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# Opioid-free anesthesia with lidocaine for improved postoperative recovery in hysteroscopy: a randomized controlled trial

NH Cha<sup>1†</sup>, Y Hu<sup>1†</sup>, GH Zhu<sup>1†</sup>, X Long<sup>1</sup>, JJ Jiang<sup>1</sup> and Yuan Gong<sup>1\*</sup>

## Abstract

**Background** Anesthesia with opioids negatively affects patients' quality of recovery. Opioid-free anesthesia attempts to avoid these effects. This study aimed to evaluate the effect of opioid-free anesthesia on the quality of recovery, using lidocaine on patients undergoing hysteroscopy.

**Methods** A parallel-group, randomized, double-blind, controlled trial was conducted in Yichang Central Peoples' Hospital, Hubei Province, China, from January to April, 2022. We included 90 female patients (age: 18–65 years, American Society of Anesthesiologists Physical Status Class I–II) scheduled for elective hysteroscopy, 45 of whom received lidocaine (Group L), and 45 received sufentanil (Group S). Patients were randomly allocated to receive either lidocaine or sufentanil perioperatively. The primary outcome was the quality of postoperative recovery, which was assessed using the QoR-40 questionnaire (a patient-reported outcome questionnaire measuring the quality of recovery after surgery).

**Results** The two groups were similar in age, American Society of Anesthesiology physical status, height, weight, body mass index, and surgical duration. The QoR scores were significantly higher in Group L than Group S. The incidence of postoperative nausea and vomiting, as well as the time to extubation were significantly lower in Group L than Group S.

**Conclusion** Opioid-free anesthesia with lidocaine achieves a better quality of recovery, faster recovery, and a shorter time to extubation than general anesthesia with sufentanil.

**Trial registration** The trial was registered on January 15, 2022 in the Chinese Clinical Trial Registry (<http://www.chictr.org.cn/showprojen.aspx?proj=149386>), registration number ChiCTR2200055623.(15/01/2022).

**Keywords** Opioid-free anesthesia, Opioids, Postoperative nausea and vomiting, Quality of recovery (QoR)

<sup>†</sup>NH Cha, Y Hu, GH Zhu contributed equally to this work.

\*Correspondence:

Yuan Gong  
gy-yc@163.com

<sup>1</sup>Institute of Anesthesiology and Critical Care Medicine, Three Gorges University & Yichang Central People's Hospital, No. 183 Yiling Avenue, Wujiagang District, 443000 Yichang City, Hubei, China



## Background

Hysteroscopy is traditionally performed under general anesthesia for pain management. Opioids are an essential part of anesthesia for their antinociceptive effects; however, they are associated with side effects, including altered mental status, hyperalgesia, nausea, and vomiting, which have a negative effect on patients' experience [1, 2].

Opioid-free anesthesia (OFA) is a multimodal approach to inducing anesthesia without opioids. The drugs used for OFA include, among others, local anesthetics. Lidocaine is a local amide anesthetic that blocks sodium channels and N-methyl-D-aspartate receptors [3]. The rationale for OFA is to avoid the side effects of opioids, which can impact the patient's postoperative outcome [4]. In other words, better recovery can be expected in hysteroscopic patients undergoing OFA. Recent developments in the anesthesia field are ensuring faster recovery from anesthesia, and optimizing surgical patients' subjective postoperative experience. Studies have demonstrated that patient-reported outcome measures can improve patient experience after surgery [5]. QoR-40 is a patient-reported outcome questionnaire that measures the quality of recovery after surgery; the results are a useful end-point in perioperative clinical studies [6].

The use of OFA is highly controversial, with limited evidence on the potential benefits; one study showed severe side effects [7, 8]. This study aimed to compare the quality of recovery, recovery time, and risk of side effects of between OFA with lidocaine and general anesthesia with opioids in patients undergoing ambulatory hysteroscopy.,

## Methods

### Study design

This was a parallel-group, randomized, double-blind, controlled trial. Ethical approval for this study (HEC-KYJJ-2021-145-01) was provided by the Institutional Review Board of Yichang Central People's Hospital, Wujiagang District, Yichang City, Hubei Province (contact: Yan Kejun) on January 7, 2022. The trial was registered on January 15, 2022 in the Chinese Clinical Trial Registry (<http://www.chictr.org.cn/showprojen.aspx?proj=149386>), registration number ChiCTR2200055623. The study was conducted from January 25 to April 30, 2022 at Yichang Central People's Hospital. All patients provided written informed consent. The patients were randomly assigned to two groups in a 1:1 ratio by computer-generated randomization. One anesthesiologist, who was blinded to the study, generated the random allocation sequence and assigned each patient a patient code.

