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EFFECTS OF INSPIRATORY OXYGEN CONCENTRATION ON ENDTIDAL CARBON MONOXIDE CONCENTRATION

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Patrick Schober, MD, Melanie Kalmanowicz and Stephan A. Loer, PhD, MD, MSc. Effects of inspiratory oxygen concentration on endtidal carbon monoxide concentration.

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ABSTRACT. Objective. Carbon monoxide (CO) is eliminated mainly via the lungs so that exhaled carbon monoxide concentration reflects endogenous production. In this context, we studied the effects of inspiratory oxygen concentration and endotracheal intubation on endtidal CO concentrations. **Methods.** In patients undergoing general anaesthesia, endtidal CO concentrations were measured while breathing room air, oxygen as well as after induction of general anaesthesia and endotracheal intubation. To exclude time-dependent effects, patients were assigned to two groups. Patients in group 1 ($n = 20$) were preoxygenated for 5 minutes, whereas patients in group 2 ($n = 20$) were preoxygenated for 10 minutes. We also studied the effects of different inspiratory oxygen concentrations in volunteers ($n = 20$) breathing room air, 50% and 100% oxygen. **Results.** Breathing oxygen for 5 minutes increased endtidal carbon monoxide concentrations in all patients (in group 1 from 7.6 ± 4.9 to 12.6 ± 5.0 ppm, $p < 0.001$; in group 2 from 7.1 ± 6.1 to 16.4 ± 8.6 ppm, $p < 0.001$). No further change of CO concentration was detected after 10 minutes of preoxygenation (16.4 ± 9.0 vs. 16.4 ± 8.6 ppm, $p > 0.05$). Endtidal CO values however significantly increased with induction of anaesthesia and endotracheal intubation (in group 1 to 21.5 ± 6.3 ppm, $p < 0.001$, in group 2 to 26.1 ± 13.1 ppm, $p < 0.001$). In volunteers, mean endtidal CO values increased from 10.7 ± 5.9 to 14.8 ± 7.3 ppm after breathing 50% oxygen for 3 minutes ($p < 0.001$). Breathing pure oxygen had no additional effect on endtidal CO values (16.0 ± 6.0 ppm, $p > 0.05$). **Conclusions.** Endtidal carbon monoxide levels are influenced by inspiratory oxygen concentrations. Induction of anaesthesia and endotracheal intubation further increases endtidal CO concentrations beyond the effects attributable to preoxygenation alone.

KEY WORDS. carbon monoxide, oxygen, anaesthesia, intubation, mechanical ventilation

INTRODUCTION

Increased exhaled carbon monoxide (CO) levels have been suggested to indicate systemic and airway inflammation [1–5] and critical illness [6, 7]. In previous studies CO concentrations were measured in gas collected from the expiratory outlet of a respirator [5, 8] or from the respiratory circuit [6]. This approach allows to estimate mean CO production during a given sampling period, however, does not allow to determine actual alveolar, and thus also capillary concentration.

This concentration can be measured in samples of endtidal gas. In this context we developed an approach to determine CO concentrations in the last portion of expired gas in intubated anaesthetized patients. Their lungs

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are inflated to total lung capacity and subsequently allowed to exhale passively to functional residual capacity. We were specifically interested to study the effects of inspiratory oxygen fraction (FiO_2) and induction of general anaesthesia with endotracheal intubation on endtidal CO concentrations. We also studied the effects of different inspiratory oxygen concentrations on endtidal CO concentrations in healthy spontaneously breathing volunteers.

METHODS AND MATERIALS

Patients

Measurements were performed in patients ($n = 40$) undergoing anaesthesia for general ($n = 12$) or cardiovascular ($n = 28$) surgery (11 female, 29 male, age 65.4 ± 10.4 years, height 171.7 ± 7.1 cm, weight 80.4 ± 11.4 kg). Current smokers and patients with lung disease were excluded. Informed consent was obtained from all participants and measurements were approved by the Institutional Review Board.

