

CORRESPONDENCE

Anesthesiology
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The Effective Dose of Midazolam

To the Editor: Midazolam maleate is a water-soluble benzodiazepine used for intravenous anesthesia induction. In reviewing the initial paper by Fragen and co-workers,¹ a problem emerges which has plagued midazolam research, *i.e.*, what is the effective dose? Fragen stated, "based upon unpublished studies, 0.15 mg/kg is the suggested induction dose" of midazolam; however, his results revealed that the actual induction dose was 0.177 mg/kg (mean weight = 68.4 kg and mean induction dose 12.1 mg).¹ We subsequently used as an induction dose 0.2 mg/kg.² Dundee stated that the variation in individual response to midazolam "places limits on its use as an induction agent."³ It is presently our feeling that at least part of the observed midazolam induction failures and clinical impressions of great variability are because of inadequate dosing. For this reason, we have examined with probit analysis our earlier published data² to predict an ED₅₀ and ED₉₉ for midazolam.

The data base comes from 30 unpremedicated healthy (ASA I-II) patients. Three groups of ten patients were given induction dosages of 0.1, 0.15, and 0.2 mg/kg of midazolam maleate administered over 15 s. Induction was defined as loss of lid reflex and failure to respond to oral command. In the three groups induction occurred in three, five, and ten patients of the 0.1, 0.15, and 0.2 mg/kg groups, respectively. Probit analysis, based on methodology by Finney,⁴ was performed and table 1 was generated predicting the effective dosages for midazolam along with 95 per cent fiducial limits. Note that the ED₅₀ is 0.13 mg/kg, ED₉₅ is 0.20 mg/kg, and ED₉₉ 0.23 mg/kg. It would appear from these data that to be certain of induction in all patients, >0.23 mg/kg of midazolam should be administered. That dosages this high may be safely administered has recently been shown by Melvin and co-workers who infused dosages of midazolam up to 0.6 mg/kg.⁵ Because of the narrow range of dosages and because all patients in the 0.2 mg/kg group were successfully induced, the probit analysis is subject to some error and has wide fiducial limits. Nevertheless, these

TABLE 1. Probit Analysis of Midazolam Induction Dosages in Healthy Unpremedicated Patients

ED	Dose (mg/kg)	95 Per Cent Fiducial Limits (mg/kg)
1	0.03	0-0.08
5	0.06	0-0.10
25	0.10	0.03-0.13
50	0.13	0.10-0.16
75	0.16	0.14-0.22
95	0.20	0.17-0.33
99	0.23	0.19-0.42

data may explain the failure of induction seen with lower dosages of midazolam¹⁻³ and could account for the clinical impression that there is great individual variation to the drug.

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Uvular Edema without Endotracheal Intubation

To the Editor:—Recently, two cases of uvular edema following general endotracheal anesthesia have been

reported.^{1,2} In each, the proposed mechanism of this complication was trapping of the uvula between an

endotracheal tube and an oral airway. We report a case of uvular edema that occurred in the absence of an endotracheal tube.

A 19-year-old woman, 12-weeks pregnant, was admitted for a therapeutic abortion. The patient had no known medical problems, was not taking any medications, and had no known allergies. The patient was given Maalox[®], 30 ml po, 45 min before surgery. She had no other premedication. Anesthesia was induced with sodium thiopental, 300 mg, iv, and fentanyl, 100 μ g, iv, and the anesthesia was maintained with N₂O and O₂. An oral airway was inserted to facilitate ventilation by mask. An additional 450 mg sodium thiopental were given in divided doses during the case. Upon awakening in the recovery room 45 min after the procedure, she complained of a sore throat and marked difficulty in swallowing. The patient had no respiratory obstruction.

Examination revealed a markedly swollen uvula and an erythematous oral pharynx. The patient was afebrile and a throat culture taken at this time, later showed no growth. The patient was given diphenhydramine, 50 mg, iv, and hydrocortisone, 100 mg, iv. Twelve hours later, the sore throat had improved and the uvula was decreased in size.

In reviewing the literature, the only cases of uvular edema asso-

ciated with anesthesia were believed caused by either a reaction to scopolamine or atropine, or as a complication of endotracheal intubation.^{1,2} In the absence of an endotracheal tube or anticholinergic drugs, we believe the marked uvular edema we observed may have been due to entrapment of the uvula between the hard palate and the oral airway.

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An Unusual Cause of Leakage in an Anesthesia System

To the Editor:—A complete, daily check of the anesthesia machine is a mandatory part of safe anesthetic practice. Recently, we observed an unusual leak in an anesthesia system which was not found by routine recommended safety checks.¹

Following topical anesthesia and an intravenous induction, the patient was nasally intubated with the aid of succinylcholine. Ventilation was effective with a semi-closed circle system before and after intubation. The pressure relief valve was closed and the flexible connector hose from a previously adjusted and tested

Isolette[®] Ventimeter Ventilator* was connected to the conventional bag fitting in the anesthesia circuit. The ventilation appeared adequate and breath sounds were satisfactory.

Elevation of the operating table and anesthesia circuit to the surgeon's operating level caused excessive strain and kinking of the ventilator connector hose. The ventilator, which was attached to the anesthesia machine by the machine connector pipe in a pin clamp

* NARCO Medical Co., Warminster, Pennsylvania.

FIG. 1. Machine connector pipe displaying the fine longitudinal cracks.

