

# The Effect of Halothane, Isoflurane, or Sufentanil on the Hypertensive Response to Cerebellar Retraction during Posterior Fossa Surgery

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The blood pressure (BP) response to cerebellar retraction during microvascular decompression of the fifth cranial nerve was investigated in 26 ASA physical status 2 or 3 patients with trigeminal neuralgia. One surgeon performed all operations. To determine the effect of three anesthetic techniques on the BP response, patients were randomly assigned to receive halothane, isoflurane, or sufentanil in sufficient doses with 60% nitrous oxide to achieve a precerebellar retraction systolic BP that was 10–20% below the average ward systolic BP (as per standard clinical practice). The resultant doses were halothane  $1.65 \pm 0.27$  (mean  $\pm$  SD) MAC, isoflurane  $1.56 \pm 0.17$  MAC ( $P > 0.05$ ), and sufentanil  $2.7 \mu\text{g}/\text{kg}$  (MAC values include 0.6 MAC contribution from 60% nitrous oxide). In all patients BP increased during the cerebellar retractor placement period compared with the preretractor placement period ( $P < 0.05$ ). The peak increase in systolic BP in response to cerebellar retraction was  $17 \pm 6$  mmHg for halothane,  $38 \pm 20$  mmHg for isoflurane, and  $26 \pm 19$  mmHg for sufentanil. The difference between halothane and isoflurane was significant ( $P < 0.05$ ). Mean and diastolic BP showed similar significant differences. The authors conclude that halothane attenuates the hypertensive response to cerebellar retraction more than isoflurane when administered in approximately 1.6 MAC concentrations (MAC value includes contribution from nitrous oxide). (Key words: Anesthesia; neurosurgical. Anesthetic: halothane; isoflurane; sufentanil. Blood pressure: hypertension. Surgery: microvascular; neurologic.)

CARDIORESPIRATORY CHANGES can occur during posterior fossa surgery.<sup>1–5</sup> Reported cardiac rhythm changes include bradycardia,<sup>1,2</sup> ventricular extrasystoles,<sup>1,3</sup> ventricular tachycardia,<sup>1</sup> sinus arrhythmia,<sup>1,4</sup> and cardiac arrest.<sup>5</sup> Associated blood pressure (BP) changes include hypertension<sup>3,4</sup> or hypotension.<sup>1–4</sup> During posterior fossa craniectomy for microvascular decompression of the fifth cranial nerve in patients suffering from trigeminal neuralgia, the authors routinely observe an increase in BP associated with retraction of the cerebellum. We performed this study to determine if there were differences

among three anesthetic techniques in their ability to attenuate this hypertensive response.

## Materials and Methods

This investigation was approved by the institutional committee for human research. Twenty-six ASA physical status 2 or 3 adult patients gave written informed consent to participate. One surgeon performed all operations and was blinded to anesthetic technique. Individual patients were excluded from the study if they had: 1) preoperative average ward BP greater than 160/100 mmHg; 2) pulmonary disease; 3) history of hepatic disease, or 4) history of daily opioid use to control pain.

Average preoperative ward systolic and diastolic BP was obtained after hospitalization and prior to premedication using a sphygmomanometer and auscultation with a stethoscope. Average ward BP represents at least four recorded measurements. All patients received triazolam 0.125 mg po 1 h preoperatively. An iv catheter and a radial arterial catheter were inserted under local anesthesia. Anesthesia was induced in all patients with thiopental 4 mg/kg iv and lidocaine 1 mg/kg iv. Vecuronium 0.1 mg/kg iv was administered, and the patient's lungs were ventilated with 60% nitrous oxide in oxygen *via* a face mask. In addition, the patients were randomly assigned to receive one of three anesthetic drugs: halothane ( $n = 8$ ), isoflurane ( $n = 9$ ), or sufentanil ( $n = 9$ ). The trachea was intubated and ventilation controlled to maintain  $\text{PaCO}_2 = 30 \pm 3$  (mean  $\pm$  SD) mmHg. Patients were placed in the lateral decubitus position. The arterial BP transducer was zeroed to the dependent external auditory meatus and was continuously recorded with the electrocardiogram on a calibrated Hewlett-Packard 7402A strip chart recorder. For the 10-min period prior to cerebellar retraction, the anesthesiologist was instructed to deliver enough anesthetic to maintain systolic BP at a stable level 10–20% below the average systolic ward BP. The sufentanil group received sufentanil 0.5–1.0  $\mu\text{g}/\text{kg}$  iv during induction of anesthesia and then increments up to a total dose of  $2.7 \pm 0.9 \mu\text{g}/\text{kg}$  iv to attain the desired precerebellar retraction BP. Vasodilators and beta-adrenergic blocking drugs were not administered intraoperatively. Airway concentrations of all anesthetic gases, oxygen,  $\text{CO}_2$ , and  $\text{N}_2$  were monitored continuously by mass spec-

