The effect of general anaesthesia and neuromuscular blockade on Eustachian tube compliance: a prospective study

Akeelesh Mungur, Guy Cochard, Yves Ozier and Pierre Lafère

Abstract

(Mungur A, Cochard G, Ozier Y, Lafère P. The effect of general anaesthesia and neuromuscular blockade on Eustachian tube compliance: a prospective study. *Diving and Hyperbaric Medicine*. 2016 September;46(3):166-169.)

Objective: The most common complications of hyperbaric oxygen treatment (HBOT) are related to pressure changes on gas-containing cavities. Therefore, inability to auto-inflate the middle ear may result in transient or permanent hearing loss. However, it seems that middle ear barotrauma (MEBt) does not develop more often in mechanically ventilated patients than in ambulatory patients. This might be explained by deep sedation of these patients. Therefore, the aim of this study was to determine whether anaesthesia and/or neuromuscular blockade can influence Eustachian tube (ET) function.

Methods: Forty patients who were undergoing surgery under general anaesthesia were enrolled in this prospective study. ET function was evaluated by tympanography performed three times: before induction of general anaesthesia (baseline), after induction with sufentanyl/propofol and after full blockade was achieved with a long-acting neuromuscular blocking agent.

Results: There were no differences in ear volume ($P = 0.19$) and ear pressure ($P = 0.07$). There was a significant variation in compliance on tympanography after the induction of general anaesthesia ($P = 0.009$). Compared to the baseline, this variation was characterized by an increase after induction of anaesthesia ($24 \pm 7.13\%$, $P < 0.01$) and neuromuscular blockade ($23 \pm 8.9\%$, $P < 0.05$). The difference between after induction and after neuromuscular blockade was not statistically significant ($P = 0.13$).

Discussion: the findings of this trial suggest that the administration of hypnotic drugs associated with opioids improves ET compliance. Therefore it may have favourable prophylactic effects on MEBt in ventilated intensive care unit patients scheduled for HBOT.

Key words

Tympanometry; middle ear; ear barotrauma; ENT

Introduction

Multiple studies have examined the use of hyperbaric oxygen treatment (HBOT) in several acute pathologies with mixed results. Therefore, every few years, the European Committee for Hyperbaric Medicine publishes its recommendations concerning the clinical indications for HBOT. Several proposed conditions, such as iatrogenic gas embolism, decompression sickness, carbon monoxide poisoning and necrotizing soft tissue infections may require intensive care (ICU) hospitalisation and mechanical ventilation.[1,2]

The most common complications of HBOT are due to the effects of pressure changes on the gas-containing cavities of the body. Failure to equalize the pressure gradient between the affected body cavity and the external environment during chamber operation results in barotrauma, most commonly middle ear barotrauma (MEBt).[3] Known risk factors for MEBt include female sex, older age, artificial airways (intubation) and a history of Eustachian tube (ET) dysfunction or the inability to auto-inflate the middle ear such as sedated and ventilated ICU patients who are unable to perform a Valsalva manoeuvre to prevent MEBt. Damage to the components of the auditory system (ossicular chain, tympanic membrane in case of MEBt) may result in transient or permanent impairment, such as hearing loss and tinnitus.[4,5]

According to the literature, reported incidences of MEBt after HBOT range from 8% to 68.7% and up to 91% in patients unable to auto-inflate their middle ear.[3,6–8] However, in a recent study, although the incidence was twice as high in the intubated group compared to the conscious group of patients (24.4% vs. 12.4%), this result was not statistically significant. In this particular 'acute-only' setting, there was no influence of age, sex or mechanical ventilation on the occurrence of MEBt.[9] This might be explained by deep sedation of the patients while HBOT was performed, as it may have helped the relaxation of the tube-opening muscles (*m. tensor* and *m. levator veli palatini*) and unconscious pressure equalization.

We conducted the present prospective study to determine whether or not anaesthesia/sedation and/or neuromuscular blockade (NMB) could influence ET compliance.

Methods

This was a prospective, observational study conducted on 40 patients who were undergoing surgery under general anaesthesia. After local ethics committee approval, EudraCt registration (2015-003022-14) and obtaining written informed consent, patients were subjected to otolaryngological examination to rule out any disorder affecting hearing and ET function. Patients with a history of recent ear discharge, abnormal external auditory canal, acute infections of the ear or a perforated tympanic membrane were excluded. We also excluded patients in whom a rapid sequence induction was indicated.

Tympanometry analysis was done using an AT 235 impedance meter (Interacoustics, Assens, Denmark). A small probe was inserted which emits a sound of low frequency (226 Hz) via a tube into the auditory canal and a continuous change of positive and negative pressure was created by the pump of the instrument in the external auditory canal in front of the tympanic membrane. The compliance was measured simultaneously. This measurement was done three times: before induction (Baseline), after injection of hypnotic drugs (Induction) and after NMB, once full blockade was achieved (no response to 'train-of-four' stimulation of a peripheral nerve). Demographic data were recorded for each patient including age, sex, height, weight and ASA classification.

