Use of High-Flow Nasal Cannula to Prevent Desaturation Episodes in the Morbidly Obese Patient Undergoing Colonoscopy: A Prospective Randomized Clinical Trial

NCT Number: NCT03148262

Date of Documents: 09/22/2017

The University of Texas Southwestern Medical Center at Dallas
Institutional Review Board

Protocol

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1. Introduction and Purpose:

It is standard practice in the United States and many parts of world to perform Gastrointestinal (GI) endoscopy with the patient under deep sedation (1). Obesity is accepted as a patient specific risk factor for hypoxic events during procedural sedation for GI endoscopic procedures. The Obese population has a higher prevalence of obstructive sleep apnea (OSA) which is characterized by repeated obstruction of the upper airway, and leads to apnea and desaturation. This prospective, randomized study was designed to compare the effectiveness of the high flow nasal cannula and the standard nasal cannula in morbidly obese (BMI > 40) patients receiving deep intravenous sedation during colonoscopies. This study will assess whether use of the high flow nasal cannula (HFNC) leads to less intraoperative desaturation events compared to the current standard of care.

Hypothesis 1- The HFNC group will have significantly lower incidence of desaturation episodes (SpO2 <90) than the standard nasal cannula group during procedural sedation for colonoscopies.

Primary objective: To compare the frequency of desaturation episodes during procedural sedation in obese patients undergoing colonoscopies.

Hypothesis 2- The HFNC group will require fewer interventions to treat hypoxic events than the standard nasal cannula group during procedural sedation for colonoscopies.

Secondary objective1: To compare the number of interventions made by the anesthesia providers required to treat desaturation events during procedural sedation in patient undergoing colonoscopies.

Hypothesis 3- Use of HFNC would decrease sedation-related adverse events in obese subjects with OSA.

Secondary objective2: To determine the frequency of desaturation episodes during procedural sedation in obese patients with undiagnosed OSA.

2. Background:

The prevalence of morbid obesity is increasing worldwide. As the severity of obesity increases, the incidence of diagnosed obstructive sleep apnea also rises. Studies have shown an incidence of sleep apnea as high as 64% in patients with a body mass index (BMI) over 40 and 100% in patients with a BMI greater than 60 (2). Patients with OSA have been shown to have significant desaturations under intravenous sedation due to airway narrowing and obstruction. Several studies have also shown that morbidly obese subjects, independent of a diagnosis of OSA, run a higher perioperative risk of adverse

airway events, including hypoxia. Quadeer et al found a 51% overall incidence of desaturation below 90% in a prospective observational study with 79 patients undergoing endoscopy under "conscious sedation." They also found a significant difference in the frequency of desaturation events between obese (BMI > 30) and non-obese patients (3). Many morbidly obese subjects present to our institution for GI procedures under deep sedation. Providing anesthesia for this patient population is challenging and requires careful titration of drugs and superb airway management skills.

The current standard of care for oxygen delivery in this setting is a Salter nasal cannula. There are no prospective, randomized studies that compare the use of a high flow humidified nasal cannula system and standard nasal cannula in morbidly obese patients presenting for colonoscopy under anesthesia. Patel et al have been working with a transnasal high flow device (THRIVE) and have shown it to increase apnea times in patients with difficult airways post induction of general anesthesia (4). These patients received neuromuscular blockade and made no respiratory effort, however, the patency of their airway was maintained with a manual jaw thrust by anesthesia providers. They concluded that the device combines the benefits of apneic oxygenation with continuous positive airway pressure and gaseous exchange occurs through flow-dependent dead space flushing (5).

