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Nikethamide Alleviates Low SpO_2 during Gastrointestinal Endoscopy under Total Intravenous Anesthesia with Propofol Combined with Sufentanil: A Randomized Controlled Trial

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ABSTRACT

Background: Gastrointestinal Endoscopy under Total Intravenous Anesthesia (GETIVA) is used for gastrointestinal disease investigation. Total intravenous anesthesia with propofol and opioids is usually applied but could result in respiratory depression or low oxygen saturation. This study aimed to test the effectiveness of nikethamide (respiratory stimulant) for alleviating low oxygen saturation induced by combined propofol and sufentanil use during GETIVA.

Methods: This randomized controlled trial was performed in an in one center in Wuxi City, China, in total, 135 patients scheduled to undergo painless gastrointestinal endoscopy were enrolled and divided into nikethamide and saline groups. Nikethamide was intravenously injected following sufentanil and propofol intravenous administration in the nikethamide group; an equivalent volume of normal saline was injected in the saline group. The primary outcomes were the incidence of low oxygen saturation, oxygen flow increase, lower jaw lifting, oxygen inhalation (with facemask), and assisted ventilation.

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Results: The incidences of increased oxygen flow, lower jaw lifting, and oxygen inhalation (with mask) were lower in the nikethamide group versus the saline group (P<0.05). No significant differences in the mean arte-rial pressure, heart rate, or oxygen saturation were observed at any point between the groups. The sufentanil dose, endoscopy time, post-anesthesia care unit awaking time, and satisfaction of the patients and endoscopy physicians were not significantly different. The propofol dose was higher in the nikethamide group than in the saline group (P<0.05).

Conclusions: Nikethamide could decrease respiratory depression during GETIVA performed with combined propofol and sufentanil use; however, it increased the required propofol dose.

Keywords: Nikethamide; Propofol; Sufentanil; Gastrointestinal Endoscopy; Total Intravenous Anesthesia

INTRODUCTION

Many gastrointestinal endoscopies are conducted using propofol for sedation. Propofol is a ground breaking intravenous anesthetic and provides shorter onset and faster recovery but does not provide analgesia. The decrease in blood pressure, respiratory apnea, and myocardial perfusion reduction attributed to propofol should be prevented. Sufentanil is an opioid that provides strong analgesia and is suitable for use during painless endoscopy (Zhang, 2014). Combined propofol and sufentanil use offers good sedation and analgesia. However, the possibility of respiratory depression or low oxygen saturation (SpO_2) remains, especially for patients with debility or obesity. Respiratory depression should be prevented and clinically evaded. Lidocaine is a sodium channel blocker, used as an adjunct to decrease the dose of propofol administered (Kamal,2021) and reduce oxygen desaturation and apnea episodes during painless colonoscopy (Li, 2020). Dexmedetomidine, a α2 agonist, has been used to reduce propofol consumption during endoscopy (Padiyara, 2020); however, it may increase the risk of adverse reactions in patients with bradycardia (Amri, 2018). Doxapram works as a respiratory stimulant and antagonist of respiration inhibition attributed to anesthetic medicine and could ameliorate respiratory depression during Gastrointestinal Endoscopy under Total Intravenous Anesthesia (GETIVA) (Gu, 2019). Vigilance is warranted regarding the possibility of hypoxemia induced by propofol combined with opioids in the clinical setting.

Nikethamide is a central nervous system stimulant. The therapeutic effect of this drug is principally attributed to the stimulation of centers in the medulla. It increases respiratory related rhythmic discharge activity (RRDA) partly via 5-HT(2A) receptors (Qian, 2008). Some studies have demonstrated that its enhancement of RRDA can be partially mediated by the Gamma-Aminobutyric Acid (GABA) type A ($GABA_A$) receptor (Qian, 2008). In addition, it has a beneficial effect on the heart, with dilation of the coronary arteries and inconsistent increase in the cardiac output (Ball, 2018). We hypothesized that intravenous nikethamide could lower the prevalence of low SpO_2 during GETIVA. Therefore, we conducted a prospective, double-blind, randomized controlled trial to explore whether intravenous nikethamide administration could alleviate respiratory depression in patients during GETIVA.

