test (for data with an abnormal distribution) between the two groups. Because most vital values presented an abnormal distribution, repeated-measures generalized estimating equations were employed to assess group and time effects and the interaction effect of SBP, DBP, HR, and SpO<sub>2</sub> values. Additionally, the Friedman and Kruskal-Wallis *H* tests were used to assess differences in these values at various time points within each group and among the three groups at each time point. Categorical data



**Figure 2.** Flow chart of the study.

are presented as numbers and percentages and data sets were compared using the Pearson chi-squared and Fisher's exact tests. The Mann-Whitney  $U$  test was used to compare satisfaction evaluation scores, NRS scores for pain, PONV, and the ASA physical condition. Statistical significance was set at a two-tailed  $p$  value of  $<0.05$ .

## Results

### *The process of the study*

A total of 160 patients were initially enrolled in this study. However, two patients withdrew due to unanticipated surgical expansion to laparoscopy with the need for endotracheal intubation, and an additional three withdrawals for patient's refusal to continue with the study protocol. Three cases were lost to follow-up. Consequently, data from the remaining 152 patients (alfentanil: 78; sufentanil: 74) were analyzed (Figure 2).

### *Demographics and baseline values*

There were no significant differences between the groups with regard to age, weight, height, ASA

physical status classification, or diagnosis. Furthermore, there were no significant differences in baseline values for SBP, DBP, HR, and  $SpO_2$  (Table 1).

### *Primary outcomes*

The incidence of hypoxemia was significantly lower in Group A: in Group S, 15 (20.3%) patients required transient mask positive pressure ventilation for hypoxemia, compared to 3 (3.8%) in Group A ( $p=0.002$ ; Table 2).

### *Secondary outcomes*

The incidence of PONV was lower in Group A ( $p=0.021$ ). In Group S, 14 (18.9%) patients experienced PONV, including one who had severe PONV and required antiemetics, whereas only 5 (6.4%) patients in Group A had PONV. There were no obvious differences in the incidence of other complications including intraoperative body movement, bradycardia, hypotension, additional analgesia, dizziness, pruritus, or delirium between the two groups (Table 2).

**Table 1.** Demographics and baseline values.

Characteristic	Alfentanil group (n=78)	Sufentanil group (n=74)	p Value
Age (y)	42.40 ± 10.83	39.50 (33.00, 44.00)	0.119
Weight (kg)	57.70 (50.00, 65.00)	56.62 ± 8.88	0.308
Height (cm)	158.00 (155.00, 160.00)	158.00 (153.75, 161.25)	0.695
ASA (I/II)	68/10	60/14	0.304
Diagnosis			
Endometrial polyps	45 (57.7%)	48 (64.9%)	0.527
Intrauterine adhesion	13 (16.7%)	12 (16.2%)	
Uterine malformation	2 (2.6%)	2 (2.7%)	
Submucous myoma	2 (2.6%)	1 (1.4%)	
Contraceptive ring incarceration	4 (5.1%)	0 (0%)	
Abnormal uterine bleeding	12 (11.8%)	11 (14.9%)	
SBP prior to anesthesia induction (mmHg)	126.00 (118.00, 138.00)	128.96 ± 15.27	0.665
DBP prior to anesthesia induction (mmHg)	76.00 (69.50, 82.00)	77.36 ± 12.20	0.605
HR prior to anesthesia induction (min <sup>-1</sup> )	75.00 (10.00, 82.00)	75.50 (64.00, 87.00)	0.905
SpO <sub>2</sub> prior to anesthesia induction (%)	98.00 (98.00, 99.00)	99.00 (98.00, 100.00)	0.104
Values given as mean ± SD, median (inter-quartile range), or numbers (percentage). There were no significant differences between the two groups for all variables. ASA, American Society of Anesthesiologists; DBP, diastolic blood pressure; HR, heart rate; SBP, systolic blood pressure.			

In terms of the overall trend, the NIBP and HR of both groups exhibited a significant decrease at the start of surgery (T1) compared to baseline values (T0) and this decrease persisted throughout the duration of the surgery (Figure 3(a)–(c)). Group A exhibited a smaller reduction in NIBP after anesthesia and a quicker return to higher values than Group S (Figure 3(a) and (b)). DBP and HR values in both groups returned to preoperative levels after patients were transferred to the PACU (Figure 3(b) and (c)). In group A, SpO<sub>2</sub> remained significantly higher after anesthesia induction compared to T0, and it was higher than that in group S after the start of surgery (Figure 3(d)). It appears that alfentanil had a less detrimental effect on hemodynamics and better oxygen saturation.