Humidified high flow nasal cannula (HFNC) oxygen therapy utilizes an air oxygen blend allowing from 21% to 100% FiO2 delivery and generates up to 60 L/min flow rates (6,7). The gas is heated (35 to 40 degree Celsius) and humidified through an active heated humidifier and delivered via a single limb heated inspiratory circuit (to avoid heat loss and condensation) to the subject through a large diameter nasal cannula (8, 9). Theoretically, HFNC offers significant advantages in oxygenation and ventilation over conventional methods (9). Constant high flow oxygen delivery provides steady inspired oxygen fraction (FiO2) and decreases oxygen dilution (10). It also washes out physiologic dead space and generates positive end expiration pressure (PEEP) that augments ventilation (10, 11). In the current narrative review, Sotello et al. summarized factors explained the improvement in respiratory parameters by using HFNC (12). (1) Washout of the nasopharyngeal dead space; (2) Reduction in inspiratory resistance associated with gas flow through the nasopharynx; (3) Improvement in respiratory mechanical parameters associated with gas temperature and state of humidification; (4) Reduction in metabolic work associated with gas conditioning; (5) Provision of mild distending pressure.

Some studies have demonstrated a positive effect of HFNC on the apnea-hypopnea index (AHI) showing that use of HFNC could decrease hypoxic episodes in subjects with repetitive upper airway obstruction such as obstructive sleep apnea. The STOP-BANG questionnaire (SB) has been used successfully to screen patients undergoing therapeutic endoscopic procedures at higher risk for sedation-related adverse events (14). Mehta et al (15) evaluated the prevalence of undiagnosed OSA at their endoscopy center and the relationship between a positive SB result and sedation-related adverse events. They found that 48.5% (118/243) of patients were SB+ and exhibited a higher level of potentially adverse medical conditions, with 66.3% (161/243) being classified with an SB score of 3.

We are hypothesizing that the HFNC will help maintain a patent airway and improve gaseous exchange in the morbidly obese patients undergoing deep sedation for colonoscopies and will result in a significant decrease in intraoperative desaturation events, thus improving morbidity and overall safety for this subgroup.

3. Concise Summary of Project: The study population for this randomized prospective clinical trial will consist of male and female subjects, between the ages of 18-80, with a BMI over 40 undergoing colonoscopies. Consent will be obtained by research coordinator or anesthesia providers involved in

the study. OSA screening questionnaire (Stop Bang) will be completed during review of the patient's history and physical exam and subjects will be stratified based on STOPBANG score of ≥5 versus ≤4. Subjects will then be randomized in a stratified fashion to either the HFNC (Comfort Flo System) group or the Salter cannula group. Then subjects will be brought into the procedure room and placed on all standard ASA monitors (BP cuff, EKG, pulse oximetry). In the HFNC group, the nasal cannula will be placed on the patient at a setting of FiO2 36% and up to 60L/min depending on patient tolerance. 60 L/min is the max flow rate and will be used as tolerated for maximum benefit. The HFNC setting will start at 40 L/min and will be titrated up to the max flow rate of 60 L/min depending on subjects' tolerance.

Research intervention: The Comfort Flo system (Teleflex Medical, Research Triangle Park, NC, USA) will be used for high flow nasal cannula during colonoscopy. The Comfort Flo System has an air-O_2 blender setting and a FiO2 analyzer to confirm FiO2 delivered to the patient. This FiO2 has been shown to be equal to the FiO2 measured using the Salter cannula at 4L/min (13)**.**

Control group: A Salter nasal cannula will be used at 4L/ minute during the colonoscopy.

The cannulas will be placed on the patients 5 minutes prior to the start of the anesthetic.

All patients will receive a similar intravenous anesthetic with a propofol infusion titrated to a Richmond Agitation-Sedation Scale (RASS) score of 3-4. A lidocaine bolus of up to 100 mg can be used prior to the start of the propofol infusion for initial tolerance of the drug. Patient saturation is recorded every minute during the anesthetic on the electronic medical record and is available for review. The duration and frequency of all measurements at or below 90% will be recorded by the Electronic Medical Record (EMR). The anesthesia providers will be instructed to intervene only when the patient's saturation falls below 90%, by either manually performing a jaw thrust, placing a nasal or oral airway, bag mask ventilation, increasing the patients FiO2 or decreasing the rate/ pausing the propofol infusion or endotracheal intubation. They will be instructed to write a quick note at the time of intervention in the EMR describing their maneuver. Duration of the study will be the length of the procedure through discharge from the Postoperative Anesthesia Care Unit (PACU).

