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STUDY PROTOCOL

Comparison of Nasopharyngeal Airway with Endoscopic Respiratory Mask for Hypoxemia in Painless Gastrointestinal Endoscopy in Obese Outpatients: Study Protocol for a Randomized Controlled Trial

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Introduction: Sedatives and anesthetics can modify airway tone and induce respiratory depression, exacerbating the gas exchange impairments associated with obesity. In obese patients undergoing gastrointestinal endoscopy, upper airway obstruction and hypoventilation are prevalent, leading to frequent occurrences of hypoxemia during the procedure. This study aims to investigate the effects of the nasopharyngeal airway in mitigating hypoxemia via alleviating upper airway obstruction in obese outpatients during painless gastrointestinal endoscopy procedure.

Methods: This is a prospective single-center randomized controlled study. After signing the written informed consent, eligible outpatients scheduled for painless gastrointestinal endoscopy will be randomly allocated into the nasopharyngeal airway group (group N) and control group (group C), with 88 patients in each group. Patients in group N will undergo intubation of the nasopharyngeal airway prior to examination, whereas patients in group C will receive oxygen therapy through an endoscopic respiratory mask at a flow rate of 10 L/min during the procedure. All patients in two groups will receive propofol and opioids for procedural sedation. The primary outcome will be the incidence of hypoxemia. The secondary outcomes will be the incidence of epistaxis, suspended examination due to hypoxemia, manual ventilation, the times of attempt to nasopharynx airway insertion, duration of insertion of nasopharyngeal airway, tracheal/laryngeal mask intubation, adverse cardiovascular events, gastrointestinal complications, VAS score of nasopharynx pain after removing the nasopharyngeal airway, satisfaction score of patients, endoscopist and anesthesiologists.

Discussion: This study evaluates the effects of nasopharyngeal airway insertion on hypoxemia caused by procedural sedation in obese patients undergoing gastrointestinal endoscopy. The results of this study are expected to provide evidence for the use of nasopharyngeal airway in obese outpatients.

Trial Registration Number: ChiCTR2300078892.

Keywords: nasopharyngeal airway, hypoxemia, obese outpatients

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Introduction

Painless gastrointestinal endoscopy has been developed rapidly worldwide.[1,2] Many patients prefer receiving gastrointestinal endoscopy under procedural sedation as a part of physical examination, or diagnosis and treatment of gastrointestinal diseases.[3] Propofol combined with opioids is the most frequently used sedation plan in painless gastrointestinal endoscopy due to the rapid onset, short maintenance and rapid recovery.[4–6] However, this combination of medications has respiratory depression effects, which contributes to hypoxemia and increases the risk of procedural sedation and anesthesia.[7–10] According to our pilot study, the incidence of hypoxemia in obese patients induced by the combination of propofol and opioids was high as 40% when oxygen was inhaled through the endoscopic respiratory mask, which is consistent with previous research findings.[7,8]

Patients with obesity are at increased risk of developing hypoxemia due to the changes in the anatomical structure of the respiratory tract, such as the short neck, decreased functional residual volume, reduced chest wall compliance, and a narrow airway.[9,10] Moreover, a dose-dependent use of propofol in obese patients often increases the risk of apnea and hypoxemia during the anesthetic procedure.[5] Therefore, upper airway obstruction and hypoventilation are frequent in obese patients during painless gastrointestinal endoscopy,[11–13] which are also the key reason of hypoxemia induced by procedural sedation. It is reported that opioid-free (propofol- or remimazolam- balanced) anesthesia for gastrointestinal endoscopy can reduce the incidence of severe hypoxemia in obese patients.[10] The use of high-flow nasal oxygen had fewer hypoxemic events during gastrointestinal endoscopy, but it is difficult to apply it to all patients in clinical scenarios and patients.[7] While the strategy has not evolved to reduce the risk to zero percent, there are ways to mitigate the risk of hypoxemia.

