THE EFFECT OF DIAZEPAM (VALIUM®) ON MINIMUM ALVEOLAR ANAESTHETIC REQUIREMENT (MAC) IN MAN*

JERRY A. PERISHO, LCDR (MC), USN, D. R. BUECHEL, CAPT., (MC) USN, AND
RONALD D. MILLER, M.D.†

DIAZEPAM (VALIUM®) has been used as a premedicant,^{1,2} sedative, and anticonvulsant. The reported amnesia and analgesia associated with diazepam administration has popularized its use during cardioversion.^{3,4} Because of minimal cardiac depression with diazepam during cardioversion, some have suggested it may be a better drug for induction of anaesthesia than the ultra-short acting barbiturates. The recommended dose of diazepam ranges from 0.2 mg/kg to 0.45 mg/kg.^{5,6} The present study was undertaken to determine the effect of a single intravenous injection of diazepam on anaesthetic requirement for halothane.

METHODS

Our standard of potency was the minimum alveolar concentration of anaesthetic (MAC) required to eliminate gross movement in 50 per cent of patients in response to surgical incision. The technique used by us has been described previously.⁷ All patients studied were healthy 18- to 35-year-old males, 52 to 102 kg in weight, undergoing elective herniorrhaphy. The patients received either no medication or atropine sulfate, 0.4 mg intramuscularly preoperatively. Oesophageal temperature was maintained between 35 to 38°C. All patients were informed of any difference between the anaesthetic they would receive and our usual general anaesthetic technique.

Anaesthesia was induced in 22 patients with nitrous oxide-oxygen (4:2 liters) and halothane using a Fluotec vaporized and a semi-closed circle system with a carbon dioxide absorber. After intubation of the trachea, anaesthesia was maintained with oxygen (6 liters) and halothane, without nitrous oxide. All patients were maintained under anaesthesia for at least 90 minutes prior to incision. When the desired halothane end-tidal concentration had been maintained for 15 to 30 minutes, the incision was made. End-tidal halothane concentrations were determined with a Mayo Vapor Analyzer which was calibrated using known concentrations of halothane.⁷ Seventeen of the patients received diazepam 0.2 mg/kg and the other five patients received diazepam 0.4 mg/kg intravenously 15 to 30 minutes prior to the incision.

Arterial PO_2 , P_{CO_2} and pH were drawn from a radial artery cannula and determined with appropriate electrodes⁸ immediately before, 1, 3, 10, and 15 minutes after the administration of diazepam.

*The views expressed are those of the authors, and in no way reflect those of the Naval Medical Department or Naval Service at large.

†Department of Anesthesiology; US Naval Hospital; San Diego, California 92134 and Department of Anesthesia, University of California, San Francisco, California 94122. Reprint requests to: Ronald D. Miller, M.D., Department of Anesthesia, University of California, San Francisco, California 94122.

RESULTS

In the 17 patients receiving 0.2 mg/kg of diazepam intravenously 15 to 30 minutes prior to the incision, all moved at an end-tidal concentration of halothane below 0.44 per cent. In contrast no patient moved at a concentration greater than 0.49 per cent. The resultant MAC for halothane was 0.475 per cent (Figure 1). Thus, administration of 0.2 mg/kg of diazepam results in a 35 per cent reduction in the

FIGURE 1. The upper portion of the graph illustrates the data used to determine the MAC in the presence of diazepam, 0.2 mg/kg. If the patient moved in response to a surgical incision, an upward deflection was recorded at the appropriate alveolar concentration. If the patient did not move, a downward deflection was recorded. The data were grouped to arrive at the graph presented in the lower portion of the figure. Starting from the lowest concentration, patients were taken into groups of four. For each group the percentage of those who moved was plotted on the vertical axis, while the alveolar concentration was plotted on the horizontal axis. A visually-determined line was drawn through these points.

MAC of halothane, since the MAC of halothane has been previously determined by us in unmedicated patients as 0.73 per cent.⁷ Although the mean P_{aCO_2} was elevated three minutes after injection of diazepam, the differences from control were statistically not significant (Figure 2). Twenty-three per cent of the patients had a transient apnoea of a mean duration of 37 seconds immediately after administration of diazepam. Although respiratory volumes were not measured, tidal volume appeared to decrease while respiratory rate either remained unchanged or increased, which is consistent with previous observations.⁹

In those patients receiving 0.4 mg/kg of diazepam, all moved at end-tidal concentration below 0.39 per cent and none moved at a concentration above 0.43 per

POST DIAZEPAM 0.2mg/Kg ADMINISTRATION

FIGURE 2. Correlation between PaCO_2 determined at intervals of time after intravenous administration of diazepam, 0.2 mg/kg, during halothane anaesthesia. PaCO_2 values did not differ significantly.

