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The effect of positive airway pressure during pre-oxygenation and induction of anaesthesia upon duration of non-hypoxic apnoea

THESE

Préparée sous la supervision du Dr Lennart Magnusson, PD et MER

et présentée à la Faculté de biologie et de médecine de l'Université de Lausanne pour l'obtention du grade de

DOCTEUR EN MEDECINE

par

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Médecin diplômée de la Confédération Suisse

Originaire de Genève

Lausanne 2006

Résumé de l'étude.

Effet de l'application d'une pression positive sur la durée d'apnée non hypoxique pendant la phase d'induction d'une anesthésie générale

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L'application d'une pression positive (PEEP) pendant la phase d'induction d'une anesthésie générale peut prévenir la formation d'atélectasies pulmonaires. Ceci pourrait permettre d'accroître la durée d'apnée non hypoxique par l'augmentation de la capacité pulmonaire résiduelle fonctionnelle (CRF).

Nous avons étudié le bénéfice de l'application d'une PEEP durant la phase d'induction d'une anesthésie générale sur la durée d'apnée avant que la saturation périphérique en oxygène atteigne 90%.

Quarante patients ASA I-II ont été randomisés en deux groupes distincts.
- Dans le groupe PEEP (n=20), les patients ont été pré-oxygénés durant 5 minutes avec une FiO2 à 100% par l'intermédiaire d'un appareil de CPAP (6cmH2O). Après induction de l'anesthésie, les patients furent ventilés mécaniquement (PEEP 6cmH2O) durant 5 minutes supplémentaires.
- Dans le groupe ZEEP (n=20), aucune pression positive (ni CPAP, ni PEEP) ne fut utilisée. La durée d'apnée pour atteindre une saturation périphérique de 90% fut mesurée.

La durée d'apnée non hypoxique était plus longue dans le groupe PEEP par rapport au groupe ZEEP (599 +/- 135 s vs 470 +/- 150 s, p= 0,007).

Nous concluons que l'application d'une pression positive durant la phase d'induction d'une anesthésie générale chez l'adulte prolonge la durée d'apnée non hypoxique de plus de 2 minutes.

The effect of positive airway pressure during pre-oxygenation and induction of anaesthesia upon duration of non-hypoxic apnoea

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Summary

Positive end-expiratory pressure (PEEP) applied during induction of anaesthesia may prevent atelectasis formation in the lungs. This may increase the duration of non-hypoxic apnoea by increasing the functional residual capacity. We studied the benefit of PEEP applied during the induction of anaesthesia on the duration of apnoea until the SpO_2 reached 90%. Forty ASA I–II patients were randomly allocated to one of two groups. In the PEEP group ($n = 20$) patients were pre-oxygenated using 100% O_2 administered using a CPAP device (6 cmH_2O) for 5 min. Following induction of anaesthesia, patients were mechanically ventilated (PEEP 6 cm H_2O) for a further 5 min. In the ZEEP group ($n = 20$), no CPAP or PEEP was used. The duration of apnoea until SpO_2 reached 90% was measured. Non-hypoxic apnoea duration was longer in the PEEP group compared to ZEEP group (599 ± 135 s vs. 470 ± 150 s, $p = 0.007$). We conclude that the application of positive airway pressure during induction of anaesthesia in adults prolongs the non-hypoxic apnoea duration by > 2 min.

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Induction of general anaesthesia causes an increase in intrapulmonary shunt [1], which is mainly caused by atelectasis formation [2]. Atelectasis appears within minutes of induction of anaesthesia in the lungs of 85–90% of healthy, non-obese patients [3, 4].

In cases of difficult airway management, duration of non-hypoxic apnoea, defined as apnoea with $SpO_2 > 90\%$, depends on the reserves of oxygen held within the body, which are mainly in the functional residual capacity (FRC) [5]. To a lesser degree, intrapulmonary shunt will also influence the duration of non-hypoxic apnoea. Therefore, avoiding atelectasis formation may increase the duration of non-hypoxic apnoea and, in consequence, increase the margin of safety.

It has been shown that FiO_2 used during pre-oxygenation greatly influences atelectasis formation. Even a FiO_2 of 0.8 will prevent atelectasis formation compared to 100% oxygen, although, at the cost of a decrease in the non-hypoxic apnoea duration from 411 to 303 s [6].