Pre-anesthesia assessment practices vary globally. For instance, in some institutions, these patients are seen only on the day of the procedure after a questionnaire-based assessment beforehand. Although most outpatients usually undergo pre-anesthesia evaluation a few days before examination, the preoperative examination may not be as comprehensive as that of the inpatients. Because some important invasive respiratory and imaging examinations may be incomplete. Thus, it is important to note that patients with obesity are classified as level II according to the American Society of Anesthesiologists (ASA) status, which indicates that the presence of additional comorbidities may elevate the ASA level for obese patients. Higher ASA grades are related to a higher risk of anesthesia.[14] Outpatients may also not have sufficient preoperative preparation before gastrointestinal endoscopy procedure due to the lack of standard care provided in hospital.[15,16] This may result that the anesthesiologists cannot fully understand the patient's conditions and preparations before anesthesia or procedural sedation. Therefore, outpatients with obesity deserve more attention. It is very necessary to establish a safe and effective airway for obese outpatients when they experience painless gastrointestinal endoscopy.

The nasopharyngeal airway is a simple ventilation device that functions as an artificial airway from the nasal cavity to the glottis. It effectively alleviates upper airway obstruction caused by the tongue falling backward, thereby maintaining an unobstructed airway. A previous study successfully applied nasopharyngeal airway to replace laryngeal mask airways in plastic surgery under general anesthesia.[17] This indicates the effectiveness of nasopharyngeal airway in upper airway management. Compared with the endoscopic respiratory mask, the common oxygen inhalation device for gastrointestinal endoscopy, the nasopharyngeal airway is expected to be a simple and effective device to alleviate hypoxemia.

In the present study, we postulate that inserting the nasopharyngeal airway before endoscopy examination can well alleviate hypoxemia induced by propofol and opioids during painless gastrointestinal endoscopy in obese patients, without increasing the incidence of perioperative complications.

Methods

Study Design

This is a prospective single-center randomized controlled study to detect whether the nasopharyngeal airway insertion before endoscopy can reduce the incidence of hypoxemia during painless gastrointestinal endoscopy among obese outpatients. The subjects will be recruited in Deyang People's Hospital, Deyang City, Sichuan province, People's Republic of China. Table 1 shows the study schedule in accordance with the SPIRIT guidelines.[18] Figure 1 shows the flowchart of this study. All researchers will be trained to conduct the study in a standard and uniform protocol. This training will encompass the preparation of research teams in areas such as patient recruitment, assessment, intervention, follow-up, privacy protection, data collection, and data management.

Table 1 The Study Schedule of Enrollment, Interventions and Assessments

Time Point	Study Period								
	Enrollment	Allocation	During Induction	During Endoscopy	During Recovery	After Awakening	Follow-Up Period		
	T-1	T0	T1	T2	T3	T4	T5	T6	T7
Enrollment									
Eligibility screening	X								
Inclusion Criteria	X								
Exclusion Criteria	X								
Informed consent	X								
Randomization	X								
Demographic data	X								
Allocation		X							
Interventions									
With nasopharyngeal airway intubation (Group N)			X						
Without nasopharyngeal airway intubation (Group C)			X						
Assessments									
Vital signs (ECG, HR, NIBP, SPO_2)	X	X	X	X	X				
MOAA/S			X	X					
$EtCO_2$			X	X	X				
Low SpO_2			X	X	X				
Times of attempt for NA intubation			X						
Duration Of NA intubation			X						
Epistaxis			X	X	X				
Suspended examination for hypoxemia				X					
Respiratory adverse events			X	X	X				
Cardiovascular adverse events			X	X	X				
Gastrointestinal complications			X	X	X				
Satisfaction scores						X			
VAS score of nasopharynx pain						X	X	X	X

Notes: T5, 1 postoperative day after removing the nasopharynx airway; T6, 3 postoperative days after removing the nasopharynx airway; T7, 7 postoperative days after removing the nasopharynx airway.

