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Diazepam and Intracranial Pressure

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In neurosurgical anesthesia, drugs which decrease cerebral blood flow (CBF) are assumed to decrease intracranial pressure (ICP) probably as a result of a decrease in cerebral blood volume (CBV).^{1,2} Diazepam is known to decrease CBF in both humans³ and animals,^{4,5} and hence may decrease ICP. However, in dogs, Campan *et al.*⁶ observed no significant change in ICP with diazepam. The effect of diazepam on ICP in humans has not been described except for a case report by Phirman and Shapiro.⁷ Therefore, we measured ICP after intravenous injection of diazepam in neurosurgical patients.

METHODS

The study was approved by the Human Experimentation Committee of the Hospital and was performed during the induction of general anesthesia on ten neurosurgical patients who were divided into two groups of five patients each: hypertensive (ICP > 15 torr) and normotensive (ICP < 15 torr). Their age ranged from eleven to seventy-six years old. Four cases of intracranial hematoma, three cases of brain tumor, two cases of hydrocephalus and one case of subarachnoid hemorrhage were included. Glasgow

coma scale[¶] was 15 in five patients, 14 in two patients, and 13, 11, and 10, respectively, in the remaining three patients. An intraventricular catheter or a subdural balloon, which was connected to a transducer (Statham[®] P23ID), was installed one or two days before surgery, under local anesthesia. On the day of surgery, a central venous catheter was inserted from the basilic vein, and a catheter inserted in the radial artery. Direct arterial pressure, ICP, ECG, and rectal temperature were monitored continuously. Arterial pressure, central venous pressure (CVP) and ICP were zero-referred to the level of external auditory canal. Cerebral perfusion pressure (CPP) was calculated as the difference between mean arterial pressure (MAP) and mean ICP. After monitoring was started, at least 10 min elapsed to permit the measured variables to become constant. The measurements were performed before, and for 15 min after diazepam (0.25 mg/kg for one min) administration. CVP was measured by open manometry before, 5, 10, and 15 min after diazepam. Arterial blood gases, heart rate, and hematocrit were measured before and 10 min after diazepam was given. After the measurements, all the patients were hyperventilated and neuroleptanesthesia was started. The subsequent course of anesthesia in all cases was uneventful. Results were analyzed statistically using a Student's *t* test for paired data to compare the values before and after diazepam in each group, and for unpaired data to compare the values before diazepam between both groups. *P* < 0.05 was considered to be significant.

RESULTS

Figure 1 shows individual ICP before and after diazepam. Table 1 shows mean values of ICP, MAP

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¶ The Glasgow coma scale consists of points for the best possible responses to vocal or noxious stimuli as characterized by eye opening, verbalization, and motor activity. Normal responses result in a score of 15, with 3 being the lowest possible value.

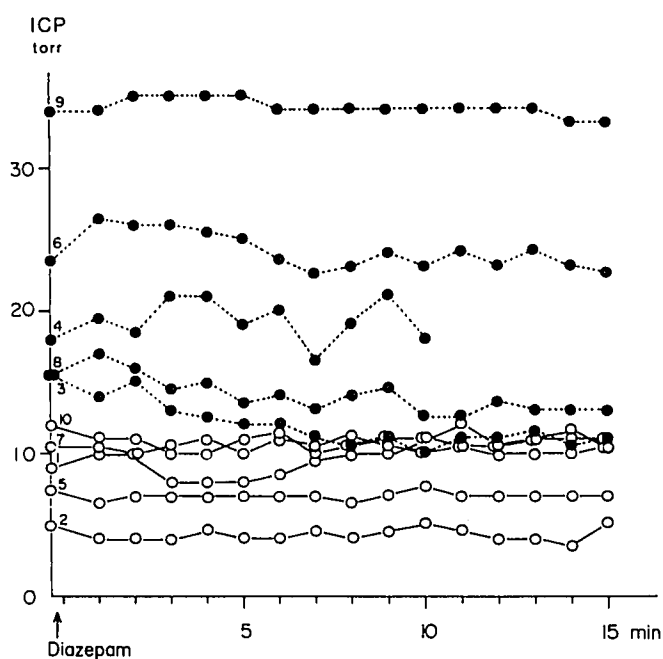


FIG. 1. Individual values of ICP before and after diazepam (0.25 mg/kg). Solid circle (Patient 3, 4, 6, 8, 9) indicates hypertensive group; open circle (Patient 1, 2, 5, 7, 10) indicates normotensive group.

and CPP in both groups. In the hypertensive group, ICP did not change, while MAP and CPP decreased significantly after diazepam to 82 and 77 per cent of control values at 5 min, respectively. In the normotensive group, ICP significantly decreased only at 5 min while MAP and CPP remained unchanged. There were no significant differences of the values before diazepam between the two groups in MAP, CPP, CVP, blood gases, heart rates, hematocrit and body temperature. P_{aCO_2} values before and after diazepam were 37 ± 1 (mean \pm SEM) and 39 ± 1 torr in the hypertensive group, and were 40 ± 2 and 39 ± 3 torr in the normotensive group, respectively.

