Research Study Protocol

Title: Determination of the Optimal Pre-oxygenation Interval Using THRIVE and Facemask Oxygenation in Parturients: A Biased-Coin Sequential Allocation Trial

Abbreviated Title: OPTI-sat (Optimal Pre-oxygenation Time Interval Sequential Allocation Trial)

ClinicalTrials.gov Unique Identifier:

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Peer Review:

Background:
Pregnancy invokes anatomical and physiological changes that increase the difficulty of airway management and decrease the time available to manage the airway following induction of general anesthesia (GA). Given these challenges, GA is a time-pressed and often stressful procedure in obstetric patients[1]. To mitigate the rapid desaturation, adequate oxygenation before rapid-sequence induction and intubation (RSI) is performed when a GA is required, often in a time-critical fashion. Adequate oxygenation before RSI (i.e. pre-oxygenation) is necessary to avoid hypoxemia and helps to create an oxygen reservoir, prolonging the safe time interval for airway management between induction of anesthesia and successful intubation (i.e. apnea time). However, despite the importance of pre-oxygenation in obstetrics, it is often performed poorly due to air entrainment[2].

Advances in oxygenation using transnasal humidified rapid insufflation ventilatory exchange (THRIVE) have been widely published in the critical care setting, management of the difficult airway and morbid obesity [3-5]. Transnasal humidified rapid insufflation ventilatory exchange allows both pre-oxygenation and apneic oxygenation with a degree of continuous positive airway pressure during induction [4]. When 3 minutes of THRIVE pre-oxygenation was compared to standard facemask pre-oxygenation during RSI in non-obstetric patients, the THRIVE group had a significantly longer apnea time without desaturation (248 vs. 123 seconds, $p<0.001$)[6]. However, there is currently limited published evidence for using THRIVE in obstetric anesthesia with only a case report describing THRIVE during a maternal cardiac arrest, a conference presentation and a letter [7-9].

High flow nasal pre-oxygenation could offer significant clinical benefits in obstetric anesthesia[10]. It can be prepared ahead of time for immediate use during an emergency Cesarean delivery. During THRIVE pre-oxygenation, the anesthesiologist can prepare drugs, equipment or attempt neuraxial anesthesia

instead of holding a mask. It can also continue during airway manipulation, permitting apneic oxygenation, which may transform managing the difficult obstetric airway from a time-pressed, anxious situation to one where there is time to carefully make considered decisions[11].

Recently, our department conducted a study (REB (#H17-01996) Pre-Oxygenation in Pregnancy (POP study), ClinicalTrials.gov identifier: NCT03310723) comparing THRIVE pre-oxygenation to conventional facemask for healthy, term parturients [12]. Pre-oxygenation using THRIVE was non-inferior to conventional tight-fitting facemask following 3 minutes of tidal volume breathing and was well tolerated[12]. However, this study did not examine which technique could provide more rapid pre-oxygenation. Knowledge of this information would be immensely helpful and could help anesthesiologists decide the best technique for rapid pre-oxygenation. For example, in situations such as in emergency Cesarean deliveries where the baby needs imminent delivery and there is limited time for optimal pre-oxygenation, the best technique is unknown. Furthermore, the maximum rate of oxygenation using THRIVE has not been measured in any patient group.

The purpose of this study is to identify the effective time interval using THRIVE to achieve an end tidal oxygen (EtO_2) >=90% in 90% of healthy parturients (i.e. effective time interval (EI90)) using a biased-coin design. We also seek to directly compare EI90 of THRIVE to EI90 of facemask using the same protocol.

Study design and methodology
This will be a prospective, randomized, sequential allocation study with a biased-coin design. The purpose of this study is to identify the EI90 using THRIVE versus conventional facemask to pre-oxygenate 90% of healthy parturients to an EtO_2 >=90%.

Hypothesis:
We hypothesize that in healthy parturients undergoing tidal volume breathing, the EI90 for THRIVE pre-oxygenation will be shorter than the EI90 for facemask pre-oxygenation.

Primary objective:
1. To determine the EI_{90} for THRIVE and facemask pre-oxygenation using tidal volume breathing.

Primary outcome:
1. Duration to achieve EtO2 >=90% after tidal volume breathing using THRIVE and facemask pre-oxygenation.

