The Safe Limits of Mechanical Factors in the Apnea Testing for the Diagnosis of Brain Death

ÇİMEN OLGUNER,¹ UĞUR KOCA,¹ MERT AKAN,¹ AYŞE KARCI¹ and ZAHİDE ELAR¹

¹Department of Anesthesiology and Reanimation, Dokuz Eylül University, School of Medicine, Izmir, Turkey

OLGUNER, Ç., KOCA, U., AKAN, M., KARCI, A. and ELAR, Z. *The Safe Limits of Mechanical Factors in the Apnea Testing for the Diagnosis of Brain Death.* Tohoku J. Exp. Med., 2007, **211** (2), 115-120 — Apneic oxygenation is an apnea testing method in the diagnosis of brain death. In this method, oxygen (O₂) is delivered into the trachea via an O₂ catheter (O₂C). However, barotrauma may develop during O₂ insufflation into the trachea. Oxygen catheter diameters, O₂ catheter tip position in the trachea, and O₂ flow rate have been proposed as causes of barotrauma. This study was designed to highlight the airway pressure changes during apneic oxygenation in a model consisting of an anesthesia bag, which was connected to a pressure transducer and to an endotracheal tube (ETT). The pressure of the system was monitored while delivering O₂ continuously to the system through O₂C of different diameters, which were placed in the ETT. Tested variables were ETT/O₂C ratio, O₂C tip position in ETT (proximal 1/3 of the ETT, mid point of the ETT, and distal 1/3 of the ETT) and O₂ flow rate (6, 8, and 10 L min⁻¹). The increase in the airway pressure significantly correlated with O₂C tip position in ETT ($p = 0.017$). ETT/O₂C ratio smaller than 1.75 caused significantly high airway pressures ($p < 0.05$). The pressure was significantly higher at the flow rate of 10 L min⁻¹ O₂ compared with the flow rate of 6 L min⁻¹ O₂ ($p < 0.01$). Thus, ETT/O₂C ratio, O₂C tip position in ETT and O₂ flow rate are the important factors that determine the airway pressure in the trachea during O₂ insufflation. In conclusion, overlooked mechanical factors dangerously increase airway pressure during apnea testing. ——— brain death; apnea testing; barotrauma; organ donation; airway simulator

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Brain death (BD) is defined as irreversible loss of the brain functions, including the brainstem. Unresponsiveness or coma, absence of brainstem reflexes and apnea have been accepted as diagnostic criteria for BD by American Academy of Neurology (AAN) (The Quality Standards Subcommittee of the American Academy of Neurology 1995). Apnea testing (AT) is one of the cardinal requisites that should be

completed in the diagnosis of BD (Saposnik et al. 2000).

Preventing from hypoxemia while allowing the arterial partial carbon dioxide pressure to rise above the threshold level, is the key point of AT. There are mainly three methods to provide sufficient O₂ to patient during AT; apneic oxygenation, hypoventilation and continuous positive airway pressure (CPAP) (Lang and Heckmann 2005;

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Correspondence: Çimen Olguner, Dokuz Eylül University School of Medicine, Department of Anesthesiology and Reanimation, Balçova, 35340, İzmir, Turkey.
e-mail: cimen.olguner@deu.edu.tr

Levésque et al. 2006). In the hypoventilation and CPAP methods the patient is not disconnected from mechanical ventilator but minute ventilation volume is reduced to a very low level such as $0.5 - 2 \text{ L min}^{-1}$ (Lang and Heckmann 2005) or ventilation mode is changed to CPAP mode with 100% O_2 (Levésque et al. 2006), respectively.

Apneic oxygenation is still widely accepted method for AT and described as follows in the guideline of AAN; ventilatory assistance is discontinued and 6 L min^{-1} 100% O_2 is delivered into the trachea via an O_2 catheter optionally placed “at the level of the carina” while waiting for spontaneous respiratory movements (The Quality Standards Subcommittee of the American Academy of Neurology 1995). However, even if apneic oxygenation is performed as described in the AAN guideline, hypoxemia, bradycardia, respiratory acidosis, hypotension and pneumothorax may occur (Rudolf et al. 1998; Saposnik et al. 2004). Although pneumothorax was described as a rare complication in the literature, authors proposed that it is more frequently encountered in clinical practice (Zisfein and Marks 1999). Diameter of the O_2 catheter and O_2 flow rate are the suggested factors that may lead to pneumothorax during apneic oxygenation (Bar-Joseph et al. 1998). However, there is no agreement on the diameter and position of the O_2 catheter and O_2

flow rate that are used for O_2 delivery into the trachea during the apneic oxygenation. We designed a simple model to determine the effect of the position and diameter of O_2 catheter and the O_2 flow rate on the airway pressure in the simulated model of airway and lung.

