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Oxygenation during Apnea: An Assessment of Six Methods Using an Ex Vivo Experimental Model

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Abstract

Introduction: In emergency medicine and pre-hospital care, oxygenation techniques are frequently used in case of apnea. However, among the different methods, the choice is often based on recommendations with little level of evidence. This study is a preliminary investigation on a mechanical model that provides experimental data on six modalities of oxygenation during apnea.

Design: A mechanical model of the human airways was created to simulate gas evolution during apnea. Six methods of oxygenation were applied: the Bag-Valve-Mask (BVM) without ventilation, the nasal cannula, the high concentration mask (HCM), the nasopharyngeal cannula, the high-flow nasal cannula (HFNC) and the laryngeal tube with passive oxygen flow. For each method, the fraction of « pulmonary » oxygen (F«p»02) was monitored three times for 400 seconds. Subsequently, the data were statistically compared.

Main results: After 400 seconds, the best performing method appeared to be the laryngeal tube with passive oxygen flow followed by the HCM. The third best method was HFNC then the nasal cannula. The BVM device proved to be the least effective method. The differences in F«p»02 between 100 and 400 seconds were found to be statistically significant using Friedman's repeated measurements analysis. Dunn's test for post-hoc multiple comparison with Bonferroni corrections showed that the differences between all pairs were statistically significant ($p < 0,0001$) except for the HFNC-HCM pair.

Conclusion: This study provides data on the capacity of various methods to oxygenate a mechanical model of the pulmonary system during apnea. Considering pre-hospital constraints, the results highlight the efficiency of the simple HCM method for oxygenation. Nevertheless, this work is exclusively based on a mechanical model, more investigation and clinical research is needed before issuing practical recommendations.

Keywords: Oxygenation; Pre-hospital; Apnea; Pre-oxygenation; Pulmonary model

Introduction

In the pre-hospital setting, clinical situations of patients with respiratory difficulties, which may lead to bradypnea or even to apnea, are frequently encountered, and intubation is sometimes necessary. In this case, apnea is created with anesthetic drugs and the preoxygenation and oxygenation of the patient is considered as essential. Though many clinical studies encourage preoxygenation [1], there is still little experimental work published [2] on the best method to use to provide oxygen (O_2) during apnea and no experimental work has been published for the pre-hospital setting. In this framework, there is a tendency to precipitate BVM application, yet medical staff is still too preoccupied with setting up for intubation to provide optimal ventilation, resulting in a misuse of BVM.

The recommendations of the French Society of Anesthesia and Resuscitation for intubation of the critical care patient consider preoxygenation with a BVM or ventilation by high-flow nasal canula (HNFC) for non-hypoxemic patients and non-invasive ventilation (VNI) for hypoxemic patients. They specifically exclude the field of pre-hospital medicine from their review of the literature and thus from their recommendations [3].

The primary objective of this study is to investigate the ability of different methods to oxygenate a mechanical pulmonary system. By modelling the respiratory system and reproducing human apnea, we quantitatively assessed the fraction of oxygen in the « lungs » (F«p»0_2) and measured the effect of six different oxygenation techniques on this simulator, allowing us to compare the techniques with one another. These results can be used as a basis for further investigation and clinical studies.

Materials and methods

We built a mechanical prototype of the airways simulating « lungs » in apnea (see Figure 1 below). An intubation exercise head (VBM, Medizintechnik Gmbh, Sulz am Neckar, Germany) was connected to a trachea on the one hand and to the reproduction of an esophagus on the other hand. The bronchial tree was made of polyvinyl chloride and silicone tubes. The trachea was divided into two branches of 16 mm diameter. The tube on the right was divided into three sections of 5mm diameter while the tube on the left was divided into two sections of 5 mm diameter. The stem bronchial tubes were connected to two silicone balloons with a maximum total capacity of 4.6 L. These « lungs » were placed between two plexiglass plates. The movement of the upper plexiglass plate was limited in expansion by springs and in retraction by rods. These springs and rods allowed the system to be calibrated to reproduce the compliance, volume and residual volume of these modelled « lungs ». Resistance was controlled by bronchial diameter.