METHODS

Ethics

Ethical approval for this study (Ethical Committee No. KS2019053) was provided by the Ethics Committee of Nanjing Medical University Affiliated Wuxi People's Hospital, Wuxi, China (Chairperson Prof Bing Wu) on October 18, 2019. Our trial was registered on 29 November 2019 in the Chinese Clinical Trial Registry (ChiCTR1900027816; main researcher: Zhengfeng Gu) before recruitment of the first patient. The trial was conducted in accordance with the tenets of the Declaration of Helsinki, and it adhered to the CONSORT guidelines. Written informed consent was obtained from all enrolled patients. This study was carried out between January 2020 and October 2024.

Participants

One hundred and twenty patients (American Society of Anesthesiology Physical Status I–II) scheduled to undergo painless gastrointestinal endoscopy at our hospital were enrolled. There were 80 male and 55 female patients aged 33–65 years with a weight of

36–82 kg and height of 148–183 cm. The patients were randomly and equally allocated into a nikethamide (group N) and a normal saline (group S) group using a computer program (60 patients per group). One anesthesiologist, in charge of allocation, generated the random allocation sequence, enrolled the participants, assigned the participants to interventions, and prepared the randomized sequence in an opaque envelope. The exclusion criteria were: 1) medical history of medication, such as diazepam, neuroleptics, and anticonvulsants that interfere with the heart rate; 2) anaphylaxis caused by drugs used in the study; 3) cardiovascular diseases, such as hypertension, arrhythmia, and abnormal electrocardiographic (ECG) readings; 4) abnormal liver and/or kidney function; 5) lung disease, such as chronic obstructive pulmonary disease; 6) abdominal laparotomy; 7) body mass index >30 kg/m^2; 8) age >75 years or <18 years; 9) clinical suspicion of intestinal sub-occlusion or stenosis; 10) colorectal tumours; 11) psychiatric diseases; 12) requirement for complex therapeutic procedures during diagnostic gastrointestinal endoscopy; 13) airway assessed as difficult; 14) allergy to propofol, sufentanil, or nikethamide; and 15) refusal to provide written informed consent.

Anesthesia and Intervention

Patients who met the inclusion criteria were screened. All patients fasted routinely before endoscopy without premedication. An anesthetist nurse opened the envelope and prepared nikethamide 0.375 g diluted with normal saline to 3 ml or normal saline of the same volume. Both the patients and anesthesiologists were blinded to the allocation. All patients were continuously monitored using pulse oximetry (SpO_2), ECG, bispectral index (Bis) and a noninvasive blood pressure measurement apparatus; variables were assessed every 1 min in the first 5 min and then at a 5 min intervals following nikethamide or normal saline administration. Oxygen (5 L/min) was inhaled through a nasal cannula. Capnographic monitoring of ventilation activity was performed with an expired carbon dioxide detector attached to the tip of the nasal cannula. Each patient in group N received an intravenous infusion of sufentanil 0.1 μg/kg and propofol 1–2 mg/kg sequentially, followed by intravenous nikethamide 0.375 g/3 ml; while patients in group S received sequential intravenous sufentanil 0.1 μg/kg and propofol 1–2 mg/kg, followed by intravenous normal saline (same volume as that of nikethamide in group S). In both groups, propofol was slowly infused and stopped until closure of the eyelids was observed. An additional dose of 0.5–1 mg/kg was administered in the event of Bis > 60. In the event of hypotension (systolic blood pressure <90 mmHg or <20% basal value), ephedrine 6–15 mg was administered. In case of the occurrence of bradycardia (heart rate <50 bpm), atropine 0.25–0.5 was administered. The treatment was repeated if necessary. Either of the following applications was carried out when the SpO_2 was <90%: 1) increasing the oxygen flow to 10 L/min, 2) face mask covering the patient's nose and mouth, 3) lifting the mandibles, and 4) assisted ventilation with a simple breathing balloon. The procedure would be terminated if assisted ventilation was performed with gastroscope withdrawal, or the colonoscopy stop.