Abbreviations: ECG, electrocardiogram; HR, heart rate; $EtCO_2$, end-tidal carbon dioxide; MOAA/S, modified observer's assessment of alertness/sedation scale; SpO_2, peripheral oxygen saturation; NA, nasopharynx airway; VAS, visual analogue scale.

Registration and Ethics

The study was approved by the Medical Ethics Committee of Deyang People's Hospital on November 21, 2023 (Ethics Number: 2023–03-024-K01), and the study protocol (version 3.0) was registered on the Chinese Clinical Trial Registry on December 20, 2023 (Registration Number: ChiCTR2300078892).

The researchers will explain this study to the eligible subjects and present them with informed consent forms. After signing the relevant documents, candidates will be included into the procedure. The subjects can withdraw from the study at any time. This study will be performed in accordance with the Declaration of Helsinki.

Inclusion and Exclusion Criteria

Patients scheduled for selective painless gastrointestinal endoscopy are eligible for participation in this trial if they: I) have an ASA status between II–III; II) are 18–65 years old; III) have a body mass index (BMI) ≥28 kg/m^2; IV) are outpatients; V) voluntarily take appropriate and effective contraceptive measures.

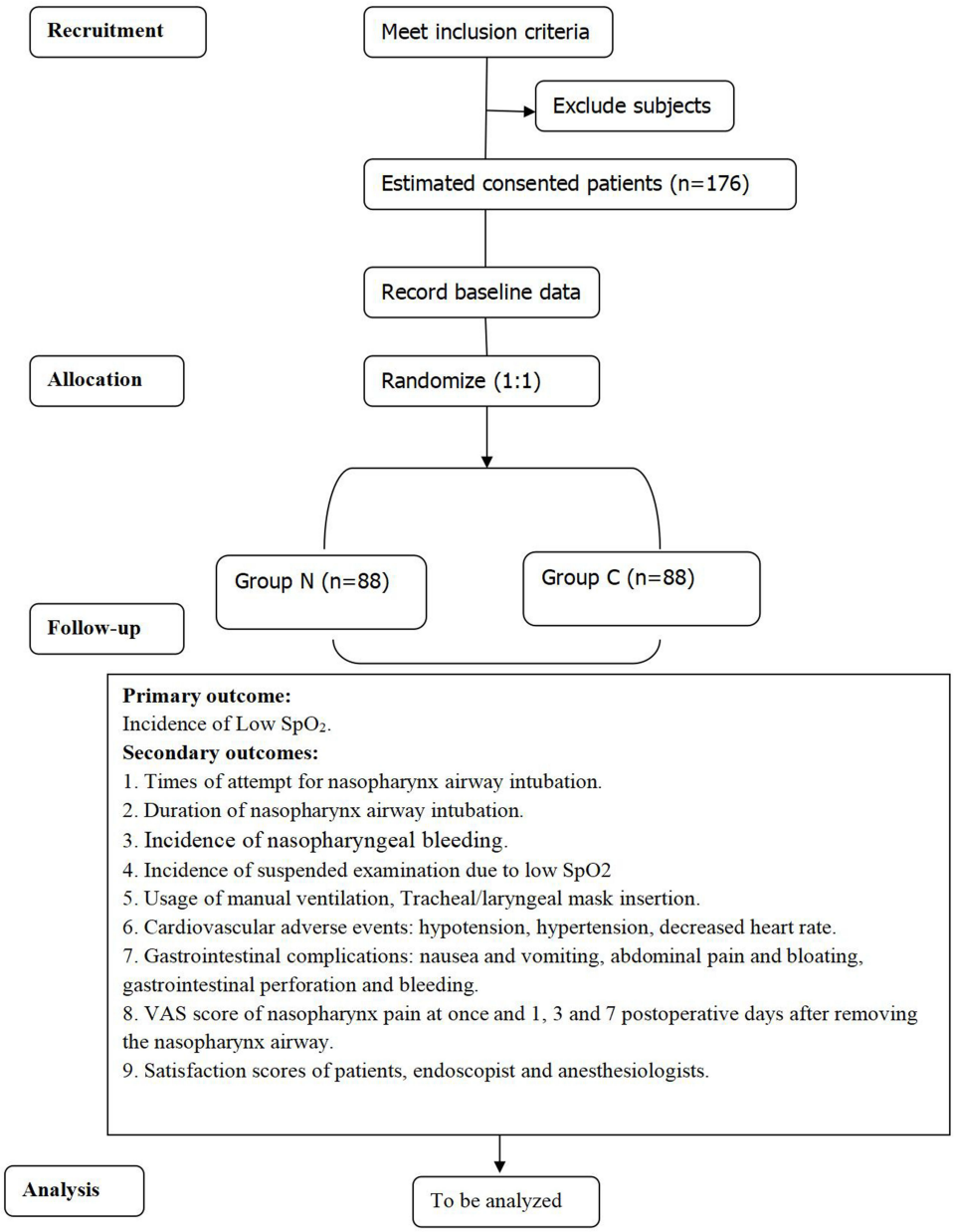

Figure 1 The flowchart of this study.

The exclusion criteria are as follows: I) a history of opioid dependence or abuse; II) severe mental illness; III) severe heart, liver, kidney, lung and organ decompensation; IV) contraindications to propofol or sufentanil; V) a history of head, chest, and intracranial surgery, or stroke within 4 weeks before examination; VI) poorly controlled hypertension; VII) pregnant or lactating women; VIII) nasopharyngeal polyps, bleeding, trauma, deformities or inflammation; IX) other situations that are not suitable for the trial.

Dropout Criteria

If patients meet one of the following situations, the cases will be stopped: I) withdrawal of the participants; II) failing to complete gastrointestinal endoscopy by a single endoscopist; III) severe allergic reactions or anesthesia accidents; IV) severe epistaxis during nasopharyngeal airway insertion. Severe epistaxis is defined as unrelieved bleed after hemostatic treatment.

Allocation and Blinding