Our hypothesis is that the patients in the high flow nasal cannula group will experience a marked reduction in intraoperative desaturation events as compared to the Salter cannula group.

Outcome Measures:

- Lowest recorded saturation
- The frequency of desaturation episodes (SpO2 <90%)
- Duration of desaturation episodes (SpO2 <90%)
- Number of apnea episodes
- Dose of propofol or other combination for sedation during colonoscopy
- Anesthesiologist intervention (intubation, airway repositioning, Chin lift)
- Type of airway used (oral airway, nasal airway, bag mask ventilation, suctioning)
- Premature termination of procedure
- Unplanned hospital admission

4. Study Procedures:

- OSA screening with the SB questionnaire: SB is made up of 8 yes or no questions (14). The anesthesiologist or certified registered nurse anesthetist will be blinded to the results of the SB.

High risk of obstructive sleep apnea if yes to ≥5 questions; low risk of obstructive sleep apnea: yes to ≤4 questions.

- Randomization to the high flow nasal cannula group or the Salter cannula group. Subjects will be randomized in a 1:1 ratio according to a computer generated randomization list provided by the study statistician.
- All standard monitoring (BP, EKG, pulse oximeter) placed on all patients in the procedure room. Cannulas placed on the patients 5 minutes prior to the start of the anesthetic and set to rate of 4/min for standard nasal cannula and 36% FiO2 up to 60 L/min for the HFNC group.
- Anesthesia achieved with a propofol infusion titrated to a RAS score of 3-4.
- All desaturation points at or below 90% recorded via intraoperative electronic charting (Epic).
- Frequency and method of intervention aimed at increasing the patient's saturation by the provider will be recorded on the EMR at the time of intervention with a quick note.

5. Sub-Study Procedures:
N/A

6. Criteria for Inclusion of Subjects:

- Age between 18-80
- Subjects undergoing colonoscopies
- Morbidly obese BMI ≥ 40

7. Criteria for Exclusion of Subjects:

- Subjects deemed hemodynamically unstable by the anesthesia team
- Subjects who are an aspiration risk and will require endotracheal intubation.
- Pregnancy
- Subjects with an allergy to propofol
- Patients who are unable to tolerate the high flow nasal cannula secondary to discomfort
- Subjects unwilling to sign consent
- Chronic obstructive pulmonary disease
- Patients that received medications other than lidocaine and propofol

8. Sources of Research Material:

- Subjects undergoing colonoscopy
- Electronic Medical Record
- Anesthesia Reports
- PHI including name, medical record number, contact information including demographic information including age, gender, race, birth date, weight, height, BMI and medical and surgical history, medication list, ASA classification.
- **Procedural sedation-related variables**: type of sedation agent used for procedural sedation, propofol dose, propofol infusion time, opioid use, any other combination agent for the procedural sedation during colonoscopy, Procedure time, premature termination of procedure.
- **Respiratory event-related variables**; Anesthesiologist intervention (intubation, airway repositioning, Chin lift); Type of airway used (oral airway, nasal airway, bag mask ventilation, suctioning), Laryngospasm or any other airway obstruction; pulse oximetry reading, the number and duration of apnea/hypoxia episodes.
- **Hemodynamic variables** such as baseline blood pressure
- **Postoperative Recovery:** Aldrete score in recovery, the time spend in PACU
- Unplanned hospital admission

- Stop Bang questionnaire for OSA screening

9. Recruitment Methods and Consenting Process:
All patient recruitment will take place in the GI endoscopy suite. Subject will be identified by reviewing daily endoscopy schedule. A designated team of anesthesiologists and nurse anesthetists involved in the study will be responsible for screening, consenting and enrolling potential subjects. The patient's chart will be reviewed to determine eligibility with the use of a HIPAA waiver form. Information about the study will be given in a pressure-free, confidential private area in a face-to-face meeting and the voluntary nature of the research will be emphasized to the subjects.

