

## MAC of Desflurane in 60% Nitrous Oxide in Infants and Children

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Desflurane, an inhaled anesthetic, may be useful for outpatient procedures in pediatric patients because its blood solubility (similar to that of nitrous oxide and less than that of commercially available potent inhaled anesthetics) may facilitate emergence and recovery from anesthesia. Although the MAC of desflurane without nitrous oxide has been determined in pediatric patients, it is likely that clinicians will administer desflurane with nitrous oxide. To determine the potency of desflurane administered with 60% nitrous oxide in pediatric patients, the authors determined the minimum alveolar concentration that prevents movement in 50% of subjects (MAC) in 12 infants aged 17 weeks–12 months and 12 children aged 1–5 yr. Anesthesia was induced with desflurane in oxygen; nitrous oxide was not administered during induction of anesthesia to minimize the likelihood of hypoxia if laryngospasm occurred. Following tracheal intubation, nitrous oxide and desflurane were administered and maintained at target concentrations for a minimum of 10 min before surgical incision. No additional anesthetic, sedative/hypnotic, or analgesic drugs were administered prior to incision. Following surgical incision, anesthesia was maintained with nitrous oxide, desflurane, and fentanyl,  $4 \pm 1 \mu\text{g}/\text{kg}$  (mean  $\pm$  SD). MAC, determined using a modification of Dixon's "up-and-down" technique, was  $7.5 \pm 0.1\%$  (mean  $\pm$  SE) for infants and  $6.4 \pm 0.2\%$  for children; similar values were obtained using logistic regression ( $7.5 \pm 0.01\%$  and  $6.3 \pm 0.03\%$ , respectively). Time from discontinuation of anesthesia to eye-opening and tracheal extubation was  $5.4 \pm 3.6$  min (mean  $\pm$  SD). Based on published data for desflurane's MAC in the absence of nitrous oxide, the authors conclude that desflurane's MAC is decreased approximately 25% by concurrent administration of 60% nitrous oxide. (Key words: Anesthesia; pediatric. Anesthetics, gaseous: nitrous oxide. Anesthetics, volatile: desflurane. Potency, anesthetic: MAC.)

DESFLURANE, an inhaled anesthetic with low blood solubility, is associated with rapid emergence from anesthesia.<sup>1</sup> Although the MAC of desflurane administered without nitrous oxide ( $\text{N}_2\text{O}$ ) has been reported in pediatric patients,<sup>2</sup> it is likely that clinicians anesthetizing infants and children will assume that  $\text{N}_2\text{O}$  contributes significantly to reducing desflurane's MAC and will therefore administer  $\text{N}_2\text{O}$  in addition to desflurane. Therefore, we determined the MAC of desflurane with 60%  $\text{N}_2\text{O}$  in pediatric patients aged 17 weeks to 5 yr.

### Materials and Methods

After obtaining approval from our local Committee on Human Research and written informed parental consent,

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we studied 13 infants aged 17 weeks–12 months ( $7 \pm 2$  months, mean  $\pm$  SD) and 13 children aged 1–5 yr ( $2.7 \pm 1.5$  yr). All patients were ASA physical status 1 or 2 and were undergoing a variety of minor surgical procedures. Exclusion criteria included premature birth, congenital heart disease, recent or chronic administration of sedative drugs, or central nervous system disorders. Patients were eligible for the study only if the surgical procedure involved a skin incision.

Patients received no preanesthetic medication. Anesthesia was induced with desflurane in 5–10 l/min flows of oxygen using a pediatric circle system with a  $\text{CO}_2$  absorber. The inspired desflurane concentration was increased from 6.0% to 15.0–18.0% during the first 2–3 min of administration. No sedatives, hypnotics, local anesthetics, or analgesics were administered prior to the determination of MAC. Tracheal intubation was performed without the use of muscle relaxants, and the patient's lungs were mechanically ventilated to maintain an end-tidal  $\text{P}_{\text{CO}_2}$  of 30–43 mmHg. Patients were maintained normothermic. Following tracheal intubation,  $\text{N}_2\text{O}$  was added to the inspired gas to produce an end-tidal  $\text{N}_2\text{O}$  concentration of 60%, and desflurane concentrations were adjusted in each patient to produce the desired target concentrations. In each age group, the target concentration of desflurane was 6.0% for the first subject. If the subject moved an unincised body part purposefully during the 1 min following surgical incision, the target concentration for the next patient in that age group was increased 0.5%, *i.e.*, to 6.5%. If the subject did not move, the target concentration for the following patient was decreased 0.5%. Grimacing or coughing was not considered to be purposeful movement. Anesthetic concentrations were maintained constant at the target concentration for at least 10 min (and typically  $> 20$  min) before skin incision in each subject. End-tidal concentrations of desflurane, sampled at the Y-connector of the breathing circuit, were determined using infrared absorption spectroscopy (Datex PB254, Puritan-Bennett, Tewksbury, MA); end-tidal  $\text{N}_2\text{O}$  concentration and  $\text{P}_{\text{CO}_2}$  were measured by mass spectrometry. Both devices were calibrated with known standards before each MAC determination.