As for the digestive part of the simulator, an overpressure valve was placed in the esophagus, making it possible to reproduce the normal opening of the esophagus after an increase of 15-20 mmHg in the upper respiratory tract.

This device was calibrated by a ventilator (Dragër Evita V500, Dragër medical Gmbh, Lübeck, Germany) connected to a tracheal tube positioned in the trachea. Gas analyses were carried out on each « lung » (Masimo Radical 7 and Root, Masimo Corporation, Irvine, California, the USA). The transmitted pressure was measured in the « lungs » via a manometer (Masimo Corporation, Irvine, California, the USA).

This study was based on a normal lung, i.e., with a capacity of 4.6 L and a residual volume of 400 mL, a compliance of 1440 mL. kPa^{-1} and a resistance of 0,56 $kPa.L^{-1}.sec^{-1}$.

The gas composition was that of a healthy lung, ventilated 12 times at 500 mL per minute with 21% inspired fraction of oxygen (FiO_2). Carbon dioxide (CO_2) was injected into the « lung » until a stable end-tidal CO_2 ($ETCO_2$) of 35 mmHg was reached at the end of the tracheal tube. This is represented by the first 100 seconds in Figure 2. This partial pressure in CO_2 (P«p»CO_2) was expressed in mmHg by the measurement device. When balance was reached, ventilation was maintained for up to 400 seconds and then stopped before the endotracheal tube was removed. The next step consisted of a stabilization phase. Once a linear decrease in CO_2 in the « lungs » was observed, we performed a discontinuous « pulmonary » injection of CO_2 («CO_2 IN» in Figure 1) in order to obtain an increase in P«p»CO_2 of 3 to 5 mmHg/min as observed in humans [4]. We were therefore able to reproduce human apnea.

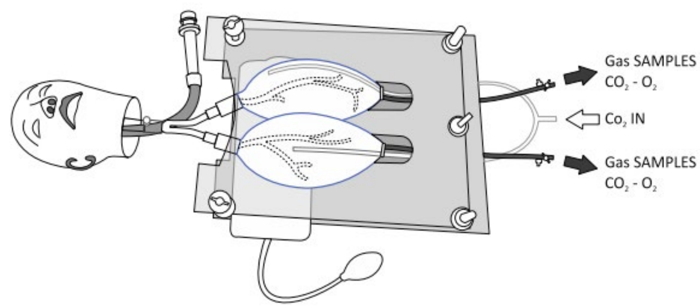

Figure 1: Upper and lower airway simulator.

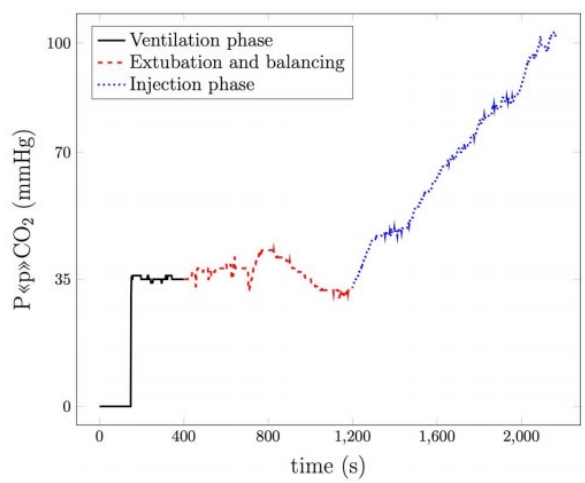

Figure 2: Example of the evolution of the partial pressure in « pulmonary » CO2 during an apnea simulation.

The six oxygenation methods were chosen to reflect the methods commonly used in experimental studies described in literature [5,6] as well as in human clinical practice [7,8].

The oxygen flow rate is calibrated to be in accordance with rates used for each method in clinical practice.