The purpose of the study and risks and potential complications of the study will be explained. Adequate time will be given to read consent form to consider whether or not participate in the study. All questions will be answered before the patient is asked to sign the consent form. If the patient agrees to participate, then he or she will sign the consent form and HIPAA Authorization Form prior to any study procedures.

10. Potential Risks:
This study has minimal risk. The anesthetic management in either group will not differ from the current standard of care.

Risk for HFNC*:*
There may be minimal risk for mucosal injury with HFNC. This risk is not higher than standard nasal cannula because HFNC systems deliver heated, humidified gas.

HFNC may produce distending pressure in the lung, similar to CPAP pressures. There may be potentially unpredictable pressures generated by HFNC which may be significant in pediatric but not adult obese population. Mild distending pressure may provide better patent airway in obese subjects. Flow rate of HFNC will be adjusted for maximum benefit to the subject (40-60 L/minutes).

Psychological Stress: Some of the questions related to the study may make the subject feel uncomfortable. Subjects may refuse to answer any of the questions, or take a break or stop participation in the study at any time.

Loss of Confidentiality: Any time information is collected; there is a potential risk of loss of confidentiality. Every effort will be made to keep your information confidential.

11. Subject Safety and Data Monitoring:
Investigators will ensure patient safety throughout the procedure. This will include following all standards of care with regard to conducting a safe anesthetic in the endoscopy suite. All standard ASA monitors will be used, adequate O2 delivery will be ensured and the proper interventions by the providers will be carried out during significant desaturation episodes. Subjects will recover from the anesthetic in the endoscopy suite recovery room. All data will be collected by the EMR as per usual (EPIC).

12. Procedures to Maintain Confidentiality:
All participants will be given an identification number such that identifiable, personal information will not be used. Every effort will be made to keep all data collection sheets confidential and any electronic data sets will be password protected and secure. Electronic documents will be de-identified according to information security policies. Paper documents will be shredded.

13. Potential Benefits:
There is no benefit to subjects. Use of the Comfort Flo high flow nasal cannula may lead to a significant decrease in hypoxic events in morbidly obese, likely sleep apneic, patients undergoing deep sedation for colonoscopies. Information gained from this study will increase patient safety and decrease the morbidity and possibly, mortality, in this challenging patient population.

14. Biostatistics:
The study is powered to detect a 50% reduction in the frequency of desaturation episodes in patients with HFNC compared to patients using a standard nasal cannula. Quadeer et al. (3) reported a 51% incidence rate for desaturation episodes below 90% in patients with standard nasal cannula. Thus to detect a difference of 25% with 80% power and a type 1 error rate of 0.05, the study would need a sample of 59 per group (total n = 118). Assuming a 10% loss of subjects, the total sample size to be enrolled is 130. An interim analysis will be performed at 50% of the enrolment. Based on the interim analysis results, study may be stopped for futility if there is no difference in interim analysis or for early termination for effectiveness if the observed difference at the time is large enough. Obrien-Flemming α-spending function approach would be used to develop acceptance or rejection boundaries. Continuous data will be summarized using means and standard deviations and categorical data will be summarized using frequencies and percentages. The proportions of desaturation episodes below 90% in the two groups will be compared using a Z test or Fisher's exact test. Mean durations of desaturation episodes and mean numbers of interventions to treat hypoxic events in the two groups will be compared using Student's t-tests or Wilcoxon-Mann-Whitney tests. Frequencies of sedation-related adverse events will be compared using chi-square tests or Fisher's exact tests. Normality of the sample data will be assed using normal quantile plots. Level of significance will be set at 0.05 and Bonferroni corrections will be made for all primary hypotheses tests.

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