The patients were placed in the left lateral position. Gastrointestinal endoscopy was performed by the same endoscopist using an Olympus OEV262H video system with gastroscopic tubes of the GIF-H290 series and colonoscopic tubes of the CF-H2901 series. The endoscopists sequentially performed gastroscopy and colonoscopy. The patients were transferred to the post anesthesia care unit (PACU) for recovery. The time the patient remained in the unit and the adverse events were recorded.

Another anesthesiologist, who was blinded to the study group assignment, recorded the blood pressure, heart rate, and SpO_2 at the time before anesthesia (T0); at 1 min (T1), 3 min (T3), and 5 min (T5) after induction; and after the end of endoscopy (Te), as well as other outcomes. Low SpO_2 was considered significant when the SpO_2 was <90% [10]. The doses of propofol and sufentanil, application of low SpO_2 management, time of endoscopy, and degree of satisfaction of the patient and endoscopist were recorded.

Outcomes

The primary aim of the study was to investigate the effects of nikethamide on low SpO_2. The secondary

outcomes were increased oxygen flow, lower jaw lifting, oxygen inhalation with a mask, and assisted ventilation. Additional secondary outcomes were Mean Arterial Pressure (MAP); heart rate; SpO_2 at T0, T1, T3, T5, and Te; the dose of propofol, sufentanil, ephedrine and atropine; time of PACU stay (defined as time from the end of the procedure to discharge from the PACU); satisfaction of the patients and endoscopists (evaluated with a Visual Analog Scale [VAS] from 0 to 10; the higher the score, the greater the satisfaction); and prevalence of adverse events (e.g., cardiac dysrhythmias, bradycardia, hypotension, nausea/vomiting).

Sample Size Calculation

Sample size calculation was performed with the probability of type I error (α) at 0.05, a power (1-β) of 0.80, and a low SpO_2 of 50% and 25% in the control and intervention groups, respectively, with a 1:1 ratio. Thus, 58 patients were required for each group. Considering the probability of loss to follow up, we included 60 patients in each group.

Statistical Analyses

Statistical analyses were performed using MedCalc software (version 20.006, MedCalc Software bvba, Ostend, Belgium) [6]. The D'Agostino-Pearson test was used for normally distributed variables. The sex proportions and cases of low SpO_2 and respiratory treatment were compared using Pearson's Chi-squared test. Levels of the outcome variables, expressed as mean ± standard deviation, were analyzed using independent samples *t*-tests after confirming that the variables were normally distributed. The Mann–Whitney test (independent samples) was employed if the variables were not normally distributed. Repeated measurement analyses (within subject factors) were used to compare MAP, heart rate, and SpO_2 within the groups. A *P*-value <0.05 was considered statistically significant. The age, weight, and height of the patients, total examination duration, total propofol consumption, blood pressure, heart rate, and SpO_2 were recorded, together with profiles of low SpO_2, face mask use, jaw lifting, and

