Decreased respiratory depression during emergence from anesthesia with sevoflurane/N_2O than with sevoflurane alone

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Purpose: To investigate ventilation and gas elimination during the emergence from inhalational anesthesia with controlled normoventilation with either sevoflurane/N_2O or sevoflurane alone.

Methods: Twenty-four ASA I-II patients scheduled for abdominal hysterectomy were randomly allocated to receive either 1.3 MAC sevoflurane/N_2O (n=12) or equi-MAC sevoflurane (n=12) in 30% oxygen (O_2). Expired minute ventilation volumes (V_E), end-tidal (ET) concentrations of O_2, carbon dioxide (CO_2), sevoflurane and N_2O as well as pulse oximetry saturation (SpO_2) and CO_2 elimination rates (VCO_2) were measured. The ET concentrations of sevoflurane and N_2O were converted to total MAC values and gas elimination was expressed in terms of MAC reduction. Time to resumption of spontaneous breathing and extubation were recorded and arterial blood gas analysis was performed at the end of controlled normoventilation and at the beginning of spontaneous breathing.

Results: Resumption of spontaneous breathing and extubation were 8 and 13 min less, respectively, in the sevoflurane/N_2O than in the sevoflurane group. Spontaneous breathing was resumed in both groups when pH had decreased by 0.07-0.08 and $PaCO_2$ increased by 1.3-1.5 kPa. Depression of V_E and VCO_2 were less, and MAC reduction more rapid in the sevoflurane/N_2O than in the sevoflurane group.

Conclusions: Respiratory recovery was faster after sevoflurane/N_2O than sevoflurane anesthesia. Changes in pH and $PaCO_2$ rather than absolute values were important for resumption of spontaneous breathing after controlled normoventilation. In both groups, the tracheas were extubated at about 0.2 MAC.

Objectif : Observer la ventilation et l'élimination des gaz pendant la récupération de l'anesthésie par inhalation avec une normoventilation contrôlée, en utilisant un mélange de sévoflurane/N_2O ou seulement du sévoflurane.

Méthode : Vingt-quatre patientes ASA I-II, dont l'hystérectomie abdominale était prévue, ont été réparties au hasard pour recevoir soit 1,3 CAM de sévoflurane/N_2O (n = 12) ou la CAM équivalente de sévoflurane (n = 12) dans 30 % d'oxygène (O_2). On a pris les mesures suivantes : volumes expirés de ventilation-minute (V_E), concentrations d'O_2 de fin d'expiration, gaz carbonique (CO_2), sévoflurane et N_2O, saturation en oxygène par oxymétrie pulsée (SpO_2) et vitesses d'élimination du CO_2 (VCO_2). Les concentrations de sévoflurane et de N_2O de fin d'expiration ont été transformées en valeurs de CAM totales et l'élimination des gaz a été exprimée en termes de réduction de CAM. Le temps nécessaire au retour de la respiration spontanée et à l'extubation a été noté, l'analyse des gaz du sang artériel a été réalisée à la fin de la normoventilation contrôlée et au début de la respiration spontanée.

Résultats : Le retour de la respiration spontanée et l'extubation ont demandé 8 et 13 min de moins, respectivement, avec le sévoflurane/N_2O qu'avec le sévoflurane seul. La reprise de la respiration spontanée s'est faite dans les deux groupes après une baisse du pH de 0,07 - 0,08 et une augmentation de la $PaCO_2$ de 1,3 - 1,5 kPa. La baisse de V_E et de VCO_2 a été moindre avec le sévoflurane/N_2O, mais la réduction de CAM a été plus rapide avec le sévoflurane/N_2O.

Conclusion : La récupération respiratoire s'est faite plus rapidement après l'anesthésie avec un mélange de sévoflurane/N_2O qu'avec du sévoflurane employé seul. Les changements de pH et de $PaCO_2$, plutôt que les valeurs absolues, ont été importants pour le retour de la respiration spontanée après la normoventilation contrôlée. Dans les deux groupes, l'extubation a été faite à environ 0,2 CAM.

