**‘Apnoeic Oxygenation: A comparison of Nasal Prongs to Nasopharyngeal Cannula on Oxygenation During Laryngoscopy’.**

After induction of general anaesthesia and administration of a muscle relaxant, the patient becomes apnoeic. If ventilation of the patient is not achieved by other means, such as when face – mask ventilation is impossible or contraindicated, the time until successful endotracheal intubation is achieved and ventilation commenced is an apnoeic period. If the apnoeic period is long, such as when intubation is difficult, critical arterial oxygenation desaturation of the patient may occur.

Many authors have explored means of maintaining oxygenation during this period of apnoea with various airway adjuncts. The term ‘apnoeic oxygenation’ has been generated to describe such efforts. The physiological basis of the term rests in the different solubilities of Oxygen and Carbon Dioxide. During apnoea, the rate of oxygen extraction from the alveoli is approximately 250 ml min-1. This is considerably more than the amount of Carbon Dioxide entering the alveoli, due to the fact that it is much more water soluble than Oxygen. Indeed, only 10% of the CO2 produced every minute reaches the alveolar space. The total volume of gas within the lungs decreases rapidly and the intrathoracic pressure decreases at a rate dependent upon Oxygen consumption and thoracic compliance. A patent airway allows Oxygen to diffuse into the apnoeic lung, resulting in ‘apnoeic mass-movement Oxygenation’, which has been shown in animal and simulated human studies to maintain oxygen saturation for up to 100 minutes.

The purpose of this study is to explore simple, yet potentially effective means to improve the delivered Fraction of Inspired Oxygen concentration (FiO2) during this apnoeic period. We aim to compare the effects of the administration of Oxygen at 15L/minute with nasal prongs to nasopharyngeal cannula. Our measured primary endpoint is FiO2 at the laryngeal inlet, measured by a gas sampling line after three minutes of apnoea, prior to intubation. Our secondary endpoints are peripheral arterial oxygen saturation (SpO2) after three minutes of apnoea, and the proportion of patients who desaturate to ≤ 94% within three minutes of apnoea.

Previous studies have described the potential beneficial effects of various additional oxygenation devices during the peri-intubation period. However, the application of nasal prongs during this time has not been compared to a nasopharyngeal cannula as a means of oxygenation in human subjects. Furthermore, only one study we found measured Fi02 as the primary endpoint as opposed to oxygen saturations.

Our Intervention

Multiple research and review articles describe the benefits and possibilities of using apnoeic oxygenation and extending time to critical desaturation during intubation attempts. Many others have attempted to determine the best method for achieving this.

Oxygenation during intubation via nasal prongs or nasopharyngeal cannulae have been demonstrated to serve this purpose. We wanted to utilise, and take advantage of these two pieces of equipment common to most emergency departments and operating environments. Additional benefits of these include the low cost, safe and easy application, ability to be kept on the patient without interfering with any other aspect of the intubation routine, including view obtained at laryngoscopy. Our study attempts to directly compare the effects of nasal prongs versus nasopharyngeal cannula for apnoeic oxygenation in human subjects. We will also include a control group of no additional oxygen during the apnoea period.

Oxygen Flow Rate

Near 100% FiO2 can be obtained with nasal cannula, at high flows (15L/minute) in the apnoeic patient. Concerns about potential discomfort in the awake patient, with a nasal Oxygenation device at higher flow rates have been raised. 15 Litres/minute is usually advocated during emergency procedures rather than 6 Litres/Minutes usually adopted to be acceptable in terms of patient comfort and tolerance. Several authors have challenged this notion. . Brainardt et al (12) determined the participants’ ability to tolerate 10 minutes of nasal cannula oxygen at increasingly higher flow rates. Higher-flow nasal cannula oxygen at 15 Litres/minute was associated with some discomfort, but the discomfort quickly dissipated and caused no adverse events.

Our Endpoint

We chose to measure Fi02 values at the pharyngeal inlet as our primary endpoint. Peripheral oxygen saturations have been used by many previous studies. By using Fi02 levels, we are able to evaluate the effect of each device upon the delivery of oxygen to the patient’s laryngeal inlet. The measurement of oxygen saturations are exposed and influenced by many more variables other than that of simple oxygen delivery. The effects of shunting, increased metabolic demand, anaemia, volume depletion, and decreased cardiac output are synergistic in dramatically reducing oxygen storage in the lungs and shortening safe apnoea in critically ill patients. This is reflected by oxygen saturation measurements and are factors we, as clinicians have limited control of during the process of intubation.