Endtidal carbon monoxide concentrations

Expired CO concentrations were measured with a portable electrochemical monitor (microPac, Dräger, Lübeck, Germany). In this analyzer carbon monoxide is oxidized at the sensing electrode (anode) according to the formula $CO + H_2O \rightarrow CO_2 + 2H^+ + 2e^-$. Simultaneously, oxygen present in the exhaled gas is reduced to water at the counter electrode according to the formula $\frac{1}{2} O_2 + 2H^+ + 2e^- \rightarrow H_2O$ resulting in an overall chemical reaction of $CO + \frac{1}{2}O_2 \rightarrow CO_2$. The generated current is proportional to the carbon monoxide concentration which is displayed in parts per million (ppm). According to the manufacturer CO is measured in the range from 0 to 400 ppm. In preliminary measurement, we observed a reproducibility of endtidal CO measurements of ±4.2% before endotracheal intubation and ±3.1% after intubation in 20 double determinations. The response time of the analyzer (time from the initial deflection to 90% of the plateau value) was 13.1 ± 1.5 seconds when measured 10 times using a calibration gas of 250 ppm. Before each measurement we ensured that no CO was present within the breathing circuit. For this purpose we measured CO concentrations in the breathing circuit, flushed the circuit with a high fresh gas flow (>12 l/min) for three minutes and measured the CO concentration again to exclude any potential accumulation of CO within the breathing system. In addition, we ensured that ambient CO level was 0 ppm to exclude any exogenous CO sources.

Endtidal gas analyzes in spontaneously breathing volunteers

In order to obtain samples of endtidal gas from spontaneously breathing patients, subjects were instructed to exhale slowly from total lung capacity over a period of 20 seconds into a disposable mouthpiece connected to the analyzer via a 30 cm hose (volume 5.9 ml).

Endtidal gas analyzes in anaesthetized intubated patients

Before induction of anaesthesia, pure oxygen (gas flow 12 l/min) was administered via a tightly fitting face mask (preoxygenation) as a safety precaution to minimize the risk of hypoxia in case difficulties in airway management occur. In order to determine time-dependent effects of preoxygenation on alveolar carbon monoxide concentrations, patients were assigned to two groups: Patients of group 1 were preoxygenated 5 minutes whereas patients of group 2 were preoxygenated for 10 minutes prior to induction of general anaesthesia. Measurements of endtidal carbon monoxide concentrations were performed after 5 minutes (both groups) and after 10 minutes of preoxygenation (only group 2).

After induction of anaesthesia (3–5 mg/kg thiopental, 1–3 microgram/kg fentanyl) and muscle relaxation 0.6 mg/kg rocuronium or 0.1 mg/kg pancuronium, patients were ventilated with a mask and pure oxygen for 5 minutes awaiting the onset of muscle relaxation. Thereafter endotracheal intubation was performed (internal diameter 7.5–8.5 mm). In order to obtain endtidal gas samples ventilation was stopped in endinspiration. The endotracheal tube was clamped and disconnected from the breathing system of the ventilator. Subsequently, the hose of the CO analyzer was connected to the endotracheal tube via an airtight adapter. Then the clamp was released so that all gas from the lungs was exhaled through the CO monitor passively to residual functional capacity. Because the last portion of gas flowing through the analyzer represented a sample of endtidal alveolar gas, the highest value measured at this time was defined as endtidal CO concentration (etCO, see Figure 1 for an individual registration). Because of complete muscle relaxation endexpiration could be hold long enough until the analyzer had reached this plateau value (usually within 30 seconds).

Additional etCO measurements were performed after 15 minutes of mechanical ventilation (Julian, Dräger, Lübeck, Germany; FiO_2 1.0, positive endexpiratory

