Effect of Severity of Pulmonary Disease on Nitrous Oxide Washin and Washout Characteristics†

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Abstract

The influence of chronic obstructive pulmonary disease (COPD) on the nitrous oxide (N_2O) washin and washout characteristics was evaluated in 90 (ASA II-III) males undergoing elective peripheral surgery under general anaesthesia with controlled ventilation. Patients were classified by preoperative bedside pulmonary function testing into three groups. Group I (n=30), patients without COPD (FEV_1/FVC > 80% predicted values; control group); Group II (n=30), patients with mild COPD (FEV_1/FVC = 65-79% of predicted values); and Group III (n=30), patients with moderate COPD (FEV_1/FVC = 50-64% of predicted values).

The anaesthetic technique was standardized for all patients. The Datex Capnomac Ultima™ monitor was used to measure the inspired and expired concentrations of nitrous oxide (N_2O), carbon dioxide (CO_2), and isoflurane. The duration of both N_2O washin (time from start of N_2O administration to equilibrium of inspired and expired N_2O concentrations) and 5 per cent washout (time from discontinuation of N_2O to an expired N_2O concentration of 5 per cent of the equilibrium value) were recorded. The duration of N_2O washin and washout were significantly prolonged in Groups II and III ($P < 0.001$) as compared to the control group (Group I). The end-tidal CO_2 concentration decreased significantly during N_2O washout without causing oxygen desaturation ($Sp0_2$ < 90%). We conclude that the duration of N_2O washin and washout were significantly prolonged in anaesthetized patients with COPD which may delay the induction and recovery from N_2O anaesthesia.

The low blood-gas partition coefficient of nitrous oxide (N_2O) produces not only a rapid equilibrium of the alveolar concentration (F_A = end-tidal concentration) and the inspired concentration (F_I), but also a rapid clearance[1]. In healthy patients, the inspired concentration of N_2O approaches 90 per cent of the delivered concentration within 3-6 min[2]. However, the effect of pul-

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monary disease on these characteristics has not been previously reported.

Wagner et al[3] showed that patients with moderate degrees of airway obstruction developed ventilation-perfusion (V_A/Q) mismatching after induction of anaesthesia. Furthermore, patients with severe pulmonary disease developed greater gas exchange disturbances during general anaesthesia[4]. The increased V_A/Q mismatch and increased functional residual capacity (FRC) in patients with chronic obstructive pulmonary disease (COPD) may affect N_2O kinetics[5]. Therefore, the aim of this investigation was to study the effect of the severity of COPD on the duration of N_2O washin and washout characteristics in mechanically ventilated anaesthetized patients.

MATERIAL AND METHOD

Ninety consenting males (ASA II-III) undergoing elective peripheral surgery under general anaesthesia were studied according to an institutional review board approved protocol. Baseline pulmonary measurements were performed in the preoperative holding area using a Respiradyne hand-held pulmonary function testing device (Sherwood Medical, St. Louis, Missouri). Patients with the history of asthma, cardiovascular disease, FEV_1 < 1 L, PaO_2 < 55 mmHg, SaO_2 < 90 per cent at rest, and haematocrit < 30 per cent or > 60 per cent were excluded from the study. Patients were divided into three groups according to the results of their preoperative pulmonary function tests. Group I (n=30), patients without COPD (FEV_1/FVC > 80 per cent of predicted value; control group), Group II (n=30), patients with mild COPD (FEV_1/FVC = 65-79 per cent of predicted value), and Group III (n=30), patients with moderate COPD (FEV_1/FVC = 50-64 per cent of predicted value). In addition, the patients in group II and III had an FEV_1 of less than 50 per cent of their calculated predicted value.

After insertion of an intravenous cannula and placement of routine monitoring devices, a standardized general anaesthetic protocol was followed. Following preoxygenation with 100 per cent oxygen (0_2) for 5 min, general anaesthesia was induced with intravenous fentanyl (1-2 $\mu g \cdot kg^{-1}$) and thiopental (4-5 $mg \cdot kg^{-1}$). Vecuronium (0.1 $mg \cdot kg^{-1}$) was used to facilitate tracheal intubation with a size 8 tracheal tube. Following tracheal intubation, patients were mechanically ventilated with 0.5 MAC isoflurane in 9 $L \cdot min^{-1}$ of O_2 for 5 min through circle system with the Ohmeda 7000 ventilator (BOC Health Care, Madison, Wisconsin). Ventilation was adjusted to maintain end-tidal carbon dioxide ($ETCO_2$) concentrations at 35-40 mmHg. No changes were made in the respiratory parameters and the inspiratory minute ventilation was maintained constant during the study period.

