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High-flow nasal oxygenation versus standard oxygenation for gastrointestinal endoscopy with sedation. The prospective multicentre randomised controlled ODEPHI study protocol

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ABSTRACT

Introduction Hypoxaemia is a major complication during gastrointestinal endoscopy (GIE) procedures (upper/lower) when performed under deep sedation in the procedure room. Standard oxygen therapy (SOT) is used to prevent hypoxaemia. Data suggest that risk factors for hypoxaemia under deep sedation during GIE are obstructive sleep apnoea syndrome, a body mass index above 30 kg/m², high blood pressure, diabetes, heart disease, age over 60 years old, high American Society of Anesthesiologists physical status class and the association of upper and lower GIE. High-flow nasal oxygenation (HFNO) may potentially improve oxygenation during GIE under deep sedation. We hypothesised that HFNO could decrease the incidence of hypoxaemia in comparison with SOT.

Methods and analysis The ODEPHI (High-flow nasal oxygenation versus standard oxygenation for gastrointestinal endoscopy with sedation. The prospective multicentre randomised controlled) study is a multicentre randomised controlled trial comparing HFNO to SOT during GIE (upper and/or lower) under deep sedation administered by anaesthesiologists in the procedure room. Three hundred and eighty patients will be randomised with a 1:1 ratio in two parallel groups.

The primary outcome is the occurrence of hypoxaemia, defined by a pulse oximetry measurement of peripheral capillary oxygen saturation (SpO_2) below or equal to 92% during the GIE procedure. Secondary outcomes include prolonged hypoxaemia, severe hypoxaemia, need for manoeuvres to maintain upper airway patency and other adverse events.

Ethics and dissemination This study has been approved by the ethics committee (CPP Sud Est Paris V, France), and patients are included after informed consent. The results will be submitted for publication in peer-reviewed journals. As provided for by French law, patients participating in the study are informed that they have the possibility to ask the investigators, once the study is completed, to be informed of the overall results of the study. Thus, a summary of the results will be sent by post to the participants on request.

Trial registration number ClinicalTrials.gov Registry (NCT03829293).

Strengths and limitations of this study

- This is the first pragmatic randomised multicentre study comparing high-flow nasal oxygenation (HFNO) to standard oxygen therapy (SOT) for the oxygenation of patients at risk of hypoxaemia while undergoing gastrointestinal endoscopy (upper and/or lower).
- Rather than comparing HFNO with high fraction of inspired oxygen (FiO_2) versus SOT with, as usual, low oxygen flow and consequently lower FiO_2, roughly the same apparent level of applied FIO_2 is targeted in both groups, by adjusting gases flows; this is intended to test whether HFNO may improve oxygenation through positive end-expiratory pressure and/or dead space washout effects.
- The exact FiO_2 cannot be guaranteed in the SOT group, that is why we used pre-existing abacus to get the best equivalence.
- Technically, the practitioners, other caregivers and patients cannot be blinded to the study arm, but the occurrence of peripheral capillary oxygen saturation less than or equal to 92%, the primary outcome measure, is recorded and printed out, thereby allowing delayed reading by an assessor blinded to treatment allocation.
- In this real-life and pragmatic study, the type and dosages of sedative drugs are not standardised, but the use of opioids that may depress respiration even at low doses is recorded and constitutes a variable of stratification.

INTRODUCTION

Most gastrointestinal endoscopy (GIE) procedures are performed under deep sedation managed by an anaesthesiology team in the

operating room.[1] Sedation during upper and/or lower GIE improves the quality of examination, patient comfort and allows performing complex procedures.[2–4] The recent British guidelines suggest that deep sedation, under the responsibility of anaesthesiologists, should also be considered for, but not limited to, cholangiopancreatography endoscopic retrograde, digestive echoendoscopy and any prolonged therapeutic procedure.[5]