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trometry and recorded. For the 10-min period prior to cerebellar retraction, the average end-tidal alveolar concentrations of halothane or isoflurane were determined and the respective MAC values (including the MAC contribution from nitrous oxide 60% = 0.6 MAC) were calculated.<sup>6</sup>

A retromastoid craniectomy was performed. After adequate hemostasis was obtained, the cerebellum was exposed. The surgeon retracted the cerebellum with a malleable retractor, which was then fixed to the skull with a self-retaining apparatus. The study was divided into two periods: 1) the 10-min period prior to cerebellar retraction (preretraction) and 2) the time from initiation of cerebellar retraction until the malleable retractor was fixed to the skull (retractor placement period). These times were easily discernible because retraction began immediately after the dissecting microscope was positioned over the surgical field and could be observed with an in-room video monitor. These events were recorded on the strip chart. The greatest systolic, diastolic, and mean BP change during the retractor placement period was noted.

Mean BP was calculated according to the formula

$$\text{mean BP} = \text{diastolic BP} + 1/3 (\text{systolic BP} - \text{diastolic BP})$$

The duration of the retractor placement period was obtained from the strip chart recording. Average MAC values for halothane and isoflurane (with 60% nitrous oxide) during the 10-min preretraction period were compared by Student's *t* test. The average maximum changes in systolic, diastolic, and mean BP were compared among groups by analysis of variance (ANOVA). Ninety-five percent confidence intervals were then used to test for differences among groups. ANOVA was used to test for differences among the groups in age, weight, average ward BP, preretraction BP, and duration of the retractor placement period. Statistical significance was considered when *P* < 0.05.

### Results

There were no significant differences among the anesthetic groups (halothane *vs.* isoflurane *vs.* sufentanil, respectively) in terms of age ( $57 \pm 11$  [mean  $\pm$  SD] *vs.*  $62 \pm 8$  *vs.*  $51 \pm 13$  years), weight ( $81 \pm 20$  *vs.*  $69 \pm 13$  *vs.*  $75 \pm 21$  kg), average ward BP (systolic mean  $\pm$  SD/diastolic mean  $\pm$  SD =  $136 \pm 13/85 \pm 13$  *vs.*  $130 \pm 14/77 \pm 14$  *vs.*  $136 \pm 19/80 \pm 9$  mmHg), average precerebellar retraction BP ( $117 \pm 9/73 \pm 14$  *vs.*  $104 \pm 11/60 \pm 7$  *vs.*  $123 \pm 15/70 \pm 7$  mmHg), or duration of the retractor placement period ( $7.1 \pm 2.8$  *vs.*  $6.8 \pm 3.1$  *vs.*  $8.3 \pm 2.5$  min). Preretraction systolic BP represented 14%, 20%, and 10% reductions from average ward systolic BP for the halothane, isoflurane, and sufentanil groups, respec-

tively. The MAC values (including nitrous oxide) for the halothane and isoflurane groups were not significantly different ( $1.65 \pm 0.27$  *vs.*  $1.56 \pm 0.17$ ).

In every patient BP increased during cerebellar retraction. The increases in systolic (fig. 1), diastolic ( $10 \pm 5$  *vs.*  $26 \pm 13$  *vs.*  $13 \pm 10$  mmHg for halothane, isoflurane, and sufentanil, respectively), and mean BP (fig. 2) were less in the halothane group than the isoflurane group (*P* < 0.05). BP increases in the sufentanil group were intermediate and not statistically different from either the halothane or the isoflurane groups. BP in two patients in the sufentanil group could not be controlled at any level below the average ward BP during the preretraction period despite receiving 6 and 12  $\mu\text{g}/\text{kg}$  sufentanil, respectively. Thus, these two patients did not meet protocol requirements and were excluded from this analysis. Four of the remaining seven patients in the sufentanil group required naloxone to restore spontaneous ventilation at the end of the surgery. In one patient receiving sufentanil, the heart rate decreased from 75 to 35 beats/min during the retraction period. All other heart rate changes were within 10 beats/min of the preretraction value.