### Patients

We included female patients (age: 18–65 years, American Society of Anesthesiologists Physical Status Class I–II) scheduled for elective hysteroscopy. Patients were divided into two groups: Group S, who received general anesthesia (sufentanil, Yichang Renfu Pharmaceutical Co. LTD, Yichang city, China) and Group L, who received OFA (lidocaine, Anhui Changjiang Pharmaceutical Co. LTD, Wuhu City, China). The exclusion criteria were as follows: history of drug abuse, refusal to provide consent, history of psychotropic medication or psychological disorders, treatment using angiotensin-converting enzyme inhibitors, gastro-esophageal reflux, morbid obesity ( $BMI \geq 30 \text{ kg/m}^2$ ), allergy to any of the study drugs, use of medications or nutraceuticals that affect blood pressure (BP) or heart rate (HR), surgical procedure exceeding one hour in duration, unexpected bleeding complications, or repeated laryngeal mask airway insertion attempts.

### Perioperative anesthetic care

Preoperatively, all patients fasted for 8 h and were asked to avoid oral intake of clear fluids for 2 h. Upon entry into the operating room, non-invasive BP, HR, and pulse oxygen saturation were measured, and electrocardiography was performed using a multifunctional monitor (GE Healthcare, Chicago, IL, USA), with 5 min of stabilization after each measurement. A 24-gauge intravenous catheter was subsequently placed into a vein on the dorsum of the hand.

After preoxygenation, either  $1.5 \text{ mg kg}^{-1}$  lidocaine or  $0.3 \mu\text{g kg}^{-1}$  sufentanil was injected intravenously over a 3 s period with activation of the pump, followed by either  $1.5 \text{ mg kg}^{-1} \text{ h}^{-1}$  lidocaine or 0.9% saline, respectively, at the same rate and volume. The anesthetic nurse who prepared the research treatment solutions and activated the pump was blinded to the study groups. Two minutes after activation, general anesthesia was standardized with  $2.0 \text{ mg kg}^{-1}$  propofol (Fresenius Kabi Deutschland GmbH, Homburg, Germany) and  $1 \text{ mg kg}^{-1}$  scoline (Xi'an Hanfeng Pharmaceutical Co. LTD, Xi'an City, China). If the patient exhibited no eyelash reflex, an appropriately sized laryngeal mask airway was selected using standard guidelines and the patient was intubated. After intubation without complications,  $0.3 \text{ mg kg}^{-1}$  of rocuronium (Zhejiang Xianju Pharmaceutical Co., Ltd., Taizhou City, China) was administered to maintain muscle relaxation. Anesthesia was maintained using 2–3% sevoflurane (Maruishi Pharmaceutical Co., Ltd., Osaka, Japan) and 50% oxygen.

At the end of the surgery, sevoflurane and the infusions were discontinued. Patients were administered  $0.04 \text{ mg kg}^{-1}$  neostigmine (Zhejiang Xianju Pharmaceutical Co., Ltd., Taizhou City, China) and  $0.02 \text{ mg kg}^{-1}$  atropine (Suicheng Pharmaceutical Co., LTD, Xinzheng City,

China) to antagonize any residual neuromuscular blockade, after evaluation with a neuromuscular monitor. During anesthesia, an anesthesiologist blinded to the group assignments oversaw patients' emergence from anesthesia and graded their postoperative pain. Oral suction was performed immediately after surgery, with the patient still under anesthesia. Extubation was performed when the patient regained consciousness, with confirmation of adequate tidal volume, a regular spontaneous respiratory pattern, and purposeful behavior (eye opening upon request). After extubation, patients were monitored for  $\geq 5$  min to ensure regular spontaneous respiration, and were subsequently transferred to the post-anesthesia care unit (PACU). Here, patients were monitored with electrocardiography, peripheral pulse oximetry, and non-invasive BP measurements.

Patients were discharged from the PACU when their Steward score reached  $>4$ . Other operative care was provided according to usual clinical practice. Postoperative quality of recovery was investigated using the QoR-40 questionnaire. Postoperative pain was quantified using a 100-mm visual analog scale (VAS), marked from "no pain" to "severe pain." [9]. If the VAS score was  $\geq 30/100$  at rest, the attending PACU nurse administered 30 mg  $\text{kg}^{-1}$  of intravenous propacetamol. The QoR-40 questionnaire was performed in the ward 24 h postoperatively by an anesthetist that was blinded to the study.

**Primary outcomes**

The primary outcome was the quality of recovery 24 h postoperatively as assessed using the QoR-40 questionnaire.