Hypoxaemia is the most common complication during GIE procedures performed under sedation, and may occur in 1%–85% of the procedures. This variation is explained by the heterogeneity of studied populations and different definitions of hypoxaemia.[6–17] Hypoxaemia is multifactorial: pharyngeal obstruction caused by endoscope introduction in upper GIE and insufflation during the procedure (upper or lower) are responsible for a respiratory mechanical disorder through diaphragm compression. Myorelaxation and respiratory depression induced by sedation may cause upper airway obstruction and a drop in functional residual capacity, which in turn may lead to hypoxaemia.[18] Hypoxaemia can affect morbidity and mortality as a result of myocardial ischaemia, cardiac rhythm disorders or cerebral hypoxia.[12 19 20]

Several studies have identified the main risks factors for hypoxaemia during GIE: obstructive sleep apnoea syndrome (OSA) diagnosed or highly suspected with the STOP-BANG questionnaire (STOP-BANG ≥3),[17 21] obesity defined by a body mass index (BMI) ≥30 kg/m²,[22 23] high blood pressure, diabetes, heart disease,[24] elderly patients over 60 years old,[6 8 23] high American Society of Anesthesiologists (ASA) physical status class and the association of upper[8 25] and lower GIE.[24]

To prevent and to treat hypoxaemia, standard oxygen therapy (SOT) is recommended by the ASA and the American Society of Gastrointestinal Endoscopy. However, there is no recommendation about the device to be used for oxygenation. Many techniques such as jet ventilation or new interfaces for oxygenation aimed at reducing hypoxaemia have been studied, but none have really modified current clinical practice.[26–28]

High-flow nasal oxygenation (HFNO) could be an interesting alternative. Gases are heated, humidified and dispensed through large bore nasal cannula, improving patient comfort and tolerance. The gas flow is usually set as high as 40–70 L/min and allows the administration of a precisely known inspired oxygen fraction (FiO_2) (21%–100%). The high gas flow maintains a slight positive end-expiratory pressure (PEEP) in the airway by opposing resistance to expiration and also exerts a dead space washout effect.[29–34]

HFNO is commonly used in intensive care units but is still underused in the operating room.[35 36] Guidelines of the French Society of Anaesthesiology recommend the use of HFNO for patients at risk of desaturation during tracheal intubation to safely extend the apnoea time if necessary.[37] HFNO showed a benefit in various perioperative procedures such as during awake fibreoptic intubation.[38] Some studies showed a benefit of HFNO as compared with SOT, especially to safely extend the apnoea time in laryngeal surgery[32 39 40] or in morbidly obese patients.[41] In dental surgery under sedation, HFNO also reduced hypoxaemia and decreased the blood carbon dioxide concentration with a flow set at 50 L/min compared with SOT.[42]

Endoscopic retrograde cholangiopancreatography retrograde and digestive echoendoscopies are complex procedures often carried out under general anaesthesia. In this context, HFNO may help to reduce the need for tracheal intubation by improving the respiratory tolerance of deep sedation.[43]

In a recent multicentre randomised trial in 1994 patients, HFNO (FiO_2 100% and gas flow from 30 to 60 L/min) significantly decreased the incidence of hypoxaemia (from 8.4% to 0%) compared with SOT (2 L/min with nasal cannula) in healthy (ASA I and II) patients during gastroscopy.[44] These results were also found in a recent single-centre randomised trial which showed that HFNO decreased hypoxaemic events compared with SOT during upper GIE in healthy patients (ASA I and II).[45] The comparison was made between three arms: standard bite-block with standard oxygen (O_2) cannula (5 L/min of O_2; control arm) versus standard bite block with HFNO (30 L/min, 100% O_2) versus mandibular advancement (MA) bite block with standard O_2 cannula. There were significant reductions of hypoxaemia in the HFNO and MA groups versus control group. However, the rate of hypoxaemia was higher in the HFNO group than in the MA bite block, a finding potentially due to a too low flow (30 L/min) used for HFNO.