The breathing circuit was disconnected from the tracheal tube, purged with the mixture of N_2O 6 $L \cdot min^{-1}$ and O_2 3 $L \cdot min^{-1}$ for 30 sec and then reconnected. The Datex Capnomac Ultima™ (Datex Medical Instrumentation, Tewksbury, Massachusetts) was used to monitor respiratory rate, inspired and expired concentrations of O_2, N_2O, CO_2, and isoflurane. Data from the respiratory monitor was recorded on a laptop computer every 10 sec using a Datex software program. In addition, heart rate, non-invasive blood pressure, temperature, oxygen saturation (SpO_2), neuromuscular function, peak airway pressures, tidal volume, and minute ventilation were also recorded during the study period.

Fifteen minutes after N_2O reached equilibrium (i.e., the difference between the inspired and expired concentrations of N_2O was less than 5%), N_2O was turned off, the breathing circuit was disconnected from the tracheal tube and purged with O_2 (9 $L \cdot min^{-1}$) for 30 sec before reconnecting. The study was terminated when the expired concentrations of N_2O were less than 5 per cent of the equilibrium value. The duration of both N_2O washin (time from start of N_2O to equilibrium) and 5 per cent washout (time from discontinuation of N_2O to an expired N_2O concentration of 5 per cent of equilibrium value) were recorded.

Data are expressed as mean values ± standard deviation (SD). Statistical analysis was performed using a two-way ANOVA with Bonferroni's correction or Kruskuall-Wallis test where appropriate. A p-value of less than 0.05 was considered statistically significant.

RESULTS

There were no differences between the three groups with respect to demographic data (Table 1). During N_2O washin, the end-tidal N_2O concentration (F_A) reached the inspired concentration (F_I) more rapidly in Group I as compared to the other groups (Fig. 1A). The time related ratio of end-tidal N_2O concentration (F_A) to inspired

Table 1. Demographic distribution, duration of nitrous oxide washin and washout, and end-tidal carbon dioxide (mmHg) during the nitrous oxide washin and washout of the patients in the three groups.

	Control (I)	Mild (II)	Moderate (III)
Demographic distribution			
Age (yr)	63 ± 5	60 ± 10	62 ± 7
Height (cm)	171 ± 2	169 ± 2	170 ± 2
Weight (kg)	90 ± 9	89 ± 12	86 ± 11
Duration of N_2O washin and washout			
Washin (min)	5.4 ± 0.7	7.5 ± 0.6**	9.1 ± 0.7** #
5% Washout (min)	7.4 ± 0.7	9.8 ± 0.9**	14.7 ± 1.3** #
$ETCO_2$ during washin and washout			
Washin	34.6 ± 3.4	33.7 ± 3.7	33.5 ± 3.7
5% Washout	30.8 ± 3.3*	30.2 ± 3.4*	30.7 ± 4.3*

Values are mean ± SD

* Significantly different from group I (control), $p<0.05$

** Siginificantly different from group I (control), $p<0.001$

\# Siginificantly different between group II (mild) and III (moderate), $p<0.001$.

FIGURE 1 [A]

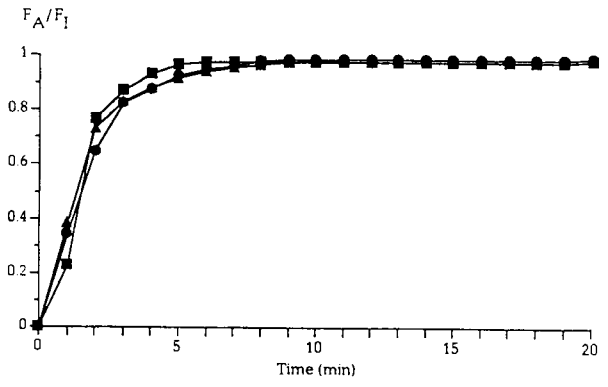

FIGURE 1 [B]

