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Minimum Alveolar Concentration of Desflurane in Patients Older Than 65 Yr

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Background: **The minimum alveolar concentration (MAC) of desflurane/oxygen is 7.25% in the 18–30-yr age group, and 6.0% in the 31–65-yr age group. The addition of 60% N_2O reduces MAC to 4.0 and 2.83%, respectively. Because MAC of other inhaled anesthetics is less than that for younger adults, we determined MAC of desflurane in adults aged 65 yr and older.**

Methods: **Thirty-nine patients, 21 of whom received 60% N_2O/O_2/desflurane, and 18 of whom received desflurane/oxygen, scheduled for surgery, were enrolled. They received no premedication, intravenous induction agent, opioid, or neuromuscular blocking agent for intubation. After 10 min or more at a steady end-tidal desflurane concentration, the incision was made. In both groups, six crossover pairs of patient responses (movement–no movement) provided a mean end-tidal concentration. Minimum alveolar concentration was defined as the average of the six crossover midpoints in each subgroup.**

Results: **MAC was 5.17 ± 0.6% (mean ± SD) in the desflurane/oxygen group. It was 1.67 ± 0.4% in the desflurane/nitrous oxide/oxygen group.**

Conclusions: **In the geriatric patient, MAC of desflurane, with or without nitrous oxide, is less than that reported in patients aged 18–65 yr. This is in agreement with results with all other inhalation agents. (Key words: Anesthesia, geriatric. Anesthetics, gases: nitrous oxide. Anesthetics, volatile: desflurane. Potency: minimum alveolar concentration.)**

THE minimum alveolar concentration (MAC) of desflurane, with or without nitrous oxide, has been shown to be less in patients 31–65 yr of age than in those 18–30 yr of age.[1] MAC of other volatile agents is also less in the older age group.[2–7] Because so many geriatric patients undergo surgery and anesthesia, we hypothesize that less desflurane is needed in patients over the age of 65 yr. Consequently, we determined the potency (MAC) of desflurane in oxygen and nitrous oxide/oxygen in patients 65 yr of age or older.

Materials and Methods

Thirty-nine patients were enrolled after the investigators obtained approval of the protocol from the University of Miami, School of Medicine, and the Sub-Committee on Human Research, VA Medical Center, Miami. Written informed consent was obtained from all patients. All patients were 65 yr of age or older, and ASA physical status 2 or 3. All were scheduled for elective surgery requiring a skin incision. Exclusion criteria included laboratory evidence of severe hepatic disease (aspartate amino transferase > 35 U/L, alanine amino transferase > 50 U/L); renal disease (creatinine > 1.5 mg/dL); history of cardiac disease (recent congestive heart failure, infarct); central nervous system disease (brain tumor), chronic use of drugs that may alter MAC, including severe alcoholism or recreational drug use; and general anesthesia during the 7 days before scheduled surgery. All patients were divided into two groups that determined whether they were to receive: 1) desflurane in 60:40 N_2O:O_2 (done first), or 2) desflurane in oxygen.

All patients were monitored by continuous electrocardiography, pulse oximetry, and a self-inflating blood-pressure cuff. Patients received no preanesthetic medication and, after an intravenous infusion was started, no intravenous agent was used for induction of anesthesia. Anesthesia was induced by the inhalation of desflurane in nitrous oxide/oxygen or oxygen *via* a tight-fitting face mask. Desflurane was vaporized by a modified Ohmeda DM 5000 vaporizer (Madison, WI) and delivered through a semiclosed circuit. Airway gases were monitored continuously with an infrared absorption spectrometer, Datex PB-254 (Puritan-Bennett, Tewksbury, MA), calibrated using a specially designed calibration gas with the analyzer modified to

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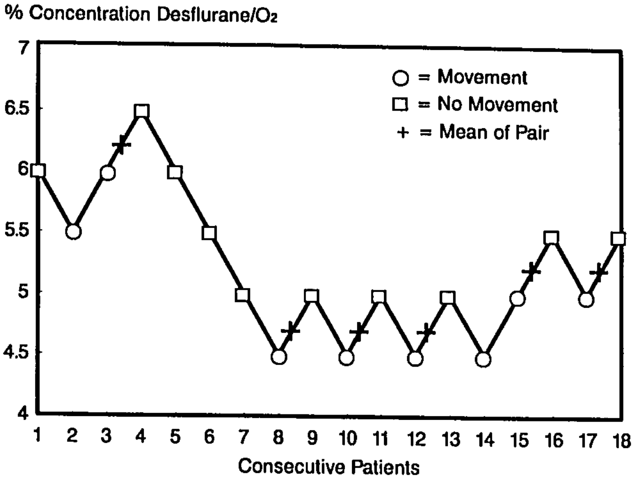