No statistically significant differences were found within each group in terms of anesthetic data, including the total propofol dose, duration of

surgery, patient satisfaction evaluation, NRS for pain in PACU and 2-h after surgery, or the time to awakening (Table 3).

### Discussion

The study investigated whether the opioids alfentanil and sufentanil, when employed as components of a balanced anesthesia technique, could be linked to distinct analgesic efficacy, hemodynamic conditions, and the potential for adverse events during daytime hysteroscopic procedures. The TCI method was employed to achieve similar plasma drug levels in both groups. Both opioids were found to facilitate rapid recovery from anesthesia and provide effective pain relief. Hemodynamic parameters demonstrated greater stability in the group that received alfentanil, which also experienced lower rates of hypoxemia and PONV.

**Table 2.** Perioperative adverse outcomes.

Characteristic	Alfentanil group (n = 78)	Sufentanil group (n = 74)	p Value
Hypoxemia, n (%)	3 (3.8%)	15 (20.3%)	0.002
Intraoperative body movement, n (%)	11 (14.1%)	9 (12.2%)	0.724
Bradycardia, n (%)	10 (12.8%)	5 (6.8%)	0.210
Hypotension, n (%)	7 (9.0%)	12 (16.2%)	0.177
Hypertension, n (%)	0	0	/
Additional analgesia, n (%)	8 (10.3%)	5 (6.8%)	0.441
PONV(I/II/III/IV), n	73/3/2/0	60/9/4/1	0.021
Dizziness, n (%)	3 (3.8%)	4 (5.4%)	0.714
Pruritus, n (%)	0 (0%)	1 (1.35%)	0.487
Delirium, n (%)	0 (0%)	0 (0%)	/

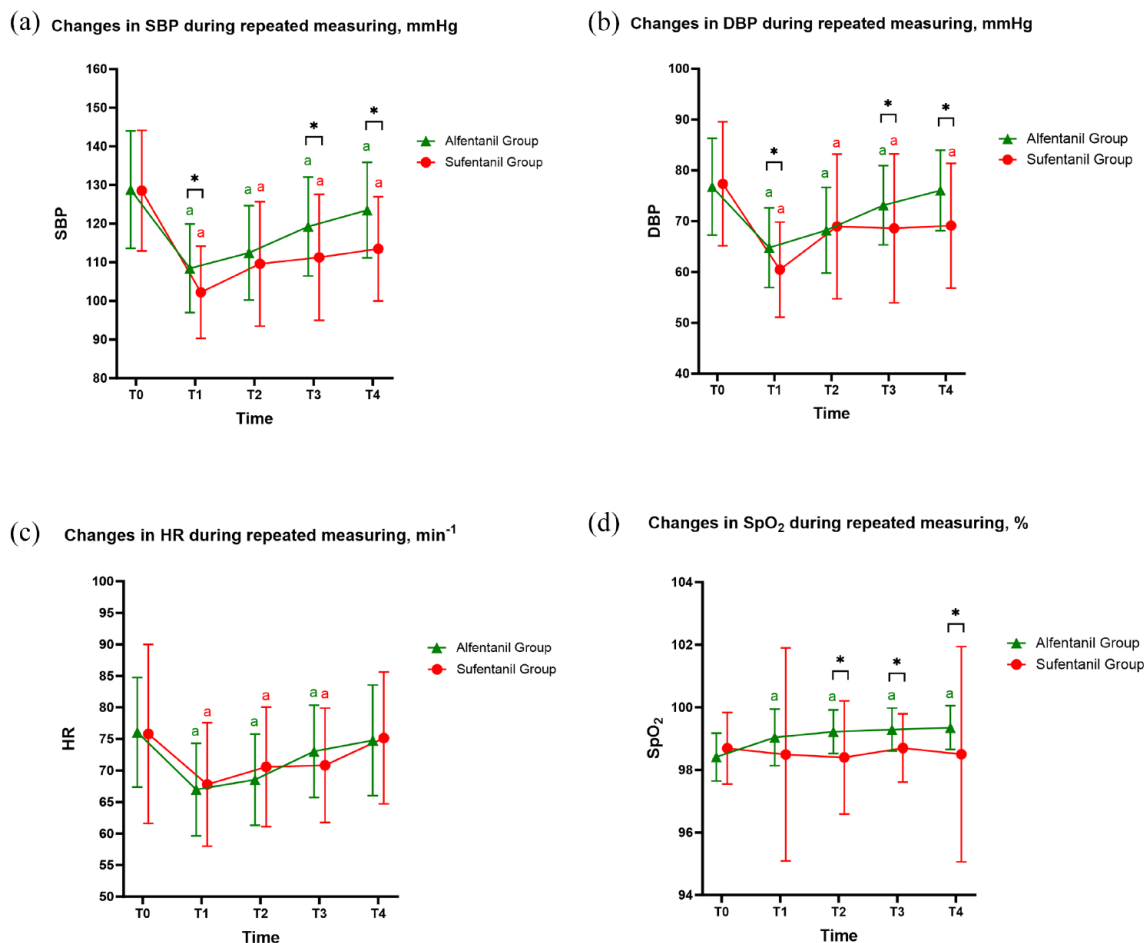
Values given as mean  $\pm$  SD, median (inter-quartile range), or numbers (percentage).  
PONV, postoperative nausea and vomiting.

