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Intraocular Pressures in Children during Isoflurane and Halothane Anesthesia

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The effects of isoflurane and halothane on intraocular pressure (IOP) were studied in 28 children. Measurements were made during spontaneous ventilation and at various levels of reduced Pa_{CO_2} achieved by controlled ventilation. Control IOP values were determined prior to anesthesia following premedication with chloral hydrate, pentobarbital, or pentobarbital with meperidine. At roughly equivalent levels of anesthesia, mean IOP values during spontaneous ventilation ranged from 16.3 to 17.6 torr for each anesthetic. These values were significantly less ($P < 0.01$) than control values only in those patients receiving chloral hydrate who did not cooperate. In contrast, no significant change in IOP was found in more sedated and cooperative patients who received pentobarbital and meperidine. Moderate hypocarbia and hypercarbia over a range of $Pa_{CO_2} > 42$ torr had little influence on IOP. We conclude that IOP's during isoflurane and halothane anesthesia do not differ significantly from IOP in the sedated, cooperative, healthy pediatric patient. (Key words: eyes: intraocular pressure; Anesthetics, volatile, halothane; Anesthetics, volatile, isoflurane.)

INTRAOCULAR PRESSURE (IOP) in children often is measured during anesthesia because it is difficult to obtain adequate cooperation from the awake patient. Evaluation of the impact of anesthetic drugs on IOP is imperative for the accurate diagnosis and treatment of congenital glaucoma. This knowledge also is essential in avoiding untoward alterations in IOP during intraocular surgery, which may lead to grave ocular complications.

It is widely believed that IOP is reduced by halothane and other inhalation anesthetic agents.[1-3] Isoflurane (Forane¶), a new halogenated volatile ether, shows promise in pediatric patients.** Since the effects of isoflurane on IOP have not been reported, we measured IOP during isoflurane anesthesia in a group of children. For comparison, similar studies were performed at roughly equivalent levels of halothane anesthesia. With each anesthetic, measurements of IOP were made during spontaneous ventilation and at several levels of controlled hyperventilation to evaluate the influence of arterial partial pressure of carbon dioxide (Pa_{CO_2}) on IOP.

Methods

Studies were performed on 28 children, ranging in age from 1 to 17 years (mean 6.9 years). Fifteen patients were given isoflurane and 13 patients, halothane, on a random basis (table 1). Only patients scheduled for elective operations on the extraocular muscles and without a history of glaucoma were studied. Two children who previously had received corrective surgery for strabismus were included, and one child was anesthetized on two separate occasions, once with each anesthetic. Informed consent was obtained from the patient's parent or guardian. The experimental protocol received the ap-

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proval of the University's Committee for the Protection of Human Subjects.

In order to simulate the usual conditions of pediatric IOP measurement used in the eye clinic, and to facilitate patient cooperation during awake measurements, all patients preoperatively received one of three sedative drug schedules: chloral hydrate, 25 mg/kg per rectal suppository; pentobarbital, 2.2 to 4.4 mg/kg intramuscularly, alone, or with the addition of meperidine, 1.1 mg/kg. Each patient also received atropine, .02 mg/kg, intramuscularly. In three poorly sedated patients, additional doses of pentobarbital were given intravenously (50 to 75 mg total additional dosage) until sedation and cooperation adequate for control values were obtained.

Studies were conducted in a quiet room adjacent to the operating theater. Following corneal application of 0.5 per cent proparacaine hydrochloride ophthalmic solution, IOP was measured in both eyes with the MacKay-Marg electronic applanation tonometer.[4] Prior to induction of anesthesia, a Godart capnograph was used to measure end-tidal carbon dioxide concentration. Anesthesia then was induced with either isoflurane, 3 to 4 per cent, or halothane, 1.5 to 3 per cent, in combination with nitrous oxide and oxygen in a proportion of 1:1. A semi-closed circle system with a CO_2 absorber was employed for patients weighing more than 15 kg. A Mapleson D, a modification of Ayre's t-piece, was used for patients weighing less than 15 kg. Care was taken to avoid any increase in end-expired positive pressure. Lead II of the electrocardiograph was monitored and arterial blood pressure was measured by the auscultatory method.