Only one study showed different results during colonoscopy. This single-centre trial in morbidly obese patients was stopped for futility. At similar FiO_2 (36%–40% at 60 L/min in HFNO group vs O_2 flow of 4 L/min in SOT group), HFNO did not reduce the rate of hypoxaemia (39.3% vs 45.2%, respectively, p=0.79).[46] However, there was a trend favouring HFNO in patients at risk of sleep apnoea syndrome. To explain the lack of between-group difference, the authors stated that knowledge of the intervention may have influenced the anaesthesiology team administering propofol, leading them to adjust the depth of sedation based on their own beliefs regarding the safety and performance of the device being used. The gas flow was 60 L/min for HFNO, but the gas flow could be raised to 70 L/min to increase the positive pressure effect.

Up to now, HFNO has never been studied in patients at risk of desaturation during GIE (upper and/or lower) under deep sedation. Moreover, the settings of HFNO were very different in the previous studies described above: a FiO_2 of 100% was often compared with low flow of standard oxygen, and the HFNO flows used were also different between studies.

Hence, we hypothesise that HFNO during GIE under sedation could decrease the incidence of hypoxaemia in comparison with SOT through its PEEP and dead space washout effects. For this purpose, similar initial FiO_2 is set in both groups of patients at risk of desaturation.

METHODS AND ANALYSIS

Design

This is an investigator-initiated, prospective, multicentre (four centres) randomised, controlled, superiority trial comparing HFNO with SOT during GIE (upper and/or lower) performed under sedation in the operating room. Our main hypothesis is that HFNO may reduce the incidence of hypoxaemia in comparison with SOT. Three hundred and eighty eligible patients will be randomised in a 1:1 ratio into 2 parallel groups of 190 patients each.

A computer-generated randomisation is performed with stratification according to the centre and the use of opioids in a 1:1 ratio, using a centralised web-based management system (EOL Random, Medsharing, France). Investigators are blinded to the block sizes. After randomisation, the intervention (HFNO or SOT) is initiated. The allocated group assigned by randomisation is recorded in the patient medical chart and in a dedicated chart gathering the whole randomised patient population of the trial.

Oral and written information is given during the anaesthesia consultation several days to several weeks before endoscopy. Written consent is obtained after verification of the eligibility on the day of the GIE procedure. Patients have the right to withdraw their consent and discontinue their participation at any time for any reason.

Patients are expected to be included during an 18-month period starting in March 2019.

- March 2019: protocol approval from the ethics committee and trial tools development (case report form, randomisation system).
- 2019–2020: inclusion of patients.
- 2020: cleaning and closure of the database. Data analysis, writing of the manuscript and submission for publication in a peer-reviewed journal.

Study setting

The trial is carried out in four medical centres, three public hospitals (Orléans Regional Hospital; the Tours University Hospital; the Dax Hospital, in France) and one private hospital (Oréliance Pôle Santé, Orléans, France). The sponsor (Centre hospitalier regional d'Orléans, France) organises on-site training and support regarding methods and ethics before and during the study.

Study objectives

The primary study objective is to compare the rate of hypoxaemia during GIE, defined as an SpO_2 ≤92% observed between anaesthesia induction and the end of the procedure between the intervention group (HFNO) and the standard care (or control) group (SOT).

The secondary objectives are to compare between groups:

- The incidence of hypoxaemia (defined as SpO_2 ≤92%) in the recovery room.
- The number of episodes of apnoea (defined as respiratory rate ≤6/min).
- The incidence of hypoxaemia with an SpO_2 ≤90%.
- The incidence of severe hypoxaemia (defined as SpO_2 ≤85%).
- The incidence of prolonged hypoxaemia (SpO_2 ≤92% during ≥60 s).
- The rate of modifications of oxygen flow in both groups and of the FiO_2 in the HFNO group.
- The need to use mask ventilation or to perform any airway intervention.
- The evolution of the SpO_2, respiratory rate, heart rate and blood pressure.
- The incidence of bradycardia (defined by a heart rate <50/min).
- The need for non-invasive ventilation, laryngeal mask airway or for intubation.
- The need to stop the procedure.
- The incidence of the failure of the endoscopic procedure.
- The duration of the endoscopy.
- The duration of sedation (from the induction to the awakening of the patient).
- The time spent in recovery room.
- The number of ambulatory patients who needed to be hospitalised after the procedure.
- The frequency of serious adverse events.