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SEVOFLURANE produces respiratory effects that share many similarities with other inhalational anesthetics. Thus, sevoflurane causes dose-related reductions in tidal volume (V_T) and minute volume (V_E) with resultant increases in $ETCO_2$ and $PaCO_2$.[1] Subanesthetic concentrations also cause depression of the hypoxic ventilatory response.[2] Because of its relatively low blood/gas solubility coefficient, sevoflurane has pharmacokinetic properties permitting rapid recovery. Nitrous oxide used in combination with sevoflurane is known to reduce the respiratory depression caused by high concentrations of sevoflurane.[3] Compared with older vaporised agents the emergence time from sevoflurane, as assessed by variables such as response to command and eye opening, is shorter which may be important for the efficiency in the operating room.[4-6] In contrast to cognitive functions, the respiratory consequences of sevoflurane anesthesia with or without N_2O during emergence have not been evaluated.

The purpose of this study was to compare the recovery profile, with focus on respiration (time to resumption of spontaneous breathing and extubation, ventilation volumes, oxygenation, arterial blood gases, elimination of carbon dioxide and anesthetic gases) after equivalent MAC anesthesia with sevoflurane with or without N_2O and controlled normoventilation in patients after a standardised surgical procedure, abdominal hysterectomy.

Methods

The study was approved by the local ethics committee. After informed consent, 24 ASA I-II women scheduled for elective hysterectomy were studied. A circle absorber system was used. A canister of two litre volume was inserted in the expiratory line to obtain mixed gas concentrations. The fresh gas flow (FGF) was 4.5 $L \cdot min^{-1}$ during the first six minutes and was then reduced to < 1 $L \cdot min^{-1}$ according to the Göteborg low flow concept.[7] Ports permitted sampling of inspired, end-tidal and mixed expired gas. An Eger type C circle system was used, in which the fresh gas flow enters the system up-stream of a unidirectional valve in the inspiratory limb.[8] The effect of FGF on measured mixed expired gas concentrations was thereby minimised. A Datex Ultima SV (Datex Instrumentarium OY, Helsinki, Finland) was used to measure SpO_2, inspired, end-tidal and mixed expired concentrations of O_2, CO_2, N_2O and sevoflurane, and V_E. Measurements of V_T have a stated accuracy of ± 6% within the range 250-2000 ml. The gas analyses were collected on line to a computer employing an IdaCare (Hermes Systems S.A., Angleur, Belgium) software program. The product of mixed expired CO_2 fraction minus inspired CO_2 fraction ($FICO_2$) multiplied by V_E was used to calculate VCO_2. A new disposable soda-lime absorber was used for each patient and the $FICO_2$ never exceeded 0.2 vol%. Carbon dioxide production was normalised by weight to $ml \cdot 70\ kg^{-1} \cdot min^{-1}$ and is given as ambient temperature and pressure, dry (ATPD) at 23°C.

Anesthesia

The patients received 0.5-1 mg flunitrazepam *po* for premedication. Anesthesia was induced using 2 $\mu g \cdot kg^{-1}$ fentanyl, 2-3 $mg \cdot kg^{-1}$ propofol, and 0.1 $mg \cdot kg^{-1}$ vecuronium. Fentanyl was not repeated during maintenance of anesthesia but propofol and vecuronium were given when clinically needed. Intravenous bolus doses of ephedrine were used for treatment of hypotension. After intubation, an arterial line was placed in the radial artery for continuous blood pressure monitoring and blood gas sampling. The patients were randomly assigned for maintenance of anesthesia with:

Group sevoflurane/N_2O: sevoflurane (ET 1.35%) and N_2O (ET 65%).
Group sevoflurane: sevoflurane (ET 2.7%).