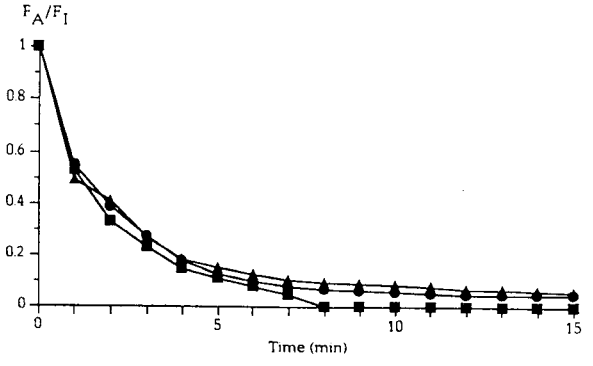

Fig. 1. The effect of severity of COPD on nitrous oxide washin (A) and washout (B) as illustrated by the ratio of end-tidal N_2O concentrations (F_A) to inspired N_2O concentrations (F_I) -■- Control, -●- Mild, - ▲- Moderate.

N_2O concentration (F_I) after it was discontinued was used to illustrate the N_2O washout curve (Fig. 1B). The duration of N_2O washin and washout was significantly longer in patients with COPD (Groups II and III) as compared to the control group (Table 1). The duration of N_2O washin and 5 per cent washout was also significantly longer in the patients with moderate COPD (Group III) as compared to those with mild COPD (Group II).

No differences were found in the $ETCO_2$ concentration between the three groups during N_2O washin and washout measurements (Table 1). However, within each group the $ETCO_2$ concentrations were significantly lower at 5 per cent N_2O washout than at N_2O equilibrium. All patients were hemodynamically stable during the study period (data not included). None of the subjects had oxygen desaturation (SpO_2 < 90%) during the N_2O washout measurements.

DISCUSSION

These results demonstrate that increasing severity of COPD significantly prolongs the duration of N_2O washin and washout. This suggests that the time for induction and recovery with N_2O may be delayed in patients with COPD undergoing balanced anaesthesia. We used FEV_1/FVC ratio to quantify the degree of COPD because there is a good correlation between FEV_1/FVC ratio and the degree of V_A/Q mismatching and shunt development during anaesthesia[3]. In addition, patients in group II and III had an FEV_1 < 50 per cent of their

calculated predicted value which is an indicator of pulmonary impairment[6]. Ventilation was controlled throughout the study, eliminating the problems associated with hypoventilation and irregular respiration.

The duration of N_2O washin and washout in the normal patients evaluated in this study was similar to that reported previously[2,5]. Prolonged N_2O washin and washout duration seen in patients with COPD may be due to an increase in their FRC and increased V_A/Q mismatching followed induction of general anaesthesia[3,5]. Using an electrical analogue model, Eger and Severinghaus[7] measured the effects of V_A/Q mismatching on the duration of induction of cyclopropane, ether, and halothane and suggested that V_A/Q mismatching could significantly delay the induction of anaesthesia with insoluble agents (e.g., N_2O). This delay was greater in emphysematous patients with high lung volumes [7]. Forkert et al[8] suggested that the increase in gas density produced by N_2O might impair the distribution of gas within the lung and create V_A/Q inequalities. It is possible that N_2O may further increase the V_A/Q inequalities in patients with COPD.

The significant fall in the $ETCO_2$ in our study is similar to that reported by Rackow et al[9]. This fall in $ETCO_2$ persisted until the completion of the N_2O washout period. In our patient population, the decrease in $ETCO_2$ occurred inspite of a constant minute ventilation, suggesting a dilution effect. Rackow et al[9] suggested that the fall in $ETCO_2$ may be another cause of the hypoxemia observed during recovery from N_2O anaesthesia. With the prolonged duration of CO_2 dilution in COPD patients, the duration of hypoxemia may also be prolonged.