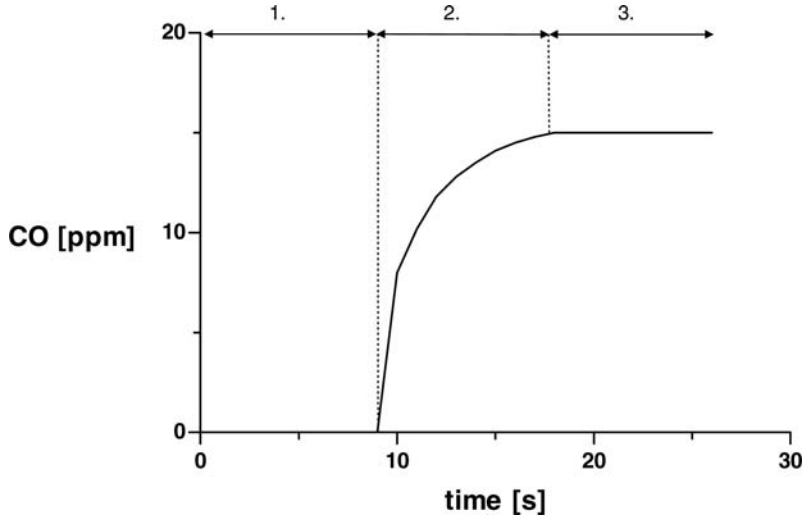

Fig. 1. Registration of expiratory carbon monoxide concentrations of an intubated anaesthetized patient. The CO analyzer was connected to the endotracheal tube in end-inspiration. Thereafter the lungs were allowed to deflate passively. In phase 1, no CO was measured. Phase 2 is characterized by an increase of the reading which reaches a plateau (phase 3) representing the endtidal CO concentration (15 ppm).

pressure 5 mbar, tidal volume 8 ml/kg and a respiratory rate set to maintain normocapnia) to assess time-dependent effects.

Variation of inspiratory oxygen concentration

In order to evaluate the effect of different FiO_2 on endtidal carbon monoxide levels, etCO measurements were performed in 20 healthy, non-smoking volunteers (6 female, 14 male, age 30.8 ± 5.8 years, height 177.9 ± 10.1 cm, weight 74.6 ± 11.7 kg). We ensured that they were not exposed to second hand smoke. All measurement were performed within a non-smoking area with climatisation and no CO was measured in the ambient air. The mode of sampling alveolar gas was identical to the method described above for spontaneously patients before induction of anaesthesia. Measurements were performed during breathing of room air, at a FiO_2 of 0.5 and of 1.0.

Statistics

Data are presented as mean ± standard deviation. Results were analyzed by the Prism 4.0 statistical package (GraphPad Software, San Diego, CA, USA). Differences in etCO concentrations at different time points were analyzed by one way repeated measures analysis of variance (ANOVA) corrected for multiple comparisons by Bonferroni's post hoc test. An alpha-adjusted p-value of less than 0.05 was considered statistically significant.

RESULTS

Carbon monoxide concentration time-curves during expiration

Expired CO concentrations could be measured easily in all patients during spontaneous respiration as well as during mechanical ventilation. Carbon monoxide concentrations increased during expiration from zero to a plateau value at end expiration (see Figure 1 for an example in an intubated patient). From the obtained concentration time-curves three different phases could be distinguished. In the first phase no CO was detected, phase two is characterized by an increase of the reading which reaches a plateau value in phase three. This value represented the concentration of alveolar gas and was defined as endtidal carbon monoxide concentration.

Effects of preoxygenation (FiO_2 1.0) on endtidal CO-concentrations in patients

Endtidal CO values significantly increased after 5 min breathing of oxygen in both groups, Figure 2. No further increase in etCO concentration was detected in group 2 where the subjects underwent additional preoxygenation for 5 minutes.