The MAC of sevoflurane was not adjusted for age and was taken as 2.1%[9] and the MAC of N_2O was regarded as 104% of one atmosphere.[10] It was assumed that the MAC multiple of sevoflurane was additive to that of N_2O[11] and a total of 1.3 MAC was used. The inspired oxygen fraction (FIO_2) was kept at 0.30 and $ETCO_2$ was kept between 4.5 and 5.0 vol%.

Interventions

-10 min (skin closure finished); neuromuscular blockade was reversed with 0.5 mg glycopyrrolate and 2.5 mg neostigmine *iv* and 0.05 $mg \cdot kg^{-1}$ ketobemidone *iv* was administered to provide postoperative analgesia. Ketobemidone is a synthetic opioid with a plasma half-life of 2.3 hours after an *iv* injection, and 1 mg has an equianalgesic potency of 1.0-1.5 mg morphine. Moderate hypoventilation was induced by the respirator. The respiratory frequency was changed from 16 to 8 $breaths \cdot min^{-1}$ while maintaining V_T. The FGF was increased to 4.5 $l \cdot min^{-1}$. Sevoflurane administration was discontinued in Group sevoflurane/N_2O and 1.5 L O_2 and 3.0 L N_2O were given per minute. In Group sevoflurane, the sevoflurane vaporiser was set at 1.35% with FGF of 0.8 $l \cdot min^{-1}$ O_2 and 3.7 $l \cdot min^{-1}$ room air.

0 min: The administration of N_2O and sevoflurane in fresh gas was discontinued in Group sevoflurane/N_2O and Group sevoflurane, respectively. The FGF was

adjusted to 8 l·min^{-1} with a FiO_2 of 30% (1 l·min^{-1} O_2 and 7 l·min^{-1} room air). Controlled hypoventilation was continued with 8 bpm until resumption of spontaneous breathing.

The start of spontaneous breathing was defined by a $ETCO_2$ >1 vol% during non-assisted breathing. At this moment, the sample does not represent the alveolar CO_2 concentration, but merely indicates that there is muscular activity resulting in gas exchange. Endotracheal extubation took place when the patients coughed or opened their eyes during spontaneous breathing. The ET concentrations and ventilation volumes presented are those measured prior to extubation. Arterial blood gas samples were taken at -10 min, 0 min, at resumption of spontaneous breathing, and at 15 and 30 min after the administration of anesthetic gas was discontinued.

Statistics

Data are expressed as median values and ranges if not stated otherwise and 95% confidence intervals were calculated when appropriate. Statistical significance analyses were performed by comparing the -10 min value with the -5, 0, 5, 10, 15 and 30 min values. Within group comparisons were made by Friedman's test which can be considered as a non-parametric method of ANOVA for repeated measures. If significant changes were found, comparisons were also performed when relevant between the –10 min value and subsequent values using Wilcoxon signed rank test, two-tailed. Differences between the groups were studied with ANOVA and multiple comparisons by Duncan's method. If significant differences were obtained, comparisons were also performed with the Mann-Whitney U-test, two-tailed. Statistical significance was assumed for values of $P < 0.05$.

Results

The groups were comparable with regard to age, height, weight, body surface area (BSA) and anesthesia time (Table I). During maintenance of anesthesia, Group sevoflurane/N_2O and Group sevoflurane received (median (range)); 20 (0-60) mg and 0 (0-40) mg propofol ($P = 0.02$), 3.5 (0-7) mg and 1 (0-5) mg vecuronium and 2.5 (0-30) mg and 22.5 (0-65) mg ephedrine ($P = 0.009$) respectively. Thus, Group sevoflurane received less propofol and more ephedrine.

