Smoking Status and Body Size Increase Carbon Monoxide Concentrations in the Breathing Circuit During Low-Flow Anesthesia

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The major sources for intraoperative carbon monoxide (CO) in the breathing circuit are related to patient's hemoglobin catabolism, smoking and the degradation between absorbent and anesthetics. We performed this study to evaluate their combined effects on CO production during low-flow anesthesia. We used a direct-measurement instrument to measure real-time CO concentrations in the breathing circuit during different anesthetic conditions for patients who received desflurane or isoflurane. By applying multiple linear regression models, we determined the significant factors related to CO concentrations in the circuit. We identified patients' smoking status, preoperative smoking and

body weight as well as gas flow rates as important factors for affecting peak and time-weighted CO levels. These four factors predicted approximately 44.1% and 42.7% of peak and mean inspiratory CO concentrations respectively. We found that chronic and preoperative smokers and patients with larger body weights are associated with increased CO concentrations, whereas increase in gas flow rates could decrease CO concentrations. After controlling these four important factors, we found that inspiratory CO concentrations were not significantly associated with the choice of anesthetic and its concentration during low-flow anesthesia.

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Low-flow anesthesia reduces anesthetic consumption and operating room pollution. However, this practice can result in the accumulation of carbon monoxide (CO) from the catabolism of hemoglobin (1). Low fresh gases also increase carboxyhemoglobin (COHb) levels (2). One recent study reports that preoperative smoking, which is measured by expired breath CO concentration, increases ST depression for patients without a history of ischemic heart disease during general anesthesia (3). Many *in vitro* studies also report that the reaction between desiccated carbon dioxide (CO₂) absorbent and volatile anesthetics is a major source of CO production (desflurane > isoflurane) (4-7). Real-time and continuous CO monitoring may identify exposure to large CO concentrations (8), especially for patients suffering from ischemic heart disease. The goal of this study is to measure CO concentrations continuously during low-flow anesthesia to determine the contribution of CO accumulation in the breathing circuits by different anesthetic

conditions and patient characteristics, such as anesthetic types and concentrations, gas flow rates, gender, body weight, and smoking status.

Methods

Our IRB on human subjects has approved this study, and all participating patients have given their informed consents. We randomly selected 218 patients, who received inhaled anesthesia with desflurane or isoflurane for scheduled operations. Patients with pulmonary dysfunction, asthma, or who were receiving cardiac and vascular surgery were excluded. We recorded patient's age, sex, and body weight and obtained their smoking status, including smoking history, cigarette consumption per day, and preoperative smoking information. We defined patients as smokers if they had smoked at least one cigarette per day within the last month. We defined preoperative smoking as a patient's cigarette consumption before operation on the morning of surgery.

To measure CO exposures and variations during anesthesia, the anesthetic types, concentrations, and gas flow rates of inhaled anesthesia were decided by

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Figure 1. The direct-measurement system of monitoring intraoperative carbon monoxide (CO) concentrations, temperature and relative humidity. 1 = temperature and relative humidity sensor probe, 2 = upper canister, 3 = temperature and relative humidity monitor, 4 = gas from anesthesia machine, 5 = silicon tube and connector, 6 = polyethylene sampling chamber, 7 = direct-measurement CO monitor, 8 = suction pump.

anesthesiologists. The choice of anesthetics, however, was not dependent on patients' smoking history. The anesthesiologists were not aware of our study design when they performed the anesthesia. Each day we replaced at least one canister of fresh soda lime (SO-DASORB®; W. R. Grace & Co., Cambridge, MA) in the anesthesia machine (Modulus® CD Anesthesia System, Ohmeda Inc., Madison, WI) before the first induction of anesthesia. We recorded gas flow rates and concentrations of inhaled anesthesia intraoperatively and used time-weighted averages to represent gas flow rates and anesthetic concentrations for the entire period. We recorded the inhaled anesthetic concentrations from the gas monitor in the anesthesia machine that directly measured the anesthetic concentrations in the breathing circuit.