To avoid any bias related to the anaesthetic procedure, it was standardized with propofol 4 $mg \cdot kg^{-1}$ preceded by sufentanyl 0.3 $\mu g \cdot kg^{-1}$ and followed by atracurium 0.5 $mg \cdot kg^{-1}$ administered through a 18g intravenous cannula in the patient's antecubital fossa. NMB was monitored by acceleromyography. Since it has been demonstrated that the use of nitrous oxide as an anaesthetic gas can increase middle ear pressure, which may theoretically result in expulsion of middle ear fluid through an open ET, nitrous oxide was not used. Also, to avoid any effective volume variation of the middle ear (fluid displacement), no positive pressure ventilation was applied between the first (Baseline) and second (Induction) tests.

STATISTICAL ANALYSIS

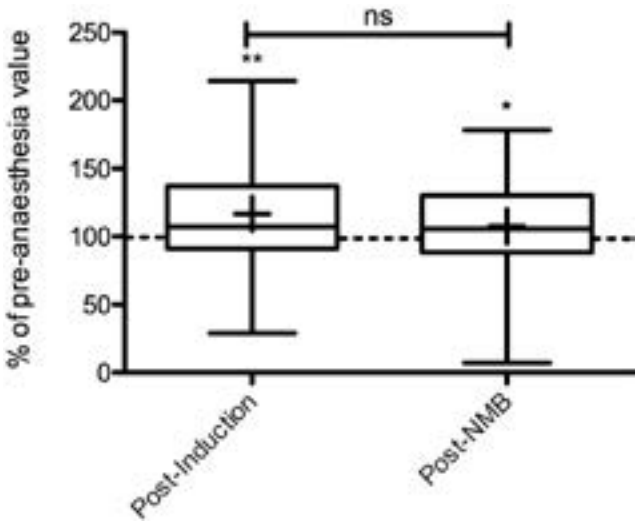
All tests were performed using a standard computer statistical package, GraphPad Prism version 5.00 for Mac (GraphPad Software, San Diego California USA). Since each candidate was their own control, a power analysis indicated that a sample size of 66 ears was required to detect a difference in ET compliance with an effect size of at least 20% (= 0.05, (1 -) = 0.95).

The Kolmgorov-Smirnov normality test was used to determine whether the data were normally distributed. A Gaussian distribution could be assumed for heart rate, mean arterial pressure (MAP), diastolic pressure and patient demographics. For these parameters, a one-way analysis of variance was used. Post-hoc comparisons were then made using Bonferroni's multiple comparison tests.

In all other cases (compliance, ear volume and pressure, systolic blood pressure), a Friedman test with Dunn's multiple comparison tests or Wilcoxon matched-pairs signed rank tests were used. Compliance changes were expressed as a percentage (median and 25–75 interquartile range) of the baseline value recorded during the pre-induction phase before any drugs were injected. This has allowed an appreciation of the magnitude of change rather than the absolute values. A threshold of $P < 0.05$ was considered statistically significant.

Figure 1

Box and whisker plots of variation in middle ear compliance compared to the value recorded before induction of anaesthesia (dotted line = 100%), indicating median, 25–75 percentiles and minimum and maximum observations; "+" marked in the boxes indicate the means; NMB – neuromuscular blocking agent; ns – not significant; * $P < 0.05$; ** $P < 0.01$ (Dunn's test)



Results

All subjects were selected from a large surgical population in order to obtain a group of comparable health status (ASA I and II). There was no variation of heart rhythm ($P = 0.21$), a 15% drop of the blood pressure after the injection of hypnotic drugs was observed (systolic BP: 136 ± 19 to 115 ± 19mmHg; diastolic BP: 75 ± 13 to 66 ± 13mmHg; MAP: 98 ± 13 to 83 ± 14mmHg). There was no further variation after injection of NMB agents.

Of the 80 tested ears, 12 data sets were excluded because of incomplete results leaving 68 ears available for analysis. The loss of data was mostly due to leaking during the compliance measurement and the inability for the operator to correct the problem before intubation was mandatory.

There were no statistically significant differences in ear volume ($P = 0.19$) or pressure ($P = 0.07$) during the different measurements. There was a significant change in compliance (Figure 1) after the induction of general anaesthesia ($P = 0.009$, Friedman test). Compared to Baseline, this variation is characterized by an increase in middle ear compliance after induction of anaesthesia to 107% (91–137%, Dunn's test $P < 0.01$) and after NMB 106% (88–130%, Dunn's test $P < 0.05$). However, the difference between post induction and after NMB was not statistically significant ($P = 0.13$, Wilcoxon matched-pairs signed rank test).