Spontaneous breathing and extubation

Spontaneous breathing was resumed eight minutes earlier in Group sevoflurane/N_2O than in Group sevoflurane, at -7 min and 1 min, respectively ($P = 0.009$) (Table II). At the start of breathing, pH was 7.30 in both groups and $PaCO_2$ was 6.6 and 6.7 kPa in Group sevoflurane/N_2O and Group sevoflurane, respectively. Calculated 95% confidence intervals for the decrease in pH between the end of 1.3 MAC anesthesia with controlled ventilation and resumption of spontaneous breathing were 0.05-0.08 and 0.07-0.09 in Group sevoflurane/N_2O and Group sevoflurane, respectively. Corresponding increases in $PaCO_2$ were 1.0-1.6 kPa and 1.2-1.7 kPa, respectively. Extubation took place at 6 (1-17) and 19 (6-33) min in Group sevoflurane/N_2O and Group sevoflurane, respectively ($P = 0.003$). At extubation, median total MAC values and $ETCO_2$ did not differ between the groups. The MAC was 0.22 (0.12-0.56) and 0.19 (0.13-0.29), in Group sevoflurane/N_2O and Group sevoflurane, respectively (Figure 1). The $ETCO_2$ was 5.6 (4.8-6.6) and 5.4 (4.8-6.3) vol% in Group sevoflurane/N_2O and Group sevoflurane, respectively.

V_E, $ETCO_2$, ETO_2, and SpO_2 (Figure 2)

At the end of 1.3 MAC anesthesia (-10 min) the V_E was 99 and 90 ml·kg^{-1}·min^{-1} in Group sevoflu-

TABLE I

Group	*1*	*2*	*P*
n	12	12	
Age (yr)	53 (37 - 80)	51 (29 - 68)	NS
Height (cm)	164.5 (158 - 174)	167.0 (153 - 172)	NS
Weight (kg)	66.5 (55-105)	64.5 (49 - 90)	NS
BSA (m^2)	1.75 (1.59 - 2.08)	1.72 (1.49 - 2.01)	NS
Anaesthesia time (min)	134 (74 - 313)	150 (107 - 319)	NS

Patient data for Group Sevoflurane/N_2O (1) and Sevoflurane (2): (median (range)).

TABLE II

Group	*1*	*2*	*P*
Time (min)	-7 (-10-13)	1.0 (-8-12)	0.009
$ETCO_2$ (%)	6.0 (4.8-6.7)	5.7 (4.7-6.7)	NS
SpO_2 (%)	96.5 (86-99)	97.5 (84-99)	NS
Total MAC	0.91 (0.19-1.26)	0.57 (0.28-0.86)	0.008
Blood gases			
pH	7.30 (7.24-7.34)	7.30 (7.26-7.36)	NS
$PaCO_2$ (kPa)	6.6 (5.6-7.3)	6.9 (5.6-7.6)	NS
PaO_2 (kPa)	14.4 (7.9-30.1)	15.1 (7.5-24.2)	NS
Base excess (mmol·l^{-1})	-3.1 (-5.3- -1.1)	-2.5 (-4.7- -0.6)	NS
SaO_2 (%)	97.6 (86.8-99.6)	97.8 (84.4-99.4)	NS

Spontaneous breathing for Group Sevoflurane/N_2O (1) and Sevoflurane (2):

Time, $ETCO_2$, SpO_2, total MAC and arterial blood gas analyses at resumption of spontaneous breathing: (median (range)). "Time" represents the time from "0 minutes".

