Effect of positive end-expiratory pressure on gastric insufflation during induction of anaesthesia when using pressure-controlled ventilation via a face mask

A randomised controlled trial

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BACKGROUND  Face mask ventilation (FMV) during induction of anaesthesia is associated with risk of gastric insufflation that may lead to gastric regurgitation and pulmonary aspiration. A continuous positive airway pressure (CPAP) has been shown to reduce gastric regurgitation. We therefore hypothesised that CPAP followed by FMV with positive end-expiratory pressure (PEEP) during induction of anaesthesia would reduce the risk of gastric insufflation.

OBJECTIVE  The primary aim was to compare the incidence of gastric insufflation during FMV with a fixed PEEP level or zero PEEP (ZEEP) after anaesthesia induction. A secondary aim was to investigate the effects of FMV with or without PEEP on upper oesophageal sphincter (UES), oesophageal body and lower oesophageal sphincter (LES) pressures.

DESIGN  A randomised controlled trial.

SETTING  Single centre, Department of Anaesthesia and Intensive Care, Örebro University Hospital, Sweden.

PARTICIPANTS  Thirty healthy volunteers.

INTERVENTIONS  Pre-oxygenation without or with CPAP 10 cmH2O, followed by pressure-controlled FMV with either ZEEP or PEEP 10 cmH2O after anaesthesia induction.

MAIN OUTCOME MEASURES  A combined impedance/manometry catheter was used to detect the presence of gas and to measure oesophageal pressures. The primary outcome measure was the cumulative incidence of gastric insufflation, defined as a sudden anterograde increase in impedance of more than 1 kΩ over the LES. Secondary outcome measures were UES, oesophageal body and LES pressures.

RESULTS  The cumulative incidence of gastric insufflation related to peak inspiratory pressure (PIP), was significantly higher in the PEEP group compared with the ZEEP group (log-rank test \( P < 0.01 \)). When PIP reached 30 cmH2O, 13 out of 15 in the PEEP group compared with five out of 15 had shown gastric insufflation. There was a significant reduction of oesophageal sphincter pressures within groups comparing pre-oxygenation to after anaesthesia induction, but there were no significant differences in oesophageal sphincter pressures related to the level of PEEP.

CONCLUSION  Contrary to the primary hypothesis, with increasing PIP the tested PEEP level did not protect against but facilitated gastric insufflation during FMV. This result suggests that PEEP should be used with caution after anaesthesia induction during FMV, whereas CPAP during pre-oxygenation seems to be safe.

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pressure (CPAP) during pre-oxygenation, followed by pressure-controlled face mask ventilation (FMV) with a positive end-expiratory pressure (PEEP) during induction of anaesthesia.\textsuperscript{4} CPAP during pre-oxygenation, and FMV with PEEP during induction of anaesthesia, are thus frequently recommended.\textsuperscript{5,6} During pre-oxygenation and induction, CPAP increases FRC and thereby the oxygen reserve, with a prolongation of time to desaturation in the case of poor airway control.\textsuperscript{7,8} However, PEEP has some relevant disadvantages, in particular, circulatory compromise and elevated peak inspiratory pressure (PIP).\textsuperscript{9} With higher PIP during FMV, the risk for gastric insufflation increases.\textsuperscript{10,11} Insufflation of gas into the stomach may elevate intragastric pressure, thus increasing the risk for regurgitation of gastric contents and pulmonary aspiration.\textsuperscript{12} Even though pulmonary aspiration during anaesthesia is a rare event, it is one of the leading causes of mortality related to general anaesthesia.\textsuperscript{13,14}

Significantly, it has been observed that CPAP has a protective effect regarding reflux symptoms in CPAP-treated patients with obstructive sleep apnoea syndrome (OSAS) and in patients with nocturnal gastro-oesophageal reflux without OSAS, because of an increased lower oesophageal sphincter (LES) pressure.\textsuperscript{15–17}

Since PEEP is frequently used in clinical practice during mask ventilation, despite increased PIP, we sought to investigate whether the protective mechanisms, seen in CPAP-treated patients, also would apply during FMV under anaesthesia induction. In previous studies, a PIP of 15 cmH\textsubscript{2}O has been considered safe regarding gastric insufflation\textsuperscript{10,18}; therefore, we chose to study the possible protective effect of PEEP in patients with PIP between 15 and 30 cmH\textsubscript{2}O.