Data collection

Multiparameter monitoring data recordings (SpO_2, heart rate, blood pressure, respiratory rate and capnography if available) are made automatically.

SpO_2 is recorded every minute during intervention by the usual multiparameter monitor (Datex Ohmeda or Carescape B450 or Carescape B650, General Electric Healthcare) enabling the capture of prolonged hypoxaemia defined as an SpO_2 ≤92% for ≥60 s. Outcomes are collected on paper case report forms (CRF). Collection of data stops when the patient leaves the recovery room. The trends of vital signs, including SpO_2 recordings, are printed out and put in an envelope with the CRF. The medical history is collected from the anaesthesia consultation chart and reported on the CRF. Any protocol deviations are recorded in either the CRF or the medical records; both are checked by a clinical research assistant to ensure that all protocol deviations and adverse events are in the database.

Investigators not involved in the care of enrolled patients and blinded to the allocated intervention will read the recordings of SpO_2 captured and check if they were in concordance with events reported by clinicians on the paper CRF. SpO_2 values≤92% observed on these records will define hypoxaemia unless technical reasons for poor SpO_2 signal are reported by the clinicians. In every case, in the absence of specific comments on the CRF, SpO_2 values≤92% recorded by the usual multiparameter monitor will be considered as reflecting hypoxaemia.

Sample size

In a short preliminary observational study conducted on 100 patients undergoing GIE with the usual SOT, we

found a 24% incidence of hypoxaemia (SpO_2 ≤92%). Based on published studies that showed a two-to-threefold decrease in hypoxaemia rate with different oxygenation devices compared with standard oxygenation,[26 27 47] we assume that the oxygenation with HFNO will decrease the incidence of hypoxaemia from 24% to 12%. With a 2-side alpha risk set at 5% and a statistical power of 80%, 176 patients in each group are needed to demonstrate such a difference. We chose to increase this number to 190 patients in each group to anticipate possible dropouts for any reason and possible unreliable SpO_2 readings for technical reasons as determined by the anaesthesiology team.

Recruitment and informed consent

Explanatory posters are displayed in the waiting room of the anaesthesia consultation service.

During the anaesthesia consultation, the information letter and explanations of the study are given to the patient by an investigator (see online supplementary file 1).

The patients who accept to participate sign the written informed consent form on the day of the GIE during the preanaesthetic visit (see online supplementary file 2). Then, the randomisation is performed at the entrance in the operating room. Figure 1 shows the schedule of enrolment, interventions and assessments.

Eligibility criteria

Inclusion criteria

- Patients older than 18 years old.
- Patients scheduled for GIE (upper and/or lower endoscopy), for which sedation with maintenance of spontaneous breathing is planned (as determined during the anaesthesia consultation).
- Patients who have provided signed consent.
- At risk of hypoxaemia with at least one of the following criteria:
  - Underlying cardiac pathology (left ventricular dysfunction with a left ventricular ejection fraction ≤45%, documented ischaemic heart disease,