- BVM with 15 L/min oxygen flow placed hermetically on the mouth and the nose of the exercise head without any manual ventilation (AMBU MARK IV, Ambu A/S, Ballerup, Denemark)
- Nasal cannulas with an oxygen flow rate of 6 L/min.
- HCM with an oxygen flow rate of 15 L/min.
- Nasopharyngeal cannula 15 L/min.
- HFNC 50 L/minute humidified $FiO_2$100% with the nasal interface pasted on exercise head with mouth open (Airvo 2 Fischer and Pyckle Healthcare limited, Auckland, New Zealand).
- Laryngeal tube with a passive oxygen flow rate of 15 L/min.

The creation of artificial apnea was carried out in the same way as described above before testing each oxygenation method. An increase in « pulmonary » CO_2 of 3 to 5 mmHg per minute was observed until a P«p»CO_2 of 35 mmHg was reached. It is from this moment that we applied each method of oxygenation during « apnea ».

Each test was carried out three times for 400 seconds on the simulator. The only exception is the BVM for which we had two measurements of 400 seconds and one of 200 seconds.

The 400 second period was chosen arbitrarily due to the lack of data on typical time between arrival of a medical team on site and intubation. Furthermore, these apnea times are known and studied in the context of rapid sequence induction in the operating theatre (median time 23 to 27 seconds) [9]. To our knowledge, there are no reliable studies estimating airway management times in pre-hospital care.

The fraction of oxygen in the modelled lung (F«p»0_2) was measured every 2 seconds and expressed as a percentage (%). The « lungs » were ventilated between each test until the F«p»0_2 returned to 21% and the P«p»CO_2 to 35 mmHg.

Data were plotted graphically and were also reported in an ordered table (minimum value, median, maximum value) every 100 seconds. Using repeated measurements analysis, statistical inference was used to determine whether the differences observed with the limited set of measurements could be reproducible. We focused on the five methods for which three measurements were performed for the full length of the 400 seconds time window. We adopted the 0.05 significance threshold.

Results

Figure 3 indicates that during the first 100 seconds, the various methods are not clearly distinguishable, since the F«p»0_2 remained in the physiological range [19%, 23%] and the small differences between methods did not appear to be meaningful. After 100 seconds, differentiation started to occur, as shown by the numerical values indicatively reported in Table 1.

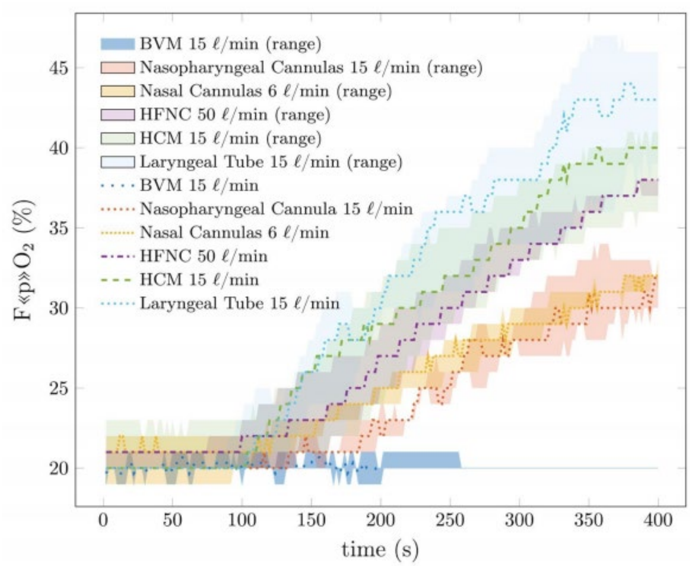

Figure 3: Evolution of « pulmonary » oxygen as a function of time, represented by the median of the measurements at every time step. The shading corresponds to the range of the measurements. Since only two measurements are available for the BVM beyond 200 seconds, the median was not plotted past that time.