Sequential allocation method with a biased-coin design:
1. Positive response is defined as an EtO_2 concentration ≥90%
2. Negative response is defined as an EtO_2 concentration <90%
3. Increment:
    a. THRIVE pre-oxygenation – first participant starts at 3 minutes, increments of 1 minute (except lowest interval of 30 seconds), maximum 8 minutes, minimum 30 seconds. Possible time intervals 30s-1-2-3-4-5-6-7-8 minutes.
    b. Facemask - first participant starts at 3 minutes, increments of 1 minute (except lowest interval of 30 seconds), maximum 8 minutes, minimum 30 seconds. Possible time intervals 30s-1-2-3-4-5-6-7-8 minutes.

4. Allocation:
    a. The time interval for pre-oxygenation for subsequent study participants is based on the whether the previous participant achieves a negative or positive response (as defined above).
    b. The time for pre-oxygenation for subsequent participants will be adjusted using a biased coin up–down sequential allocation method described by Durham and Flournoy with the aim of estimating the EI90[13]. When EI90 is to be determined ($\tau = 0.9$), the probability (B) = $(1 - \tau)/\tau = (1 - 0.9)/0.9 = 0.1/0.9 \approx 0.11$.
    c. If a negative response is achieved (EtO_2 concentration <90%), when the next participant uses the same pre-oxygenation method, they will receive the next upper time interval for that pre-oxygenation method. For example, if the first participant achieves an EtO_2 concentration <90% using THRIVE for 3 minutes, the next participant who uses THRIVE pre-oxygenation will do so for 4 minutes.
    d. If a positive response is achieved (EtO_2 concentration ≥90%), when the next participant uses the same pre-oxygenation method, they will receive with probability $B \approx 0.11$ the next lower time interval and with probability $1 - B = 0.89$, the same time interval as the previous participant. For example, if the first participant achieves an EtO_2 concentration ≥90% using THRIVE for 3 minutes, the next participant who uses THRIVE pre-oxygenation will stay at the same level breathing for 3 minutes.
    e. If a participant is excluded after randomization they will be removed from the study. The next recruited participant will be subjected to random group allocation (THRIVE versus facemask), and the EI90 assignment will be adjusted based on the same biased-coin sequential allocation process as if the excluded participant had not been randomized.

Inclusion criteria:

- Pregnant patients ≥36 weeks gestation.
- Non-laboring patients admitted for elective Cesarean delivery under neuraxial anesthesia
- American Society of Anesthesiologists (ASA) class 2.
- Patients who are ≥ 19 years of age.

Exclusion criteria:

- Any medical conditions that are likely to affect gas exchange including recent respiratory infection, chronic respiratory disease (e.g., obstructive sleep apnea) or diseases of pregnancy (e.g. preeclampsia).
- Obstructed nasal passage, thus are only able to breathe through their mouth.
- Patients who express concerns or unwillingness to try on a conventional facemask.
- Body Mass Index ≥40 kg/m^2 as this may affect gas exchange while lying flat.
- Patients who are in active labor (i.e. cervical dilation ≥4cm).
- Patients who are unable to give informed consent because of a language barrier as the study team only speaks English and will be unable to complete the consent process and study procedures appropriately.

Withdrawal criteria:

- Inability to form a tight seal with facemask.
- Inability to form a tight seal around the mouth piece when measuring EtO_2 concentration.
- Inability to tolerate THRIVE or facemask.
- Withdrawal of consent at any time.

Recruitment

Patients having an elective Cesarean delivery typically arrive 60-90 minutes prior to their scheduled procedure. Upon arrival, patients check in at the admitting desk where the admitting nurse will provide eligible patients with a Patient Information Sheet describing our study. The patients are then brought to the pre-operative waiting area to await their procedure. After approximately 30 minutes and once the patient and her support personnel have had a chance to read the information sheet, one of the study team members will approach the patient to fully explain what the study entails (i.e. why we are doing it and how it will affect her care if she chooses to participate) and answer any questions. We will also show the patient the facemask, nasal cannula system, and mouthpiece that she will have to use if she chooses to participate. This is to allow full transparency for the patient to make a decision on whether or not to participate. We will then leave her with the consent form to further read about the study and discuss it with her support persons. Approximately 30 minutes prior to her elective Cesarean delivery, we will ask the nurse what the patient has decided. If the patient agrees, one of the study team members will formally go through the consent process with the patient, obtaining their informed written consent prior to transfer of the patient to the operating room for the study and their Cesarean delivery.

