

High flow nasal cannula oxygen in patients having anesthesia for GI endoscopy (HIFLO-ENDO)

Designation: Clinical Research

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1.1 Rationale

Patients often receive anesthesia during endoscopy to ensure comfort and unconsciousness during the procedure. Upper gastrointestinal endoscopy (EGD) may require particularly deep anesthesia because the patient's gag reflex must be suppressed to tolerate the endoscope. One of the principal risks of anesthesia is that anesthesia drugs depress normal breathing, which can lead to serious harm. Specifically, patients can develop low blood oxygen levels or high blood carbon dioxide levels, which are patient safety risks. Usually, these changes do not cause death or obvious injury because the anesthesiologist treats them. Nevertheless, best medical practice should be to avoid these changes as their long term impact on the patient's well-being is not known. Also low blood oxygen levels or elevated carbon dioxide levels can lead to cardiovascular depression, cardiac arrhythmia, or the need for emergent intubation (placement of a breathing tube). Emergent intubation is a high risk procedure and can cause pulmonary aspiration, vocal cord injury, or oropharyngeal injury.

The current standard of care is for anesthesiologists to provide supplementary oxygen to patients during anesthesia for endoscopy. This helps to maintain blood oxygen levels even when normal breathing is depressed. This is typically done by placing a nasal cannula (small plastic tube) in the patient's nose which allows oxygen to flow into their airway while they breathe. The nasal cannulas that are normally used

are connected to an oxygen flowmeter on the wall and provide oxygen flows between 2 and 6 liters per minute.

High flow nasal cannula oxygen systems are relatively new and can deliver 5 to 10 times more oxygen to a patient. These systems have been used primarily in critically ill patients to improve gas exchange, but they may be useful in other settings including anesthesia. High flow nasal cannula oxygen provides advantages over traditional nasal cannula oxygen including: reduced work of breathing, reduced anatomic dead space, and continuous positive airway pressure, which may improve oxygenation.¹ Traditional nasal cannula oxygen is limited by the fact that it can only increase the inspired oxygen concentration to around 35%.² Alternatively, high flow nasal cannula can deliver inspired oxygen concentrations as high as 91%.³ High flow nasal cannula oxygen has also been shown to increase the distending pressure in the upper airway, which may decrease upper airway obstruction in anesthetized patients and improve ventilation.⁴ Because GI endoscopies are performed in millions of patients each year and up to 17% of patients experience hypoxemia, it is critical to develop strategies for reducing the risk of this problem. Even if the number of patients who die or have permanent brain injury from low oxygen levels is low, best medical practice should avoid low blood oxygen levels.

1.2 Risks/Benefits

Benefits-The purpose of the study is to improve overall patient safety during anesthesia for GI endoscopy by providing higher levels of supplementary oxygen to patients.

The study's potential benefits are higher blood oxygen levels, lower blood carbon dioxide levels, more stable/normal blood pressure, and less need for emergency intubation (placement of a breathing tube into the trachea) during anesthesia.

Risks-The potential risks of the study are:

- 1) The device used to measure blood carbon dioxide levels causes a tingling sensation on the skin related to warming.

- 2) High flow nasal cannula oxygen can change the way that patients are monitored during anesthesia. A patient's breathing is normally monitored in several ways including visual inspection of chest movement, plethysmography, and by measurement of exhaled carbon dioxide levels. High flow nasal cannula oxygen could affect exhaled carbon dioxide measurements because the device is designed to wash carbon dioxide out of the upper airway. We do not anticipate that this will have a significant impact on patient safety because breathing is monitored in multiple ways during anesthesia.

1.3 Study Conduct

The study will be conducted in compliance with the protocol approved by the institutional review board (IRB) and according to good clinical practice standards. No deviation will be implemented without prior authorization from the IRB.

1.4 Population

Enrollment goal = 262 patients

The study enrollment criteria will be:

- 1) Age >18
- 2) Having a non-emergent upper GI endoscopy procedure.

Exclusion criteria will be:

- 1) Propofol, fentanyl, or midazolam allergy. This will be based on the pre-procedure medical history.
- 2) Pre-procedure plan for general anesthesia with an endotracheal tube (at the discretion of the attending anesthesiologist)
- 3) Pregnancy. This will be determined by a urine pregnancy test. Urine or plasma pregnancy tests are performed on all patients having elective anesthesia/surgery as part of normal clinical practice.
- 4) Use of electrocautery during the procedure. High oxygen levels in patients who require electrocautery could increase the risk for fire.

2.1 Study Objective

The principal objective of the study will be to determine whether high flow nasal cannula oxygen delivery decreases the rate of hypoxemia during anesthesia for GI endoscopy. The secondary objectives will be to determine whether high flow nasal cannula oxygen delivery improves ventilation (reduces blood carbon dioxide levels), improves blood pressure (reduces hypotension), and reduces the incidence of rescue intubation (breathing tube placement) during anesthesia.