Historically, detection of air insufflation has been performed by auscultation with a stethoscope over the epigastic area, a method with uncertain reliability.\textsuperscript{19} With a combined high-resolution manometry and impedance catheter (HRIM), it is possible to detect gas and liquids flowing through the oesophagus and simultaneously perform manometric measurements of oesophageal pressures.\textsuperscript{20} With these properties, the technique seemed to be an ideal method to use in this study.

The primary aim of the current study was to investigate the effects of PEEP on gastric insufflation during pressure-controlled FMV after anaesthesia induction. A secondary aim was to investigate the effects of FMV with PEEP on upper oesophageal sphincter (UES), oesophageal body and LES pressures during induction of anaesthesia.

**Materials and methods**

**Study participants**

The study protocol (ClinicalTrials.gov registration number NCT02238691) was approved by the Central Ethics Review Board, Uppsala, Sweden (Dnr 2014/343, approval date 11/19/14). The trial was conducted at the Department of Anaesthesiology, Örebro University Hospital, Sweden, February 2015. Thirty healthy volunteers, 18 males and 12 females, were recruited to participate in this randomised controlled trial. All participants received verbal and written information about the study details before written consent was obtained. All volunteers received financial compensation. A pre-operative evaluation was performed including airway status assessment. All participants had a Mallampati score of I to II and none had other clinical signs of difficult mask ventilation. Inclusion criteria were age 18 to 40 years, American Society of Anesthesiologists physical status class 1, and a BMI of 18.5 to 30 kg m\textsuperscript{2}. Exclusion criteria were pregnancy, breastfeeding, fasting not suitable or a history of gastro-intestinal disease.

**Equipment**

All participants were ventilated using a turbine-driven ventilator (Dräger Zeus Infinity Empowered, Dräger Medical, Lübeck, Germany). Manometric and impedance measurements were performed with an HRIM catheter (Sierra Scientific Instruments, Los Angeles, California, USA). The catheter, a solid-state assembly, consists of 36 circumferential manometry sensors at 1 cm intervals, and 18 impedance segments at 2 cm intervals. The closely positioned pressure transducers enable detailed assessment of oesophageal and gastric pressure characteristics. It is thus possible to simultaneously measure pressure variations in the UES, oesophageal body, LES and the stomach. The technique has been validated for oesophageal measurements in the field of gastroenterology and is today considered the gold standard in evaluating oesophageal motility disorders.\textsuperscript{21,22}

Oesophageal impedance monitoring is performed by measuring the impedance of an alternating electric current generated between pairs of impedance segments mounted on the catheter. After insertion of the catheter, baseline recordings are made. Variations in impedance are then observed, high values corresponding to the low conductivity of gas and low values when fluids are present. Recorded data are presented on a real-time topographic plot with pressures and impedance plotted on the \(y\)-axis and time on the \(x\)-axis. In this plot the direction and force of the oesophageal pressure wave, as well as the direction of flow of gas or liquids are visualised. All manometric and impedance data were recorded, stored and later analysed using the ManoView software (Sierra Scientific Instruments, Los Angeles, California, USA). Before each recording, the catheter was calibrated in a pressurised chamber according to the manufacturer’s instructions.