We have recently shown that atelectasis formation can be effectively prevented by the application of positive end-expiratory pressure (PEEP) applied during the induction of anaesthesia, despite the use of 100% of oxygen [7]. Therefore, applying PEEP during the entire induction of anaesthesia with 100% O_2 may increase the duration of the non-hypoxic apnoea.

The aim of this study was to assess the efficacy of the application of PEEP during induction of anaesthesia in prolonging the apnoea period before a critical desaturation to a $SpO_2 < 90\%$ occurred.

Methods

The study was approved by the Local Research Ethics Committee of the University Hospital of Lausanne,

Switzerland. All patients gave their written informed consent to participate in the study. Forty patients, ASA I or II, aged 16–60 years, admitted for elective surgery were enrolled into the study. Exclusion criteria included $SpO_2 < 97\%$ breathing room air, body mass index > 25 kg.m^{-2} and all medical conditions that contraindicated even a short desaturation or rise in $PaCO_2$ such as coronary artery disease, cerebrovascular disease, intracranial hypertension, epilepsy and severe pulmonary disease. We also excluded patients who had been in hospital for > 24 h with bed rest prior to induction of anaesthesia, because atelectasis may already be present in these patients. Patients were randomly allocated to either PEEP (positive end expiratory pressure) or ZEEP (zero end expiratory pressure) groups.

Patients were premedicated using 7.5 mg midazolam orally. In the operating room, in addition to the routine monitoring, the same pulse oximetry was used for all patients (Datex-Engstrom division, type F-LMP1-00–00, Helsinki Finland).

Both groups were preoxygenated for 5 min with 100% O_2. Anaesthesia was induced using fentanyl 3 µg.kg^{-1}, propofol (Diprifusor; AstraZeneca, Macclesfield, Cheshire, UK) with a target concentration of 4 µg.kg^{-1} and rocuronium 1 mg.kg^{-1}. Following induction, mechanical ventilation of the lungs (Dräger Oxylog, Drägerwerk AG, Lübeck, Germany) (VT 8 ml.kg^{-1}; rate 10 min^{-1}) was applied for a further 5 min using a facemask with 100% O_2 followed by tracheal intubation. In the PEEP group ($n = 20$), pre-oxygenation was undertaken using a CPAP device (6 cmH$_2$O) and ventilation was performed with PEEP maintained at 6 cmH$_2$O. In ZEEP group ($n = 20$), patients were identically ventilated but without CPAP or PEEP.

Following intubation, no pressure was applied to the airway and correct placement of the tracheal tube was confirmed using fibroscopy. The tracheal tube was left open to air at atmospheric pressure and the patient remained apnoeic until SpO$_2$ reached 90%. Capnography was used to monitor involuntary breathing. Patients were then reoxygenated using 100% O_2 and a recruitment manoeuvre applied until SpO$_2$ reached initial values.

The SpO$_2$ in ambient air and following 4 min of mechanical ventilation using a facemask was recorded. Blood gas measurements were performed following 4 min of mechanical ventilation (prior to apnoea) and when SpO$_2$ reached 92%. Apnoea duration was measured from the end of mechanical ventilation to the time when SpO$_2$ reached 90%.

Statistical analysis
The calculation of the sample size was based on previous studies [8]. The size was calculated to detect a difference of 50% in atelectasis between the groups, with p = 0.05 and a power of 80%. Values are expressed as mean +/− standard deviation (SD). Paired and unpaired Student's *t*-tests were used for comparisons within and between groups, respectively. Chi-square was used to compare discrete variables. The Pearson product-moment correlation coefficient was calculated to assess relationship between the duration of non-hypoxic apnoea and various parameters. A p-value < 0.05 was considered significant. The statistical package used was JMP (Version 5.01; SAS Institute, Cary, NC).

Results

The two study groups were similar (Table 1). We were unable to successfully perform arterial puncture in one patient of each group.

The mean (SD) duration of non-hypoxic apnoea was found to be significantly longer in the PEEP group compared to the ZEEP group (Fig. 1) (599 ± 137 s vs. 470 ± 150 s, respectively). PaO$_2$ measured prior to apnoea was higher and PaCO$_2$ lower in the PEEP group than in ZEEP group (Table 2). When SpO$_2$ reached 92% there was no difference between groups for PaO$_2$ or PaCO$_2$.

Table 1 Patient characteristics.