We will not attempt to consent patients in the days before their surgery as this would often require an extra hospital visit and thus place an onerous burden on their time. However, we will provide the Patient Information Sheet to all women once the decision to deliver via Cesarean delivery is made. This decision usually occurs in the obstetric care provider's office and once made the patient is usually given an information pack regarding their Cesarean delivery. This information pack is compiled by the admissions team at BC Women's Hospital, and they have agreed to allow study investigators to add their Patient Information Sheet to the packs sent out to the obstetric care providers. The Patient Information Poster will also be e-mailed to all the obstetric offices to print and display on their respective notice boards. Finally, the information poster will also be placed in the operating room admission area and research notice boards around the hospital, with the aim that patients will recognize the study when they come in for their elective Cesarean delivery. Investigators will educate anesthesiologists, surgeons and operating room nursing staff about the study directly through departmental rounds and by email.
All study procedures will take place in the operating rooms at BC Women's Hospital (BCWH). These will be conducted by one of the study team; however, the study team will not then be involved with the care of those participants who have a scheduled Cesarean delivery.

Randomization:
Microsoft Excel 2010 will be used to generate a randomization sequence that will be used to allocate participants to either the THRIVE or facemask (control) group. Depending on the outcome of the previous participant, the time interval probability formula (defined above) will be used to determine the duration of pre-oxygenation for subsequent participants.

Blinding:
Blinding is not possible due to the nature of the study.

Interventions (Study Protocol):
Participants will be randomly assigned to one of 2 groups: THRIVE or facemask (control). Participants in the THRIVE group will first receive pre-oxygenation using the Optiflow™ THRIVE nasal high-flow cannula system (Fisher and Paykel Healthcare Ltd, Auckland, New Zealand) followed by pre-oxygenation via a conventional anesthetic facemask, as is performed in routine clinical practice. Participants in the facemask (control) group will first receive pre-oxygenation via a conventional anesthetic facemask followed by pre-oxygenation using the Optiflow™ THRIVE nasal high-flow cannula system. It is anticipated that participation in this study will take approximately 30 mins (15 mins for informed consent and 15 minutes to complete the study protocol).

Baseline recording

Each participant will be taken to the operating room, usually where their elective Cesarean delivery will take place if applicable. The participant will be placed on the operating table, lying down in a ramped position using the Troop™ (Goal Medical, LLC, Eugene, OR, USA) elevation pillow (Figure 1) and with a right lateral pelvic wedge to minimize aortocaval compression. This is the same position used during an elective Cesarean delivery. Before assessing the different pre-oxygenation techniques, each participant will be asked to breathe 21% oxygen (room air) at a rate of 12 $L.min^{-1}$, in a normal way for 30s, via a mouthpiece with a clip on their nose. This will allow time for the participant to get used to the nose clip and to both practice making a tight seal around and breathing through the mouthpiece. The mouthpiece will be connected to an anesthetic circle system with a 2L reservoir bag, heat moisture exchange filter and an oxygen analyzer. Baseline values will be recorded for EtO_2 concentration, oxygen saturation, respiratory rate, and heart rate after the 30s have been completed. In order to record an accurate EtO_2 concentration using THRIVE, we plan to quickly remove the THRIVE system and change to a mouthpiece and nose clip attached to an anesthetic breathing circuit, as used in our previous study[12].

In the THRIVE group, after the initial baseline recordings, the following 2 stages will take place.

Stage 1: THRIVE pre-oxygenation

1. The THRIVE system will be applied, with 100% oxygen at an oxygen flow rate of 50 $L.min^{-1}$.

2. An AirLife™ Adult Oxygen Mask will then be applied overtop of the THRIVE system (Figure 2).
3. The participant will be asked to breathe normally (tidal volume breathing) with their mouth closed.
4. The duration of the pre-oxygenation will be 3 minutes (determined by our previous study) for the 1st participant. Based on the sequential allocation biased coin method, we intend to use 1 minute increments, either increasing or decreasing the duration of pre-oxygenation based on the response of the previous participant.