Following determination of MAC, anesthesia was maintained with 60%  $\text{N}_2\text{O}$  and desflurane (mean  $\pm$  SD  $7.9 \pm 1.4\%$ ; range 4.8–10%). Fentanyl (mean  $\pm$  SD  $4 \pm 1 \mu\text{g}/\text{kg}$ ; range 1–12  $\mu\text{g}/\text{kg}$ ) was administered at the discretion of the attending anesthesiologist. At the completion of surgery, 13 patients received caudal blocks or local infiltration with 0.25% bupivacaine,  $\leq 1.0$  ml/kg.

The incidence and severity of laryngospasm, breath-holding, coughing, use of succinylcholine, and incidence of hemoglobin oxygen saturation by pulse oximetry ( $SpO_2$ ) < 90% during induction of anesthesia were recorded. We also recorded the duration of anesthesia, the end-tidal desflurane concentration at the time at which anesthetic gases were discontinued, the time from discontinuation of anesthetic gases to eye-opening (at which time the trachea was extubated), recovery time (defined as the time from entry in the postanesthesia care unit to satisfying discharge criteria of a modified Aldrete score > 9), and the incidence of vomiting or requirement for opioids during recovery. Differences between infants and children were determined using chi-square with the Yates continuity correction or unpaired *t* tests; values are reported as percentages or as mean  $\pm$  SD.

MAC was determined, using a modification of Dixon's technique,<sup>3</sup> by calculating the average target concentration for each pair of consecutive subjects whose response to surgical incision differed (crossover). A minimum of four independent crossovers was obtained (*i.e.*, a sequence of move-no move-move-no move represents two independent crossovers) for each age group. MAC was defined as the mean  $\pm$  SE of the crossover values. MAC also was determined using logistic regression.<sup>4</sup> For all comparisons,  $P < 0.05$  was considered statistically significant.

### Results

Desflurane MAC, determined from the crossover values, was  $7.5 \pm 0.1\%$  for infants and  $6.4 \pm 0.2\%$  for children (fig. 1). Similar values were obtained using logistic regression ( $7.5 \pm 0.01\%$  for infants and  $6.3 \pm 0.03\%$  for children). Data for two patients were not included in these analyses. The first infant studied, aged 6 months and without any identifiable factor likely to alter MAC, did not move with a target desflurane concentration of 6.0% (fig. 1). Because the resulting crossover was more than six standard deviations from the remaining crossovers for infants, we believed that the response of this patient was an outlier, and it was not included in the estimate of MAC. Had data from this patient been included in the analysis, the MAC for infants would have been 7.2% (using the modified Dixon technique) or 7.4% (using logistic regression). A second patient, aged 54 weeks and born at 28 weeks' gestation, moved with a target desflurane concentration of 7.0% (data not shown in fig. 1). Because this patient did not meet the exclusion criteria of premature birth and because correcting the patient's postnatal age for the premature birth would have reclassified the child as an infant, the patient's data were omitted from the MAC analysis.

During induction of anesthesia, laryngospasm occurred in 73% (19% mild, 46% moderate, and 8% severe) of patients, coughing in 50%, and breathholding in 46%.

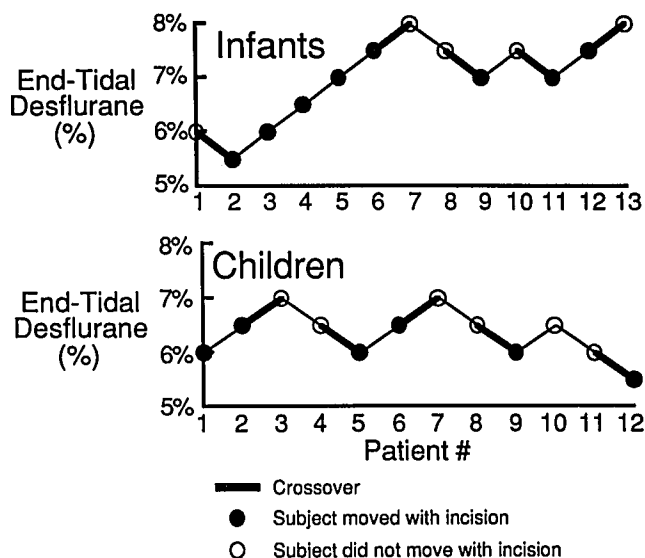


FIG. 1. Target desflurane concentrations administered during consecutive MAC determinations are shown. Each point represents the end-tidal desflurane concentration administered to a single infant (*top*) or child (*bottom*). Heavy lines (crossovers) connect consecutive patients whose response to surgical incision differed; *e.g.*, one moved and the other did not. The midpoint concentration of these crossovers was used to estimate MAC with the modified Dixon technique. MAC also was estimated using logistic regression.