### Discussion

This study documents a consistent BP increase in response to placement of a cerebellar retractor and dem-

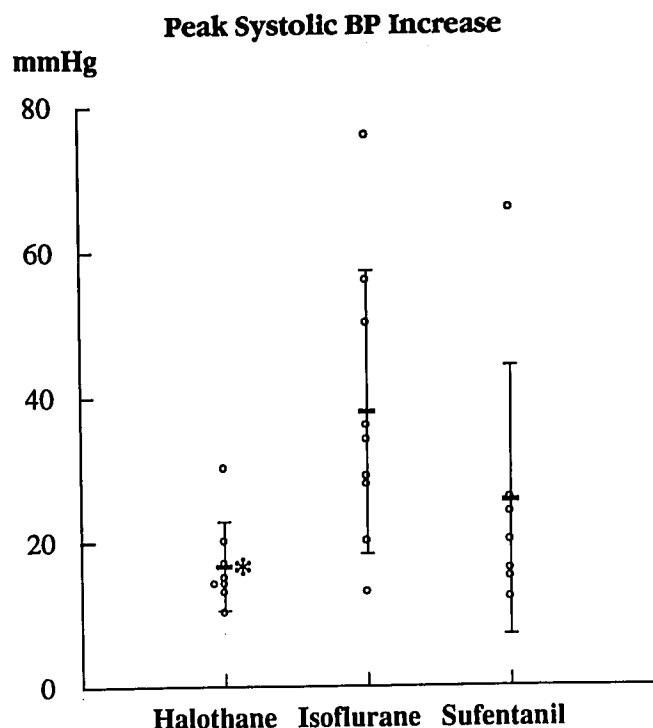


FIG. 1. The maximum change in systolic BP with cerebellar retraction from preretraction values for the three anesthetic groups. Each circle represents one patient's response. Bars are mean  $\pm$  SD. \*Halothane is different from isoflurane by ANOVA (*P* < 0.05).

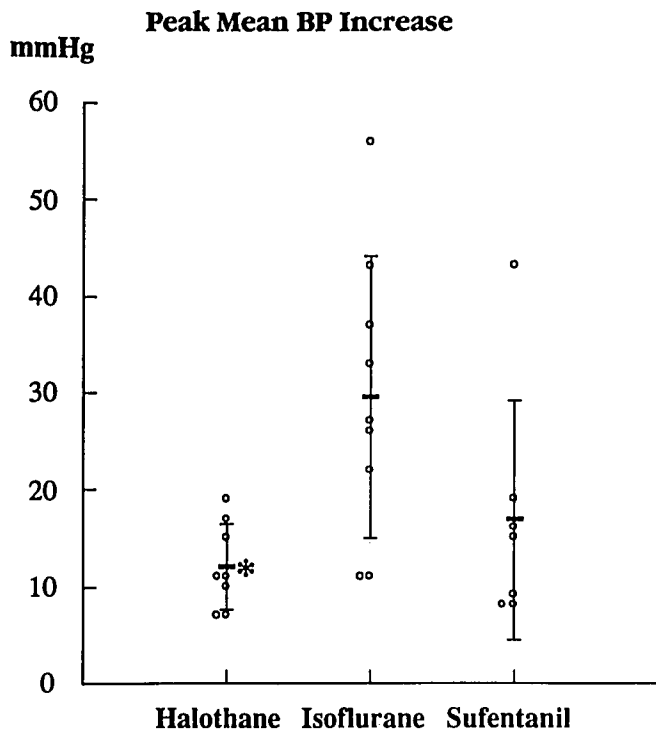


FIG. 2. The change in mean arterial BP with cerebellar retraction from preretractor values for the three anesthetic groups. Each circle represents one patient's response. Bars are mean  $\pm$  SD. \*Halothane is different from isoflurane by ANOVA ( $P < 0.05$ ).

onstrates that the magnitude of this hypertensive response is dependent on the anesthetic drugs administered. Our results suggest that halothane is more effective than isoflurane (at equipotent concentrations) in attenuating the hypertensive response.