	ZEEP group (n = 20)	PEEP group (n = 20)
Age; years	36 ± 8	34 ± 13
Sex; M/F	12/8	11/9
BMI; kg m^{-2}	22 ± 2	22 ± 2
ASA; I/II	8/12	13/7
Smoker; yes/no	9/11	4/16

Data are presented as mean ± SD.
ZEEP = zero end-expiratory pressure; PEEP = positive end-expiratory pressure; BMI = body mass index.
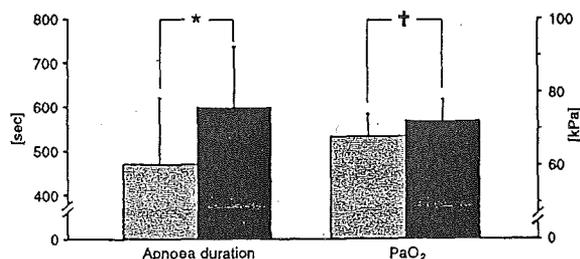

Figure 1 Duration of non-hypoxic apnoea and PaO$_2$ before apnoea in ZEEP (zero end-expiratory pressure) and PEEP (positive end-expiratory pressure) patients. *p = 0.007 and †p = 0.03 for comparison between groups. □ – ZEEP, ■ – PEEP.

Table 2 Blood gases (all units are in kPa).

	ZEEP group (n = 19)	PEEP group (n = 19)	p
PaO$_2$ before apnoea	68.0 ± 6.4	72.5 ± 5.7	0.030
PaCO$_2$ before apnoea	6.0 ± 0.9	5.5 ± 0.5	0.014
PaO$_2$ at SpO$_2$ = 92%	9.8 ± 1.6	10.1 ± 1.1	0.500
PaCO$_2$ at SpO$_2$ = 92%	8.5 ± 1.3	8.8 ± 0.9	0.556

Data are presented as mean ± SD.
ZEEP = zero end-expiratory pressure; PEEP = positive end-expiratory pressure.

We found no correlation between the duration of non-hypoxic apnoea with PaO$_2$ before apnoea (R^2 = 0.026), BMI (R^2 = 0.019), smoking (R^2 = 0.033) or age (R^2 = 0.005). In subgroup analysis, female patients showed a tendency towards shorter non-hypoxic apnoea duration compared to male patients in the PEEP group (536 ± 95 s for female vs. 645 ± 147 s for male, p = 0.062). This difference was not observed in ZEEP group (458 ± 165 for female vs. 479 ± 146 for male).

Discussion

The main finding of this study was that the application of PEEP during the induction of anaesthesia increased the duration of non-hypoxic apnoea by 2 min.

During apnoea, oxygenation depends on the oxygen reserves stored within the body. These stores are quantitatively low and are mainly localised in three compartments: the lungs, plasma and red cells. The normal stores of oxygen are approximately 1500 ml, and this may be increased to 3700 ml following pre-oxygenation with 100% oxygen [5]. Half of this increase is due to the increase in the oxygen concentration in the functional residual capacity (FRC). During general anaesthesia, up to 85–90% of patients develop atelectasis in dependent lung regions within 5 min of induction [3]. Atelectasis results in a decrease in FRC and a reduction in the oxygen stored in the body. In addition, it also increases intrapulmonary shunt [9], which will hasten desaturation to hypoxic levels. Application of PEEP during induction of anaesthesia therefore increases the duration of non-hypoxic apnoea by preventing atelectasis formation, increasing oxygen stores and decreasing intrapulmonary shunt.

It has been shown that, in the UK during the 1980s, three pregnant women died during induction of general anaesthesia every year due to difficulties associated with ventilation or intubation. It has been estimated that difficulties in airway management during induction of anaesthesia may kill up to 600 patients every year [10].

Difficult airway management is not easily anticipated, so prevention of atelectasis formation during induction of anaesthesia may have benefits for many patients.

Previous studies have shown that decreasing FiO$_2$ [11], or avoiding pre-oxygenation [12], will prevent atelectasis formation; however, the cost of this is a reduction in the time before significant hypoxaemia occurs. A recent study has shown that oxygen concentrations as high as 80% are sufficient to diminish atelectasis formation compared to 100% O$_2$; however, the time of non-hypoxic apnoea is decreased by > 90 s [6]. In a previous study, we have shown that the application of PEEP throughout the induction of anaesthesia effectively prevents atelectasis formation despite the use of 100% O$_2$ [7]. This study demonstrates that this technique also has a direct positive effect in producing an increased margin of safety by increasing the non-hypoxic apnoea duration by 2 min.