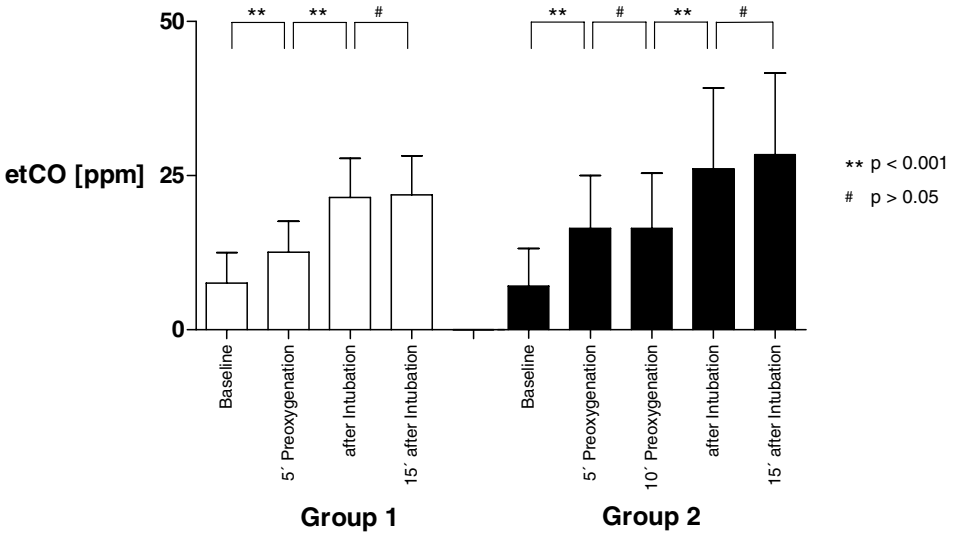

Fig. 2. Endtidal carbon monoxide concentrations of patients (n = 20 in each group, Mean + SD) before preoxygenation, after preoxygenation, immediately after endotracheal intubation and 15 minutes after intubation. Preoxygenation for five minutes caused a marked increase in endtidal carbon monoxide concentrations (etCO). In group 2, etCO concentrations after 10 minutes of preoxygenation did not differ significantly from readings measured after 5 minutes. In all patients, higher CO concentrations were measured after intubation. After 15 minutes of mechanical ventilation, endtidal carbon monoxide concentrations did not differ significantly as compared to immediately after intubation.

Effects of intubation on endtidal CO-concentrations in patients

In both groups, endtidal CO concentrations significantly increased with induction of anaesthesia and endotracheal intubation as compared to values obtained after preoxygenation, however before induction of anaesthesia, Figure 2. No further changes in endtidal CO levels were observed during subsequent mechanical ventilation.

Effects of FiO_2 on endtidal CO concentrations in volunteers

Breathing 50% oxygen for 3 minutes significantly increased mean endtidal CO values as compared to baseline values, Figure 3. Increasing FiO_2 to 1.0 showed no further effect on endtidal CO values. Endtidal CO values subsequently declined after breathing room air for 10 minutes to values comparable to baseline values.

DISCUSSION

Endogenous CO is mainly eliminated via the lungs so that measurements of alveolar carbon monoxide concentrations in intubated patients may be a useful diagnostic tool, for instance in patients with inflammation or critical illness [1–7]. We studied a new approach allowing to measure endtidal concentrations in intubated anaesthetized patients and determined the effects of inspiratory oxygen fraction on endtidal CO concentration.

Critique of methods

Carbon monoxide concentrations were measured with an electrochemical analyzer allowing to plot concentration time-curves. With the last portion of the expired gas (representing a sample of alveolar air) a plateau value was reached which was defined as endtidal concentration. Since cigarette smoking [9, 10] and airway inflammation [1–4] are known to increase expiratory carbon monoxide concentrations, current smokers as well as subjects with acute or chronic lung disease were excluded from measurements. In addition all measurements were performed in a non-smoking area to exclude second hand smoke.

For the measurements in intubed anaesthetized patients their lungs were inflated to total lung capacity and allowed to deflate passively to functional residual lung volume after airtight connection of the analyzer to the endotracheal tube. Because patients underwent muscle relaxation there was no spontaneous respiration during the measuring period. Therefore, at the end of passive expiration gas flow slowly ceased and end-tidal concentrations could be measured.

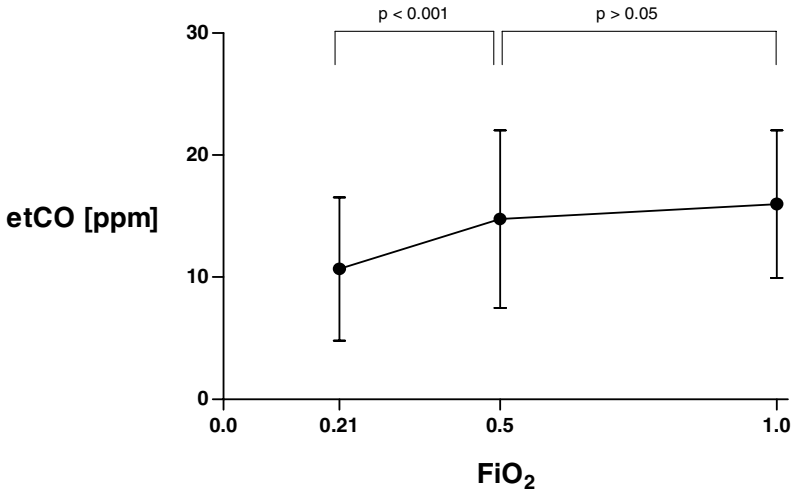

Fig. 3. Endtidal carbon monoxide concentrations in healthy volunteers (n = 20, Mean + SD) breathing varying inspiratory oxygen fractions (0.21, 0.5, 1.0). In all subjects, endtidal carbon monoxide concentrations increased after increasing the inspiratory oxygen fraction from 0.21 to 0.5. No change was observed after increasing the inspiratory oxygen fraction from 0.5 to 1.0.