Following induction of anesthesia, the trachea was intubated without the use of muscle relaxants and care was taken to avoid patient straining or coughing. Inflow concentrations of insoflurane and halothane were maintained at 1.5 and 1.0 per cent, respectively. We had previously determined that this technique produced roughly equivalent levels (MAC) of anesthesia. Patients then breathed spontaneously while intravenous and intra-arterial catheters were placed percutaneously. Esophageal temperatures were measured with a thermistor probe and maintained between 35 and 37 C. After an interval of 12 to 15 minutes to permit equilibration of the eyes with the Pa_{CO_2} and arterial partial pressure of anesthetic, IOP was remeasured in each eye and, simultaneously, an arterial blood sample obtained. The blood was analyzed for Pa_{O_2}, Pa_{CO_2}, and pH_a using an Instrumentation Laboratory 1300 blood–gas analyzer. All values were corrected to the patient's body temperature. Anesthetic concentrations in arterial blood were determined by gas chromatography. Calculations of arterial (alveolar) anesthetic partial pressures (concentrations) were made using the method described by Fink and Morikawa.[5]

Following these measurements during spontaneous ventilation, IOP determinations were repeated at one or two lower levels of Pa_{CO_2}. Controlled ventilation then was utilized to maintain constant end-tidal CO_2 for an interval of at least 6 minutes, after which an arterial blood sample was obtained to confirm the Pa_{CO_2} and IOP was again measured. In this manner, studies were made in all patients at Pa_{CO_2}'s roughly equivalent to awake control values. In approximately half the patients, measurements of IOP also were performed at Pa_{CO_2}'s approximately 15 torr lower than control values.

The effects of several other factors on IOP were evaluated in a few patients. In one child, aged 10 years, IOP was measured before and after intravenous administration of 1 mg/kg pentobarbital. In three patients determinations of IOP were repeated 15 minutes after nitrous oxide was discontinued without altering Pa_{CO_2} or halothane (two patients) or isoflurane. In one isoflurane and one halothane patient, IOP measurements were repeated following administration of 0.5 mg/kg *d*-tubocurarine. This dose of muscle relaxant abolished the ulnar nerve response to the Wellcome peripheral nerve stimulator in both patients. Statistical analysis of data was performed using Student's t test.

Results

Induction of isoflurane or halothane anesthesia was rapidly accomplished in all patients without crying or straining. The usual clinical signs of depth of anesthesia, such as systolic blood pressure, heart rate, and respiratory rate, were similar with the two

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TABLE 1. Distribution and Vital Statistics of Patients Studied*

	Number of Patients	Premedication†	Patients' Ages (Years)	Patients' Weights (kg)
Isoflurane	8	Choral hydrate	7.6 ± 4.0 (2–12)	27.2 ± 11.9 (14–46)
	3	Pentobarbital	7.0 ± 3.1 (4–12)	21.2 ± 6.4 (14–30)
	4	Pentobarbital and meperidine		
Halothane	7	Chloral hydrate	9.1 ± 5.6 (3–16)	33.1 ± 23.4 (16–71)
	2	Pentobarbital	3.2 ± 1.5 (1–5)	17.0 ± 9.4 (11–34)
	4	Pentobarbital and meperidine		

* Values represent means ± SD (and ranges).
† See text for dosage.

anesthetics. There was no hypotension or cardiac arrhythmia.

IOP was measured in both eyes during control and anesthetized states. For most patients values obtained for the two eyes were equal. However, in some patients differences between eyes ranged from 1 to 4 torr. The effects of isoflurane and halothane on IOP in 15 children premedicated with chloral hydrate are shown in table 2. A significant decrease in IOP was seen with each agent following induction of anesthesia. However, decreases in IOP were accompanied by increases in Pa_{CO_2} of 9.3 torr in the isoflurane group and 13.5 torr in the halothane group. When Pa_{CO_2} was returned to the initial value or below with controlled ventilation, no further decrease in IOP occurred.