Random sequences generator (Mac, USA) will be used to generate randomized sequence. The allocation information is going to be concealed in opaque envelopes kept by a nurse anesthetist. Once a patient is recruited, the anesthesiologist in the examination room will open an envelope. According to the randomized grouping information, the patients will be divided into nasopharyngeal airway group (group N) and control group (group C) in a 1:1 ratio. This is an open and unblinded clinical trial. Since the SpO_2 is an objective parameter that is shown on screens of the monitors. In addition, patients can judge the grouping by whether there is discomfort in the nasal passage.

Interventions and Assessments

All participants will be asked to fast before the examination. No medication will be given preoperatively. Gastrointestinal preparation will be in accordance with the Chinese guidelines. Once the patients enter the pre-anesthesia room, the baseline of vital signs will be collected in the left lying position, including noninvasive blood pressure (NIBP), electrocardiogram (ECG), heart rate (HR), SpO_2, and respiratory rate (RR). Peripheral venous access will be opened immediately before painless gastrointestinal endoscopy. A bag of 500 mL physiological saline solution will be slowly infused. Subsequently, 2% lidocaine gel will be used for surface anesthesia of the nasopharyngeal mucosa. Local anesthesia will be applied 3 times to the nasal mucosa with 5-minute intervals between each application. The total dosage of lidocaine gel is 10 mL. The relatively unobstructed nostril is determined to be inserted for patients in group N.

After entering the endoscopy room, SpO_2, ECG, NIBP and RR will be continuously monitored for all patients in the left lateral position and oxygen will be inhaled at a rate of 10 L/min through a respiratory mask in both groups. After anesthesia induction, the nasopharyngeal airway (Supplemental Figures 1 and 2) will be placed in group N. Then, end-tidal carbon dioxide ($EtCO_2$) monitoring and oxygen inhalation will also be conducted through the nasopharyngeal airway, whereas patients in group C will receive oxygen therapy through the respiratory mask for digestive endoscopy, with a flow rate of 10 L/min during the procedure. And $EtCO_2$ monitoring will also be carried out through the respiratory mask. Emergency devices, including self-inflating bag, anesthesia machine, tracheal intubation tools and laryngeal mask will be in a standby mode.