Fig. 1. The 18 consecutive patients and their corresponding inhalational concentrations of desflurane in oxygen. The crosses correspond to the average of six crossover movement–no movement patient pairs. When six averages (representing six pairs of patients) are averaged, MAC is calculated to be 5.17.

read desflurane concentrations. Total gas flow rates during induction were approximately 5 l/min. We began with 3% desflurane in nitrous oxide/oxygen and 6% desflurane in oxygen for the first patients in each group, respectively. The inspired concentration of desflurane was increased slowly, approximately 2% per minute, until anesthetic depth was judged suitable for laryngoscopy and tracheal intubation without the need for a neuromuscular blocking agent. This usually required 13–15 min after the face mask was applied. The endotracheal tube was coated with a thin layer of lidocaine ointment.

After tracheal intubation, fresh gas flow rates were continued at 5 l/min, and the inspired concentration of desflurane was adjusted to maintain a stable end-tidal concentration for at least 10 min at the test concentration selected for the individual patient. End-tidal carbon dioxide concentrations were maintained between 30–35 mmHg, and the patient's lungs were ventilated mechanically. Normothermia was maintained with a warming blanket.

The test concentration of desflurane for each individual patient was determined with the use of a modification of Dixon's up-and-down method.[8] In each group, the first patient was tested at his prescribed concentration, and subsequent patients were tested at a concentration defined by the previous patient's response to incision. If the previous patient moved, the test concentration was increased by 0.5% desflurane; in the absence of movement, the desflurane concentration was decreased by 0.5%. A positive response to incision was defined by purposeful movement of one or more extremities or the head within 1 min after incision. Coughing or bucking was not considered a positive response. Values for MAC were obtained by calculating the midpoint concentration of all independent pairs of patients involving a crossover, *i.e.*, movement to no movement. We also calculated the six crossover pairs, no movement to movement. We required that six pairs be obtained for each of the two groups to obtain MAC. Minimum alveolar concentration was defined as the average of the crossover midpoints in each crossover subgroup. We further analyzed our data by logistic regression. See Appendix. This provided an additional calculation of MAC for each study group and a plot of the probability of no movement *versus* end-tidal concentration of desflurane. Statistical analysis also included standard t tests, and significance was accepted at $P < 0.05$.

Results

Figures 1 and 2 depict responses of the two groups of patients. Thus, 21 patients were needed to obtain 6 pairs in the nitrous oxide group, and 18 patients were needed to obtain 6 pairs in the oxygen group. Minimum alveolar concentration was 5.17 ± 0.6% and 1.67 ± 0.4% for desflurane in oxygen and nitrous oxide/oxy-

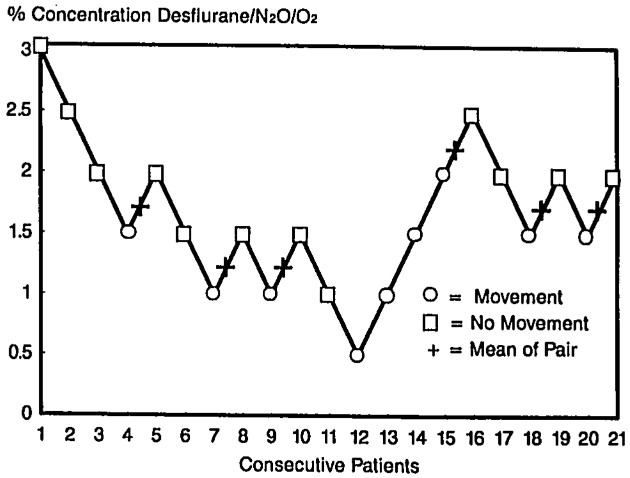

Fig. 2. The 21 consecutive patients who received desflurane in nitrous oxide/oxygen. The six pairs of movement–no movement patient combinations provide an average of 1.67, which is the MAC for desflurane/nitrous oxide/oxygen.