Advancements in surgical technology, including versatile electrosurgical bipolar systems, have made hysteroscopy less invasive, which led to rapid developments in daytime hysteroscopic procedures, which developed rapidly in the late 1990s.<sup>13</sup> While hysteroscopic daytime surgery is simple and accessible, it has also been reported to elicit underappreciated source of pain.<sup>14,15</sup> It is universally acknowledged that administering analgesics can play a significant role in reducing pain during hysteroscopic procedures,<sup>16</sup> even though hysteroscopy was sometimes considered to eliminate the need for anesthesia.<sup>13</sup> Total intravenous anesthesia (TIVA) implemented using TCI of propofol, can enhance patient satisfaction, resulting in a rapid onset of anesthesia, and promote fast awakening, making it a widely utilized drug for daytime surgeries.<sup>17,18</sup> The combination of TIVA with propofol and short-acting opioids such as sufentanil<sup>19</sup> or alfentanil<sup>20</sup> is commonly employed for short and daytime surgical anesthesia. In our hospital, a balanced anesthetic protocol for hysteroscopic daytime surgery has been implemented to enhance patient comfort and reduce the risk of adverse events.

Based on previous research, the analgesic potency of sufentanil is known to be approximately 60–70 times that of alfentanil.<sup>8,21,22</sup> This data served as the basis for the dosages of two opioid drugs

chosen and used in our study, ensuring that the analgesic effects of both groups were at the same level.

Research has demonstrated a higher incidence of respiratory events in remote locations, with inadequate oxygenation and ventilation being the most common.<sup>23</sup> The use of opioids during the perioperative period has been linked to significant adverse effects, including respiratory depression and consequent hypoxemia.<sup>24</sup> Opioid-induced respiratory depression has been associated with prolonged hospital stays, increased the rate of readmissions, involved higher costs<sup>25</sup> and even catastrophic outcomes.<sup>26</sup> Therefore, one of the primary objectives for anesthesiologists, particularly during procedural sedation, is to select anesthetics with a lower risk of eliciting respiratory depression thus enhancing patient safety. Previous research found the incidence of respiratory depression related to opioids ranged from 0.3% to 21%<sup>27–29</sup> and was likely to be underestimated: A large prospective multicenter observational trial reported that 46% of 1335 general care floor patients experienced one or more respiratory depression episodes after receiving parenteral opioids, including 13.1% who experienced hypoxemia episodes.<sup>30</sup> In our prospective study, the overall incidence of hypoxemia related to opioids was 11.7%, and all cases of hypoxemia were



**Figure 3.** Changes in hemodynamic parameters: (a) changes in SBP during repeated measuring, (b) changes in DBP during repeated measuring, (c) changes in HR during repeated measuring, and (d) changes in SpO<sub>2</sub> during repeated measuring. Time points are T0 (prior to anesthesia induction); T1 (at the commencement of surgery); T2 (5 min after surgery started); T3 (at the end of surgery); and T4 (in PACU).  
<sup>a</sup>Significant differences between T0 and other time points ( $p < 0.05$ ).  
<sup>\*</sup>Significant differences between two groups ( $p < 0.05$ ).  
 DBP, diastolic blood pressure; HR, heart rate; PACU, post-anesthesia care unit; SBP, systolic blood pressure.