MATERIALS AND METHODS

A model was designed for the evaluation of airway pressure changes during apneic oxygenation. This model was consisting of a 2.3 L anesthesia bag that connected to a pressure transducer, and to an endotracheal tube (ETT) via an “L” connector (Fig. 1). Oxygen catheters (O_2C) (Biçakçılar, Istanbul, Turkey) in different diameters were inserted into the ETT (Kendall-Gammatron, Sampran, Thailand) for O_2 insufflation. Pressure of the model was measured by a transducer (Pressure Monitoring Set, Biçakçılar, Istanbul, Turkey) and a monitor (Hewlett-Packard Viridia Component Monitoring System, Hewlett-Packard GmbH, Böblingen, Germany) in three different O_2 flow rates. The pressure transducer and the monitor were specially calibrated for air. ETTs with internal diameter (ID) 7 mm, 7.5 mm, and 8 mm and O_2Cs with external diameter 2.66 mm, 3.33 mm, 4 mm, and 4.66 mm (8 F, 10 F, 12 F, and 14 F, respectively) were used. All the O_2Cs were in the same shape with a single end hole and two side holes. ETT/ O_2C ratio was calculated by dividing an internal diameter of ETT with an external diameter of O_2C . Twelve kinds of ETT/ O_2C ratio were resulted with this formulation. Other variables

Fig. 1. The model was created with 2.3 L anesthesia bag that connected to a pressure transducer and to an ETT via an “L” connector. O_2 catheters in different diameters were inserted into the ETT. Pressure of the system was measured by a pressure transducer and a pressure monitor under three different O_2 flow rates. ETT, endotracheal tube.

were O₂C tip position in ETT and O₂ flow rate. O₂ catheter tip positions in ETT were as follows; 1) proximal 1/3 of the ETT, 2) mid point of the ETT, and 3) distal 1/3 of the ETT (near the tip of the ETT). The O₂ flow rates were 6, 8, and 10 L min⁻¹. Nine measurements were performed for each ETT/O₂C ratio (3 different O₂C position and 3 different O₂ flow rate). When each parameter was changed (i.e., O₂ flow rate or O₂C position), airway pressure measurements were performed after stabilization of the model (at least 5 min after each parameter change). Data were presented as mean $\pm$ standard error of mean (S.E.M.). Pearson's correlation and ANOVA were used for statistical analysis of the data. Multiple comparisons were made using Tukey's procedure. A *p* value < 0.05 was considered significant.

RESULTS

Overall 108 measurements were performed (at 12 different ETT/O₂C ratio with 3 different O₂C tip positions in the ETT and different O₂ flow rates). Mean airway pressure was 2.7 ± 0.35 mmHg, mean O₂ flow was 8 ± 0.15 L min⁻¹ and mean ETT/O₂C ratio was 2.1 ± 0.04 . Increase in the airway pressure significantly correlated with O₂ flow rate (*p* = 0.01, correlation constant = 0.248), O₂C tip position in ETT (*p* = 0.017, correlation constant = 0.229) and inversely correlated with ratio of ETT/O₂C (*p* < 0.01, correlation constant = -0.631) (Figs. 2 and 3). The airway pressure significantly increased with the decrease in ETT/O₂C ratio and with the increase in O₂ flow

Fig. 2. Scatterplot graph of airway pressure changes according to ETT/O₂C ratio and O₂C tip positions within ETT.

Airway pressure is inversely correlated with ratio of ETT/O₂C (*p* < 0.01, correlation constant = -0.631) and correlated with position of O₂C tip in ETT (proximal: 1/3 proximal of the ETT, mid point: mid point of the ETT, distal: distal 1/3 of the ETT "near tip of the ETT") (*p* = 0.017, correlation constant = 0.229). There is a significant increase in pressure for ETT/O₂C ratios smaller than 1.75 (*p* < 0.05).

ETT, endotracheal tube; O₂C, oxygen catheter.