The tendency for a shorter non-hypoxic apnoea duration in women in the PEEP group may be explained by a 10% lower FRC commonly seen in women [13]. Atelectasis is probably not the cause of this difference. In previous work we have not seen that the prevention of atelectasis by application of PEEP is less effective in females compared to male patients [7]. On the contrary, in fact in the ZEEP group atelectasis developed during the induction of anaesthesia [7], which decreases FRC. The absence of differences between male and females, in ZEEP group may indicate that the decrease in FRC produced by atelectasis formation reduces the gender differences.

No difference was observed between smokers and non-smokers with regard to the duration of non-hypoxic apnoea. Tobacco smoking is known to be associated with hypoxemia and an increase in PA–aO$_2$ gradient due to decreased diffusion capacity [14]. It seems that this diffusion defect has no clinical implication in our selected group of patients. Indeed, our exclusion criteria included any pulmonary symptoms and a SpO$_2$ in room air of < 97%. Therefore, it may be that we have selected light smokers without significant pulmonary sequelae.

One limitation of this study is that it is not possible to distinguish between the effects of CPAP applied during pre-oxygenation and PEEP applied during the initial phase of artificial ventilation. It has been shown that atelectasis occurs within minutes of induction of anaesthesia [15], but that no atelectasis will occur in awake, healthy, non-obese patients when breathing 100% oxygen [7]. Therefore the application of PEEP may be more important. Nevertheless, this technique may also be applied to patients more at risk of desaturation, such as morbidly obese patients [16], or when no mechanical ventilation will be applied such as during rapid sequence

induction. We therefore consider the combined CPAP-PEEP approach as the more generally applicable technique.

Application of CPAP (6 cmH$_2$O) for 5 min in conscious patients followed by 5 min of mechanical ventilation with PEEP (6 cmH$_2$O) in sedated patients is safe, simple and well accepted by patients. CPAP at 6 cmH$_2$O applied in awake patients is unlikely to have any cardiovascular effects as it is frequently used at this pressure level in the postoperative period with little cardiovascular side effects. On the other hand, PEEP may have deleterious effects as it may increase mean airway pressure. As we ventilated the patients using the pressure-controlled mode, the mean airway pressure was easily controlled and was maintained at lower levels than when manually ventilating patients. Therefore, application of low level of PEEP during the induction period is unlikely to have produced deleterious cardiovascular effects.

A potential risk of mechanical ventilation using a facemask with PEEP is to expose a sedated, paralysed patient to stomach insufflation and, as a result, increase the risk of regurgitation and aspiration. This risk exists with an inflation pressure > 20 cmH$_2$O, which can be easily obtained using manual ventilation [17, 18]. Alarm limits of the ventilator can be set to 20 cmH$_2$O and it is also possible to ventilate patient in the pressure-controlled mode, which will prevent the use of increased pressure via the facemask. Therefore, the proposed technique may even decrease these risks.

At the end of mechanical ventilation PaCO$_2$ was lower in the PEEP group (Table 2). The ventilation was standardised (Vt 8 ml.kg^{-1} at 10 breaths per min); therefore the mode of ventilation cannot be the cause of this difference. This difference may be related to the fact that PEEP helped to maintain airways open and may therefore have increased the alveolar minute ventilation. In contrast, the application of PEEP may cause overdistension of already expanded alveoli with reduction of perfusion and therefore increasing alveolar dead space. In healthy lungs, this effect is not observed unless PEEP levels > 10–15 cmH$_2$O are used [19]. Nevertheless, if this phenomenon had occurred in our study, PaCO$_2$ should have been higher (and not lower) in the PEEP group. Therefore, application of PEEP had probably no effect on dead space in our study.

We therefore, conclude that application of CPAP (6 cmH$_2$O) for 5 min during pre-oxygenation followed by 5 min of mechanical ventilation with PEEP (6 cmH$_2$O) during induction of anaesthesia is safe, simple and well accepted by patients. It prolongs the non-hypoxic period of apnoea by 2 min. This technique may have advantages if not for all patients, at least for those in which difficult airway management is anticipated.

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