For anesthesia induction, a bolus of sufentanil (0.1 μg/kg) will be administered intravenously, followed by propofol (2 mg/kg) in both groups. All patients will continuously inhale pure oxygen for over 10 deep breaths at a rate of 10 L/min before sedation.[19] When the eyelash reflex and body movement disappear, and the modified observer's assessment of alertness/sedation scale (MOAA/S)[20] (Table 2) is less than 2 points. The nasopharynx airway will be placed in group N. Then, endoscopy will be performed by a skillful endoscopist, whereas the examination in group C will start when MOAA/S is less than 2 points. During endoscopy procedure, additional boluses of propofol (0.5 mg/kg) will be administered if necessary to keep the MOAA/S score <2 points. The fluctuation of NIBP will be kept within 20% of the baseline value by injecting metaraminol or nicardipine intravenously. Atropine (0.5 mg/bolus) will be administered when the HR is below 45 beats/min. Simple airway maneuvers, such as head-tilt/chin lift and jaw-thrust, will be performed by the anesthesiologist when the SpO_2 is below 90%. If the hypoxemia is not improved by these maneuvers, manual ventilation by anesthesia machine will be consequently applied, and further, emergency tracheal intubation or laryngeal mask insertion will be performed if necessary. Other perioperative security incidents will also be noted and treated in accordance with the clinical operation standards of Deyang People's Hospital.

After completing the endoscopy, patients will be transferred into the post anesthesia recovery room with continuous monitoring. Adverse events in the recovery room will be documented by the nurse anesthetist. Attending anesthesiologists will participate in the treatment of adverse events. In addition, satisfaction of the patients, endoscopists and anesthesiologists will also be determined by a 10-point Likert scale (1=highly unacceptable, 10=outstanding)[22] (Table 3). The patients with a Steward score ≥4 and stable vital signs will be allowed to leave the anesthesia recovery room accompanied by their family members.

Table 2 The Modified Observer's Assessment of Alertness/Sedation Scale

Sore	Meaning
5	Responds readily to name spoken in normal tone (alert)
4	Lethargic response to name spoken in normal tone
3	Responds only after name is called loudly and/or repeatedly
2	Responds only after mild prodding or shaking
1	Does not respond to mild prodding or shaking
0	Does not respond to deep stimulus

Note: Reprinted from Gastroenterology, volume 133(2). Cohen LB, DeLegge MH, Aisenberg J, et al. AGA Institute Review of Endoscopic Sedation. 675-701, Copyright 2007, with permission from Elsevier.[21]

Table 3 The 10-Point Likert Scale

Sore	Meaning
10	Outstanding
9	Excellent
8	Very good
7	Good
6	Above average
5	Average
4	Below average
3	Less than acceptable
2	Unacceptable
1	Highly unacceptable

Outcomes

Primary Outcome

The primary outcome is the incidence of hypoxemia during the endoscopic examination and in post-anesthesia recovery room. The hypoxemia is defined as SpO_2 <90%.[23,24] Considering the high risk of hypoxemia during general anesthesia in obese patients, it will be treated immediately when SpO_2 is below 90%.

Secondary Outcomes

Secondary outcomes are as follows:

1. Times of attempt for nasopharynx airway intubation.
2. Time to successful nasopharynx airway intubation.
3. Incidence of epistaxis.
4. Incidence of suspended examination due to hypoxemia.
5. Usage of manual ventilation, Tracheal/laryngeal mask insertion.
6. Incidence of cardiovascular adverse events: hypotension, hypertension and bradycardia.
7. Incidence of gastrointestinal complications: nausea and vomiting, abdominal pain and bloating, gastrointestinal perforation and bleeding.
8. VAS score of nasopharynx pain at once and 1, 3 and 7 postoperative days after removing the nasopharynx airway.
9. Satisfaction scores of the patients, endoscopist and anesthesiologists.