For the measurements in healthy volunteers oxygen was given via a tightly fitting face mask and all subjects were instructed not to breathe any room air prior to exhaling completely through the hose into the analyzer and to hold breathing in end-expiration.

Prior to the measurements we excluded that any CO was present in the ambient air or within the breathing circuits. We avoided volatile anaesthetics because they may result in CO accumulation within the breathing circuit due to degradation of volatile anaesthetics by dry soda lime [11, 12]. To exclude other sources of CO, we measured CO concentrations within the breathing system before each measurement, flushed the system with high fresh gas flows (>12 l/min) and measured the CO concentration again. Because no CO was detected in the ambient air or within the breathing circuit all measured CO represented endogenous carbon monoxide of the patients and volunteers.

Interpretation of results

Effects of FiO_2 on endtidal CO concentration

Before induction of general anaesthesia and endotracheal intubation patients are routinely preoxygenated with oxygen (FiO_2 1.0). Compared to the baseline concentration we observed an increase in etCO concentration after 5 minutes of preoxygenation. Preoxygenation for a longer time period (10 min) had no additional effect suggesting that the maximum effect of inspiratory oxygen on endtidal carbon monoxide had already occurred within 5 minutes. This observation may be explained by a displacement of CO from its bond with haemoglobin with increasing alveolar oxygen concentrations. This process may result in an increased carbon monoxide elimination from the organism [13].

A similar directed, although much smaller effect of inspiratory oxygen concentration on expired CO amounts was observed in intubated critically ill patients. Inspiratory oxygen fraction was increased from 0.5 to 1.0 resulting in an increase in exhaled CO concentration from 0.63 ± 0.13 to 1.54 ± 0.16 ppm [8]. However, in this study mean exhaled concentrations and not alveolar concentrations were measured [8], so that the differences in results are likely explained by the difference in sampling and measuring techniques.

In volunteers an increase in FiO_2 from 0.21 to 0.5 significantly increased endtidal carbon monoxide concentrations, whereas a further increase showed no additional effect. During subsequent breathing of room air endtidal CO concentration returned to baseline values within a few minutes.

Effects of anaesthesia and endotracheal intubation on endtidal CO concentrations

Immediately after induction of anaesthesia and endotracheal intubation, alveolar carbon monoxide concentrations increased significantly as compared to values measured after preoxygenation, suggesting effects independent from the displacement of CO from haemoglobin. Because no

CO was detected within the ambient air or the breathing system, the increased amount of endtidal CO derived endogenously. This observation may be explained by the ventilation of different lung regions following muscle relaxation and endotracheal intubation or by cardiopulmonary effects associated with induction of anaesthesia, such as vasodilation and negative inotropy decreasing cardiac index and changing pulmonary perfusion. Since CO is known to have a high affinity to haemoglobin [14], an increased time for carbon monoxide to dissociate from haemoglobin during lung passage possibly results in higher alveolar concentrations. Further explanations, although speculative, are an increased endogenous carbon monoxide production after induction of anaesthesia or a displacement of CO from its binding sites in tissues, for instance within the brain.

CONCLUSION

Measurements of endtidal CO concentrations can be easily performed in intubated patients with an electrochemical analyzer. The lungs are inflated to total lung capacity and subsequently allowed to deflate passively to functional residual capacity. We observed that endtidal carbon monoxide levels depend on inspiratory oxygen concentrations. Moreover, induction of anaesthesia and endotracheal intubation further increase endtidal carbon monoxide concentrations beyond the effect attributable to preoxygenation by a yet unknown mechanism. These factors need to be considered for measurements and interpretation of endtidal carbon monoxide concentrations.

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