2.2 Primary Endpoint

The primary endpoint will be hypoxemia during anesthesia. Hypoxemia will be defined as $SpO_2 < 92\%$ for at least 15 seconds. This is a definition that has previously been used in the anesthesia literature.

Secondary endpoints will be

- 1) Hypercarbia. This will be defined as a $PCO_2 > 20$ mmHg above the baseline value.
- 2) Hypotension. This will be defined as a mean arterial blood pressure less than 25% of the baseline value.
- 3) Rescue intubation. This will be defined as the need for emergent placement of a breathing tube during anesthesia.

2.3 Study design/type

The study design is a single-blinded randomized controlled clinical trial. The anesthesia providers will not be blinded to treatment group, as they will be providing oxygen to patients. However, study outcomes will be determined from electronic medical records by persons that are blinded to group assignment.

2.4 Study duration

The expected study duration is two years.

3.1 Inclusion Criteria

- 1) Age > 18
- 2) Having a non-emergent upper GI endoscopy procedure expected to last longer than 15 minutes.

3.2 Exclusion Criteria

- 1) Propofol, fentanyl, or midazolam allergy. This will be based on the pre-procedure medical history.

- 2) Pre-procedure plan for general anesthesia with an endotracheal tube (at the discretion of the attending anesthesiologist)
- 3) Pregnancy. This will be determined by a urine pregnancy test. Urine or plasma pregnancy tests are performed on all patients having elective anesthesia/surgery as part of normal clinical practice.
- 4) Use of electrocautery during the procedure. High oxygen levels in patients who require electrocautery could increase the risk for fire.

3.3 Subject withdrawal

Subjects will be withdrawn from the study at the discretion of the primary anesthesia provider if there is any perceived threat to patient safety related to the study.

4.1 Clinical evaluations

Clinical evaluations will consist of standard vital sign recordings (blood pressure, pulse, respiratory rate, and oxygen saturation) that are performed for patient care as well as transcutaneous blood carbon dioxide measurements, which are not part of usual care. These measurements will be performed using a transcutaneous monitor manufactured by radiometer (TCM CombiM). The device uses a skin electrode that is similar to a sticker and measures blood carbon dioxide levels.

4.2 Laboratory evaluations

None

5.1 Adverse event review

We will perform an adverse event review after every 20 patients enrolled in the study.

5.2 Safety review

A safety monitoring board will be created and will contain 3 members who are not directly involved in the research. The board will meet every 6 months and review all adverse events or potential adverse events related to the study.

6.1 Quality control and assurance

The PI and institution are responsible for conducting the study in compliance with the IRB-approved protocol, all applicable regulations,

and the International Conference on Harmonization, E6 Good Clinical Practice guidelines, by adhering to the requirements for collecting, documenting and reporting complete and accurate data. A separate Data Quality Assurance (QA) Plan will be developed to describe the frequency of review of study related data and the roles and responsibilities for activities related to Quality Control (QC).

7.1 Study measurements

Study measurements will include routine clinical vital signs data, which are normally collected for patients having anesthesia and also transcutaneous blood carbon dioxide measurements as described in section 4.1.

7.2 Statistical analysis

The rate of hypoxemia at our own institution during GI endoscopy was 18% in the last 500 patients as determined by a query of our IRB approved metavision anesthesia registry. The study's sample size was calculated using this information and was based upon what the investigator believed would be a clinically significant difference as well as what reduction in hypoxemia was thought to be plausible using high flow nasal cannula oxygen delivery. In the PIs anecdotal experience, high flow nasal cannula oxygen can lead to dramatic improvements in oxygenation when compared to regular nasal cannula oxygen, particularly in patients with compromised breathing.

Assuming that hypoxemia occurs in 18% of patients in the control group (regular nasal cannula), a total of 262 patients will be necessary to detect a 66% reduction in hypoxemia in the treatment group with a power of 80% and a type 1 error level of 5%. Alternatively, if hypoxemia occurs in only 10% of patients in the control group, the study will have adequate power to detect a 90% reduction in hypoxemia with 80% power and a type 1 error level of 5%.

The study's primary outcome variable (hypoxemia), which will be a dichotomous outcome variable, will be compared between groups using a

Chi Squared test or Fisher's exact test. Secondary outcome variables will be analyzed in the same way.

8 Data management

Confidentiality will be maintained to the extent required by law. All clinical data will be collected on case report forms and will also be entered into a password protected excel spreadsheet. The spreadsheet will be kept on a desktop computer in the PIs office and will be backed up on the departmental network drive. Only study investigators will have access to the study data.

9. References

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3. Tiep B, Barnett M. High flow nasal vs. high flow mask oxygen delivery: tracheal gas concentrations through a heat extension airway model (abstract). *Respir Care*. 2002; 47 (9): 1079.
4. Groves N, Tobin A. A High flow nasal oxygen generates positive airway pressure in adult volunteers. *Aust Crit Care* 2007;20(4):126-131.