Data Collection and Management

Baseline demographic data including age, height, body weight, gender, BMI, ASA score, modified Mallampati score, blood pressure, heart rate and SpO_2 will be recorded when subjects enter the anesthesia preparation room.

The data recorded during gastrointestinal endoscopy are as follows: blood pressure, heart rate and SpO_2, nasopharyngeal bleeding, times of attempt for nasopharynx airway intubation, time to successful nasopharyngeal airway intubation, suspended examination for hypoxemia, cardiovascular and respiratory adverse events. Gastrointestinal complications, VAS score of nasopharynx pain after removing the nasopharyngeal airway, satisfaction of the patients, endoscopist and anesthesiologists will be collected postoperatively. Preoperative, intraoperative and postoperative data will be documented on three pieces of paper by different investigators. Namely, the nurse anesthetists are responsible for recording the preoperative and postoperative data, while anesthesiologists in the examination room for the intraoperative ones. All data will be input and stored in the SPSS software by an independent researcher. Professor Xianjie Zhang and Wenya Chen will be responsible for managing the data. All the researchers will be trained, such as the eligibility evaluation, randomization, privacy protection, and interview skills before the study.

Sample Size Determination

The results of our pilot test (Supplemental Table 1) indicated that the incidence of hypoxemia of outpatients with obesity accepting oxygen therapy through endoscopic respiratory mask was 40%, which is similar to previous research reports.[9,22] We aimed to detect a 20% difference in hypoxemia rate between the groups. The sample size was determined by the model of Compare 2 Proportions: 2-Sample, 2-Sided Equality in https://www.sci-inn.com/. We hypothesized an alpha level of 0.05 and a power level of 0.8. Therefore, we estimated that 79 subjects were needed in each group. Considering a 10% dropout, we decided to include 176 patients, namely 88 in each group.

Recruitment Plan

Outpatients who plan to undergo a painless gastrointestinal endoscopy are required to complete a preoperative evaluation of anesthesia. After a thorough evaluation, the study protocol, risks and benefits will be explained to the eligible patients in detail. The related documents were reviewed and approved by the Ethics Committee of Deyang People's Hospital. No persuasive advertising will be used to help with recruitment. To promote participant retention and completion of follow-up, we will inform the patients that the time of phone calls during recruitment period and reserve at least 2 records of contact number. The recruitment was started on March 4, 2024, and is estimated to end on June 30, 2025.

Statistical Analysis

SPSS 26.0 (SPSS, Inc., IL, USA) will be used for all statistical analyses. The normality of the data distribution will be assessed by the Shapiro–Wilk test. Normally distributed data will be summarized as mean ± standard deviation (SD), while non-normally distributed data will be expressed as median (25th and 75th percentile). Categorical data will be shown as frequency and percentages. Continuous data will be compared by Student's *t*-test or Wilcoxon-Mann–Whitney test based on viability of the normality assumption. Chi-square or Fisher's exact test will be used to compare the categorical data. Significance is set as a two-sided p value < 0.05.

Discussion

This study is designed to assess whether a nasopharyngeal airway placed before endoscopy as the ventilation device can alleviate the incidence of hypoxemia in painless gastrointestinal endoscopy in obese outpatients. Hypoxemia is a common complication occurring in patients during painless gastrointestinal endoscopy,[25] especially the obese patients.[26] To date, researchers have made numerous attempts to enhance the management of hypoxemia during gastrointestinal endoscopy in obese patients. These attempts include the use of anesthetic medications with mild respiratory suppression effects, conscious sedation, nasal high-flow oxygen inhalation, tracheal intubation anesthesia, and endoscopic respiratory mask.[8,10,25,27] In a previous study, a kind of nasopharyngeal airway was inserted to place the oxygen tube, resulting in less SpO_2 reduction relative to the nasal oxygen

tube.[28] In our previous study, despite the administration of medications with mild respiratory depression effects for colonoscopy in obese patients with oxygen inhaled through a respiratory mask, 26% of the patients experienced apnea and 32% of the patients experienced shortly hypoxemia.[29] Currently, the incidence of hypoxemia in obese patients undergoing painless gastrointestinal procedures remains high and a highly effective prevention strategy has not been reported.