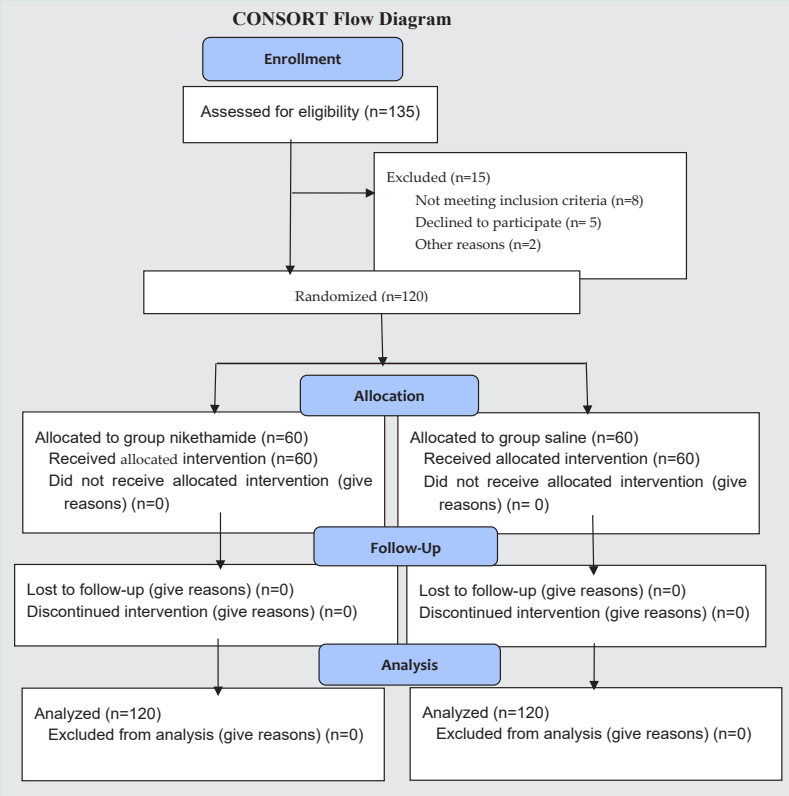

Figure 1: Participants enrollment

assisted ventilation. Study outcomes included episodes of low SpO_2 (<90%) and application of the above mentioned respiratory management measures. The variations in MAP and heart rate were compared as well as the satisfaction of both the endoscopists and patients.

RESULTS

One hundred and twenty patients were evaluated in this study. All the patients completed gastrointestinal endoscopy (Figure 1). The demographic characteristics between the two groups were comparable (Table 1). We did not observe incidents of nausea and vomiting during the endoscopy or in the PACU. The length of stay in the PACU was shorter in group N than in group S; however, there was no significant difference.

A highly significant high dose of propofol in group N was observed compared to that in group S. No significant differences in the sex, age, weight, height, body mass index, sufentanil dose, length of PACU stay, or in the satisfaction VAS scores of the endoscopists and patients were observed.

PACU, post-anesthesia care unit; VAS, visual analog scale; BMI, body mass index; MAP, heart rate, and SpO_2 were not significantly different between group S and group N at T0, T1, T3, T5, and Te (Table 2).

The results showed no significant difference in the MAP, HR, and SpO_2 at different time points. T0= before anesthesia; T1, T3, T5 =1, 3, 5 min after gastrointestinal endoscopy, respectively; Te=after gastrointestinal endoscopy.

MAP, mean arterial pressure; HR, heart rate; SpO_2, oxygen saturation; T0, before anesthesia; T1, 1 min after induction; T3, 3 min after induction; T5, 5 min after induction; Te, after the end of gastrointestinal endoscopy

The MAP in group S decreased at T1, T3, T5, and Te compared with that at T0 (Table 3). The heart rate and SpO_2 in group S demonstrated no difference at T0 compared with those at T1, T3, T5, and Te. The MAP in group N decreased at T1, T3, T5, and Te compared with that at T0. The heart rate decreased at T1 and T3 compared with that at T0 in group N (P<0.05) (Table 3). No significant differences in the heart rate were observed in group N at T0 compared with those at T5 and Te. The SpO_2 in group N demonstrated no significant difference at T0 compared with the measurements at T1, T3, T5, and Te.

Group N, nikethamide group; Group S, saline group; MAP, mean arterial pressure; HR, heart rate; SpO_2,

Table 1: Patients' demographic data presented in mean ± standard deviation, propofol and sufentanil doses, length of PACU stay, and VAS scores of endoscopist and patient satisfaction.

	Group N(n=60)	Group S(n=60)	$c^2/t/Z$	P
Sex (M/F)	36/24	42/18	0.151	0.6978
Age (years)	47.1±10.5	48.0±10.9	-0.366	0.7145
Weight (kg)	65.1±14.8	65.8±13.6	0.167	0.8685
Height (cm)	167.8±10.1	168.0±9.6	0.0642	0.9491
BMI (kg/m^2)	22.5±2.80	22.9±2.30	0.788	0.4326
Propofol dose (mg)	312.5±109.0	197.8±40.6	3.743	0.0002
Sufentanil dose (μg)	6.4±1.3	6.3±1.5	0.246	0.8060
Time of endoscopy (min)	13.9±5.2	14.1±5.8	0.135	0.8931
Time of PACU(min)	10.5±3.8	13.5±5.7	2.000	0.0527
VAS (endoscopist)	9.7±0.20	9.6±0.20	-0.130	0.8977
VAS (patient)	9.8±0.20	9.7±0.21	0.170	0.8659