**Table 3.** Anesthetic data.

Characteristic	Alfentanil Group (n = 78)	Sufentanil Group (n = 74)	p Value
Total propofol dosage (mg/kg)	3.66 ± 1.11	3.94 (3.10, 4.65)	0.078
Time to awakening (min)	6.00 (5.00, 7.00)	5.00 (5.00, 7.00)	0.053
Duration of surgery (min)	12.50 (8.75, 16.50)	12.00 (9.00, 17.00)	0.937
Satisfaction evaluation of patients (score)	9.50 (9.00, 10.00)	9.00 (8.00, 10.00)	0.241
NRS scores for pain in PACU (score)	3.00 (2.00, 3.00)	2.00 (2.00, 3.00)	0.066
NRS scores for pain 2 h after surgery (score)	1.50 (1.00, 2.00)	2.00 (1.00, 2.00)	0.814

Values given as mean ± SD, median (inter-quartile range), or numbers (percentage).  
 NRS, numerical rating scale; PACU, post-anesthesia care unit.



promptly addressed through mask ventilation, without the need for tracheal intubation. SpO<sub>2</sub> was significantly higher after the start of surgery and the rate of hypoxemia was lower in the alfentanil group (3.8% in the alfentanil group vs 20.3% in the sufentanil group,  $p=0.002$ ). Opioids are known to exert their analgesic effects by binding to the  $\mu$ -opioid receptors, which also causes respiratory depression concurrently.<sup>31</sup> One possible reason for the lower incidence of hypoxemia in the alfentanil group may be the relatively lower binding affinity of alfentanil to the  $\mu$ -opioid receptors.<sup>8</sup> Clinical trials have also confirmed that alfentanil has significantly less impact in reducing minute ventilation and respiratory rate compared to other opioids.<sup>32</sup> Furthermore, unlike other opioids, respiratory system compliance and its various subcomponents of resistance remained unchanged and within normal limits after alfentanil administration.<sup>33</sup>

Approximately 20%–30% of surgical patients experience PONV following general anesthesia,<sup>34</sup> and up to 37% of daytime surgery patients continue to experience these symptoms after discharge.<sup>35</sup> Severe PONV can be so debilitating that patients have rated it as a more serious concern than postoperative pain. It can result in delayed patient discharge from the PACU and unexpected hospital admissions after daytime surgery.<sup>35</sup> The most reliable independent predictors of PONV include female gender, nonsmoking status, younger age, and the use of postoperative opioids.<sup>34</sup> It seems likely the patients scheduled for daytime hysteroscopy are a high-risk group for PONV. To reduce PONV, we employed the TIVA technique in our study. A prospective study revealed that when administered in approximately equipotent doses, alfentanil elicited significantly less PONV, both in the outpatient surgery unit and 24-h after discharge and, this difference could not be attributed to lower relative plasma concentrations.<sup>36</sup> Our study yielded similar results, with PONV rates of 6.3% in the alfentanil group and 18.9% in the sufentanil group. Opioids stimulate the chemoreceptor trigger zone in the area postrema of the medulla, possibly through action at  $\delta$ -receptors, resulting in nausea and vomiting.<sup>37</sup> Alfentanil's relative selectivity for  $\delta$ -receptors is lower than that of sufentanil,<sup>8</sup> which may be one of the reasons for the lower incidence of PONV in the alfentanil group. Additionally, propofol possesses antiemetic effects.<sup>38</sup> Both alfentanil and propofol are rapidly

metabolized drugs with similar half-life of fast distribution ( $T_{1/2\alpha}$ ).<sup>8,39</sup> Sufentanil has a longer  $T_{1/2\alpha}$  compared to alfentanil and propofol.<sup>8</sup> In our study, the difference in the incidence of PONV between the two groups is speculated to be attributed to the simultaneous elimination of propofol and alfentanil, whereas propofol and sufentanil cannot be simultaneously eliminated. The differences in the pharmacokinetics and pharmacodynamics of these two drugs may be responsible for the variation in PONV incidence, warranting further investigation.