We will employ a standard technique to record Fi02 levels, using a gas sampling line and inserting it through the mouth and placing it under vision into the pharynx at the laryngeal inlet.

The primary endpoint will be the FiO2 thus recorded after three minutes of apnoea, or if the patient desaturates to 94% before three minutes of apnoea has been completed, the FiO2 at the time of the saturation dropping to 94%.

Methods and Protocol

 We intend to recruit patients undergoing surgery at Southern Health, who are age ≥ 16 years, able to provide informed consent and undergoing surgery requiring a general anaesthetic, muscle paralysis and insertion of an endotracheal tube. Potential study patients will be given an information sheet (Figure 1) pre-operatively, explaining the study rationale, methodology and any implications of their involvement. Written consent will be obtained.

Exclusion criteria include preoperative Oxygen saturations on room air of ≤94%. We know that 91% to 95% saturations have values close to the precipice of the steep portion of the oxyhaemoglobin dissociation curve and should be considered high risk. Patients with greater saturations are at low risk for peri-intubation desaturation. Patients requiring a rapid sequence induction, with soft tissue or nasal structure abnormalities rendering it challenging to pass a nasopharyngeal cannula or apply nasal prongs, those predicted difficult to intubation and pregnant patients are also excluded from the study.

The procedural algorithm (Figure 2) summarises the key steps within our study protocol. After written consent has been obtained, patients are randomly assigned to one of three groups. A nasopharyngeal cannula (NC) cohort, nasal prongs (NP) cohort or control group (C). If appropriate, the nasal prongs or nasopharyngeal cannula is applied and Oxygen is delivered at a rate of 15 Litres/Minute. Pre-Oxygenation with a face mask is delivered as normal, for three minutes after which time the appropriate anaesthetic agent and paralysis is given. A timer is started and the face mask removed. Laryngoscopy is performed and an assessment is made regarding the attainable view and ease of intubation. The laryngoscope is then relaxed in position (mouth open) and a gas sampling line inserted through the mouth and placed in the pharynx at the laryngeal inlet. After three minutes intubation is performed.

There are several steps within this algorithm that permit early intubation or bag-mask ventilation before the full three minuted has elapsed. Specifically, if peripheral saturations fall to ≤94% or any event requiring the urgent placement of a secure airway or prompt re-oxygenation (e.g. aspiration). Furthermore, if the initial view at laryngoscopy is considered poor or predicted difficult, then the patient is withdrawn from the study and usual procedures to optimise oxygenation and ventilation of the patient are initiated.

FiO2 at the pharyngeal inlet at two and three minutes are recorded. Peripheral saturations will also be noted after three minutes. Our primary endpoint is the FiO2 at the pharyngeal inlet prior to intubation, after three minutes of apnoeic Oxygenation Our secondary endpoints are peripheral arterial oxygen saturation (SpO2) after three minutes of apnoea, and the proportion of patients who desaturate to ≤ 94% within three minutes of apnoea. We have developed study record forms to aid documentation (Figure 3). These forms will be kept in a box within the theatre complex at Monash Medical Centre and Moorabbin Hospital.

A power analysis has been performed. We will compare FiO2 between the intervention groups with a t-test. We consider a difference of 5% or more in FiO2 between nasal prongs and nasopharyngeal cannula to be clinically significant. So to look for a difference of 5%, with an estimated standard deviation of 5% in each group, and an alpha = 0.05 (two-sided) and 90% power we will need 22 patients in each intervention group. Given the large difference expected in the control group, we estimate half this number (ie 11 patients) will be sufficient for the control group. This gives a total recruitment of 55 patients.

We hope to start this study in June 2015 and estimate it will take around 4 months to complete data collection. Prior to this study, we intend to seek ethics approval via HREC, Southern Health Ethics Committee and the Department of Anaesthetics at Monash Hospital. We hope to secure funding for this project from the Monash Anaesthesia and estimate the total costs to be approximately $100 which includes the additional equipment used in the study (22 nasal prongs, 22 nasopharyngeal cannulae) but excludes the additional Oxygen utilised, as this is challenging to calculate but is not considered to be significant.