Table 2: MAP, HR, and SpO_2 at different time points

Vital signs	Time point	group	Parameter	*t*	*P*
MAP	T0	S	88.1±12.5	-0.145	0.8852
		N	88.6±10.2		
	T1	S	72.2±9.5	1.301	0.2014
		N	76.6±9.5		
	T3	S	72.6±7.8	-0.687	0.4967
		N	70.5±11.2		
	T5	S	74.5±13.0	-0.683	0.4987
		N	71.7±12.8		
	Te	S	74.9±12.0	-1.453	0.1548
		N	70.1±8.6		
HR	T0	S	78.6±18.5	0.256	0.7990
		N	79.9±10.2		
	T1	S	74.2±13.2	-0.0844	0.9332
		N	73.9±9.6		
	T3	S	71.7±11.4	-0.270	0.7890
		N	70.9±9.0		
	T5	S	72.9±11.7	-0.0134	0.9894
		N	72.9±9.1		
	Te	S	73.5±11.7	0.563	0.57773
		N	75.5±10.2		
SpO_2	T0	S	98.9±1.2	1.321	0.1947
		N	99.4±0.6		
	T1	S	97.1±3.4	0.360	0.7209
		N	97.4±2.6		
	T3	S	98.7±1.6	-1.623	0.1131
		N	97.6±2.5		
	T5	S	98.9±1.4	-0.946	0.3504
		N	98.5±1.2		
	Te	S	98.9±1.7	-0.734	0.4678
		N	98.5±1.1		

Table 3: Within group comparisons for MAP, HR, and SpO_2

Group	MAP		HR		SpO_2	
	Time	*P*	Time	*P*	Time	*P*
Group S	T0-T1	<0.0001	T0-T1	1.0000	T0-T1	0.2014
	T0-T3	<0.0001	T0-T3	0.1086	T0-T3	1.0000
	T0-T5	<0.0001	T0-T5	0.1804	T0-T5	1.0000
	T0-Te	0.005	T0-Te	0.7163	T0- Te	1.0000
Group N	T0-T1	<0.0001	T0-T1	0.0223	T0-T1	0.0197
	T0-T3	<0.0001	T0-T3	0.0002	T0-T3	0.0282
	T0-T5	0.0008	T0-T5	0.0861	T0-T5	0.0261
	T0-Te	<0.0001	T0-Te	1.0000	T0-Te	0.0197

oxygen saturation; T0, before anesthesia; T1, 1 min after induction; T3, 3 min after induction; T5, 5 min after induction; Te, after the end of gastrointestinal endoscopy

MAP significantly decreased following the induction of anesthesia to the end of endoscopy in both groups N and S. The heart rate decreased in T1 and T3 compared with that at T0 (P=0.0223 and 0.0002, respectively) in group N; however, no significant difference was observed in the heart rate in group S. SpO_2 did not significantly vary between the groups.

The incidence of low SpO_2 was lower and oxygen flow, facemask oxygen inhalation, lower jaw lifting, and assisted ventilation were higher in group N than in group S (P<0.05) (Table 4).

DISCUSSION

Our study demonstrated that intravenous nikethamide (0.375 g/3 ml) administration following combined use of sufentanil and propofol in GETIVA could reduce the incidence of low SpO_2; however, it increased the total consumption of propofol. The heart rate in group N decreased at T1 and T3 compared with that at T0, which could be attributed to the high dose of propofol. Moreover, there were no nikethamide related adverse events.