**Protocol**

Randomisation was performed after enrolment, before start of protocol, using sequentially numbered sealed
opaque envelopes. A fasting period of 6 h was obligatory. All participants were monitored with continuous electrocardiography, pulse oximetry and automatic, noninvasive blood pressure measurement. Topical lidocaine (Lidocaine 100 mg ml$^{-1}$, AstraZeneca, Södertälje, Sweden) was used before transnasal insertion of the HRIM catheter. The catheter was positioned to record pressures and impedance signals from the hypopharynx to the stomach. All measurements were made with the subject in the supine position, with the head in a neutral position. Once the position of the catheter had been confirmed, the device was taped to the nose, followed by a 5-min stabilisation period for the participants to get accustomed to the catheter. Thereafter, pre-oxygenation with 100% oxygen during spontaneous breathing by mask was conducted for 3 min without CPAP or 10 cmH$_2$O CPAP. After pre-oxygenation, target-controlled infusions of remifentanil (Minto pharmacokinetic model, effect site concentration 6 ng ml$^{-1}$) and propofol (Marsh pharmacokinetic model, effect site concentration 6 µg ml$^{-1}$) (Alaris PK Syringe Pump, CareFusion, Basingstoke, UK) were started. No neuromuscular blocking agent was used. Approximately 30 s after loss of spontaneous breathing, a jaw thrust was performed, and with a 200 mask ventilation technique, pressure-controlled FMV using the ventilator with either zero PEEP (ZEEP) or 10 cmH$_2$O PEEP was started. No oropharyngeal airway was used due to risk of interference with the HRIM catheter. In both groups, the ventilator was set in a pressure-controlled ventilation (PCV) mode at a respiratory rate of 10 bpm with an inspiration:expiration ratio of 1:2. At initiation of PCV, inspiratory pressure above PEEP/ ZEEP ($\Delta P$) was set at 5 cmH$_2$O until detection of end-tidal carbon dioxide (EtCO$_2$) on the capnograph. When EtCO$_2$ was detected, the airway was considered to be open. Thereafter, the $\Delta P$ was elevated by 5 cmH$_2$O every 2 min until a PIP of 30 cmH$_2$O was reached or gastric insufflation occurred. Since equal PIP pressures were compared, there was a time delay of approximately 4 to 6 min in the ZEEP group because of initial titration of $\Delta P$. Throughout the procedure, a designated person listened with a stethoscope over the epigastric area, to detect sounds of gastric insufflation. When obvious gastric insufflation was auscultated, the protocol was aborted for safety reasons with no further increase in $\Delta P$.

**Measurements**

Events of gastric insufflation were defined as a sudden anterograde 1 kΩ increase in impedance over the LES, in accordance with previous studies on belching and aerophagia (Fig. 1).

Pressures at the UES, oesophageal body and LES were measured during inspiration at pre-oxygenation, during apnoea and after two to three cycles at each PIP level of FMV. Oesophageal body pressures were recorded and are presented as mean pressure, measured from the lower border of the UES to the upper border of the LES.
Statistical analyses
When designing the study, a crude estimate was made based on our hypothesis that there would be a reduction in risk for gastric insufflation by the application of PEEP at equal PIP, in accordance with results from studies on CPAP treatment in nonanaesthetised patients. A sample size was therefore calculated assuming a gastric insufflation incidence of 80% at a peak airway pressure of 30 cmH₂O in the control group and 30% in the intervention group. It would require in total 28 individuals, 14 in each group, to achieve 80% power with a 5% significance level. Power and Sample Size Calculation version 3.1.2 was used for calculations. A total of 30 volunteers were included in case of technical problems with the HRIM catheter.

For each study group, the cumulative incidence of gastric insufflation events for each increase in PIP was portrayed on a Kaplan–Meier curve, and statistical comparison performed with a log-rank test. The proportion of events was also compared between study groups for comparable PIP levels (15 to 30 cmH₂O) with Bonferroni–Holm-corrected χ² test or Fisher exact test, when appropriate. A linear mixed model for repeated measurements with unstructured correlation format was used to evaluate oesophageal pressures, using study group, ventilatory settings and their interactions as categorical variables. Oesophageal pressures were compared at five different ventilatory settings within the study groups, and as well as between the different ventilatory settings within each study group (Fig. 3a to c). Comparisons between groups were adjusted for multiple comparisons with Bonferroni correction.

A P value less than 5% was considered significant. All statistical analyses were performed using SPSS version 22 (IBM Corp., Armonk, New York, USA).

