

DOES AGING ALTER THE RATE OF ELIMINATION OF ISOFLURANE?

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Age-related physiological changes may alter drug elimination (1). The elimination rate of volatile agents in the elderly is unknown. With ethical approval and informed consent, we compared isoflurane elimination in 9 young (26 ± 4 yr) and 10 older (71 ± 4 yr) healthy surgical patients. Administration of etomidate and vecuronium was followed by tracheal intubation. Controlled ventilation maintained normocarbida. Patients received N₂O 66% in O₂, plus fentanyl 1-3 ug/kg. Isoflurane 0.8% was given for exactly 1 hour, with subsequent anesthesia maintained using halothane. Isoflurane partial pressure in arterial blood was measured immediately before discontinuing (P₀) and at 2, 5, 10, 15, 20, 30, 45, 60, 75, 90 and 120 min after discontinuing isoflurane administration. The elimination of isoflurane was compared (unpaired T test) in young and elderly using arterial partial pressures as a percentage of P₀.

Results: No demographic anesthetic or physiologic variables differed between the young and older patients. Mean P₀ (% of 1 Atm) after 60 min isoflurane administration was $.42\% \pm .09$ in the young, $.38\% \pm .04$ in the elderly.

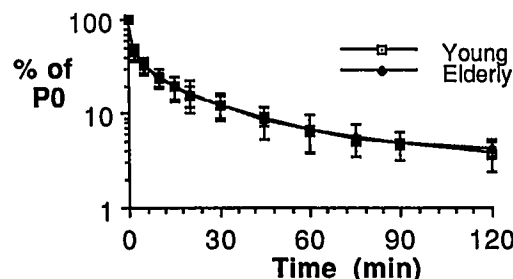


Fig. 1 Arterial isoflurane partial pressure as % P₀

Elimination of isoflurane occurred at the same rate in the young and elderly (Fig 1). The combined effects of the changes in the cardiovascular and respiratory systems and in body composition, which occur during normal aging do not alter the rate of elimination of isoflurane in healthy elderly subjects.

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A358

TITLE: AGING INCREASES SENSITIVITY TO MIDAZOLAM

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Aging has been shown to reduce the clearance of midazolam (MDZ).¹ However, this does not explain the clinical observation that MDZ dose requirements for induction are decreased in elderly patients. The present study was thus designed to determine the effect of aging on patient sensitivity to the hypnotic effect of MDZ.

Following institutional approval and written informed consent, 36 patients (39 - 77 years) undergoing elective CABG were studied. Premedication consisted of MDZ 1 - 4 mg IV before instrumentation for monitoring. Sixty to 90 min later, induction was achieved by MDZ infused for 10 min using a pharmacokinetic model driven drug infusion device (CACI) to achieve randomly predetermined set points. Plasma MDZ concentration (Cp) was measured at 5 and 10 min into the midazolam infusion to confirm the maintenance of relatively constant Cp. Patients were assessed for the presence or absence of a response to verbal command at 10 min. Cp at 10 min, age and the

observed probability of a response to command ($P = 0$: response to command, $P = 1$: no response to command) were grouped and fit to the logistic model $P = (1 + \exp(B_0 + B_1 Cp + B_2 Age))^{-1}$. Cp₅₀, that is the plasma MDZ concentration at which 50 % of patients will not respond to verbal command, was computed using $Cp_{50} = -(B_0/B_1) - (B_2/B_1)Age$.

All patients were responsive before induction. The Cp at 10 min ranged from 64 to 796 ng/ml. Age was found to be a significant predictor ($p = 0.023$) of Cp₅₀ which could be calculated as $Ln(Cp_{50}) = 7.934 - (0.037) Age$.

Previous studies have demonstrated that aging increases patient sensitivity to halothane, isoflurane and cyclopropane (reduction of MAC) (2), and to fentanyl and alfentanil (3). Our study has shown that sensitivity to the hypnotic effects of MDZ increases with age. This work differs from other studies in that the observations were not obfuscated by the use of other premedicants, and patient responsiveness was evaluated during steady state of plasma levels. These data indicate that MDZ dosages should be reduced in elderly patients in comparison to doses used in younger patients.

References

1. Anesthesiology 61:27-35, 1984
2. Anesth Analg 63:998-1000, 1984
3. J Pharmacol Exp Ther 240:159-166, 1987