Upper airway obstruction and hypoventilation are significant contributors to hypoxemia in obese patients, since they are difficult to maintain upper respiratory tract patency during sedation and anesthesia.[30,31] Although outpatients with obesity undergo preoperative evaluation at the anesthesia clinic before painless gastrointestinal endoscopy, upper airway obstruction and hypoventilation, as well as the gas exchange defects of obesity during sedation procedure are frequent.[9,32–34] The nasopharyngeal airway effectively alleviates upper airway obstruction during sedation procedure, thereby maintaining an unobstructed airway. Additionally, it can also support $EtCO_2$ monitoring, nasal high-flow oxygen ventilation or anesthesia machines for high-flow oxygen therapy if needed. Thus, compared with oxygen therapy supported by nasal oxygen tube and endoscopic respiratory mask, the nasopharyngeal airway in the present study may have significant advantages.

The nasopharyngeal airway in our study is so simple but effective ventilation device that functions as an artificial airway from the nasal cavity to the glottis. And it can be easily used by anesthesiologist, anesthesiologist nurse and endoscopist. If the results of our study meet expectations, it is anticipated that this approach may be widely promoted and adopted to alleviate hypoxemia during painless gastrointestinal endoscopy for obese outpatients.

We attempt to prevent upper respiratory obstruction in outpatients with obesity by placing the nasopharyngeal airway in advance to reduce the incidence of hypoxemia during examination and in post-anesthesia care unit (PACU). The nasopharyngeal airway is located at the glottis after placement, which keeps the airway open. Thus, it is likely that placing the nasopharyngeal airway can effectively relieve upper respiratory obstruction and improve oxygen supply, and further, decrease the incidence of hypoxemia in obese outpatients undergoing painless gastrointestinal endoscopy.

Conclusion

This is a prospective randomized controlled trial to detect whether the nasopharyngeal airway can decrease the incidence of hypoxemia induced by propofol and opioids during painless gastrointestinal endoscopy among outpatients with obesity. Therefore, the results of our study may provide a useful method to maintain oxygen supply in painless practice. In addition, we will closely monitor potential side effects and security incidents that may arise in both groups throughout the study, and they will be further analyzed.

Abbreviations

SpO_2, peripheral oxygen saturation; ASA, American Society of Anesthesiologists; SPIRIT, Standard Protocol Items for Randomized Trials; BMI, body mass index; NIBP, noninvasive blood pressure; ECG, electrocardiogram; HR, heart rate; RR, respiratory rate; $EtCO_2$, end-tidal carbon dioxide; MOAA/S, modified observer's assessment of alertness/sedation scale; PACU, post-anesthesia care unit.

Data Sharing Statement

There are no specific data in this paper. Results of this trial can be obtained from the correspondence authors 6 months after publication of the study results for reasonable requests.

Ethics Approval and Consent to Participate

The study was approved by the Ethics Committee of Deyang People's Hospital on November 21, 2023 (approval number: 2023-03-024-K01), and the version was updated on February 09, 2024 (approval number: 2023-03-024-K02). Our investigators will explain the study to eligible subjects and get written informed consents. We declare that the study procedure will be complied with the Declaration of Helsinki.

Consent for Publication

All the authors agreed to publish this manuscript.

Trial Status

The study protocol (version 3.0) was firstly registered in the Chinese Clinical Trial Registry on December 20, 2023, and the study protocol (version 4.0) was updated on January 25, 2024. Recruitment was started on March 4, 2024, and is planned to end on June 30, 2025. The first patient was enrolled on March 4, 2024.

Trial Auditing

The Ethics Committee of Deyang People's Hospital will audit ethic-related matters of this study once a year.

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Disclosure

The authors declare that there are no conflicts of interest for this work.

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