Previous studies

Weintgart et al (2, 3) provides an excellent overview of apnoeic oxygenation, its rationale, various methods and beneficial consequences.

 Taha et al (4)69 demonstrated increased maintenance (6minutes or more) of oxygenation in patients receiving low flow oxygen via the nose (5litres/minute), compared to a control group who desaturated much faster (3.65 minutes). Ramachandran et al (5)70 used nasal cannulae in the obese patient to provide apnoeic oxygenation. Once again, time to desaturation (≥95%) was significantly prolonged in the oxygenated group (5.29 minutes) compared to controls (3.49 minutes). Not only were these saturations increased, they were maintained, even after 6 minutes, compared to the control group and the minimum oxygen saturations recorded were significantly higher (94.3% versus 87.7%). Furthermore, the oxygenated cohort maintained saturations at 6 minutes compared to control and the minimum recorded oxygen saturations were significantly higher overall, (94.3% versus 87.7%).

 Tran et el (6) conducted a randomized, controlled, double-blind study in 41 patients without significant cardiac or respiratory disease undergoing elective surgery (age 18-65, ASA I-III). After pre-oxygenation and 90 seconds post induction of anaesthesia, patients received oxygen via nasal prongs at 0, 5, or 10 Litres/minute. Patients were intubated after 4.5 minutes post induction. Their results demonstrate apnoeic oxygenation with 10 L/min compared to 5 Litres/minute via nasal prongs delayed onset of desaturation and enabled maintenance of higher arterial partial pressures of oxygen during elective intubation.

The THRIVE (Transnasal Humidified Rapid-Insufflation Ventilatory Exchange) trial, conducted by Patel et al (7) used continuous delivery of transnasal high-flow humidified oxygen for increasing apnoea time in 25 patients with difficult airways, undergoing hypopharyngeal or laryngotracheal surgery. The stated advantage of this device was application of Positive End Expiratory Pressure (PEEP) in addition to provision of apnoeic oxygenation. This was used at all stages of the intubation process – pre-oxygenation, anaesthetic induction and paralysis until a definitive airway was secured. No patient was reported to have dropped arterial oxygen saturations to ≤90%. They concluded that THRIVE has the potential to “transform the practice of anaesthesia by changing the nature of securing a definitive airway in emergency and difficult intubations from a pressured stop–start process to a smooth and unhurried undertaking”.

Wijewardena et al. (8) conducted an audit to compare the standard technique of pre-oxygenation with high flow nasal oxygen therapy in adult emergency airway management scenarios. They too, demonstrated an increase in safe apnoea time and concluded that high flow nasal oxygen can make intubation safer than the conventional method.

Ching et al (9) in 2014 used a nasopharyngeal airway to deliver high flow oxygen. Although the patients recruited were spontaneously breathing, they found the nasaopharyngeal airway to be effective. They described it to be a non-invasive device, with an automatic safety feature for the release of excess pressure, via either the opposite nare or the patient's open mouth. They found this technique to be a lifesaving intervention in many different scenarios including angioedema, anaphylaxis and trauma patients. Indeed, the acronym NO DESAT (Nasal Oxygen During Efforts Securing A Tube)75 was introduced by Levitan et al (10) in 2010 . This paper describes the continued benefits of apnoeic oxygenation during intubation attempts and NO DESAT has been adopted by several authors since. It appears these simple, benign, inexpensive techniques may be useful as a routine addition to airway management.

Stride et al (11) studied the relative efficacy of nasal cannula compared to non-rebreather facemask in delivering oxygen at various flow rates during apnoea, in a mannequin model. Four different oxygen delivery methods were tested: simple nasal cannula without nasopharyngeal airway, Nasal cannula with a nasopharyngeal airway, non-rebreather facemask without oropharyngeal airway, and non-rebreather facemask with oropharyngeal oxygen. A pneumotachometer was used to determine steady state airflow in the lower airways. They found apnoeic oxygen delivery by nasal cannula was more efficacious than delivery by facemask at equivalent flow rates. Furthermore, the use of nasal cannula with bilateral nasopharyngeal airways resulted in markedly improved oxygen delivery compared to nasal cannula alone. They suggested future studies in apnoeic oxygenation should attempt to confirm this effect in human patients.