Regarding hemodynamics, NIBP and HR were significantly decreased in both opioid groups following the induction of anesthesia. These decreases may be attributed to a reduction in systemic vascular resistance or cardiac output resulting from a combination of venous and arterial vasodilation, impaired baroreflex mechanisms, and depression of myocardial contractility caused by propofol.<sup>40</sup> As is well known, opioid drugs also have a similar inhibitory effect on the sympathetic nervous system,<sup>41</sup> and when combined with propofol, the effects on hemodynamics become more prominent. In the study, the decrease in NIBP was less pronounced in the alfentanil group compared to the sufentanil group, suggesting that alfentanil contributes to a more stable hemodynamic environment. Although there were no differences in the incidence of bradycardia or hypotension between the two groups, the greater hemodynamic stability provided by alfentanil may have significant clinical implications for specific patient populations, such as the frail elderly or those with coronary heart disease. This information is crucial because the primary anesthetic goal is to maintain a stable HR and blood pressure.<sup>42–44</sup>

Ozkan *et al.*<sup>45</sup> found that a propofol-alfentanil combination yielded more favorable outcomes in terms of early recovery times, and Ahonen *et al.*<sup>46</sup> observed that patients who received alfentanil experienced shorter and more predictable extubation times compared to those given sufentanil. In our study, the time to awakening was not significantly different between the two groups. This finding may be attributed to the smaller opioid dosage used resulting from the shorter duration of hysteroscopies. A retrospective study involving 597 patients reported that procedural sedation and anesthesia comprised of propofol plus alfentanil yielded favorable sedative effects and high

satisfaction scores,<sup>28</sup> findings in good agreement with our results.

### Limitations

The present study had several limitations. This prospective single-center study lacked additional data on the anesthesia effect and the incidence of adverse effects associated with the two analgesics in daytime hysteroscopies for the entire population. Large-scale, multicenter prospective clinical trials will be required to permit more accurate and comprehensive conclusions. Furthermore, the data collection extended only until discharge, and some adverse effects such as PONV, dizziness, and severe pain might have persisted or emerged after discharge. The lack of post-discharge follow-up might result in a missed opportunity to observe the long-term effects of the anesthesia protocol.

### Conclusion

During daytime hysteroscopy procedures, alfentanil exhibited a reduced propensity to elicit hypoxemia and PONV. Additionally, it demonstrated a capacity for maintaining more consistent hemodynamics and better oxygen saturation compared to sufentanil. These findings indicate that alfentanil may be a safer option for daytime hysteroscopy surgery.

### Declarations

#### *Ethics approval and consent to participate*

The study has received ethical approval from the Medical Ethics Committee of Chongqing Health Center for Women and Children (Registration number: 2022-055) and was duly registered with the Chinese Clinical Trial Registry ([www.chictr.org.cn](http://www.chictr.org.cn); registration number: ChiCTR2200063939). All protocols were carried out in strict accordance with the relevant guidelines and regulations. Written informed consents were obtained from all participating patients. Written informed consents were obtained from the patients for publication of this study. Copies of the written consent are available for review by the Editor of this journal.

#### *Consent for publication*

Not applicable.

#### *Author contributions*

**Xiaofeng Lei:** Data curation; Project administration; Writing – original draft.

**Tinghuan Zhang:** Conceptualization; Data curation; Project administration.

**Xuezhu Huang:** Conceptualization; Data curation; Formal analysis; Project administration; Resources; Software; Writing – original draft; Writing – review & editing.

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#### *Competing interests*

The authors declare that there is no conflict of interest.

#### *Availability of data and materials*

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

#### ORCID iD

Xuezhu Huang  <https://orcid.org/0000-0002-8019-9747>

### References

1. Marsh FA, Rogerson LJ and Duffy SR. A randomised controlled trial comparing outpatient versus daycase endometrial polypectomy. *BJOG* 2006; 113: 896–901.
2. Tang L, Ye C, Wang N, et al. The median effective doses of propofol combined with two different doses of nalbuphine for adult patients during painless gastroscopy. *Front Pharmacol* 2022; 13: 1014486.
3. Stein C. [Pain inhibition by opioids-new concepts]. *Schmerz* 2019; 33: 295–302.
4. He LX, Yao YT, Shao K, et al. Efficacy of dezocine on preventing opioid-induced cough during general anaesthesia induction:

- a PRISMA-compliant systematic review and meta-analysis. *BMJ Open* 2022; 12: e52142.
5. Beloeil H, Corsia G, Coriat P, et al. Remifentanyl compared with sufentanil during extra-corporeal shock wave lithotripsy with spontaneous ventilation: a double-blind, randomized study. *Br J Anaesth* 2002; 89: 567–570.
  6. Cohen MM, Duncan PG, DeBoer DP, et al. The postoperative interview: assessing risk factors for nausea and vomiting. *Anesth Analg* 1994; 78: 7–16.
  7. Bennett MW, Shah MV and Bembridge JL. A comparison of the effect on gastric emptying of alfentanil or morphine given during anaesthesia for minor surgery. *Anaesthesia* 1994; 49: 155–156.
  8. Enno Freye JVL. *Opioids in medicine: a comprehensive review on the mode of action and the use of analgesics in different clinical pain states*. 1st ed. Dordrecht, Netherlands: Springer, 2008, p. 475.
  9. Schulz KF, Altman DG and Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. *Ann Intern Med* 2010; 152: 726–732.
  10. Hsieh CH, Lin TY, Wang TY, et al. The safety and efficacy of alfentanil-based induction in bronchoscopy sedation: a randomized, double-blind, controlled trial. *Medicine (Baltimore)* 2016; 95: e5101.
  11. Yuan Y, Zhang J, Yue HL, et al. [A preliminary study of different methods of anesthesia for painless bronchoscopy]. *Zhonghua Jie He He Hu Xi Za Zhi* 2019; 42: 106–113.
  12. Hawker GA, Mian S, Kendzerska T, et al. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). *Arthritis Care Res (Hoboken)* 2011; 63(Suppl. 11): S240–S252.
  13. D Urso V, Gulino FA, Incognito GG, et al. Hysteroscopic findings and operative treatment: all at Once? *J Clin Med* 2023; 12: 4232.
  14. Harrison R, Kuteesa W, Kapila A, et al. Pain-free day surgery? Evaluating pain and pain assessment during hysteroscopy. *Br J Anaesth* 2020; 125: e468–e470.
  15. Harrison R, Kuteesa W, van Reekum CM, et al. Regarding Mahmud et al., 2021, Benchmarking services in outpatient hysteroscopy (OPH): a quality improvement project—Letter to the Editor. *Eur J Obstet Gynecol Reprod Biol* 2021; 263: 231–232.
  16. Buzzaccarini G, Alonso PL, Vitagliano A, et al. Pain management during office hysteroscopy: an evidence-based approach. *Medicina (Kaunas)* 2022; 58: 1132.
  17. Loser S, Herminghaus A, Huppe T, et al. [General anesthesia for ambulatory surgery: clinical pharmacological considerations on the practical approach]. *Anaesthesist* 2014; 63: 865–870, 872–874.
  18. Tesniere A and Servin F. Intravenous techniques in ambulatory anesthesia. *Anesthesiol Clin North Am* 2003; 21: 273–288.
  19. Alayurt S, Memis D and Pamukcu Z. The addition of sufentanil, tramadol or clonidine to lignocaine for intravenous regional anaesthesia. *Anaesth Intensive Care* 2004; 32: 22–27.
  20. Mandel JE. Considerations for the use of short-acting opioids in general anesthesia. *J Clin Anesth* 2014; 26: S1–S7.
  21. Brunton LL, Chabner B, Goodman LS, et al. *Goodman & Gilman's: the pharmacological basis of therapeutics*. 11th ed. New York, NY: McGraw-Hill Education, 2006, pp. 257–259.
  22. Stanley TH, Egan TD and Van Aken H. A tribute to Dr. Paul A. J. Janssen: entrepreneur extraordinaire, innovative scientist, and significant contributor to anesthesiology. *Anesth Analg* 2008; 106: 451–462.
  23. Metzner J, Posner KL and Domino KB. The risk and safety of anesthesia at remote locations: the US closed claims analysis. *Curr Opin Anaesthesiol* 2009; 22: 502–508.
  24. Shanthanna H, Ladha KS, Kehlet H, et al. Perioperative opioid administration. *Anesthesiology* 2021; 134: 645–659.
  25. Oderda GM, Gan TJ, Johnson BH, et al. Effect of opioid-related adverse events on outcomes in selected surgical patients. *J Pain Palliat Care Pharmacother* 2013; 27: 62–70.
  26. Andersen LW, Berg KM, Chase M, et al. Acute respiratory compromise on inpatient wards in the United States: incidence, outcomes, and factors associated with in-hospital mortality. *Resuscitation* 2016; 105: 123–129.
  27. Cashman JN and Dolin SJ. Respiratory and haemodynamic effects of acute postoperative pain management: evidence from published data. *Br J Anaesth* 2004; 93: 212–223.