These airway-related complications resulted in  $SpO_2 < 90\%$  in 8% of patients; the lowest  $SpO_2$  was 85%. No patient required succinylcholine. At the completion of surgery, the end-tidal desflurane concentration when  $N_2O$  and desflurane were discontinued was  $2.9 \pm 2.0\%$ . The time from discontinuation of desflurane to eye opening and tracheal extubation was  $5.4 \pm 3.6$  min following anesthesia of  $132 \pm 80$  min. Recovery time was  $51 \pm 18$  min. In the postanesthesia care unit, 23% percent of patients vomited and 38% required opioids for pain management. The incidence of laryngospasm, hypoxemia, vomiting, and opioid requirement, and the times to extubation and recovery were similar for infants and children.

### Discussion

We found that the MAC of desflurane, administered with 60%  $N_2O$ , was 7.5% in infants and 6.3% in children. Recently, Taylor and Lerman<sup>2</sup> reported that the MAC of desflurane without  $N_2O$  was  $9.4 \pm 0.1\%$  at ages 1–6 months,  $9.9 \pm 0.4\%$  at ages 6–12 months,  $8.7 \pm 0.6\%$  at ages 1–3 yr, and  $8.6 \pm 0.4\%$  at ages 3–5 yr. Using these values, we estimate that 60%  $N_2O$  reduces the MAC of desflurane by 22% in infants and 26% in children. However, applying both the additivity principle and the reported MAC of  $N_2O$  in infants and children, 105% (as estimated in additivity studies involving  $N_2O$  and halo-

thane),<sup>5</sup> administration of 60% N<sub>2</sub>O should reduce the MAC of desflurane approximately 55%.

Three possibilities exist to explain this discrepancy. First, the additivity principle may not be correct or may not apply to the combination of desflurane and N<sub>2</sub>O. In support of this, Rampil *et al.*<sup>1</sup> reported that 60% N<sub>2</sub>O reduced desflurane's MAC by only 45% in adults aged 18–30 yr. (However, in adults aged 31–65 yr, the reduction was 53%, as expected.) In addition, recent studies question the validity of the additive contribution of N<sub>2</sub>O to the MAC of halothane, isoflurane, and enflurane<sup>6,7</sup>; however, Eger<sup>8</sup> disputes the results of those studies. Second, reported values for MAC of N<sub>2</sub>O in children may be in error. We note that the reported value for N<sub>2</sub>O MAC in young children, 105%<sup>5</sup> (estimated from additivity studies with halothane), is similar to that in adults; in contrast, the MAC of halothane,<sup>9</sup> isoflurane,<sup>10</sup> and desflurane<sup>2</sup> all vary with age.

A third possibility is that our values for MAC with N<sub>2</sub>O or those reported by Taylor and Lerman<sup>2</sup> for MAC in the absence of N<sub>2</sub>O may be in error. Our MAC determinations would be in error if contamination of end-tidal gas by inspired gas falsely elevated our end-tidal measurements for desflurane. We contend that this is unlikely. First, we used a valved circle system that does not have continuous flow. Second, ventilation was controlled using tidal volumes exceeding 10 ml/kg and inspiratory times > 1 s; with these settings, there was a consistent plateau in the capnographic tracing. Third, because of desflurane's low blood-gas solubility, end-tidal concentrations approach inspired concentrations, minimizing the importance of contamination. Additional studies are necessary to determine whether the reduction in MAC by N<sub>2</sub>O in infants and children is less with desflurane than with other inhaled anesthetics.

In summary, the MAC of desflurane in 60% N<sub>2</sub>O is 7.5% for infants and 6.3% for children. These values represent an approximate 25% reduction of the MAC of desflurane previously reported in the absence of N<sub>2</sub>O.

Whether the less-than-expected reduction of desflurane's MAC in pediatric patients represents an error in the results of the present study or that of Taylor and Lerman<sup>2</sup> or whether the additivity principle does not apply to desflurane and N<sub>2</sub>O remains to be determined. Finally, the relatively small contribution of N<sub>2</sub>O to desflurane's MAC may limit the importance of administering N<sub>2</sub>O during anesthesia with desflurane in pediatric patients.

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