Propofol is administered during GETIVA to relieve the discomfort caused by mechanical stimulation. Propofol is the first choice of intravenous anesthetic during GETIVA owing to its rapid onset of action, strong sedation effect, short half-life, and the fact that it does not induce nausea and vomiting (Yoo, 2012; Vasileiou, 2009). Deep sedation with propofol may lead to complications such as arterial hypotension, desaturation, bradycardia, and aspiration (Agostoni, 2011). We observed a high incidence of low SpO_2 (53.3%) in our study in patients who were administered propofol combined with sufentanil; a nearly identical result was reported by Deng, *et al.* (Deng, 2017). Methods of decreasing the incidence of low SpO_2 without affecting the quality of anesthesia during GETIVA are of particular interest to anesthetists. Sufentanil, a synthetic opioid analgesic, offers 5–10 times higher analgesia intensity compared with fentanyl and 1000 times higher analgesia intensity compared with morphine. Combining sufentanil with propofol is considered a good alternative during GETIVA owing to its satisfactory analgesic properties to compensate for the disadvantages of propofol (Zhang, 2014). However, it may lead to respiratory depression, especially when combined with propofol. Thus, the combined application may increase the risk of low SpO_2. Nikethamide, widely known by its former trade name, Coramine, is marketed as an analeptic, i.e., a central nervous system stimulant acting on the medulla. It has a wide margin of safety and beneficial effects on the heart with dilation of the coronary arteries and inconsistent increase in the cardiac output (Ball, 2018). Its effect is maintained for approximately 5–10 min with bolus intravenous injection, matching the effect of propofol. Although it is utilized in certain regions, its adoption remains limited in the United States, Europe, and several other countries.

Our results demonstrated that there was no significant difference in SpO_2 at different time points between the groups. As we immediately treated low SpO_2 with increased oxygen flow, oxygen inhalation with a face

Table 4: Cases of low SpO_2 and respiratory treatment.

	Group S (n=60)	Group N (n=60)	χ^2	P
Low SpO_2	32	15	10.1078	0.0015
Oxygen flow increasing	20	5	11.3684	0.0007
Facemask oxygen inhalation	31	12	13.0837	0.0003
Low jaw lifting	26	15	4.4829	0.0042
Assisted ventilation	6	3	1.0811	0.2985

SpO_2, oxygen saturation

mask, low jaw lifting to open the airway, or artificial assisted ventilation, we found that the dose of propofol increased in group N, which could be related to the central excitation effect of nikethamide. The incidence of low SpO_2 was lower and fewer patients needed respiratory treatment in group N than in group S. Thus, nikethamide could effectively alleviate the occurrence rate of low SpO_2 during GETIVA performed under propofol and sufentanil administration. Nikethamide can increase the excitability of neurons through increasing voltage dependent sodium currents (Qian, 2009). It increased the RRDA in transverse medullary slices partly via 5-HT (2A) receptors (Qian, 2008). It showed the most distinct effect on inspiratory time, integral amplitude, and respiratory cycle. It can reportedly enhance the RRDA of the hypoglossal nerve rootlets in the medullary slices of neonatal rats, and the effect can be partially mediated by the $GABA_A$ receptor, which participates in the respiratory enhancement induced by nikethamide (Qian, 2008). Propofol inhibits persistent sodium current fraction in cortical neurons (Martella, 2005). Moreover, the respiratory depressant action of propofol is mediated by beta 3-containing $GABA_A$ receptors; it acts on the $GABA_A$ receptors containing any of the β subunits β1, β2, or β3 (Zeller, 2005). We speculated that these actions could be the mechanisms by which the side effects of propofol are antagonized by the underlying nikethamide. It may also be the reason for the propofol dose increase in group N. Our study demonstrated that nikethamide could effectively attenuate the occurrence of low SpO_2 during GETIVA, which would result in improved patient safety.