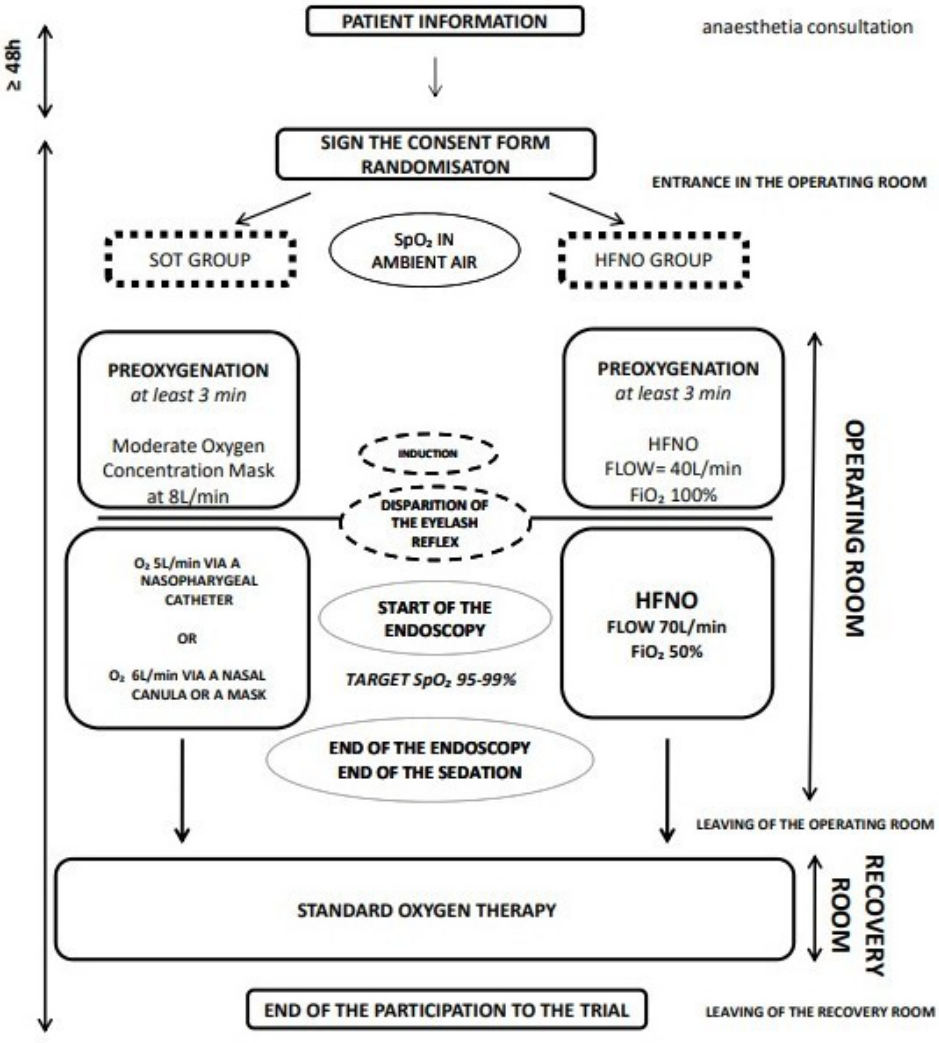

Figure 1 Chart illustrating the study. FiO_2, high fraction of inspired oxygen; HFNO, high-flow nasal oxygenation; SOT, standard oxygen therapy; SPO_2, peripheral oxygen saturation.

chronic atrial fibrillation, medical history of cardiogenic pulmonary oedema, arterial hypertension).
- Underlying respiratory pathology (chronic obstructive pulmonary disease (COPD), pulmonary emphysema, bronchiectasis, asthma, obesity hypoventilation syndrome, restrictive respiratory disease).
- Older than 60 years old.
- ASA II, III or ASA IV.
- Obesity defined by a BMI≥30 (kg/m²).
- OSA diagnosed or highly suspected with the STOP-BANG questionnaire (STOP-BANG ≥3).[48]

Exclusion criteria

- GIE performed in emergency.
- Necessity to intubate the patient for the procedure.
- Patient under oxygen therapy at home.
- Tracheostomised patient.
- Pregnancy.
- Patient not affiliated or excluded from social protection.
- Patient deprived of liberty by court or administrative decision.

Intervention

In the operating room, before starting the procedure, vital signs including ECG, non-invasive blood pressure and SpO_2 via pulse oximeter are displayed and recorded in each patient using standard anaesthesia monitors. SpO_2 is recorded in ambient air (figure 1).

Preoxygenation with the oxygen device depending on the randomly allocated intervention is performed (at 40 L/min FiO_2 100% in the HFNO group and at 8 L/min in the SOT group) for at least 3 min before starting the induction.

In this pragmatic study, investigators are free to choose the drugs administered for the induction. During the procedure, in both groups, if deemed necessary, the investigator can raise the FiO_2 or the gas flow in case of desaturation or for any reason. In case of major intolerance, HFNO or SOT can be stopped and replaced by any other oxygen therapy technique (except HFNO in the SOT group). Tracheal intubation is allowed if necessary. In every case, investigators have to record all events in the case report form.