To monitor CO production from the degradation of anesthetics by dried CO₂ absorbents, we modified the inspiratory limb of the breathing circuit to make real-time CO measurements in a bypass circuit (Fig. 1). We also modified the absorbent's canister to measure temperature and relative humidity in the gas phase intraoperatively. The CO monitor we used is based on an electrochemical oxidation principle (Drager PacIII CO detection instrument, Drager, Inc., Pittsburgh, PA). It has a detection range of from 1 to 2000 ppm and records 10-s averaged concentrations continuously. Routine calibration of the CO monitor and suction flow rate of the pump was performed according to the manufacture's instructions. In practice, we used a pump (Dual mode low-flow air sampler, LFS-113, Gilian®; Sensidyne, Clearwater, FL) to draw approximately 500 mL/min of gas from the inspiratory limb for continuous CO measurements and then it was returned to the circuit. We also put two probes (Testo 400 multifunction-measuring instrument, Testo GmbH & Co., Lenzkirch, Germany) at the points

Figure 2. A typical example of intraoperative carbon monoxide (CO) concentration (A), temperature (B) and relative humidity (C) trends recorded by the direct-measurement system for two patients. Patient #1: male, aged 54 yr, 58.7 kg, smoker, and 1 cigarette of preoperative smoking under the averaged concentration of 1.5% desflurane at 0.66 L/min of averaged gas flow rate; Patient #2: female, aged 29 yr, 47 kg, nonsmoker under the averaged concentration of 0.4% desflurane at 0.73 L/min of averaged gas flow rate.

Table 1. Description of Patient's Characteristics ($n = 218$)

Item	Category	Frequency	Percent
Gender	Male	117	53.7
	Female	101	46.3
Smoking status	Smoker	47	21.6
	Nonsmoker	171	78.4
Number of cigarettes smoked per day	0	171	78.4
	1~10	12	5.5
	11~20	26	11.9
	21~50	9	4.2
Number of cigarettes smoked before operation in smokers	0	31	66.0
	1	12	25.5
	2	3	6.4
	3	1	2.1
Anesthetic used	Desflurane	149	68.3
	Isoflurane	69	31.7

above and inside the absorbent canister to monitor changes of relative humidity and temperature in the circuit and absorbent during operation. The anesthesia

Table 2. Description of Patient's Characteristics and Anesthetic Characteristics During Operation ($n = 218$)

Item	No.	Statistics			
		Mean	SD	Maximum	Minimum
Age (yr)	218	38.7	23.0	84.5	0.1
Weight (kg)	218	51.5	20.9	117.0	0.9
Concentration of desflurane (%)	149	6.2	2.4	12.9	0.6
Concentration of isoflurane (%)	69	1.4	0.8	3.64	0.4
Concentration of peak CO (ppm)	218	24.8	19.4	145.0	1.0
Concentration of mean CO (ppm)	218	17.0	14.8	114.7	0.3
Flow rate of gas (L/min)	218	1.4	0.9	4.8	0.3
Anesthesia duration (min)	218	143.2	139.4	700.0	5.0

CO = carbon monoxide.

Figure 3. Histogram of inspiratory mean carbon monoxide (CO) concentrations for chronic smokers ($n = 47$) and nonsmokers ($n = 171$).

machine and anesthetic circuit were purged with high fresh gas flows before each operation.

We applied multiple linear regression models to evaluate the contribution of various exogenous and endogenous factors to the patient's CO exposures. We used peak and time-weighted CO concentrations as dependent variables and patient's gender, body weight, smoking status, cigarettes smoked before operation, and gas flow rates, as well as anesthetic type as predictive variables in the models. We fit separate regression models to evaluate the relation between anesthetic concentrations and CO exposures for each type of anesthetic. We used SPSS software (SPSS for windows, Release 10.0.1; SPSS Inc., Chicago, IL) to perform data analysis and set a P value <0.05 as statistically significant in the models.

Results

Our results indicate that our system could monitor intraoperative changes in CO, temperature, and relative humidity continuously for over 10 h of anesthesia (Fig. 2). The demographic data of the patients and

their characteristics during anesthesia are summarized in Tables 1 and 2.