Figure 2. AirLife™ Adult Oxygen Mask.

5. Once the pre-oxygenation is completed, the participant will be asked to take and hold a deep breath through their nose for up to 5s, to avoid breathing room air. At the same time, THRIVE and the AirLife™ Adult Oxygen Mask will be quickly removed, a nose clip will be placed on the participant's nose and the participant will be given the mouthpiece to insert into their mouth and asked to make a tight seal around it.
6. The participant will then be asked to exhale fully into the mouthpiece for the EtO_2 concentration to be analyzed and recorded (primary endpoint).
7. Oxygen saturation, respiratory rate and heart rate will be recorded at baseline and every 60s.
8. An estimate of how much time the participant managed to breathe with their mouth closed during the pre-oxygenation period will be made by the study Anesthesiologist on a 5-point Likert scale: Mouth closed the entire time, mouth open sometimes, mouth open half of the time, mouth open occasionally or mouth open the entire time.

Stage 2: Facemask (control) pre-oxygenation

1. The participant will then be asked to breathe normally, without either the mouthpiece or THRIVE for 5 minutes. This should allow the EtO_2 concentration to return to the baseline value. During this time, the mouthpiece will be re-applied (set at 21% oxygen (room air) and a rate of 12 $L.min^{-1}$) to check the EtO_2 concentration has returned to within 10% of the baseline value. If it has not, the participant will be asked to continue breathing room air until baseline EtO_2 has returned to within 10% of the baseline value.
2. After returning to the baseline EtO_2 concentration, the participant will be asked to breathe normally via the conventional face mask held by the study anesthesiologist set at 100% oxygen and at a rate of 15 $L.min^{-1}$.
3. The duration of this pre-oxygenation will again be 3 minutes for the 1st participant. Based on the sequential allocation biased coin method, we intend to use 1 minute increments, either increasing or decreasing the duration of pre-oxygenation based on the response of the previous participant.
4. Once the pre-oxygenation is completed, the participant will be asked to take and hold a deep breath for up to 5s. The facemask will be quickly removed, a nose clip will be placed on the

participant's nose and the participant will be given the mouthpiece to insert into their mouth and asked to make a tight seal around it.

5. The participant will then be asked to exhale fully into the mouthpiece for the EtO_2 concentration to be analyzed and recorded (primary endpoint).
6. Oxygen saturation, respiratory rate and heart rate will be recorded at the start of the second pre-oxygenation period and every 60s until completed.

In the facemask (control) group, after the initial baseline data recordings, the following 2 stages will take place:

Stage 1: Facemask (control) pre-oxygenation

1. Participants will be assigned to receive pre-oxygenation via a conventional facemask held by the study anesthesiologist, set at 100% oxygen and a rate of 15 $L.min^{-1}$.
2. The duration of this pre-oxygenation will be 3 minutes for the 1st participant. Based on the sequential allocation biased coin method, we intend to use 1 minute increments, either increasing or decreasing the duration of pre-oxygenation based on the response of the previous participant.
3. Once the pre-oxygenation is completed, the participant will be asked to take and hold a deep breath for up to 5s. The facemask will be quickly removed, a nose clip will be placed on the participant's nose and the participant will be given the mouthpiece to insert into their mouth and asked to make a tight seal around it.
4. The participant will then be asked to exhale fully into the mouthpiece for the EtO_2 concentration to be analyzed and recorded (primary endpoint).
5. Oxygen saturation, respiratory rate and heart rate will be recorded at the start of the second pre-oxygenation period and every 60s until completed.

Stage 2: THRIVE pre-oxygenation

1. The participant will then be asked to breathe normally, without either the mouthpiece or THRIVE for 5 minutes. During this time, the mouthpiece will be re-applied (set at 21% oxygen (room air) and a rate of 12 $L.min^{-1}$) to check the EtO_2 concentration has returned to within 10% of the baseline value. If it has not, the participant will be asked to continue breathing room air until baseline EtO_2 has returned to within 10% of the baseline value.
2. After returning to the baseline EtO_2 concentration, the participant will be asked to breathe normally with their mouth closed via the THRIVE system, with 100% oxygen at an oxygen flow rate of 50 $L.min^{-1}$. In addition, an AirLifeTM Adult Oxygen Mask, which is a loose fitting clear facemask, will be placed over-top of the THRIVE system.
3. The duration of the pre-oxygenation will be 3 minutes for the 1st participant. Based on the sequential allocation biased coin method, we intend to use 1 minute increments, either increasing or decreasing the duration of pre-oxygenation based on the response of the previous participant.
4. Once the pre-oxygenation is completed, the participant will be asked to take and hold a deep breath through their nose for up to 5s, to avoid breathing room air. At the same time, THRIVE

will be quickly removed, a nose clip will be placed on the participant's nose and the participant will be given the mouthpiece to insert into their mouth and asked to make a tight seal around it.