TABLE III

Group	*1*	*2*	*1*	*2*	*1*	*2*	*1*	*2*
Minutes	-10		0		15		30	
pH	7.36 (7.32-7.40)	7.38 (7.32-7.46)	7.32† (7.19-7.35)	7.32† (7.25-7.38)	7.34* (7.30-7.38)	7.31† (7.25-7.38)	7.34 (7.29-7.44)	7.35† (7.29-7.39)
$PaCO_2$ (kPa)	5.4 (4.0-6.1)	5.2 (4.4-6.2)	6.3† (5.2-8.1)	6.2† (5.2-7.4)	5.8 (4.6-6.9)	6.4† (5.1-7.7)	5.6 (3.8-7.1)	6.0† (4.8-7.0)
PaO_2 (kPa)	16.9 (10.9-26.7)	18.9 (10.0-26.1)	18.0 (8.5-25.4)	17.3 (9.6-26.8)	16.6 (11.8-27.8)	21.0 (7.5-27.1)	17.0 (9.6-27.9)	20.0 (8.1-31.4)
BE ($mmol \cdot l^{-1}$)	-2.8 (-6.1—0.3)	-1.3 (-4.4 - 0.4)	-3.4* (-6.8—1.4)	-1.9* (-4.2—0.5)	-3.0 (-5.3—0.9)	-2.4* (-4.0—0.7)	-2.8 (-5.7—1.0)	-2.0 (-3.7-0.1)
SaO_2 (%)	98.5 (95.8-99.7)	98.9 (94.5-99.5)	98.7 (86.3-99.6)	98.6 (92.0-99.5)	98.4 (95.6-99.	99.1 (85.0-99.7)	98.6 (92.9-99.5)	99.0 (87.9-99.6)

Arterial blood gas analyses for Group Sevoflurane/N_2O (1) and Sevoflurane (2): (median (range)).
* $P < 0.05$, † $P < 0.01$ compared with the value at -10 min.

rane/N_2O and sevoflurane respectively. After resumption of spontaneous breathing the V_E in Group sevoflurane was depressed compared with the value at -10 min throughout the measurement period, whereas the V_E in Group sevoflurane/N_2O was not. The $ETCO_2$ was increased throughout the measurement period in both groups. The only difference in ETO_2 between the groups was at 0 min, 23.5 *vs* 21.0 vol% in Group sevoflurane/N_2O and Group sevoflurane, respectively ($P = 0.002$). The median SpO_2 never decreased below 97% and there were no differences between the groups.

VCO_2 (Figure 3) and MAC reduction (Figure 1)

At -10 min, VCO_2 was 163 $ml \cdot 70\ kg^{-1} \cdot min^{-1}$ in Group sevoflurane/N_2O (Figure 4). At five minutes the VCO_2 had increased to 186 $ml \cdot 70\ kg^{-1} \cdot min^{-1}$ ($P = 0.0037$). In Group sevoflurane, VCO_2 decreased from a baseline 154 $ml \cdot 70\ kg^{-1} \cdot min^{-1}$ to 91 ($P = 0.0029$) and 97 $ml \cdot 70\ kg^{-1} \cdot min^{-1}$ ($P = 0.037$) at -5 and 0 min, respectively. The VCO_2 was lower in Group sevoflurane than in Group sevoflurane/N_2O at -5, 0 and 5 min ($P = 0.02$, 0.007 and 0.03 respectively). The ET concentrations of sevoflurane and N_2O were converted to MAC values, and in Group sevoflurane/N_2O the sevoflurane and N_2O MAC values were added to get a total MAC value which could be compared to the MAC values of Group sevoflurane (Figure 1). At five minutes MAC was lower in Group sevoflurane/N_2O, 0.24, than in Group sevoflurane, 0.33 ($P = 0.002$).

Blood gas analyses (Table III)

Base excess was lower in Group sevoflurane/N_2O than in Group sevoflurane at 0 min, -3.4 *vs* -1.9 $mmol \cdot l^{-1}$, respectively ($P < 0.05$). Otherwise, there were no differences in arterial blood gas analyses between the groups. The pH was decreased at 0 min compared with the value at -10 min in both groups. It remained decreased during the measurement period in both groups, except at 30 min in Group sevoflurane/N_2O where pH no longer was decreased compared with the value at -10 min. The maximum increase in $PaCO_2$ was 6.3 kPa at 0 min and 6.4 kPa at 15 min in Group sevoflurane/N_2O and Group sevoflurane, respectively.