TABLE I

	Patient number				
	1	2	3	4	5
End-tidal halothane concentration (%)	0.28	0.38	0.39	0.42	0.43
Time at test concentration prior to incision (minutes)	25	15	20	15	20
Response	move	move	no move	move	no move

TABLE II

Patient number	PaCO_2 (Torr)					
	Control	1*	3	10	15	30
1	34	50	52	50	47	46
2	37	54	61	52	46	
4**	33	38	40	34	31	31
5	47	46	44	45	45	48

*Time in minutes post Diazepam 0.4 mg/kg administration intravenously.

**Patient number 3 did not have arterial blood gases drawn.

cent (Table I). Some of these patients had a large increase in PaCO_2 (Table II). All patients experienced some apnoea the mean duration being 1.70 minutes (range 0.25 to 4.0 minutes).

DISCUSSION

The use of diazepam as an induction agent has become increasingly popular at our institution. This study demonstrates a significant reduction in the MAC of

halothane with 0.2 mg/kg of diazepam. Doubling the dose of diazepam results only in minimal additional reduction of halothane anaesthetic requirement over that obtained with 0.2 mg/kg. Fox, Wynands, and Bhambhani¹⁰ found maintenance of anaesthesia required less halothane when diazepam was substituted for thiopentone. However, end-tidal concentrations of halothane were not monitored in their study.

That diazepam either has no effect¹¹ or actually augments myocardial contractibility¹² suggests it may have certain advantages over thiopentone as an induction agent. Although administration of 0.2 mg/kg of diazepam during halothane anaesthesia resulted in little change in the P_{aCO_2} (Figure 2), 0.4 mg/kg of diazepam resulted in rather dramatic increases in P_{aCO_2} in some patients (Table II). Since reduction of halothane anaesthetic requirement is not much greater with 0.4 mg/kg than 0.2 mg/kg of diazepam, there seems little advantage to using the larger dose.

Those who have proposed diazepam as an induction agent for general anaesthesia^{5,6,9,10} based their recommendations on the lack of stimulation of adverse reflex activity and the cardiovascular stability associated with the drug. The facts gathered from our study indicate that diazepam potentiates the analgesia of halothane or adds analgesic effects of its own. Because of longer duration of action as compared to thiopentone and for the reasons elaborated above, diazepam might well be considered as the induction agent of choice in many cases. The use of diazepam for induction and in supplemental doses along with halothane anaesthesia will significantly decrease the amount of halothane needed.

SUMMARY

The MAC of halothane was 0.475 per cent in 17 patients 15 to 30 minutes after the intravenous administration of diazepam in doses of 0.2 mg/kg. This represents a 35-per cent reduction from the halothane MAC in unmedicated patients. No significant respiratory depression was observed.

In contrast significant respiratory depression occurred in some patients when diazepam 0.4 mg/kg was administered. Yet, halothane anaesthetic requirement was not significantly reduced over that determined with 0.2 mg/kg of diazepam. Thus, there appears to be no advantage to giving the larger dose of diazepam.

RÉSUMÉ

La concentration alvéolaire minima (MAC ou CAM) de l'halothane a été de 0.475 pour cent chez 17 malades de 15 à 30 minutes après l'injection par voie endoveineuse de diazépam à la dose de 0.2 mg/kilo. Ceci représente une réduction de 35 pour cent de la CAM d'halothane chez des malades non prémédiqués. Nous n'avons pas observé de dépression respiratoire importante.

Par contre, chez des malades qui avaient reçu 0.4 mg/kilo de diazépam, nous avons observé une dépression respiratoire notable. Encore chez ces malades, la dose d'halothane a dû être maintenue à peu près la même que chez les malades qui avaient reçu 0.2 mg/kilo de diazépam. Il semble donc qu'il n'y ait pas d'avantage à donner une plus grosse dose de diazépam.

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