	100 s	200 s	300 s	400 s
BVM 15 L/min	(19, 20, 21) %	(19, 20, 20) %	(20, -- , 20) %	(20, -- , 20) %
Nasopharyngeal Cannulas 15 L/min	(20, 20, 20) %	(22, 22, 24) %	(27, 28, 29) %	(30, 32, 32) %
Nasal Cannulas 6 L/min	(20, 21, 22) %	(24, 25, 26) %	(28, 29, 30) %	(31, 32, 33) %
HFNC 15 L/min	(20, 22, 23) %	(25, 27, 29) %	(32, 33, 35) %	(37, 38, 38) %
HCM 15 L/min	(20, 20, 23) %	(24, 29, 31) %	(33, 35, 38) %	(36, 40, 41) %
Laryngeal Tube 15 L/min	(20, 20, 23) %	(29, 30, 31) %	(34, 38, 40) %	(39, 43, 46) %

Table 1: Measurements of F«p»0_2 reported every 100 seconds. The data are written as (minimum value, median, maximum value) in %.

Measurements indicate that the application to the mechanical model of BVM without ventilation does not induce an increase in F«p»0_2. From a descriptive point of view, the superiority of the laryngeal tube method closely followed by the HCM technique is noticeable. It appears that the HFNC method is less effective than the HCM approach. Nasal cannulas performed better than the nasopharyngeal tube up to approximately 300 seconds, after which the two methods seem indistinguishable.

Our goal was to statistically investigate the differences recorded over time between the five alternatives to BVM without ventilation at 100 seconds intervals from 100 seconds to 400 seconds. Since the assumptions (both normality and sphericity) of a repeated measurements ANOVA were not met in this experience, we turned to Friedman's test, a non-parametric alternative. This test revealed that the differences between the distributions are significant ($p < 0.0001$). Multiple comparisons using Dunn's test with Bonferroni corrections for the Type I error showed statistically significant differences ($p < 0.0001$ for each pair), with the HFNC-HCM pair being the only exception ($p = 1$ after adjustment).

Discussion

Literature review

Passive oxygenation of the lungs has been studied for many years. The first experiment dates back to 1947. Drapper and al. studied the passive supply of oxygen to the lungs in animals by what they called "diffusion respiration" [10]. The first human experimental clinical data was from Frumin and al. in 1959, who studied the evolution of arterial oxygen partial pressure of anesthetized patients during elective surgery. They interrupted ventilation and left a source of oxygen in the endotracheal tube [4]. Since then, we have evidence that it is possible to oxygenate a patient while in apnea without desaturation for long periods of time ranging from 5 to 55 minutes [4]. In 2014, Mitterlechner and al. created a mechanical model of apnea [2]. Their model consisted of an intubation training head connected to a ventilator test bag. They demonstrated that deep laryngeal oxygen insufflation via a dual-purpose laryngoscope is more effective than oxygen insufflation via nasal cannulas. Our model, while distinctive in many ways, is inspired by this experiment.

With the recent advent of high flow nasal oxygenation techniques (HFNC), many authors have taken a renewed interest in the different possibilities of oxygenating a patient in apnea. Several studies demonstrated a significant decrease in desaturation during intubation in hypoxemic patients in resuscitation [11-13], who are preoxygenated using the HFNC technique and when oxygenation is maintained during apnea and laryngoscopy. Different devices allow oxygenation to continue during the apnea phase after induction of anesthesia. Oxygenation during laryngoscopy resulted in a significant decrease in the rate of desaturation [13,14]. It is of importance to note that the HFNC method requires between 40 L and 60 L of continuous oxygen, making this technique less suitable for pre-hospital practice. Unfortunately, in current practice, we do not have the materials required to bring this quantity of oxygen to the patient out of hospital.

We identified three relevant studies in the specific context of pre-hospital rescue:

Wimalasena, et al. [7] measured a 22.6% to 16.5% reduction in the rate of desaturation after the systematic introduction of a nasal cannula at 5 L/min of oxygen during preoxygenation and continued during the intubation phase.

Riyapan, et al. [8] compared patients who received 15 L of oxygen via nasal cannula during laryngoscopy to those who did not, but found no statistically significant differences.

Tae Hoon, et al. [15] exported high flow nasal oxygen therapy to their emergency department. None of the 30 patients included in their study had saturation levels below 97%.