5. The participant will then be asked to exhale fully into the mouthpiece for the EtO_2 concentration to be analyzed and recorded (primary endpoint).
6. Oxygen saturation, respiratory rate and heart rate will be recorded at baseline and every 60s.
7. An estimate of how much time the participant managed to breathe with their mouth closed during the pre-oxygenation period will be made by the study Anesthesiologist on a 5-point Likert scale: Mouth closed the entire time, mouth open sometimes, mouth open half of the time, mouth open occasionally or mouth open the entire time.

In both groups, once the final EtO_2 concentration is recorded, participants will be asked to breathe normally and all pre-oxygenation techniques will be removed. Each participant will be asked 5 questions about their satisfaction with the method of pre-oxygenation using a 5-point Likert Scale:

1. Please indicate how you felt from a comfort point of view breathing during the study using the nasal oxygen device: Completely comfortable, slightly comfortable, neutral, slightly uncomfortable, completely uncomfortable.
2. Please indicate how you felt from an acceptability point of view breathing during the study using the nasal oxygen device: Acceptable, slightly acceptable, neutral, slightly unacceptable or unacceptable.
3. Please indicate how you felt from a comfort point of view breathing during the study using the facemask: Completely comfortable, slightly comfortable, neutral, slightly uncomfortable, completely uncomfortable.
4. Please indicate how you felt from an acceptability point of view breathing during the study using the facemask: Acceptable, slightly acceptable, neutral, slightly unacceptable or unacceptable.
5. Which breathing device did you prefer: nasal oxygen device or facemask?
   After answering the questions, the participants will have completed their part in the study and routine clinical care will continue for their elective Cesarean delivery.

Dr Kelly Au (study anesthesiologist) or Dr Anton Chau (study PI) will be conducting the procedures with the participant and James Taylor (research assistant) will be recording the data. Neither of these people will then be involved in providing care for the patient's caesarean delivery as this will be completed by an anesthesiologist not involved in the study for that patient.

Flow diagram:

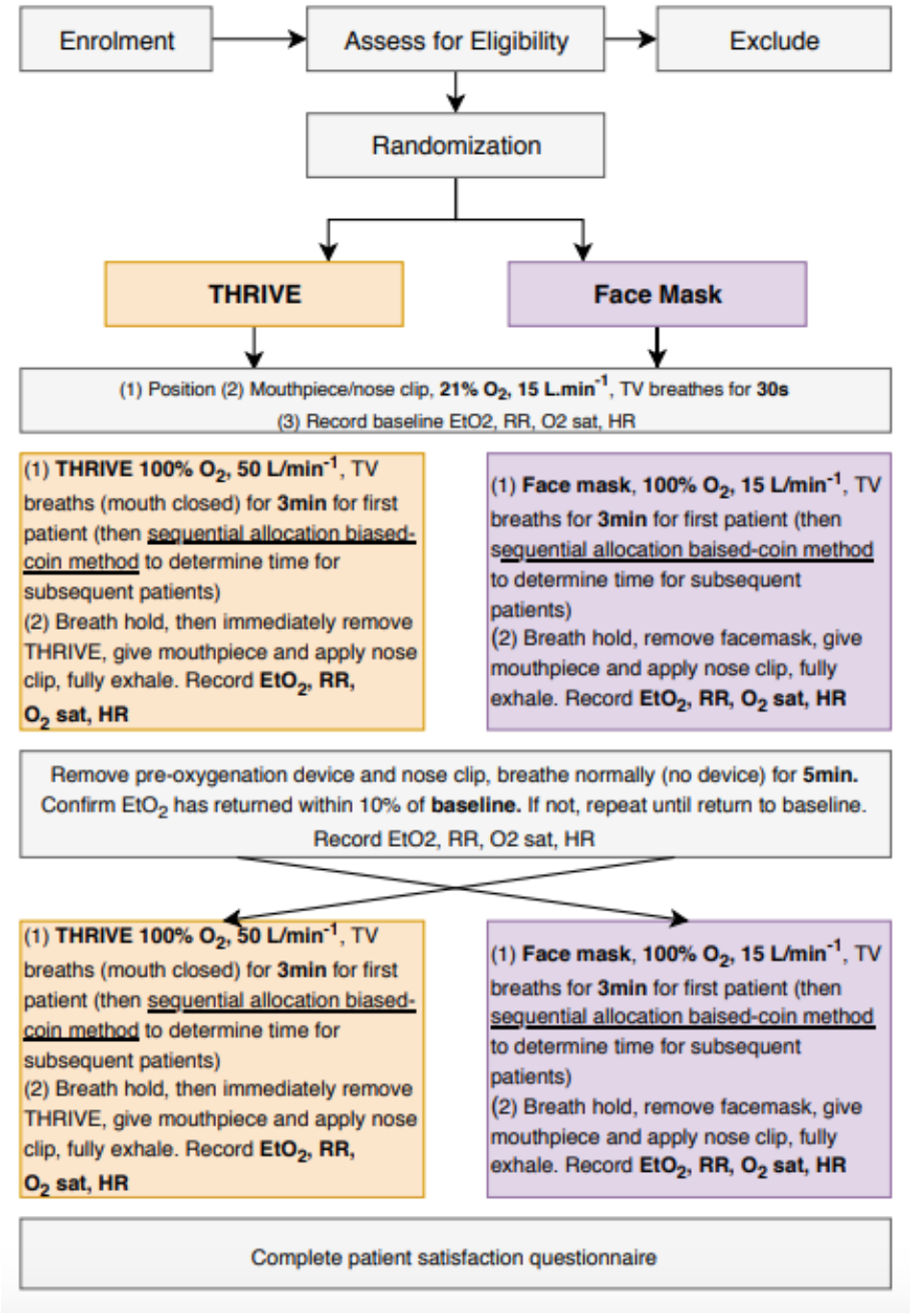

Figure 3. Study Flow Diagram. Abbreviations: Transnasal humidified rapid insufflation ventilatory exchange (THRIVE), oxygen (O_2), tidal volume (TV), End-tidal oxygen concentration (EtO_2), respiratory rate (RR), oxygen saturation (O_2 sat), heart rate (HR).

Data to be collected:

- Participant demographics including age, height, most recent weight and body mass index, gravidity, parity and gestation.
- Co-morbidities, complications of pregnancy, ASA grade, reason for admission.
- End-tidal oxygen concentration:
  - In the THRIVE group at baseline (after 30s of TV breathing) and at the end of the pre-oxygenation technique (immediately after the breath hold).
  - In the Facemask group at baseline (after 30s of TV breathing) and the end of the pre-oxygenation technique (immediately after the breath hold).
- Oxygen saturation, respiratory rate and heart rate after 30s of breathing room air (baseline), every 60s from starting pre-oxygenation technique and at time of EtO_2 measurement.
- In the THRIVE group, an estimate of how much time the participant managed to breathe with their mouth closed during the pre-oxygenation period on a 5-point Likert scale: Mouth closed the entire time, mouth open sometimes, mouth open half of the time, mouth open occasionally or mouth open the entire time.

The demographic information and medical history will be collected from the medical chart by one of the study team after the participant has given informed consent to participate in the study. The participant satisfaction data will be collected at the end of the breathing procedures by one of the study team who were conducting the study procedure. This will be done by asking the following questions listed on the Data Collection Sheet:

1. "Please indicate how you felt from a comfort point of view breathing via the nasal oxygen device/Facemask: Completely comfortable, slightly comfortable, neither, slightly uncomfortable, completely uncomfortable."
2. "Please indicate how you felt from an acceptability point of view breathing via the Nasal Oxygen device/Facemask: Acceptable, slightly acceptable, neutral, slightly unacceptable or unacceptable."
3. Which breathing device did you prefer: nasal oxygen device or facemask?