28. Vaessen H, Bruens E and Knape J. Clinical analysis of moderate-to-deep-sedation by nonmedical sedation practitioners in 597 patients undergoing gastrointestinal endoscopy: a retrospective study. *Endosc Int Open* 2016; 4: E564–E571.
29. Sun Z, Sessler DI, Dalton JE, et al. Postoperative hypoxemia is common and persistent: a prospective blinded observational study. *Anesth Analg* 2015; 121: 709–715.
30. Khanna AK, Bergese SD, Jungquist CR, et al. Prediction of opioid-induced respiratory depression on inpatient wards using continuous capnography and oximetry: an international prospective, observational trial. *Anesth Analg* 2020; 131: 1012–1024.
31. Baldo BA. Current research in pathophysiology of opioid-induced respiratory depression, neonatal opioid withdrawal syndrome, and neonatal antidepressant exposure syndrome. *Curr Res Toxicol* 2022; 3: 100078.
32. Mildh LH, Scheinin H and Kirvela OA. The concentration-effect relationship of the respiratory depressant effects of alfentanil and fentanyl. *Anesth Analg* 2001; 93: 939–946.
33. Conti G, De Cosmo G, Bocci MG, et al. Alfentanil does not increase resistance of the respiratory system in ASA I patients ventilated mechanically during general anesthesia. *Can J Anaesth* 2002; 49: 718–723.
34. Apfel CC, Heidrich FM, Jukar-Rao S, et al. Evidence-based analysis of risk factors for postoperative nausea and vomiting. *Br J Anaesth* 2012; 109: 742–753.
35. Apfel CC, Philip BK, Cakmakkaya OS, et al. Who is at risk for postdischarge nausea and vomiting after ambulatory surgery? *Anesthesiology* 2012; 117: 475–486.
36. Langevin S, Lessard MR, Trepanier CA, et al. Alfentanil causes less postoperative nausea and vomiting than equipotent doses of fentanyl or sufentanil in outpatients. *Anesthesiology* 1999; 91: 1666–1673.
37. Gropper MA, Eriksson LI, Fleisher LA, et al. *Miller's anesthesia*. 9th ed. Amsterdam, The Netherlands: Elsevier, 2019.
38. Kampo S, Afful AP, Mohammed S, et al. Sub-hypnotic dose of propofol as antiemetic prophylaxis attenuates intrathecal morphine-induced postoperative nausea and vomiting, and pruritus in parturient undergoing cesarean section: a randomized control trial. *BMC Anesthesiol* 2019; 19: 177.
39. Sahinovic MM, Struys M and Absalom AR. Clinical pharmacokinetics and pharmacodynamics of propofol. *Clin Pharmacokinet* 2018; 57: 1539–1558.
40. Kanaya N, Satoh H, Seki S, et al. Propofol anesthesia enhances the pressor response to intravenous ephedrine. *Anesth Analg* 2002; 94: 1207–1211.
41. Wong TM and Shan J. Modulation of sympathetic actions on the heart by opioid receptor stimulation. *J Biomed Sci* 2001; 8: 299–306.
42. Habib AS, Parker JL, Maguire AM, et al. Effects of remifentanyl and alfentanil on the cardiovascular responses to induction of anaesthesia and tracheal intubation in the elderly. *Br J Anaesth* 2002; 88: 430–433.
43. Mantz J, Abi-Jaoude F, Ceddaha A, et al. High-dose alfentanil for myocardial revascularization: a hemodynamic and pharmacokinetic study. *J Cardiothorac Vasc Anesth* 1991; 5: 107–110.
44. Pouraghaei M, Moharamzadeh P, Soleimanpour H, et al. Comparison between the effects of alfentanil, fentanyl and sufentanil on hemodynamic indices during rapid sequence intubation in the emergency department. *Anesth Pain Med* 2014; 4: e14618.
45. Ozkan G, Ince ME, Eskin MB, et al. Sedoanalgesia for cardioversion: comparison of alfentanil, remifentanyl and fentanyl combined with propofol and midazolam: a prospective, randomized, double-blind study. *Eur Rev Med Pharmacol Sci* 2016; 20: 1140–1148.
46. Ahonen J, Olkkola KT, Hynynen M, et al. Comparison of alfentanil, fentanyl and sufentanil for total intravenous anaesthesia with propofol in patients undergoing coronary artery bypass surgery. *Br J Anaesth* 2000; 85: 533–540.