Table 1. Adult MAC Reduction by Age and 60–70% N_2O

Anesthetic Agent	Average Age (yr)	MAC% in O_2	% Decrease from Young	MAC% in N_2O/O_2	% Decrease from Young	MAC% Decrease from O_2 to N_2O
Cyclopropane[5]	32	9.8	—	—	—	—
	81	7.6	−22	—	—	—
Halothane[3]	19–30 (young)	0.84	—	—	—	—
	31–55	0.76	−9.5	—	—	—
	70–96 (old)	0.64	−24	—	—	—
Isoflurane[2]	19–30	1.28	—	0.56	—	−56
	32–55	1.15	−10	0.50	−11	−57
	>55	1.05	−18	0.37	−34	−65
Desflurane	18–30[1]	7.25	—	4.0	—	−45
	31–65[1]	6.0	−17	2.83	−29	−53
	>65*	5.17	−29	1.67	−58	−68
Sevoflurane	38[6]	2.05	—	—	—	—
	71[7]	1.48	−28	—	—	—

Both increasing age and use of nitrous oxide reduce MAC. Primary agent with nitrous oxide in oldest group creates greatest MAC reduction.
* Current study.

gen, respectively. The midpoint of each movement–no movement pair is displayed as a cross. We also defined a crossover with a transition from a no movement–movement pair. These MACs, based on six pairs each, were calculated as 5 and 1.42%, respectively ($P > 0.05$). We did create a logistic regression model (see Appendix) and a plot of the probability of 50% response *versus* desflurane concentration for each group. The midpoint, *i.e.*, the probability of 50% response, is almost the same as that calculated by the Dixon up-and-down method (Figs. A1 and A2). The average age in the desflurane/oxygen group was 69.6 ± 4.5 yr, and, in the desflurane/nitrous oxide/oxygen group, 69.7 ± 4.3 yr. The average heights and weights in each group were: 175.7 ± 6.4 and 175.4 ± 7.2 cm, and 83.8 ± 15.8 and 77.5 ± 15.0 kg, respectively. None of these represent statistically significant differences.

Discussion

Within the framework of at least five inhalational anesthetics, advancing age is consistently associated with decreasing anesthetic requirements for cyclopropane, halothane, isoflurane, desflurane, and sevoflurane[2–7] (table 1). The simultaneous administration of 60% N_2O reduces MAC of desflurane by 45% in the 18–30-yr age group and by 53% in the 31–65-yr age group (table 1). This study indicates that, in patients over the age of 65 yr, this reduction increases to 68%. This additive effect on the potency of desflurane is comparable to the effect of nitrous oxide on other volatile agents, particularly isoflurane. Therefore, both increasing age and the use of nitrous oxide reduce desflurane requirements.

With respect to desflurane, we recalculated the data using crossover midpoints between patients as no movement–movement, and the differences of MAC were minimal and not statistically significant. We also recalculated the data using logistic regression and, once again, at the 50% line that corresponds to MAC, the difference was minimal. In conclusion, in patients older than 65 yr, MACs of desflurane in oxygen are 5.17 and 1.67% with 60% N_2O in oxygen.

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Appendix: Logistic Regression of the Probability of No Movement as a Function of End-tidal Concentration of Desflurane/Nitrous Oxide/Oxygen or Desflurane/Oxygen

A logistic regression model was fitted to the proportions (*P*) depicted in table A1. In these analyses the logit transformation, ln $(P/1 - P)$, is expressed as a linear function of the end-tidal concentration (ET_{DES}) for each treatment (*i.e.*, desflurane/N_2O/O_2 or desflurane/O_2). That is, ln $(P/1 - P) = B_0 + B_1x$, where B_0 = intercept, B_1 = slope, and x = $ET_{DES}\%$. The BMDP® LR module was used to obtain maximum likelihood estimators of the model parameters and assess goodness of fit. This was done separately for each treatment group. MAC estimates were obtained by setting $P = 0.5$ and solving the resulting equation for the ET_{DES}. Logistic regression of the natural log of concentration was also done and similar results obtained.

Results of analyses are presented in table A2. Graphs of the estimated and observed proportions are presented in figures A1 and A2. These were created using SAS/Graph software.