Discussion

Inhalational anesthetics are known to depress the response to CO_2 and the reactions to hypoxemia. Acute hypoxic ventilatory response was decreased at 0.1 MAC sevoflurane in the absence and presence of noxious stimulation.[2] As other inhaled anesthetics, sevoflurane decreases V_T and V_E and increases $PaCO_2$ with increasing depth of anesthesia.[1] In a study by Doi *et al.*, the substitution of 0.4 MAC N_2O for sevoflurane decreased $PaCO_2$ and increased V_E. At 1.3 MAC sevoflurane/N_2O anesthesia, spontaneous respiration maintained $PaCO_2$ at almost awake levels. At 1.3 MAC sevoflurane alone and at 1.5 MAC sevoflurane/N_2O anesthesia, spontaneous respiration was moderately depressed.[3] Ventilation volumes can be expected to be low in the early recovery period when vaporised anesthetics and opioids have been used.

Hypoxemia can occur after N_2O anesthesia due to dilution of alveolar O_2 if extra O_2 is not supplied, particularly in cases with low ventilation volumes.[12,13] In the present study, 30% O_2 was supplied until extubation and two litres O_2 were administered nasally thereafter. In addition, only moderate hypoventilation was allowed until resumption of spontaneous ventilation. There was no general evidence of diffusion hypoxemia in the sevoflurane/N_2O group but, as an indirect sign,

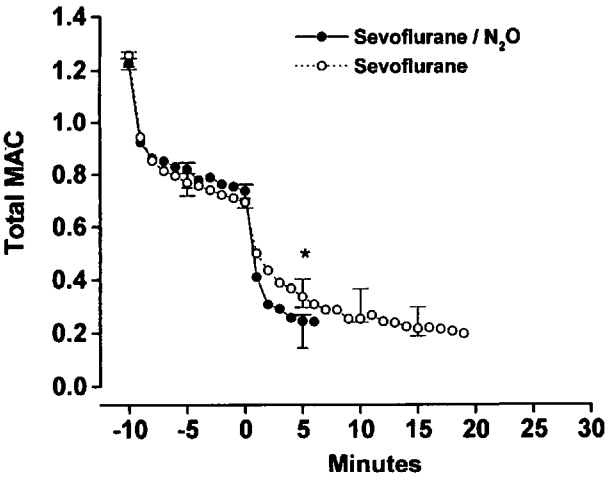

FIGURE 1 Total MAC values during emergence from anesthesia; median values and 25th-75th percentiles. Intergroup difference is denoted * $P < 0.01$.

ETO_2 tended to be lower about five minutes after the discontinuation of N_2O (Figure 2). No differences in oxygenation variables (SpO_2, ETO_2, SaO_2, PaO_2) could be observed between Group sevoflurane/N_2O or Group sevoflurane, at the end of 1.3 MAC anesthesia or in the emergence period.

In a study by Nishino and Kochi, apneic on- and off-switch thresholds for CO_2 were determined during sevoflurane anesthesia before and during surgical stimulation. The CO_2 on-switch threshold, at which post-hyperventilation apnea ceases and respiration begins during 1.2 MAC sevoflurane anesthesia, was at $P_{ET}CO_2$ 6.1 kPa (almost 6.1 vol%) before surgical stimulation and 4.7 kPa during surgery.[14] After the resumption of spontaneous breathing before surgical stimulation $P_{ET}CO_2$ decreased to a resting level of 5.7 kPa, while the resting level during surgical stimulation continued at a level of 4.8 kPa, like the on-switch threshold. Our study was very different in design, but their results compare fairly well to our resumption of spontaneous breathing which occurred at $PaCO_2$ of 6.6 and 6.7 kPa in Group sevoflurane/N_2O and Group sevoflurane, respectively. However, the individual differences in each group were quite large. The wide age range and the strict administration of opioids and volatile agents, independent of age in our study, may explain both our larger thresholds in spite of diminishing inhalational anesthetic depth and possibly the large individual differences. Findings common to both groups were the changes in arterial pH and CO_2 tension. Thus, there was a decrease in pH of about 0.07 and an increase in $PaCO_2$ of about 1.4 kPa.