Results
All participants completed the study protocol. For demographic data see Table 1. No adverse events were observed during the study. Haemodynamic monitoring data showed significant reduction of mean arterial pressure and bradycardia after anaesthesia induction in both groups but no significant difference between groups. No anticholinergic or vasoactive drugs were needed.

Impedance-detected gastric insufflation
Results are presented as Kaplan–Meier curves. The cumulative incidence of gastric insufflation related to PIP was significantly higher in the PEEP group compared with the ZEEP group (log-rank test $P < 0.01$) (Fig. 2).

At a PIP of 15 cmH₂O or below, there were no insufflation events in either group. At a PIP of 20 cmH₂O, three out of 15 in the PEEP group compared with 0 out of 15 in the ZEEP group ($P = 0.45$) showed gastric insufflation. At a PIP of 25 cmH₂O, seven out of 15 in the PEEP group compared with three out of 15 in the ZEEP group showed gastric insufflation ($P = 0.01$). At PIP 30 cmH₂O, 13 out of 15 compared with five out of 15 showed gastric insufflation ($P = 0.01$).

In analyses of impedance curves, six out of 30 participants, five in the PEEP group and one in the ZEEP group, showed gastric insufflation detected as a sudden rise in impedance, detected by the HRIM catheter over the LES, before they could be detected with the stethoscope. None of the participants had auscultatory detected insufflations before they were detected by impedance measurements.

Upper oesophageal sphincter pressure variation
No statistically significant differences in LES pressure were found between groups at any of the compared ventilatory settings (Fig. 3a). The UES pressure was significantly decreased after induction of anaesthesia in both groups, in the ZEEP group, from 104.5 during pre-oxygenation to 43.9 cmH₂O at apnoea, a mean difference of 60.6 cmH₂O (CI 95% 38.8 to 82.5, $P < 0.01$), and from 95.6 to 38.6 cmH₂O in the PEEP group, a mean difference of 57.0 cmH₂O (CI 95% 35.1 to 78.9, $P < 0.01$). A further significant decrease within groups was seen from apnoea to FMV at PIP 20, from 43.9 to 12.5 cmH₂O in the ZEEP group, a mean difference of 31.4 cmH₂O (CI 95% 17.7 to 45.1, $P < 0.01$), and from 38.6 to 13.2 cmH₂O in the PEEP group, a mean difference of 25.4 cmH₂O (CI 95% 11.7 to 39.0, $P < 0.01$) (Fig. 3a).

Oesophageal body pressure variation
Oesophageal body pressures were not significantly affected by either anaesthesia or PIP level. Mean pressures varied from 7.9 to 9.5 cmH₂O in the ZEEP group and from 7.4 to 10.3 cmH₂O in the PEEP group (Fig. 3b).

Lower oesophageal sphincter pressure variation
From spontaneous breathing to start of pre-oxygenation there was significant increase in LES pressure from 50.0 to 73.9 cmH₂O in the PEEP group, a mean difference of 23.9 cmH₂O (CI 95% 9.3 to 38.5, $P < 0.01$), whereas there was no significant difference in the ZEEP group, 59.3 compared with 64.2 cmH₂O, a mean difference of 4.9 cmH₂O (CI 95% −9.7 to 19.5, $P = 0.50$).

After induction of anaesthesia there was a significant reduction in mean LES pressure within groups, from 64.2 at pre-oxygenation to 32.3 cmH₂O at apnoea in the ZEEP group, a mean difference of 31.9 cmH₂O (CI 95% 19.7 to 44.2, $P < 0.01$), and from 73.9 to

### Table 1 Personal data

|                  | ZEEP, n = 15 | PEEP 10 cmH₂O, n = 15 |
|------------------|--------------|-----------------------|
| Sex (male/female)| 10/5         | 8/7                   |
| Age (years)      | 25.5 ± 4.7   | 26.8 ± 4.7            |
| Height (cm)      | 178 ± 9      | 177 ± 11              |
| Weight (kg)      | 74.6 ± 12.6  | 76.6 ± 16.6           |
| BMI (kg/m²)      | 23.5 ± 2.8   | 24.1 ± 2.9            |

Data presented as mean (±SD) or numbers when applicable. PEEP, positive end-expiratory pressure; ZEEP, zero positive end-expiratory pressure.
29.9 cmH₂O in the PEEP group, a mean difference of 44.0 cmH₂O (CI 95% 31.8 to 56.2, \(P < 0.01\)). After apnoea, during FMV there were no statistical differences in LES pressure within or between groups, regardless of PIP (Fig. 3c).