In our study, MAP decreased following propofol injection at T1, T3, T5, and Te. There was no difference in MAP between the groups at different points, despite the high dose of propofol in group N. Propofol possesses the effects of vascular dilation and myocardial inhibition through GABA receptors and the atrial muscarinic cholinergic receptors that lead to hypotension and bradycardia (Aguero, 2008). Coincidentally, nikethamide demonstrates weak excitation on the vasomotor centers that partly antagonize the side effects of the decreased vascular tone attributed to the relatively high dose of propofol injection. The heart rate decreased at T1 and T3 compared with that at T0 (P=0.0223 and 0.0002, respectively) in group N, showing that 0.375 g/3 ml of intravenous nikethamide could not entirely antagonize bradycardia caused by propofol combined with sufentanil, which could be related to the administered dose or other reasons. We hadn't observed aggravation of circulatory inhibition with increasing the dosage of propofol. It is suggested to regulate the dose of propofol in clinical practice. However, more study should be designed to explore the potential risks of higher doses of propofol combined with nikethamide.

There were certain limitations in our study. First, we administered the same dose of nikethamide to all patients; the optimal dose of nikethamide needs to be elucidated. Second, although we recorded the length of PACU stay and any side effects, such as nausea or vomiting, we did not assess the degree of dizziness and fatigue. Early safe and comfortable discharge of outpatients is of importance; thus, more profound investigations should be carried out in the PACU following GETIVA. In addition, what kind of extent of nikethamide antagonizing the vasodilatory effect of propofol need to further explore.

CONCLUSIONS

With intravenous administration of nikethamide (0.375 g) following combined propofol and sufentanil use during GETIVA, the incidence of low SpO_2 and need for respiratory treatments were significantly reduced; however, increase in the propofol dose was noted. Nikethamide at a dose of 0.375 g did not affect the satisfaction of endoscopists and patients and had a limited effect on MAP.

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INSTITUTIONAL REVIEW BOARD STATEMENT: The study was conducted in

accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Nanjing Medical University Affiliated Wuxi People's Hospital (protocol code: KS2019053; date of approval Jaunary 2, 2020)

INFORMED CONSENT STATEMENT: Informed consent was obtained from all subjects involved in the study.

DATA AVAILABILITY STATEMENT: All the data are included in this article.

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CONFLICTS OF INTEREST: The authors declared no conflicted interests.

ABBREVIATIONS

The following abbreviations are used in this manuscript:

MAP	Mean Arterial Pressure
PACU	Post Anesthesia Care Unit
Bis	Bispectral Index
ECG	Electrocardiography
RRDA	Respiratory Related Rhythmic Discharge Activity
GETIVA	Gastrointestinal Endoscopy under Total Intravenous Anesthesia
SpO_2	Oxygen Saturation

REFERENCES

- Agostoni, M., Fanti, L., Gemma, M., Pasculli, N., Beretta L., & Testoni, P. A. (2011). Adverse events during monitored anesthesia care for GI endoscopy: an 8-year experience. *Gastrointest Endosc*, 74,266–275. https://doi.org/10.1016/j.gie.2011.04.028
- Aguero Peña, R. E., Pascuzzo-Lima, C., Granado Duque, A. E., & Bonfante-Cabarcas, R. A. (2008). Propofol-induced myocardial depression: possible role of atrial muscarinic cholinergic receptors. *Rev Esp Anestesiol Reanim*, 55,81–85. https://doi.org/10.1016/s0034-9356(08)70
- Amri, P., Nahrini, S., Hajian-Tilaki, K., Hamidian, M., Alipour, S. F., Hamidi, S. H., Rajaei, S., & Shokri-Shirvani, J. (2018). Analgesic effect and hemodynamic changes due to dexmedetomidine versus fentanyl during elective colonoscopy: A double-blind randomized clinical trial. *Anesth Pain Med*, 8,e81077. https://doi.org/10.5812/aapm.81077
- Ball C. M., & Featherstone, P. J. (2018). Coramine and other analeptics. *Anaesth Intensive Care*, 46,3–5. https://doi.org/10.1177/0310057X1804600101
- Deng, C., Wang, X., Zhu, Q., Kang, Y., Yang, J., & Wang, H. (2017). Comparison of nalbuphine and sufentanil for colonoscopy: A randomized controlled trial. *PLOS One*, 12,e0188901. https://doi.org/10.1371/journal.pone.0188901
- Gu, Z., Xin, L., Wang, H., Hu, C., Wang, Z., Lu, S., Xu, J., Qian, Y., & Wang, J. (2019). Doxapram alleviates low SpO_2 induced by the combination of propofol and fentanyl during painless gastrointestinal endoscopy. *BMC Anesthesiol*, 19,216. https://doi.org/10.1186/s12871-019-0860-1
- Kamal, F., Khan, M. A., Lee-Smith, W., Sharma, S., Imam, Z., Jowhar, D., Henry, C., Khan, Z., Petryna, E., Patel, J. R., Qualkenbush, E. A. V., & Howden, C. W. (2021). Efficacy and safety of supplemental intravenous lidocaine for sedation in gastrointestinal endoscopic procedures: systematic review and meta-analysis of randomized