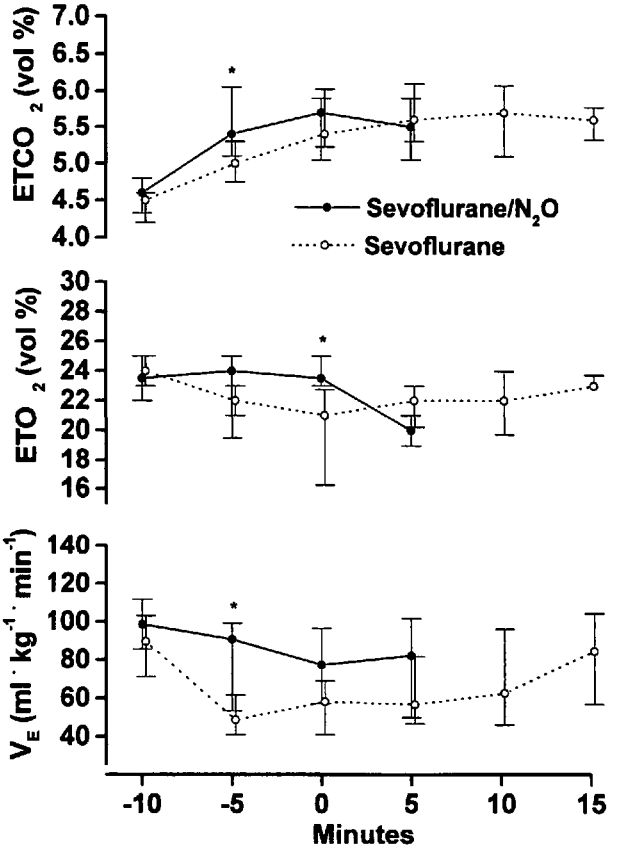

FIGURE 2 Minute ventilation volume, V_E (ml·70 kg^{-1}·min^{-1}), end-tidal oxygen concentration, ETO_2 (vol%), and end-tidal carbon dioxide concentration, $ETCO_2$ (vol%); median values and 25th-75th percentiles. Intergroup differences are denoted * $P < 0.05$.

In a series of studies we have evaluated the effect of N_2O on respiration during emergence from inhalational anesthesia with the three most commonly used volatile agents, isoflurane,[15] desflurane,[16] and now sevoflurane. All the study protocols have been identical except for the volatile agent used. The almost constant changes in arterial pH and $PaCO_2$ values from the end of 1.3 MAC anesthesia with controlled normoventilation to the start of breathing has been common in all the studies, independent of which volatile agent has been used or if N_2O has been used or not. This suggests that not only the *absolute* values of pH and $PaCO_2$ are important for the resumption of spontaneous breathing, but also the *change* from baseline arterial blood gas values at the end of anesthesia and controlled normoventilation. In the isoflurane study[15] as well as in the present study, the time to resumption of spontaneous breathing was less in the isoflu-

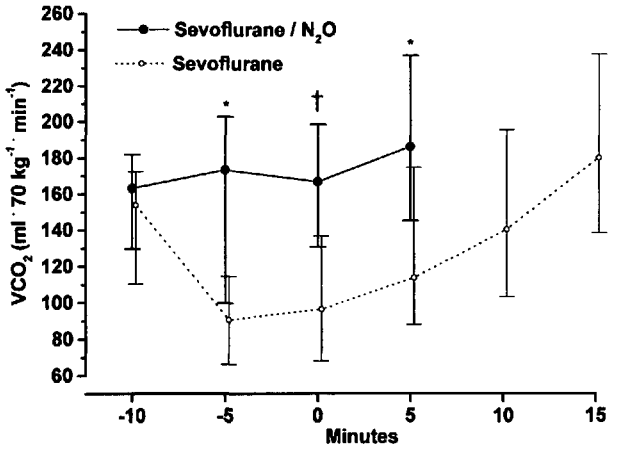

FIGURE 3 Carbon dioxide elimination rate, VCO_2 (ml·70 kg^{-1}·min^{-1}); median values and 25th-75th percentiles. Intergroup differences are denoted * $P < 0.05$, and † $P < 0.01$.