**Secondary outcomes**

Secondary outcomes included the incidence of postoperative nausea and vomiting (PONV), and time to extubation. Safety-related outcomes included intraoperative respiratory/cardiovascular complications (laryngospasm,

postoperative hypoxemia, arrhythmia) and rescue methods.

**Statistical analysis**

The sample size was calculated based on the results of our preliminary experiments and an expected QoR-40 score difference of 10 with 95% power ( $\alpha=0.05$  and  $\beta=0.1$ ), which indicated that 40 patients were required per group. The QoR-40 scores, patient characteristics (age, height, weight, and body mass index), surgery duration, time to extubation, and time to recovery are expressed as the mean  $\pm$  standard deviation, and analyzed using student's t test. The incidence of PONV was expressed as ratio using the chi-square or Fisher exact test;  $P < 0.05$  indicated statistical significance. Statistical analyses were performed using GraphPad Prism 8.4.3 (GraphPad Software Inc., San Diego, CA, USA).

**Data Availability**

The data associated with the paper are not publicly available but are available from the corresponding author on reasonable request.

**Results**

**Patients**

We enrolled 90 patients from January 25 to April 30, 2022. No significant intergroup differences were observed in patient age or physical characteristics (Table 1).

**Primary outcomes**

We discovered significant intergroup differences in the QoR-40 score 24 h postoperatively ( $P \leq 0.01$ ; Table 2).

**Secondary outcomes**

We observed a significant intergroup difference in time to extubation (L,  $6.93 \pm 0.95$  min vs. S,  $8.33 \pm 1.11$  min;  $P \leq 0.01$ ) (Table 3). The PONV incidence was lower in

**Table 1** Patient baseline and clinical characteristics

|  | Group L<br>(n=45) | Group S<br>(n=45) | P value  |
|--|-------------------|-------------------|----------|
| Age (y)                                      | 38.9 $\pm$ 6.3    | 38.7 $\pm$ 7.0    | > 0.9999 |
| Height (cm)                                  | 159.7 $\pm$ 3.9   | 159.5 $\pm$ 3.6   | 0.9996   |
| Weight (kg)                                  | 56.1 $\pm$ 8.4    | 56.3 $\pm$ 8.1    | 0.9992   |
| Body mass index (kg/cm <sup>2</sup> )        | 22.9 $\pm$ 3.7    | 22.8 $\pm$ 3.2    | 0.9993   |
| Duration of operation (min)                  | 19.3 $\pm$ 4.6    | 18.8 $\pm$ 5.5    | 0.9999   |
| Duration of anesthesia (min)                 | 29.8 $\pm$ 6.3    | 30.0 $\pm$ 7.1    | > 0.9999 |
| Operation type<br>(diagnostic vs. treatment) | 14/31             | 15/30             | 0.5164   |
| Postoperative hypoxemia                      | 0                 | 0                 |          |
| Laryngospasm                                 | 0                 | 0                 |          |
| Arrhythmia                                   | 0                 | 0                 |          |

Data are presented as either mean  $\pm$  standard deviation or counts

**Table 2** QoR-40 scores

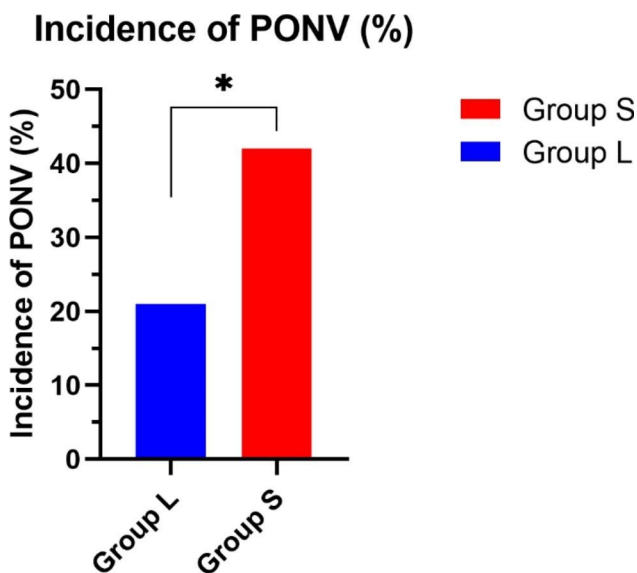
|                                    | Group L (n=45) | Group S (n=45) | P value |
|------------------------------------|----------------|----------------|---------|
| QoR-40 scores 24 h postoperatively | 177.2±6.2      | 172.6±5.3      | 0.0002  |

Data are expressed as mean±standard deviation  
QoR-40, Quality of recovery-40

**Table 3** Time of extubation

|                          | Group L (n=45) | Group S (n=45) | P value |
|--------------------------|----------------|----------------|---------|
| Time of extubation (min) | 6.9±1.0        | 8.3±1.1        | <0.0001 |

Data are expressed as mean±standard deviation



**Fig. 1** Incidence of postoperative nausea and vomiting (PONV) among the study groups  
Data are expressed as ratio

Group L than in Group S (L, 21% vs. S, 42%;  $P \leq 0.05$ ) (Fig. 1).