Fig. 3. Scatterplot graph of airway pressure changes according to O₂ flow rate and O₂C tip positions within ETT.

Airway pressure significantly increased with the change in O₂ flow rate (*p* = 0.01, correlation constant = 0.248) and position of O₂C tip in ETT (proximal: 1/3 proximal of the ETT, mid point: mid point of the ETT, distal: distal 1/3 of the ETT "near tip of the ETT") (*p* = 0.017, correlation constant = 0.229). The pressure was significantly higher in 10 L min⁻¹ O₂ flow rate compared with 6 L min⁻¹ O₂ flow rate (*p* < 0.01).

ETT, endotracheal tube; O₂C, oxygen catheter.

TABLE 1. The effect of ETT/O₂C ratio on airway pressure.

ETT/O ₂ C	<i>n</i>	Airway pressure (mmHg)
1.50	9	11.5 ± 1.8*
1.61	9	5.2 ± 0.9*
1.72	9	4.7 ± 0.8*
1.75	9	2.6 ± 0.5
1.88	9	2.1 ± 0.6
2.00	9	1.8 ± 0.7
2.10	9	1.1 ± 0.2
2.25	9	1.4 ± 0.2
2.40	9	0.6 ± 0.2
2.63	9	0.5 ± 0.5
2.82	9	0.3 ± 0.2
3.01	9	0.2 ± 0.2

ETT/O₂C ratio was calculated by dividing ETT internal diameter with O₂C external diameter. Nine measurements for each ETT/O₂C ratio were done for three different O₂ flow rates (6, 8, and 10 L min⁻¹) while keeping the O₂C tip in three different positions in the ETT (1/3 proximal of the ETT, mid point of the ETT and distal 1/3 of the ETT “near tip of the ETT”) (Fig. 2).

Airway pressure significantly increased with the decrease in ETT/O₂C ratio.

ETT, endotracheal tube; O₂C, oxygen catheter.

Data are shown as mean ± S.E.M.

**p* < 0.05 compared with other groups that have greater ETT/O₂C ratio than 1.75.

rate (*p* < 0.01) (Tables 1 and 2). The results were summarised according to ETT/O₂C ratio (Table 1 and Fig. 2) and O₂ flow rate (Table 2 and Fig. 3) while keeping the O₂C tip in 3 different positions. The pressure was not significantly influenced by the O₂C tip position (Table 3). The airway pressure was significantly higher in ETT/O₂C ratio smaller than 1.75 compared with ratio greater than 1.75 (*p* < 0.05) (Table 1). The airway pressure significantly increased in 10 L min⁻¹ O₂ flow rate compared with 6 L min⁻¹ O₂ flow rate (*p* < 0.01). The airway pressure was not significantly different in 8 L min⁻¹ O₂ flow rate compared with 6 and 10 L min⁻¹ (Table 2).

TABLE 2. The effect of O₂ flow on airway pressure.

O ₂ Flow L min ⁻¹	<i>n</i>	Airway pressure (mmHg)
6	36	1.6 ± 0.2
8	36	2.6 ± 0.3
10	36	3.8 ± 0.4*

Airway pressure was measured at each O₂ flow rate for 12 different ETT/O₂C ratio (Table 1) while keeping the O₂C tip in three different positions in the ETT (1/3 proximal of the ETT, mid point of the ETT and distal 1/3 of the ETT “near tip of the ETT”) (Fig. 3). Airway pressure significantly increased with the increase of O₂ flow rate.

ETT, endotracheal tube; O₂C, oxygen catheter.

Data are shown as mean ± S.E.M.

**p* < 0.01 compared with 6 L min⁻¹ O₂ flow rate.

TABLE 3. The effect of O₂C tip position in ETT on airway pressure.

Position	<i>n</i>	Airway pressure (mmHg)
Proximal 1/3	36	1.8 ± 0.2
Mid point	36	2.4 ± 0.3
Distal 1/3	36	3.8 ± 0.6

All measurements for each O₂C tip position in the ETT (1/3 proximal of the ETT, mid point of the ETT and distal 1/3 of the ETT “near tip of the ETT”) were done for 12 different ETT/O₂C ratio (Table 1) and for the three different O₂ flow rates (6, 8 and 10 L min⁻¹).

The O₂C tip position alone has no effect on airway pressure.

ETT, endotracheal tube; O₂C, oxygen catheter.