At the end of the GIE, patients are transferred to the recovery room and the interventional period is over. HFNO is not used in the recovery room. In the recovery room, SOT is immediately applied to all patients until deemed unnecessary, according to our current practice.

As in the study by Lin *et al*, hypercapnia is not monitored. To limit the risk of hypercapnia in our study, the FiO_2 is set at 50% with a flow at 70 L/min.[44]

Intervention group

HFNO is administered with a Optiflow Nasal High Flow device and specific anaesthesia nasal cannula fitted with a filter (Fisher & Paykel Healthcare, New Zealand).

Settings for preoxygenation are a flow rate of 40 L/min and FiO_2 of 100% for a period of at least 3 min. Induction is done after the preoxygenation time. Once the eyelash reflex has disappeared, the flow is increased to 70 L/min (for a higher PEEP effect) and the FiO_2 is set at 50%. The decision to set the FiO_2 at 50% was made to obtain a similar FiO_2 in both groups and to reduce the risk of hyperoxia and hypercapnia (particularly in patients with COPD).

Control group

The settings for preoxygenation are an oxygen flow rate of 8 L/min with a face mask for a period of at least 3 min with the FiO_2 calculated at 100% according to conversion tables. Induction is performed after the preoxygenation time. Once the eyelash reflex has disappeared, O_2 is then administered either with a nasal cannula (or a mask) at 6 L/min or with a nasopharyngeal catheter at 5 L/min (according to the current practice in each centre).

Similar FiO_2

During the preoxygenation time, FiO_2 is not exactly similar between groups. In the HFNO group, the FiO_2 is set at 100% with a flow at 40 L/min and in the SOT the flow is set to 8 L/min with pure O_2. This was chosen to obtain the most effective preoxygenation that each method may allow. To be as similar as possible, the SOT group could have benefited from a preoxygenation at 15 L/min but it requires changing the interface. A change of interface may lead to an ambient air mixture and may decrease the effectiveness of the preoxygenation. For pragmatic reasons and to favour the adherence to the protocol, we wanted to standardise and make things as simple as possible. In addition, preoxygenation is undoubtedly important for patients exposed to apnoeic periods due to neuromuscular blockage or very deep sedation. However, in this trial, the patients are supposed to keep breathing spontaneously.

During the procedure, we chose to set a similar initial FiO_2 in both groups not to disadvantage the SOT group. Furthermore, similar FiO_2 will allow to determine if the HFNO-induced PEEP and dead space washout effects could be beneficial. Similar FiO_2 is obtained by using a conversion table.[49–51] Hence, after a standardised preoxygenation period, oxygen is administered in the SOT group either with a nasal cannula (or a mask) at 6 L/min or with a nasopharyngeal catheter at 5 L/min (according to the current practice in each centre) at a calculated FiO_2 of 50% and in the HFNO group with the O_2 flow at 70 L/min and FiO_2 set at 50% ensuring a comparable FiO_2 for both groups.

Outcome

The primary outcome is the occurrence of hypoxaemia defined as an SpO_2 ≤92% during the sedation. The secondary outcomes are apnoea, prolonged hypoxaemia (SpO_2 ≤92% during ≥60 s), desaturation with a drop ≥5% in SpO_2 after preoxygenation, hypoxaemia with SpO_2 ≤90%, severe hypoxaemia defined as SpO_2 ≤85%, bradycardia (defined as heart rate <50/min) and hypoxaemia during the stay in the recovery room. Modifications of oxygenation settings, need for mask ventilation, manoeuvres to maintain upper airway patency, non-invasive ventilation, laryngeal

mask airway or intubation, duration of endoscopy, duration of sedation, time spent in recovery room, hospitalisation and serious adverse events are also recorded.