**Discussion**

In this randomised controlled study, we hypothesised that PEEP would reduce the incidence of gastric insufflation events during face mask PCV at equal PIP compared with ZEEP, in anaesthetised individuals. The results showed, to the contrary, that the cumulative incidence of gastric insufflation events was significantly higher with the application of 10 cmH₂O PEEP compared with ZEEP. No gastric insufflation was seen in either group at a PIP of 15 cmH₂O.

It is well known that high PIP increases the risk of gastric insufflation during FMV. Our study adds the important information that when PEEP was included in the PIP, the risk for gastric insufflation increased. These results were not expected beforehand, since data from previous studies on nonanaesthetised patients have shown protective properties of CPAP treatment of OSAS and reflux patients, with an increase in LES tonus and a reduction in gastric reflux.¹⁵–¹⁷

In the current study, there was an immediate significant increase in LES pressure when 10 cmH₂O of CPAP was applied, consistent with the findings from the study by Shepherd *et al.*,¹⁷ performed on spontaneously breathing patients.

The increased tonus in the LES seen with CPAP during pre-oxygenation was abolished after anaesthesia induction, and a significant reduction of LES pressure was seen, regardless of whether PEEP was applied or not. The immediate increase of LES pressure when CPAP was applied, followed by the equalisation of LES...
pressures indicates that the high LES pressures seen with CPAP before anaesthesia might be due to a reflexive mechanism that was suppressed by anaesthesia. Similarly, when the participants were awake, high UES pressures were recorded, pressures that markedly decreased after anaesthesia induction (Fig. 3).

Based on the results of this study, it seems that PEEP facilitates the passage of gas into the oesophagus during anaesthesia, and the protective mechanisms, seen at spontaneous breathing, are reversed after anaesthesia induction, with an increased risk of gastric insufflation. The reason for the higher incidence of gastric insufflation with PEEP is somewhat unclear. Indeed, there would be a higher mean airway pressure in the PEEP group than in the ZEEP group; however, all the observed gastric insufflations were observed during inspiration. Furthermore, most gastric insufflations were seen immediately after an elevation of \( \Delta P \), and even at PIP 30 cmH\(_2\)O, the calculated mean airway pressure was 17 cmH\(_2\)O in the PEEP group, which did not exceed LES pressure in our participants at this level.

When 10 cmH\(_2\)O of PEEP was applied, most of the participants showed gastric insufflation when PIP was titrated above LES pressure, whereas most of the participants in the ZEEP group resisted insufflation even when PIP exceeded LES pressure. The manometry/impedance catheter readings gave no clear explanation for this phenomenon. Theoretically, a high PEEP level could insufflate the oesophagus with gas, abolishing surface tension effect of the collapsed oesophagus, facilitating passage of gas into the stomach. However, when the impedance curves were analysed, there was no indication of gas trapping in the oesophagus, as impedance levels returned to baseline during expiration.

Even if there is an increased risk of gastric insufflation with PEEP during FMV, the use of CPAP/PEEP during pre-oxygenation and FMV after anaesthesia induction has several respiratory benefits and should therefore be used when applicable. Nevertheless, it is important to be aware that PEEP can cause gastric insufflation, especially in certain high-risk patients, who have an increased risk for regurgitation. It seems crucial to maintain PIP as low as possible. We saw no gastric insufflation events until PIP reached 20 cmH\(_2\)O in the PEEP group. We therefore recommend PCV, rather than manual or volume-controlled, to avoid peak pressures above 15 cmH\(_2\)O when PEEP is applied during FMV.\(^{18,28}\)