The distribution of inspiratory CO concentrations in Figure 3 indicate that 48 of these 218 patients (22%) exceeded the 35 ppm time-weighted exposure limit for workers by US National Institute of Occupational Safety and Health environmental exposure limits in 1972. Among them, chronic smokers (22 of 47, 47%) had a larger percentage of increased CO exposure than nonsmokers (26 of 171, 15%). On average, the temperature was $35.7 \pm 5.0^\circ\text{C}$ in the soda lime and $26.2 \pm 1.1^\circ\text{C}$ in the breathing circuit during anesthesia. The relative humidity was $86.5 \pm 5.0\%$ in the soda lime and $89.5 \pm 4.9\%$ in the breathing circuit intraoperatively.

The results of multiple linear regression models listed in Table 3 show that smoking status, preoperative cigarette consumption, gas flow rate, and body weight were four significant predictive variables affecting CO concentrations. In total, they explained approximately 44.1% and 42.7% of the variance of peak and mean CO concentrations respectively. However, gender, anesthetic type, and concentrations had no significant effect.

From our regression model, the peak and mean CO concentrations of smokers were 11.5 ppm and 7.5 ppm more than nonsmokers ($P < 0.01$). The CO concentrations were positively related to preoperative cigarette consumption (8.1 ppm for mean and 9.5 ppm for peak CO concentrations per cigarette). Increase of gas flow rate was the major factor for reduced CO concentrations in the breathing circuit (7.7 ppm for peak CO and 5.9 ppm for mean CO decrease per L/min). There was a decreasing trend in CO concentrations with increasing gas flow rates, as shown in the scatter plot of Figure 4A. The scatter plot in Figure 4B showed that patient's body weight was positively associated with inspiratory CO concentrations and the increasing rates were approximately 0.2 ppm per kg.

Discussion

In this study, we found that chronic smokers had a greater inherent probability of increased CO concentrations in the breathing circuits than nonsmokers.

Table 3. Effects of Personal Attributes and Anesthetic Conditions on Carbon Monoxide (CO) Concentrations in the Breathing Circuit by Multiple Linear Regression Model

Dependent variable	Predictors	Unstandardized coefficients		P Value	Adj. r ²
		B	SE		
Peak CO (n = 218)	Constant	18.330	3.429	0.000	0.441
	Smoker	11.471	3.002	0.000	
	Pre-smoke	9.537	3.009	0.002	
	Gas flow (L/min)	-7.661	1.068	0.000	
	Anesthetic	3.926	2.157	0.070	
	Gender	-0.267	2.122	0.900	
Mean CO (n = 218)	Body weight (kg)	0.241	0.051	0.000	0.427
	Constant	12.152	2.653	0.000	
	Pre-smoke	8.073	2.328	0.001	
	Smoker	7.500	2.322	0.001	
	Gas flow (L/min)	-5.907	0.826	0.000	
	Anesthetic	2.541	1.669	0.129	
	Body weight (kg)	0.190	0.039	0.000	
	Gender	0.048	1.642	0.977	

Adj. r² = adjusted R square; Peak CO = concentration (ppm); Smoker = 0, nonsmoker, 1, smoker; Pre-smoke = Number of cigarettes smoked before operation; Anesthetic = 0, desflurane, 1, isoflurane; Gender = 0, male, 1, female; Mean CO = concentration (ppm).

Significant for $P < 0.05$.

Acute preoperative smoking also resulted in excess CO exposures for smokers. Figure 2 shows a significant difference (90 ppm) in CO concentrations between a preoperative smoker (Patient #1) and non-smoker (Patient #2), even though gas flow rates, temperature, and relative humidity were not different. These differences likely result from the patients' personal attributes, such as smoking and body weight, than from the degradation of anesthetics.

We estimated that the average contribution of body weight to CO concentrations in the breathing circuit was approximately 0.2 ppm/kg in our regression model. We believe this estimate is reasonable because the contribution of body weight to CO in our breathing circuit for healthy and active persons should be within 2 ppm if the CO production rate of 0.36 ± 0.5 μ mole/hour/kg proposed by Bensinger et al. (9) is used.