DISCUSSION

In our previous study,⁴ diazepam (0.25 mg/kg) decreased CBF by 15 per cent in dogs. Carlsson *et al.*⁵ reported a decrease in CBF by 29 per cent with a large dose (0.75 mg/kg) of diazepam in rats. In patients who had sustained trauma to the head, Cotev *et al.*³ observed a decrease in CBF by 24 per cent with diazepam (15 mg), using ⁸⁵Kr clearance technique. The qualitative effects of anesthetics on ICP can be predicted from the drug's effects on CBF and cerebral vascular resistance. Diazepam, which is known as a cerebral vasoconstrictor which decreases CBF, will tend to decrease ICP, probably due to a decrease in CBV.^{1,2} In the present study, we found that a clinical dose of diazepam (0.25 mg/kg) did not change ICP significantly in both groups, except for a transient and small decrease in the normotensive group, which probably has no clinical significance. In the normotensive group, ICP may be little affected since larger changes of CBV would have to occur in order to induce a change in ICP. However, that no significant change in ICP occurred in the hypertensive patients whose intracranial compliance had been decreased was surprising. Thus, the known effect of diazepam on CBF did not allow us to predict the change in ICP in our hypertensive group. To clarify this point, simultaneous measurements of CBF and ICP would be necessary. In hypertensive patients, significant decrease in CPP occurred after diazepam without significant change in ICP. The decrease in MAP can be considered as the result of possible hypovolemia due to osmotic therapy and restriction of water intake. Although the critical value of CPP during diazepam administration has not been determined, CPP was maintained above 50 torr, which is considered the lower limit of autoregulation of CBF, in all hypertensive patients. In specific cases such as severely hypovolemic, elderly, debilitated patients whose MAP might decrease precipitously with diazepam, or for

TABLE 1. Effect of Diazepam on Intracranial Pressure (ICP), Mean Arterial Pressure (MAP) and Cerebral Perfusion Pressure (CPP)*

	ICP (torr)		MAP (torr)		CPP (torr)	
	Hypertensive	Normotensive	Hypertensive	Normotensive	Hypertensive	Normotensive
Before diazepam	21 \pm 3†	9 \pm 1†	104 \pm 6	102 \pm 4	83 \pm 5	94 \pm 4
After diazepam						
1 min	22 \pm 4	8 \pm 1	93 \pm 6‡	100 \pm 4	71 \pm 5‡	91 \pm 3
3 min	22 \pm 4	8 \pm 1	90 \pm 8‡	101 \pm 4	68 \pm 6‡	93 \pm 4
5 min	21 \pm 4	8 \pm 1‡	85 \pm 7‡	96 \pm 2	64 \pm 5‡	88 \pm 2
10 min	20 \pm 4	9 \pm 1	88 \pm 7‡	97 \pm 3	69 \pm 5‡	89 \pm 3
15 min	20 \pm 5	9 \pm 1	94 \pm 8‡	101 \pm 5	74 \pm 5	92 \pm 4

* Values are mean \pm SEM.

† Significantly different between the groups ($P < 0.05$).

‡ Significantly different from the values of before diazepam ($P < 0.05$).

patients who have impaired autoregulation due to intracranial pathology, a more pronounced reduction of CBF may occur than that found in our study. Therefore, MAP must be carefully maintained in these patients. The present result does not mean that diazepam is unsuitable for neurosurgical anesthesia. In fact, Phirman and Shapiro⁷ stated that prior induction of anesthesia with diazepam and thiopental was capable of blocking an increase in ICP due to nitrous oxide, suggesting the usefulness of this combination in those patients with decreased intracranial compliance. In summary, a clinical dose of diazepam does not increase ICP.

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Evaluation of a Disposable Humidifier for Use during Anesthesia

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The provision of humidity during prolonged endotracheal anesthesia has been recommended to prevent changes in ciliary cellular morphology and activity and in pulmonary mechanics.^{1,2} The method employed should reproduce the natural process and provide inspired humidity at temperatures to which the upper trachea is accustomed.¹ This paper reports a laboratory and clinical investigation of the Servo Humidifier[®] 150† with a disposable element, which appears to satisfy these physiologic needs.

MATERIALS AND METHODS

The Servo Humidifier[®] 150 (SH 150), a condenser humidifier that has a heat and moisture trap (cellu-

lose sponge) in addition to a heat and moisture screen (synthetic felt), is designed to be placed between the endotracheal tube and the breathing circuit of an anesthetic or ventilator system (fig. 1). To measure the efficiency of the SH 150, an experimental system was designed, consisting of a previously reported patient model³ and a miniature circle⁴ (fig. 2). The components of the experimental system consisted of a patient model (1, fig. 2) that produced effluent air at 32-34° C at 100 per cent relative humidity (RH; the normal moisture content and temperature of exhaled air¹), and a miniature circle (2, fig. 2) that isolated inspiration from expiration between the patient model's airway and the anesthesia system (4, fig. 2). The miniature circle was necessary to study humidity during the inspiratory phase of the SH 150, which operates on a to-and-fro principle.⁴ Temperatures of the room, exhaled air from the patient model (1C, fig. 2), air from the inspiratory (2U, fig. 2) and expiratory (2W, fig. 2) limbs of the miniature circle, and the area (2X, fig. 2) between the SH 150 and the miniature circle were measured with a Yellow Springs

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