In the ZEEP group there were no insufflations until a PIP of 25 cmH\(_2\)O, a considerably higher pressure than the findings from the study by Bouvet et al.,\(^{27}\) where insufflations were seen at PIP as low as 10 to 15 cmH\(_2\)O with ZEEP. We have no clear explanation for these differences, other than use of different techniques of measuring insufflation. In previous studies, a PIP of 15 to 20 cmH\(_2\)O has been considered as safe during FMV.\(^{18,29}\) In our opinion 15 cmH\(_2\)O is a reasonable limit, since the PIP probably needs to be greater than the LES pressure to insufflate the stomach. In line with results from several previous studies, the vast majority of the participants in our study (28/30) had a LES pressure above 15 cmH\(_2\)O during anaesthesia.\(^{30,31}\) Notably, the two participants with a LES pressure less than 15 cmH\(_2\)O both withstood insufflation during ZEEP ventilation with a PIP of 20 cmH\(_2\)O.

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The PEEP level chosen in this study setting was relatively high. It can be argued that in clinical practice more moderate PEEP levels are used. We considered a level of 10 cmH₂O as reasonable, in accordance with our primary hypothesis trying to establish a reduction in gastric insufflation. Recently, two studies have demonstrated that a PEEP level of 6 to 7 cmH₂O as a single intervention in nonobese patients results in an ‘open lung’ with minimal atelectasis, as investigated by computed tomography immediately before emergence from anaesthesia.12,33 Extrapolating from these two studies and the current study, the following implication might evolve: If pre-oxygenation starts, using first a CPAP of 6 to 7 cmH₂O and then a PEEP of the same magnitude during induction of anaesthesia, this should both give the respiratory advantages and definitely be safe in healthy, fasting patients, such as in this study, as long as PIP is no higher than 15 cmH₂O. This is assuming that the risk for gastric insufflation with lower PEEP at equal PIP per se is not higher than with PEEP of 10 cmH₂O. We suggest, that the physiological phenomenon, with PEEP facilitating gastric insufflation during mask ventilation, is assumed to be present also in all patients with increased risk of gastric regurgitation. Therefore, PEEP should be avoided after pre-oxygenation in these risk patients before the airway is secured.

The use of an HRIM catheter to measure oesophageal pressures and to evaluate gastric insufflation provides us with a unique opportunity to investigate oesophageal physiology prior to and during FMV. With this method, it is possible to detect intraluminal passage of gas and the way the oesophageal sphincters behave, simultaneously. The use of a stethoscope, which is commonly used to identify gastric insufflation, has its limitations. It is a subjective method, and the risk for false positive or negative findings is relatively high.15 In this study, the auscultatory method missed six gastric insufflations that were detected by the impedance technique.

Despite many advantages of the manometry/impedance technique, there are some limitations. The method is sensitive in detecting the presence of gas, but it cannot measure the amount of gas insufflated. Even if the catheter is equipped with manometry sensors, the compliance of the stomach is high, and small amounts of gas will not lead to a rise in pressure. If the method could be combined with the ultrasound technique described by Bouvet et al.32 an estimation of the amount of gas insufflated would also be possible.

Due to the study design, the ZEEP group had been anaesthetised for a longer time than the PEEP group at a given PIP. The time difference did not influence the observed pressures in UES, oesophageal body or LES, and therefore, in our opinion, any eventual difference in the depth of anaesthesia between the groups did not matter.

Since the primary aim was to investigate the impact of PEEP as a part of PIP on gastric insufflation, ventilatory settings resulted in supranormal tidal volumes and hypocapnia in most study participants and especially so with PEEP, as they were young adults with healthy lungs. The combination of large tidal volumes and hypocapnia might have affected the results, in spite of the fact that ventilation was pressure controlled.

Conclusion

PEEP seems to alter oesophageal protective mechanisms, enabling gastric insufflation in a manner independent of elevated PIP, which should not exceed 15 cmH₂O if applied with an unprotected airway. Using CPAP during pre-oxygenation is safe, as it seems to induce a protective reflexive increase in LES pressure.

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Conflicts of interest: none.

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