We observed no cases of severe complications such as postoperative hypoxemia, laryngospasm, or arrhythmia in this study (Table 1).

**Discussion**

The rationale of OFA is to avoid the side-effects associated with opioids on patients’ intra- and post-operative outcomes. Lidocaine is a local anesthetic, with analgesic, anti-hyperalgesic and anti-inflammatory properties. It has traditionally been used as an adjuvant during anesthesia; in this study it was administered intravenously.

Our findings revealed that, compared to general anesthesia with sufentanil, OFA with lidocaine resulted in higher QoR-40 scores in patients who underwent hysteroscopy. Moreover, lidocaine-OFA showed a shorter time to extubation and a lower incidence of PONV compared to sufentanil. Our findings demonstrate that OFA with lidocaine can provide faster and better postoperative recovery after hysteroscopy.

QoR is an important outcome measure of early postoperative health, and it is widely used for assessing patient recovery after anesthesia. The QoR-40 questionnaire includes five items: emotional state, physical comfort, psychological support, physical independence, and pain. The validity and reliability of the QoR-40 score have been proven [6]. We found statistical intergroup differences in the QoR-40 scores, however, the difference between groups did not reach our pre-set value. This may be due to sampling error in the preliminary experiment. Considering the characteristics of the QoR-40, higher scores reflect better quality of recovery. Our findings demonstrated that OFA with lidocaine allowed better QoR than general anesthesia with sufentanil did, even at 24 h postoperatively; thus, OFA with lidocaine is of clinical importance.

A longer duration of intubation has been demonstrated to result in a higher incidence of mortality [10]. The time of extubation continues to be a variable of considerable importance for patient recovery. We observed a statistically significant intergroup difference in time of extubation. This could be attributed to sufentanil having a high affinity and specificity for opioid receptors, which yields a sedative effect that enhances its effectiveness as an anesthetic [11]. PONV is a common postoperative complication, especially in younger female patients undergoing general anesthesia. It can potentially cause a highly distressing experience and a longer hospital stay [12]. Our study identified a higher rate of PONV in Group S, with a statistically significant intergroup difference (Fig. 1). No severe safety concerns such as postoperative hypoxemia, laryngospasm, or arrhythmia occurred during our study.

This study has several limitations. First, this was a single-center study; therefore, the generalizability of the findings is limited. Second, we included patients who underwent anesthesia using a laryngeal mask airway to maintain the sevoflurane concentration, which reduced the generality of our findings.

**Conclusions**

Our trial showed that OFA with lidocaine for hysteroscopy is both safe and effective, and allowed faster and better recovery than that associated with general

anesthesia with sufentanil, as assessed using QoR-40 scores. This suggests that OFA with lidocaine can be used in hysteroscopy successfully. It indicated that OFA can be performed in ambulatory surgery smoothly and effectively, and that the prospects for the use of lidocaine in anesthesia warrant further investigation.

#### Abbreviations

|      |                                   |
|------|-----------------------------------|
| HR   | Heart rate                        |
| BP   | Blood pressure                    |
| OFA  | Opioid free anesthesia            |
| PACU | Post-anesthesia care unit         |
| PONV | Postoperative nausea and vomiting |
| VAS  | Visual analog scale               |

#### Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12871-023-02152-7>.

Supplementary Material 1

#### Acknowledgements

Not applicable.

#### Author contributions

Data Curation, YH and NC; Software and Formal Analysis, YH; Resources and Investigation, NC and GZ; Project Administration, XL and JJ; Methodology, Supervision, and Validation, YG. All authors reviewed the manuscript.

#### Funding

Support was provided solely from institutional sources.

#### Data availability

The data associated with the paper are not publicly available but are available from the corresponding author (YG) on reasonable request.

#### Declarations

##### Competing interests

The authors declare no competing interests.

##### Ethics approval and consent to participate

The study has been conducted in accordance with the principles set forth in the Helsinki Declaration, and all patients provided written informed consent for participation in the research study.

Ethical approval for this study (HEC-KYJJ-2021-145-01) was provided by the Institutional Review Board of Yichang Central People's Hospital, Wujiagang District, Yichang City, Hubei Province (contact: Yan Kejun) on 07/01/2022.

#### Consent for publication

Not applicable.

Received: 21 November 2022 / Accepted: 25 May 2023

Published online: 03 June 2023

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