General conclusions cannot be drawn from these studies as they are limited by small sample sizes and the diversity of techniques makes a comparison between these studies complicated. As a matter of fact, the effects of the technique cannot be isolated from the conditions under which it is applied. The only way to do so would be to carry out tests on a hypoxemic patient left in apnea, which is not ethically achievable in human clinical research.

Regarding ventilation, rapid sequence induction classically does not include a ventilation period before laryngoscopy. This choice is based on the fear of insufflating air into the stomach [16] leading to regurgitation since the patient has lost the swallowing reflex. Controversies on this subject are not new [17]. Research shows that ventilating a patient in this sequence after a first intubation failure leads to few complications [18]. It is interesting to note that ventilating with a low pressure of insufflation before or during induction is relevant [19] and is even recommended for a hypoxemic or an apneic patient [20].

Interpretation of measurements

This study contributes to the debate on oxygenation during apnea. The measurements performed on this model confirm that using BVM without ventilation is totally useless. We deliberately used a self-filling balloon model with unidirectional valves and not the simpler single-use model. In the self-filling balloon model, if the operator does not apply manual pressure on the balloon, the valves do not open and the patient does not receive the desired oxygen. Consequently, simple facial application of the mask connected to the BVM in the patient in apnea before intubation does not allow oxygen administration. Even if this principle is known, it is not uncommon to observe such misuse in daily practice, which would therefore be a mistake in the light of the results of this study.

Moreover, tests on this mechanical model confirm that there are other effective techniques for oxygenation. The laryngeal tube method appears indeed to be the most effective in terms of oxygenation. Unfortunately, in the specific context of pre-hospital medicine, this method is not primarily used in practice, as airway safety is a priority. Therefore, this technique is usually used only when endotracheal intubation has failed [3].

Given the interesting results of the HFNC technique in intrahospital medicine, which is mainly studied in resuscitation departments on hypoxemic patients [11-13,15], one might have expected better oxygenation results with the HFNC method compared to the HCM approach. However, based on this model, we observe that this technique is not more efficient than the HCM. Moreover, as previously mentioned, it is currently complicated to export such a device outside the hospital walls.

Furthermore, this study, despite the limits of the mechanical model, presents the HCM method as a coherent possibility to oxygenate pre-hospital apnea. The HCM can be applied by any practitioner, requires no specific training and does not imply any risk of overpressure in the airways. Additionally, the HCM does not require manual action once properly positioned, freeing up hands that can be useful for other purposes. Finally, the use of HCM gives more time for acute medical care when medicalization is too dangerous or when the evacuation of victims takes precedence over any other gesture [21,22].

Limitations

Inspired by Mitterlechner's initial concept [2], this model improves the reproduction of the pulmonary anatomy but does not simulate neither the hygrometry, nor the number of alveoli, nor their microanatomy. In addition, it does not reproduce O_2 consumption, and CO_2 production is carried out by direct injection into the « lung ». Nevertheless, it reproduces the pressure conditions and gaseous environment of the normal lung. It is also distinguished by the choice of an oxygen concentration of 21% at the start of each measurement. Indeed, patients with spontaneous apnea are not preoxygenated in pre-hospital practice. To our knowledge, this is the first experiment of this kind.

Conclusion

This study provides experimental data on the performance of various oxygenation methods of a mechanical model of the pulmonary system during apnea. This study cannot directly be translated to the clinical context because of the inherent limits of modelling. With that in mind, the measurements show that the laryngeal tube is the most effective in terms of oxygenation. In addition, we show that the HNFC technique is not more efficient than the HCM approach. Finally, considering the constraints of the pre-hospital environment, the results highlight the oxygenation efficiency of the simplest technique, HCM, and the apparent total inefficiency of oxygenation with the BVM without ventilation. Due to the mechanical nature of this model, it is not possible to extrapolate clinical recommendations. Nevertheless, measurements are worth being reported, as they represent a preliminary experimental step that calls for further research.

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