Statistical analysis

R statistical software V.3.6.0 and MedCalc V.18.2.1 (MedCalc Software, OstendMariakerke, Belgium) will be used for data processing and analysis. A predefined analysis plan will be followed. The analysis report will follow the requirements of the Consolidated Standards of Reporting Trials statement.[52]

A full or modified intention-to-treat (ITT) principle will be followed, depending on (1) whether, for technical reasons, some patients will or will not show unreliable SpO_2 readings as determined by the anaesthesiology team and (2) whether some patients will or will not withdraw consent, since as required by French law, patients withdrawing their consent should not be analysed.

The primary endpoint, hypoxaemia with SpO_2 ≤92% and all the other categorical endpoints will be compared between groups using χ^2 tests adjusted for the variables of stratification. The between-group difference will be expressed as the adjusted absolute risk difference derived from a mixed-effect logistic regression taking into account the variables of stratification (centre as a random effect variable and use of opioids as a variable with fixed effect) and its 95% CI as determined by bootstrapping (2000 random samples).

Evolutions of SpO_2, arterial blood pressure and heart rate will be compared using distinct mixed linear models in which the patient will be considered as a random effect variable. The variable indicating the group of randomisation will be entered as a fixed effect variable. The interaction between randomisation and stratification variables will be tested. The results will be graphically presented in the form of estimated marginal mean evolution (and 95% CI) in each randomisation group, and possibly in each stratification group if the interaction is significant.

The duration of GIE, duration of sedation and the length of stay in the recovery room will be compared between groups using the Mann-Whitney test taking into account the stratification. The interaction between the group of randomisation and the group of stratification will also be tested.

Protocol deviations and reasons for withdrawal from the study will be described.

A per-protocol analysis in the population of patients having completed the entire procedure with the oxygenation device allocated by randomisation, if different from the ITT population, will be performed.

A subgroup analysis is planned: if there is a significant interaction between the type of endoscopy (upper, lower or both combined) and the randomisation group, the results by type of endoscopy will be presented.

In case of missing data, multivariable imputation by chained equation is planned. Missing values of SpO_2, the primary outcome measure, will not be replaced.

ETHICS AND DISSEMINATION

Investigators will make available to the persons responsible for the follow-up, the quality control or the audit of the research, the documents and individual data strictly necessary to the control, according to the provisions of law (articles L.1121-3 and R.5121-13 of the French Public Health Code).

A paper CRF is used and is considered as a source document. Data will be captured by two members of the study team into a secured spreadsheet application (Excel). Data will be handled according to French law. All original records will be archived at trial sites for 25 years. The clean database file will be anonymised and kept for 25 years. Only four members of the ODEPHI's team (the two first authors, the statistician and the last author) will have access to the final trial dataset. Investigators of each institution will not have access to the final trial dataset.

The study can be suspended or prematurely interrupted in case of unexpected serious adverse events, requiring the examination of the evolution of all the patients already included. Orléans Regional Hospital reserves the right to interrupt the study at any time if the inclusion objectives are not reached.

The investigator can definitively or temporarily stop the patient's participation for any reason which would better serve the patient's interests and especially in case of serious adverse effects. In this case, these reasons are collected, assessed and reported. An investigator at each centre is responsible for enrolling patients in the study, ensuring adherence to the protocol and completing the CRF.

Research assistants regularly monitor all the centres on site to check adherence to the protocol and the accuracy and completeness of the data recorded.

The results will be submitted for publication in peer-reviewed journals. As provided for by French law, patients participating in the study are informed that they have the possibility to ask the investigators, once the study is completed, to be informed of the overall results of the study. Thus, a summary of the results will be sent by post to the participants on request.

Informed consent

Written consent is obtained from all participants.

Patients are informed of the study orally and in writing (see information notice and consent form in online supplementary file 1 and online supplementary file 2) by the investigators before performing the procedure. The competent patient, after receiving appropriate disclosure of the potential risks and benefits of the study and having understood these explanations makes a voluntary informed decision to proceed. The participant is free to withdraw his/her consent to participate at any time and need not offer any reason for doing so. All this information appears on the information note given to the patient. Refusal or consent is recorded by the investigator on a screening log.

DISCUSSION

Hypoxaemia is one of the main concerns for anaesthesiologists during invasive procedures such as GIE performed in spontaneous breathing patients under deep sedation.