controlled trials. *Gastrointest Endosc*, 93,1241–1249,e6. https://doi.org/10.1016/j.gie.2021.01.008

- Li, X., Lv, X., Jiang, Z., Nie, X., Wang, X., Li, T., Zhang, L., & Liu, S. (2020). Application of intravenous lidocaine in obese patients undergoing painless colonoscopy: A prospective, randomized, double-blind, controlled study. *Drug Des Dev Ther*, 14,3509–3518. https://doi.org/10.2147/DDDT.S266062
- Martella, G., De Persis, C., Bonsi, P., Natoli, S., Cuomo, D., Bernardi, G., Calabresi, P., & Pisani, A. (2005). Inhibition of persistent sodium current fraction and voltage-gated L-type calcium current by propofol in cortical neurons: implications for its antiepileptic activity. *Epilepsia*, 46,624–635. https://doi.org/10.1111/j.1528-1167.2005.34904.x
- Padiyara, T. V., Bansal, S., Jain, D., Arora, S., & Gandhi, K. (2020). Dexmedetomidine versus propofol at different sedation depths during drug-induced sleep endoscopy: A randomized trial. *Laryngoscope*, 130,257–262. https://doi.org/10.1002/lary.27903
- Qian, Z., Ji M, & Song, X. (2009). Effects of nikethamide on sodium channel of hippocampal neurons in neonatal rat. *JFO Zhengzhou Univ (Med Sci)*, 44,1245–1248.
- Qian, Z. B., & Wu, Z. H. (2008). Role of 5-HT(2A) receptor in increase in respiratory-related rhythmic discharge activity by nikethamide in neonatal rat transverse medullary slices. *Sheng Li Xue Bao*, 60,216–220. https://doi.org/10.3321/j.issn:0371-0874.2008.02.009
- Qian, Z. B., Qi, Y., & Wu, Z. H. (2008). GABA A receptor participates in respiratory enhancement induced by nikethamide in neonatal rats. *Nan Fang Yi Ke Da Xue Xue Bao*, 28,301–304. https://pubmed.ncbi.nlm.nih.gov/18359677/
- Vasileiou, I., Xanthos, T., Koudouna, E., Perrea, D., Klonaris, C., Katsargyris, A., & Papadimitriou, L. (2009). Propofol: a review of its non-anaesthetic effects. *Eur J Pharmacol*, 605,1–8. https://doi.org/10.1016/j.ejphar.2009.01.007
- Yoo, Y. C., Bai, S. J., Lee, K. Y., Shin, S., Choi, E. K., & Lee, J. W. (2012). Total intravenous anesthesia with propofol reduces postoperative nausea and vomiting in patients undergoing robot-assisted laparoscopic radical prostatectomy: a prospective randomized trial. *Yonsei Med J*, 53,1197–1202. https://doi.org/10.3349/ymj.2012.53.6.1197
- Zhang, L., Bao, Y., & Shi, D. (2014). Comparing the pain of propofol via different combinations of fentanyl, sufentanil or remifentanil in gastrointestinal endoscopy. *Acta Cir Bras*, 9,675–680. https://doi.org/10.1590/s0102-8650201400160008
- Zeller, A., Arras, M., Lazaris, A., Jurd, R., & Rudolph, U. (2005). Distinct molecular targets for the central respiratory and cardiac actions of the general anesthetics etomidate and propofol. *FASEB J*, 19,1677–1679. https://doi.org/10.1096/fj.04-3443fje

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