The prolonged duration of N_2O washout in patients with COPD suggests that the duration of diffusion hypoxemia may also be increased in patients with compromised pulmonary function. Diffusion hypoxemia following administration of N_2O is one of several factors responsible for postoperative hypoxemia[10,11]. However, the clinical significance of postoperative diffusion hypoxemia in healthy patients is still highly controversial[12]. Silim et al[13] suggested that diffusion hypoxemia was clinically insignificant when ventilation is adequate and PaO_2 is at least 100 mmHg prior to N_2O washout. However, significant decreases in SpO_2 may occur for as long as 30 min following discontinuation of N_2O[14]. Similarly, Maroof et al[11] reported a higher incidence of postoperative hypoxemia (SpO_2 < 90%) in healthy patients, lasting for up to 48 h, with the use of N_2O as compared to air.

Although N_2O has a long history of apparently safe and effective use[15], its continued usage remains controversial[16]. The number of studies supporting the use of air instead of N_2O in general anaesthesia are increasing[11,16]. In addition to dilution of alveolar CO_2 and diffusion hypoxemia, N_2O may also cause depression of mucociliary function and bronchial secretion,[17] leading to atelectasis[11]. Futhermore, N_2O may increase the incidence of V_A/Q mismatch in patients with COPD, resulting in delayed induction and recovery from anaesthesia.

The relationship between the F_A/F_I ratio and the blood:gas solubility coefficient is well-recognized[5]. However, the rate of rise and the shape of the F_A/F_I curve do not represent uptake[5]. Although we used a circle breathing system instead of a nonrebreathing system, the high fresh gas flows (9 $L \cdot min^{-1}$) administered should minimize the rebreathing of N_2O. Finally, as the blood:gas coefficient of desflurane (0.42) is similar to that of N_2O (0.47), the induction and recovery with desflurane may also be delayed in patients with COPD. However, further studies are necessary to evaluate the effects of COPD on desflurane's kinetics.

In summary, our results suggest that in patients with mild-to-moderate COPD, the prolonged duration of N_2O washin and washout may delay the induction and recovery from N_2O anaesthesia.

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การศึกษาผลของความรุนแรงของโรคหลอดลมอุดกั้นอย่างเรื้อรังต่อการรับและขับถ่ายก๊าซไนตรัสออกไซด์

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คณะผู้วิจัยได้ทำการศึกษาผลกระทบของโรคหลอดลมอุดกั้นอย่างเรื้อรังต่อคุณสมบัติของก๊าซไนตรัสออกไซด์ในผู้ป่วยที่เข้ารับการดมยาสลบ จำนวน 90 ราย โดยแบ่งผู้ป่วยออกเป็น 3 กลุ่ม เท่า ๆ กัน กลุ่มที่ 1– กลุ่มควบคุม เป็นผู้ป่วยที่มีการทำงานของปอดปกติ กลุ่มที่ 2 และกลุ่มที่ 3 เป็นผู้ป่วยที่มีพยาธิสภาพของปอดอยู่ในขั้นรุนแรงน้อยและปานกลางตามลำดับ

ภายหลังจากผู้ป่วยได้รับการดมยาสลบด้วยก๊าซไนตรัสออกไซด์ และควบคุมการหายใจด้วยยาหย่อนกล้ามเนื้อแล้ว ผู้วิจัยได้ใช้เครื่องมือ Datex Capnomac Ultima™ ทำการบันทึกระยะเวลาที่ก๊าซไนตรัสออกไซด์ในปอดมีความเข้มข้นสูงสุดจนถึงภาวะสมดุล กล่าวคือ มีระดับความเข้มข้นของก๊าซไนตรัสออกไซด์ในช่วงการหายใจเข้าและออกเท่า ๆ กัน จากนั้นได้ปิดก๊าซไนตรัสออกไซด์ พร้อมกับบันทึกระยะเวลาที่ปอดสามารถขับถ่ายก๊าซไนตรัสออกไซด์ออกจนมีความเข้มข้นเหลือเพียงร้อยละ 5 ของระดับความเข้มข้นในภาวะสมดุล

ผลการศึกษาพบว่า ระยะเวลาในการนำก๊าซไนตรัสออกไซด์เข้าสู่ปอดและการขับถ่ายก๊าซไนตรัสออกไซด์ออกจากปอด มีความแตกต่างกันอย่างมีนัยสำคัญในผู้ป่วยโรคหลอดลมอุดกั้นอย่างเรื้อรังที่มีระดับความรุนแรงต่าง ๆ กัน

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