For desflurane/N_2O/O_2, the logistic model appears to give an adequate fit for the observed proportions because: (1) the

Table A1. Number of Patients (n/Total at Dose) with No Movement

Treatment	Concentration (%)	*P* = n/Total (%)
Desflurane/N_2O/O_2	0.5	0/1 (0)
	1.0	1/4 (25)
	1.5	3/7 (43)
	2.0	5/6 (83)
	2.5	2/2 (100)
	3.0	1/1 (100)
Desflurane/O_2	4.5	0/4 (0)
	5.0	4/6 (67)
	5.5	3/4 (75)
	6.0	2/3 (67)
	6.5	1/1 (100)

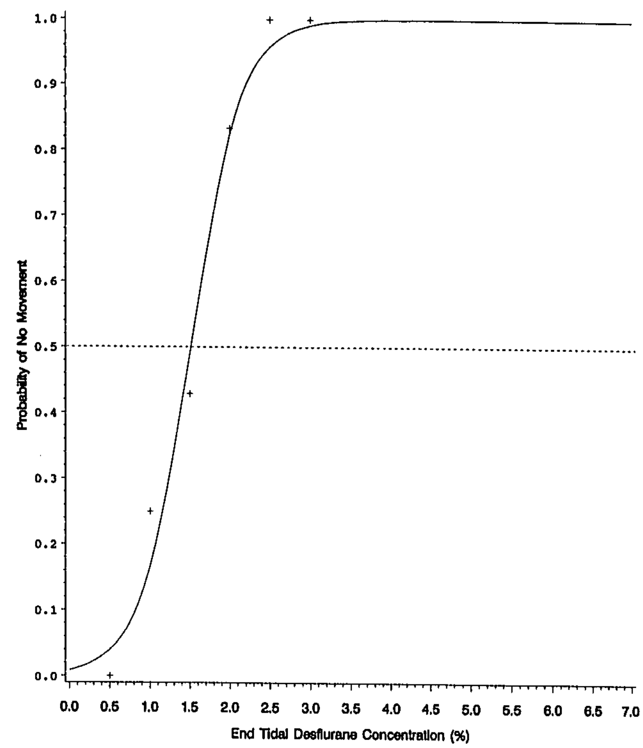

Fig. A1. Probability of no movement as a function of desflurane/nitrous oxide/oxygen concentration.

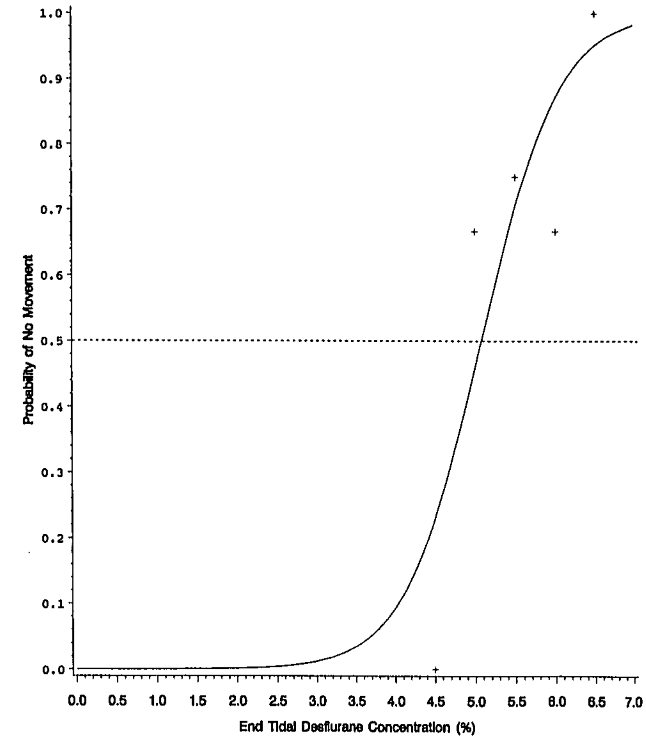

Fig. A2. Probability of no movement as a function of desflurane/oxygen concentration.

Table A2. Estimated Values of the Coefficients of Logit ($P/1 - P$) = $B_0 + B_1x$

	Desflurane/N_2O/O_2		Desflurane/O_2	
Coefficient	Estimated Value	P	Estimated Value	P
Intercept	−4.76 ± 2.3*		−10.70 ± 5.93*	
Slope	3.15 ± 1.4*	0.0286	2.10 ± 1.15*	0.0672
MAC	1.51		5.09	

Goodness of fit chi-squared (GF) P = 0.967; GF P = 0.249.
* Standard error.

P value for the slope of 0.0286 implies a statistically significant trend in the logit as a function of concentration at any significant level higher than 0.0286; and (2) the goodness-of-fit test and graphs in figure A1 suggest good agreement between the estimated and observed proportions. For desflurane/O_2, the logistic model appears to give an acceptable fit because: (1) the P value for the slope of 0.0672 is marginally significant; and (2) the goodness-of-fit test is not significant. However, the agreement between observed and estimated proportions (fig. A2) is less adequate than in the previous case. This may be due to the reversal of trend noted at ET_{DES} = 6.0%.