The mechanism for the hypertensive response to cerebellar retraction is unknown. The retractor may simply be painful. Another possibility is that the cerebellar retraction causes brain stem or cerebellar ischemia with an attendant increase in BP as an adaptive response to maintain adequate brain perfusion. In addition, it is possible that retraction causes direct stimulation of the vasomotor center and results in peripheral vasoconstriction. Wang and Ranson<sup>7</sup> and Wang<sup>8</sup> demonstrated a hypertensive response to direct stimulation of the pressor area near the floor of the fourth ventricle (an area in close proximity to the origin of the fifth cranial nerve). A reflex sympathetic effect on the heart causing only increased inotropy is doubtful because heart rate in general did not vary during cerebellar retraction and would be expected to increase if this were the mechanism.

An important observation in this study is the variable ability of anesthetic regimens to attenuate the hypertensive response to cerebellar retraction. If the hypertensive response to cerebellar retraction is due to ischemia, an explanation for the variable anesthetic effect may be found

in greater augmentation of cerebellar blood flow and hence blood volume with isoflurane than halothane at 1.6 total MAC equivalents (including nitrous oxide). Variable degrees of vasodilation between halothane and isoflurane have been demonstrated in different cortical and subcortical structures in animal models.<sup>9-12</sup> For example, Hansen *et al.* demonstrated in rats greater augmentation of neocortical blood flow with halothane compared with equipotent isoflurane despite whole-brain blood flows being similar.<sup>10</sup> One may infer that this reflected relatively greater blood flows in the subcortical regions with isoflurane. Manohar and Parks demonstrated in pigs proportionately greater increases in blood flow to the cerebellum and brain stem compared with the cerebrum during 1.0 MAC isoflurane and 50% nitrous oxide (conditions similar to those in this study).<sup>11</sup> These investigators did not compare isoflurane to halothane. However, Boarini *et al.* found in dogs that isoflurane caused significantly greater increases in posterior fossa blood flows (including the cerebellum) than equipotent concentrations of halothane.<sup>12</sup> Several cautions about extrapolation of these data to the current study are warranted, including species differences and the fact that blood flows [not blood volumes] were measured. Nevertheless, if isoflurane resulted in greater cerebellar blood volumes than halothane in our patients, then isoflurane might have resulted in increased cerebellar retractor pressure, more ischemia, and a magnified hypertensive response.

Another possible mechanism for the variable anesthetic effect is greater suppression by halothane than isoflurane of direct or reflex sympathetic nervous system pathways that regulate increases in vascular tone. Other workers have demonstrated differences between halothane and isoflurane in effects on cardiovascular control centers in the brain stem. For example, Seagard *et al.* have found that at 1 MAC halothane depresses baroreceptor reflex changes in heart rate more than isoflurane.<sup>13,14</sup>

The protocol for this study was designed to replicate our standard anesthetic techniques for microvascular decompression of the fifth cranial nerve. This is why the background anesthetic was titrated to obtain systolic BP 10–20% below the average of all ward systolic BP recorded. Fortunately, the resultant MAC values of halothane and isoflurane were not significantly different. If we had administered halothane and isoflurane to achieve a specific dosage rather than titrating the anesthetic to a clinical effect, conclusions about the BP response during equipotent halothane or isoflurane anesthesia might have been stronger. Also, the study design limited our ability to generate dose–response data and extend the testing of the anesthetic effects. Another potential limitation of this study is that the tension of retraction applied to the cerebellum was not measured. Tension may have varied among patients and affected the BP response to retraction.

However, participation of only one surgeon (blinded to anesthetic technique) and randomization of patients to different anesthetic groups would tend to offset any systematic bias.

The most important feature of this study is that it identified differences in the ability of halothane and isoflurane to attenuate the BP response to a given stimulus (cerebellar retraction) during posterior fossa surgery. Whether the findings in this study can be generalized to other surgical manipulations in the posterior fossa is unknown. If they are, the implications may be important for clinical decision making. For example, in instances in which hemodynamic change to brain stem manipulation is used as an indication of impingement on vital structures (*e.g.*, tumor resection in floor of fourth ventricle), isoflurane may be preferable to halothane. In situations in which intracranial compliance is not a concern, the anatomy is not grossly distorted, and the surgical objective does not involve resection of critical tissue, then hemodynamic stability may become relatively more important to the anesthetist. In this instance, halothane would appear to be a better choice of anesthetic than isoflurane.

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