Sample size:

We chose a sample size of 20 participants in each group (40 total participants). No formal statistical sample size analysis was performed. Simulation studies have suggested that using 20 to 40 patients in up–down sequential allocation trials will provide stable estimates of the target interval. In addition, the non-independence and unknown distribution of data of an up–down study prevent the development of theoretically rigorous rules to calculate the necessary sample size[14].

Statistical analysis:

Concentration of EtO_2 will be summarized using means and SD within each group. Data (ordinal) from Likert scales will be described using modes and percentages. Isotonic regression will be used to determine the primary outcome data.

Isotonic regression using the pooled-adjacent-violators algorithm will be used to determine the modified isotonic estimator for the ED90 interval. (Stylianou M et al. Biometrics 2002) In short, the observed success rate (percentage of patients with EtO2>=90) will be calculated for each time

interval. Isotonic regression using the pooled-adjacent-violators algorithm will then be used to obtain point estimates for the success rates that were constrained to be monotonic increasing with time interval. The modified isotonic estimator for ED_{90} will then be obtained via linear interpolation between the highest time interval with an estimated success rate <90% and the lowest time interval with an estimated success rate >90%. To provide an interval estimate for EI_{90} and for the probability of success at the sample estimate for the EI_{90}, a 95% confidence interval (CI) will be constructed using the bootstrap approach described by Stylianou et al. To account for the repeated-measures study design, ETO2 at each time points will be compared across all time points using generalized estimating equations. Using a logit link function, generalized estimating equation analyses were also performed to compare the percentage of patients with effective preoxygenation (ETO2 >=90) between different time interval groups.

This protocol has been developed with the assistance of Arianne Albert PhD, Biostatistician at the Women's Health Research Institute, BC Women's Hospital. Arianne Albert will assist with the statistical analyses of any data collected.

Data management:
De-identified participant data will only be collected by members of the research team using paper data collection forms. Once collated, the data will then be entered onto a password protected Microsoft Excel spreadsheet on a password protected computer in the locked Research Assistant's office. The paper data collection forms will be stored for 5 years following publication of the study and then destroyed using the hospital's privacy and confidentiality shredding service. Participant identifiable data will not be recorded.

Our project will be registered with the Research and Development department at the BC Women's Hospital. This study will also be registered online with http://www.clinicaltrials.gov/.

We will write up the results of the study and submit for presentation at medical conferences and publication in a medical journal so that we can tell other doctors about our findings. This may help to improve care for patients at other hospitals.

Safety:
No harm is expected from participating in this study. However, we are aware that this study aims to collect data during a potentially stressful admission to hospital. Therefore, data collection will always be secondary to the delivery of standard patient care and maternal wellbeing.

It is well described that prolonged high levels of oxygen (hyperoxia) can cause tiny parts of the lung to collapse and lead to the production of oxygen free radicals, which may cause lung inflammation[15]. However, shorter periods of hyperoxia have not been shown to cause any adverse inflammatory effects when breathing 100% oxygen for 3.5 hours[16]. In addition, increased levels of oxygen free radicals have been shown to be independent of the inspired concentration of oxygen during Cesarean delivery and this is not known to affect fetal outcomes[17][18] . During this study, participants will only be breathing 100% oxygen for a maximum of 8 minutes and therefore this should not cause any adverse effects to either the participants or their baby.

Feasibility:

At BCWH we perform 15-20 elective Cesarean deliveries under neuraxial anesthesia per week. A conservative recruitment of approximately 10% of these patients would equate to an average of 2 participants per week. We anticipate that this study would be completed in approximately 20 weeks from the start of recruitment.

Financial cost:
The current cost of a disposable anesthetic facemask, heat moisture exchange filter, mouthpiece and nose clip at BCWH are $3.01, $2.71, $0.74 and $0.98 respectively. The Optiflow™ THRIVE system has previously been purchased by the Department of Anesthesia at BCWH. The disposable components for the Optiflow™ THRIVE system are the nasal cannulae (including filter) and multi-patient circuits (which can be used for 24hrs), costing $24 and $65 respectively. This equates to a maximum total cost of approximately $7,715 for the study, but could be less if multiple patients use a single THRIVE circuit within 24hrs. We will apply for research grant funding; however, if this is not successful, it will be funded by the Department of Anesthesia at BCWH.

Disclosure:
Nothing to declare.

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