We successfully demonstrated the electrochemical method to continuously measure the real-time variations of CO concentrations in the circuit. Our data also showed that under a steady gas flow rate, CO concentrations accumulated to a plateau level rapidly. Whenever gas flow rates increased suddenly, the CO concentrations decreased accordingly (Fig. 2). Bonome et al. (2) reported a similar result of fresh gas flow's diluting effect on CO concentrations in the circuit. Our regression model predicted the decrease of approximately 7.7 ppm and 5.9 ppm in peak and mean CO concentrations for an increase of gas flow rates by 1 L/min. Although low-flow is a current trend in anesthesia, we recommended that an increasing gas flow rate should be considered (2,10) during anesthesia for smoking patients undergoing emergency and day surgery, especially for patients with excess body weights.

In this study, we found that anesthetic type and concentration did not significantly affect CO production. However, several *in vitro* studies have reported that desflurane produced more CO than isoflurane for a given minimum alveolar anesthetic concentration (4,6) as well as a positive association between CO production rates and an increase in anesthetic concentrations (4). We could attribute such a discrepancy to the fact that the soda lime during our clinical use was not dried to the condition of previous *in vitro* studies. By using relative humidity measurements in gas phase as indirect evidence for the solid absorbent's dehydration condition, we believe that our soda lime was always maintained at good hydration conditions during daily use after the replacement of fresh soda lime before the first daily induction of anesthesia (8,11). In comparison to other factors, such as smoking, gas flow rates and body weight, we believe that CO production from the degradation of anesthetics in the desiccated CO₂ absorbents became less significant during actual clinical anesthesia.

Gas monitors, such as infrared, mass spectrometry (12,13), and Raman spectroscopy monitors, cannot accurately quantify CO concentrations in the breathing circuit. Most of the CO concentration measuring methods used in previous studies used gas chromatography (GC) (2,4,6,12,14,15) because of its specificity and sensitivity. However, the process of CO analysis by GC is time consuming and fairly complicated, and thus is not suitable for measuring real-time CO concentrations in the breathing circuit during operation. In contrast, the electrochemistry instrument used in this study performs a relatively fast (1 second response time), fully automated analysis and quantification of CO with good precision (1 ppm detection

Figure 4. A, scatter plot of inspiratory mean carbon monoxide (CO) concentrations and gas flow rates for 171 nonsmokers. B, scatter plot of inspiratory carbon monoxide (CO) concentrations and patient's body weights for 171 nonsmokers.

limit) for clinical use. Thus, our CO direct measurement system can overcome the technical limitation of the GC methods and allows anesthesiologists to observe patients' CO exposure in real time and terminate iatrogenic CO poisoning in time.

We believe there are several potential applications of our monitoring system. First, we will be able to distinguish CO production from preoperative smoking, endogenous production and anesthetic breakdown by measuring expiratory and inspiratory CO concentrations simultaneously. Second, we will be able to establish a dose-response relationship between CO concentrations in the breathing circuit and COHb in blood during anesthesia by combining our measuring system with COHb measurements for patients.

Our results also showed several useful applications for clinical anesthesia. As Woehlck et al. (3) reported, expired CO concentrations are a significant predictor

for ST depression; we recommend monitoring intraoperative CO concentration continuously during anesthesia, especially for patients suffering from ischemic heart diseases. Currently CO exposure guidelines are set to maintain a COHb level at certain levels to avoid potential health risks associated with cardiovascular or pulmonary impairments under normal atmospheric conditions. Our results indicate that we need to reevaluate this standard of CO exposure under high F_{IO_2} situations during anesthesia. The preoperative smoking rate in our study (34%) might be underestimated; we believe smokers tend to conceal their smoking status before surgery. As expired-breath CO concentrations were a reasonable index for acute smoking (16,17), we needed to measure alveolar CO concentrations before anesthesia to confirm preoperative smoking. Postanesthetic complications must also be monitored because CO is a gaseous transmitter and plays a role in neuroendocrine regulation (18).

We conclude that the major sources for increased intraoperative CO exposures are related to patient attributes, such as smoking status, cigarettes smoked before operation, and body weight. Increasing gas flow rates is an effective method of decreasing CO concentrations in the breathing circuit. Our direct-measurement CO system can be applied to monitor and prevent potential CO intoxication for patients during anesthesia. If such a CO monitoring system were not available during anesthesia, we could apply our model-derived factors to predict a patient's mean and peak CO concentrations in the breathing circuit and use the predicted results to prevent unnecessary CO exposure by controlling gas flow rates.

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