Discussion

The physiological role of the ET is threefold: to protect the middle ear from sources of disease, to help drain

secretions away and to ventilate the middle ear. Although the physiological mechanisms involved in these functions are multiple, the role of ET patency is certain in the pressure equilibration process; however, it is probably not the only one involved.[10,11] Indeed, the anatomic structure of the ET is highly complex in that the lumen is surrounded by several muscular, cartilaginous, fat and connective tissue elements and is bounded by fluid-coated mucosal tissue. Therefore ET dysfunction may be due to anatomic and/or mechanical abnormalities. However, the precise mechanisms by which these structural properties alter ET opening phenomena have not been investigated.[12,13]

In healthy individuals, the tubes are physiologically closed at rest, and open primarily by synergistic action of the palatine muscles. This opening occurs during swallowing, when muscle contraction deforms the surrounding soft tissue resulting in an increase in the cross-sectional area of the lumen and a reduction in the resistance to airflow.[14] Several investigators have demonstrated that paralysis of the *tensor veli palatini* muscle, the primary muscle associated with ET function, results in negative middle ear pressures[15] and a significant decrease in the compliance or elastic properties of the ET.[16,17]

Other investigations have suggested that the elastic and viscoelastic properties of the cartilage and/or fat and connective tissue may also be important determinants of ET function.[18,19] Middle ear gas hyperoxia, which is a consequence of HBOT, has been shown to down-regulate the ET ventilatory function in patients. This has been confirmed in young adult female cynomolgus monkeys breathing either room air or 100% normobaric oxygen; higher opening, closing, and steady state pressures were observed under systemic hyperoxia.[20]

Both hyperoxia and inability to use the peritubal muscles in order to equalize ear pressure are present in mechanically ventilated patients undrgoing HBOT. This might explain why 94% of the intubated patients in one study developed MEBt, and 61% required placement of tympanostomy tubes.[21] However, these results were not supported in a recent study.[9] This might be explained by the fact that the earlier series included patients treated for head and neck surgical and radiation side effects, whereas the recent study did not. This would be in line with the hypothesis of the role of viscoelastic properties of soft tissues surrounding the ET. One other factor suggested by our results might be the deep sedation of the patients and not the effects of NMB agents, as it may have helped relaxation of the ET-opening muscles and unconscious pressure equalization.

Two aspects must be considered, a direct effect of either or both of the induction agents, sufentanyl and propofol, or an indirect effect through hypotension. Propofol was initially approved for use as an induction and maintenance hypnotic agent; however, its clinical uses have expanded over the last decades to also include intensive care sedation, although it is also known for its haemodynamic effects. Indeed, in several studies, the overall incidence of hypotension is 15.7% with 77% of the episodes recorded within 10 min of induction of anaesthesia.[22–24] Our results are in accord with these findings. However, it is less clear whether or not hypotension could have an effect on ET function. Although we cannot formally exclude this hypothesis, an extensive literature search failed to demonstrate any correlation between blood pressure and ET dysfunction.[13,25]

The muscle-relaxing mechanisms of intravenous anaesthetics, especially propofol, have been investigated in several studies.[26–28] A central mechanism (cortical and spinal cord) has been proposed to describe muscle-relaxing properties of propofol.[26–28] Bolus propofol administration impairs the central part of the motor system by decreasing α-motor neuron excitability as shown by a decreased spinal F wave.[26] Other authors have described a peripheral mechanism, reporting that anaesthetic doses of propofol decrease diaphragmatic contractility in dogs;[27] whilst inhibition of human skeletal muscle sodium channels in a voltage-dependent manner has also been described.[28] This mechanism may contribute to the reduction in muscle excitability. Contrary to the actions of propofol, sufentanil is more prone to induced muscle rigidity.[29]

Since we did not apply positive pressure ventilation between the first two tests, and others have reported that anaesthesia per se can modify the shape of the tympanogram in 30% of cases (from type B to type A),[30] we cannot be sure that the improvement in compliance was related to an improvement in ET patency. However, these tympanometric changes were mostly demonstrated in the presence of middle-ear effusion, which was not the case in our settings since we excluded all patients with a previous medical ear history or any active ear pathology. Moreover, manual ventilation of the patients prior to the injection of a NMB agent to ensure that ventilation was possible before intubation did not modify ear compliance, ear volume or ear pressure further. Therefore, it is possible to assume that the change in compliance was most probably, although not necessarily exclusively, related to ET function.

Conclusion

This trial suggests that the administration of hypnotic drugs associated with opioids may improve Eustachian tube compliance. Therefore, it may have a favourable prophylactic effect on MEBt in intubated, ventilated patients scheduled for HBOT.

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Conflicts of interest: nil

Submitted: 15 February 2016; revised 10 July 2016
Accepted: 24 July 2016

Akeelesh Mungur[1], Guy Cochard[2], Yves Ozier[1,3], Pierre Lafère[1,2,3]

[1] Department of Anaesthesiology, Hôpital de la Cavale Blanche, Brest, France
[2] Unit of Hyperbaric Oxygen Therapy, Hôpital de la Cavale Blanche
[3] Laboratoire ORPHY, Université de Bretagne Occidentale, Brest

Address for correspondence:
Laboratoire ORPHY, EA 4324
Université de Bretagne Occidentale
6 avenue Le Gorgeu, CS 93837
29238 Brest Cedex
France
pierre.lafere@chu-brest.fr