rane/N_2O group than in the isoflurane group. On the other hand, in the desflurane study there was no difference between the two groups.[16] The difference in responsiveness may reflect differences in tissue solubility. The effect of each agent on the body metabolic rate may also be important. Volatile anesthetics such as halothane,[17] enflurane,[18,19] and isoflurane[19,20] generally reduce pre- anesthetic O_2 uptake with 20-35%. Sevoflurane is also known to decrease total body oxygen consumption[4,21] and CO_2 elimination by about 20%.[21] In contrast, Lockhart *et al.*[22] found no changes in metabolic rate during desflurane anesthesia compared with awake values. In the present study, the VCO_2 was 163 and 154 ml·70 kg^{-1}·min^{-1} at the end of a 1.3 MAC sevoflurane/N_2O and sevoflurane anesthesia, respectively. In the emergence period, one would expect the total body metabolism to increase towards awake resting values. Postoperatively, the stress associated with return to consciousness and recovery of pain sensation, and the thermogenesis needed to correct a temperature fall occurring during surgery are main factors known to increase body metabolic rate.[20,23] In spite of a depression of V_E in association with controlled hypoventilation and the re-establishment of spontaneous breathing, there was a moderate increase in VCO_2 in the sevoflurane/N_2O group whereas both V_E and VCO_2 markedly decreased in the sevoflurane group during emergence from anesthesia. Provided that $PaCO_2$ is unaltered, the VCO_2 reflects metabolic production. As in the study by Nishino and Kocki[14] the $PaCO_2$ decreased after resumption of spontaneous breathing compared to the "on-switch threshold". After that the sevoflurane/N_2O patients had their peak $PaCO_2$ and minimum pH at 0 min, and the sevoflurane patients at 15 min i.e. some 10 min after spontaneous breathing was re-established. The sevoflurane group did not reach the expected normal resting VCO_2 level of about 200 ml·70 kg^{-1}·min^{-1} until 15 min after the inhalation agent had been discontinued. A mismatch between CO_2 production and elimination was indicated by an increase in $PaCO_2$ during this period.

The low blood solubility of sevoflurane and N_2O indicates that the rate of decrease of alveolar concentration should be rapid after discontinuation of the administration of the agent.[24] The blood/gas partition coefficient of sevoflurane is 0.69[25] and that of N_2O is 0.47.[26] Other tissue/blood partition coefficients also influence elimination. The fat/blood partition coefficients of sevoflurane and N_2O are 48 and 2.3, respectively.[25] The extent of washout of sevoflurane and N_2O is not only dependent on their respective solubility in blood and other tissues, but also on ventilation volumes. Thus, both lower partition coefficients of N_2O and larger ventilation volumes of Group sevoflurane/N_2O compared with Group sevoflurane may explain the differences in gas elimination and in respiratory recovery between the groups as measured by times to resumption of spontaneous breathing and extubation. At extubation, MAC was about 0.2 in both groups. In patients anesthetised with sevoflurane alone, ET-sevoflurane was 0.4 %. This is lower than the awakening concentrations of sevoflurane which was 0.62 % in a study by Katoh *et al.*[27] An explanation for the discrepancy may be found in our administration of volatile agents independent of age and of opioids for postoperative pain relief before emergence.

In conclusion, patients anesthetised with sevoflurane without N_2O had a longer delay until resumption of spontaneous breathing and tracheal extubation and a more pronounced respiratory depression in the emergence period than those anesthetised with sevoflurane/N_2O.

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