Data are shown as mean ± S.E.M.

DISCUSSION

In this in vitro study, we demonstrated that airway pressure changes significantly correlated with the ratio of ETT/O₂C, O₂C tip position in the ETT, and O₂ flow rate. Particularly, the increase in airway pressure was significant if the O₂ flow

rate was higher than 8 L min^{-1} . The pressure changes were not significant if the ETT/O₂C ratio was greater than 1.75.

The O₂C that is positioned beyond the tip of the ETT carries the risk of catheterization of one of the bronchus or being in wedge position with trachea as stated previously (Bar-Joseph et al. 1998). Although the independent effect of the O₂C tip position on airway pressure was not statistically significant, the correlation between the airway pressure and O₂C tip position in ETT was significant. Therefore the O₂C tip position in the ETT may contribute to airway pressure increase when combined with the effects of O₂ flow rate and ETT/O₂C ratio.

Apnea testing related pneumothorax was first reported by Bar-Joseph et al. In order to avoid pneumothorax, the authors proposed that the O₂C diameter should be significantly narrower than the diameter of the ETT, the tip of the O₂C should not exceed the tip of the ETT to avoid wedge position with trachea and O₂ flow rate should not exceed 6 L min^{-1} (Bar-Joseph et al. 1998). Saposnik et al. (2000) reported a case with pneumothorax and pneumoperitoneum that occurred during AT. They questioned the safety of AT and identified risk factors that were the O₂C position in the ETT and the diameter disproportion between the ETT and the O₂C. Additional three cases of pneumothorax have been reported by Vivien et al. (2001). They proposed that a 12 F catheter should be advanced only 5 cm into the ETT and the O₂ flow rate should not exceed 8 L min^{-1} to avoid this complication. After application of these rules they have not seen any such complication (Vivien et al. 2001).

All data obtained from the above cases indicate that mainly three factors may play a role in the occurrence of pneumothorax during AT. These factors are; 1) the ratio of ETT/O₂C, 2) the O₂C tip position in the ETT and 3) O₂ flow rate. In general O₂ flow rate of 6 L min^{-1} has been suggested during AT. However, different flow rates ranging from 6 to 15 L min^{-1} have been reported in the literature (Bar-Joseph et al. 1998; Saposnik et al. 2000; Vivien et al. 2001). Proper positions of the O₂C tip in trachea are not clearly described

in previous studies. The position is defined as “at the level of the carina” in the AAN guideline and “not in wedge position with trachea” by others (The Quality Standards Subcommittee of the American Academy of Neurology 1995; Wijdicks 1995; Bar-Joseph et al. 1998). The relation between the external diameter of O₂C and internal diameter of ETT is also obscure in the literature. The suggestion by authors that the use of 12 F O₂C in all patients for O₂ insufflation seems not applicable because internal diameters of ETT differ from patient to patient (Vivien et al. 2001). Moreover, AAN guideline includes any proposal about the proper O₂C diameter (The Quality Standards Subcommittee of the American Academy of Neurology 1995).

In considering the mechanical factors in AT, the shape of the O₂C is also noteworthy. Dyer et al. (2003) tested tracheal gas insufflation catheter in different shapes in a model that simulated airways. The pressure changes were minimal with the single side hole catheter and multiple side holes catheter. We standardized our study by using O₂C in one shape in different diameters in all measurements.

Because there may be other contributing factors to cause pneumothorax during in vivo conditions (i.e., pulmonary infections, acute respiratory distress syndrome and secretions), it is difficult to find a clinical threshold pressure that may cause pneumothorax. Entrapping air by secretions in the small and intermediate airways may cause localized pulmonary high-pressure zones and alveolar burst without causing high pressure within the main airways.

Organ donation contributes to survival of the patients waiting for organ transplantation. The complications such as pneumothorax occurring during AT for diagnosis of the BD may lead to donor loss (Sharples et al. 1997; Bar-Joseph et al. 1998; Goudreau et al. 2000). Thus, methods in performing AT would be revised concerning the possible complications and especially the position of the O₂C, the O₂ flow rate and the ratio of ETT/O₂C.

We are aware that our simple model is not capable enough for simulating human airways and

lungs. We concluded that the data from the present study may give an idea to clinicians about the possible dramatic airway pressure rises during AT which are easily affected from minor mechanical changes.

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