The demand for deep sedation is growing as complex diagnostic and therapeutic procedures in patients with greater comorbidities are increasingly frequent. While deep sedation and general anaesthesia allow a better tolerability and seems to improve the efficacy and/or the diagnostic yield of GIE,[5 53] ensuring the safety of the GIE procedures under deep sedation is essential.

HFNO is commonly used in intensive care units. It is now progressively spreading in the operating room to optimise preoxygenation before the induction of anaesthesia. Up to now, there are few data related to the use of HFNO during GIE and especially in patient with comorbidities. Because the incidence of hypoxaemia is low in healthy people and because HFNO is more expensive than SOT, we chose to include only patients at the highest risk of desaturation.

As the ODEPHI trial is aimed to be pragmatic, we design the study to induce minimal change in current practice and left the anaesthesiologists free of choosing the anaesthetic drugs used for induction.

Importantly, initial FiO_2 is planned to be equivalent in both groups not to disadvantage the control group. Most studies compared HFNO with 100% FiO_2 versus 2–5 L/min of standard oxygen, a gas flow that roughly results in a FiO_2 between 28% and 45% (44–46). On the contrary, in the ODEPHI trial, similar initial FiO_2 in both groups will allow to determine if the HFNO-induced PEEP and dead space washout effects could be beneficial. In addition, in the HFNO group, the gas flow is set at its maximum value (70 L/min) contrary to previous studies, and all patients undergo preoxygenation before induction.

The study was launched on 26 March 2019. This inclusion rate is rapid, which should favour high-quality data acquisition by avoiding fatigue of investigators and research teams. Until now, no serious adverse event related to the study procedures have been declared by investigators. Dropouts for any reason are rare. Together these elements give hopes for an early, full completion of the study.

To conclude, the ODEPHI trial is an investigator-initiated pragmatic randomised controlled trial undertaken to test the hypothesis that HFNO may decrease the rate of hypoxaemia during GIE under deep sedation compared with SOT at similar FiO_2. This study presents several innovative aspects. First, patients are at risk of hypoxaemia. Second, upper and/or lower GIE under deep sedation are studied. Finally, a similar initial FiO_2 is used not to disadvantage the SOT group. If the results are positive, the use of HFNO might become the standard of care to improve the safety of GIE performed under deep sedation in patients at risk of hypoxaemia.

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Contributors M-AN, LF, AE and TB designed the study and wrote the study protocol. All authors gave final approval of the manuscript. TB determined the sample size and planned the statistical analysis. M-AN is the principal investigator and coordinator of ODEPHI. M-AN, AE, LF, AA, W-SM, OB and FR designed the implementation aspects of this protocol. AE and LF have collected the data.

Funding Costs related to this research will be covered by the sponsor: Centre Hospitalier Régional d'Orléans. For this trial, the firm Fisher & Paykel (Auckland, New Zealand) provides high-flow oxygen therapy equipment to all the participating centres but has no other role in the study, with the exception of a minor assistance in preparing the manuscript.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The study was approved for all centres by the institutional review board of Orléans' Hospital, as well as the regional ethics committee (Comité de Protection des Personnes Paris Sud Est V) on 07 March 2019. "No DSMB has been established for this trial. The protocol was approved by an Ethics Committee which did not ask for a DSMB. The study has been classified as a study bringing minimal risk by the Ethics committee and the French Ministry of Health. The study is carried out in centres with an experienced anaesthesia team. Patients are continuously monitored clinically and through multiparametric monitoring by an anaesthesia team during the procedure. Several studies have been carried out on HFNO and have never encountered any major incidents. The occurrence of death and any serious adverse event during the procedure is timely reported to the sponsor (who in turn is responsible for timely declaration to the National Health Authorities)." The ethics committee (CPP of Paris Sud Est V, France) approved our study (19-ORLE-01) on March 2019. The study is conducted in accordance with the current revision of the Declaration of Helsinki, 1996, International Conference on Harmonisation Note for Guidance on Good Clinical Practise (ICH GCP) and the applicable French regulatory requirements.

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