The effects of anesthesia on IOP in 13 children premedicated with either pentobarbital alone or pentobarbital in combination with meperidine are shown in table 3. Control values of IOP prior to halothane were 6 torr lower ($P < 0.01$) than those obtained in children premedicated with chloral hydrate. We believe the increased sedation, relaxation, and cooperation following administration of pentobarbital and meperidine were responsible for the lower IOP values in the preanesthetic state. This greater sedation was accompanied by higher Pa_{CO_2}'s in both groups during awake measurements. Following induction of anesthesia no significant change in IOP occurred even though Pa_{CO_2} values showed mean increases of 16.2 torr in the isoflurane group and of 19.4 torr in the halothane group. Respiratory depression was the same in patients who received pentobarbital alone and in those who received pentobarbital in combination with meperidine. IOP remained constant when Pa_{CO_2} was returned to the control value by controlled ventilation. With halothane, a further reduction in Pa_{CO_2} following hyperventilation produced a decrease in IOP of 2 torr. This was not significantly different from the mean awake value. In all 28 patients calculated alveolar concentrations of isoflurane ranged from 0.75 to 1.52 vol per cent, and those of halothane, from .54 to .90 vol per cent. No correlation between anesthetic depth and IOP was observed. Because of the wide range in the patients' ages, we did not quantitate relative anesthetic depth in each patient. However, mean group values for isoflurane and halothane potencies were roughly equivalent. (See Discussion.)

The effects of wider ranges of Pa_{CO_2} on IOP in 22 children anesthetized with isoflurane or halothane are shown in Table 4. These data were obtained by calculating the change in IOP over a given change in Pa_{CO_2} for individual patients. Only patients who had changes in Pa_{CO_2} greater than 6 torr were included. Six patients from the halothane

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TABLE 2. Effects of Isoflurane and Halothane on IOP in 15 Children Premedicated with Chloral Hydrate (25 mg/kg Rectal Suppository)*

	IOP (torr)	P_{aco_2} (torr)	Alveolar Concentration† (Per Cent)
Isoflurane			
Control	19.9 ± 3.2 (16)	33.1 ± 1.6‡ (8)	Awake
Spontaneous ventilation	17.6 ± 2.0§ (16)	42.4 ± 4.7§ (8)	1.20 ± 0.29 (8)
Controlled ventilation	17.4 ± 3.1§ (16)	33.3 ± 4.2 (8)	1.25 ± 0.27 (8)
Halothane			
Control	21.8 ± 2.8 (14)	32.6 ± 4.4‡ (7)	Awake
Spontaneous ventilation	17.1 ± 3.0§ (14)	46.1 ± 8.2¶ (7)	0.68 ± 0.13 (6)
Controlled ventilation	16.7 ± 4.5§ (6)	27.0 ± 4.4 (3)	0.73 ± 0.17 (3)

* Numbers of determinations in parentheses.
† Calculated from arterial plasma concentration.
‡ Represents PA_{co_2}.
§ $P < .01$ from control value.
¶ $P < .05$ from control value.

TABLE 3. Effects of Isoflurane and Halothane on IOP in 13 Children Premedicated with Pentobarbital Alone (2.2 to 4.4 mg/kg) or in Combination with Meperidine (1.1 mg/kg)*

	IOP (torr)	P_{aco_2} (torr)	Alveolar Concentration† (Per Cent)
Isoflurane			
Control	18.4 ± 2.9 (14)	36.7 ± 4.9‡ (7)	Awake
Spontaneous ventilation	16.6 ± 2.6 (14)	56.1 ± 7.8§ (7)	1.17 ± .20 (7)
Controlled ventilation	16.5 ± 2.4 (14)	35.8 ± 8.9 (7)	1.33 ± .07 (7)
Hyperventilation	16.1 ± 4.9 (12)	21.8 ± 4.2§ (6)	1.35 ± .10 (6)
Halothane			
Control	15.8 ± 4.1 (12)	38.5 ± 3.4‡ (6)	Awake
Spontaneous ventilation	16.3 ± 1.8¶ (12)	54.7 ± 7.4§ (6)	0.71 ± .06 (4)
Controlled ventilation	15.3 ± 2.5¶ (8)	38.3 ± 6.7 (4)	0.82 ± .04 (3)
Hyperventilation	13.4 ± 3.1 (8)	23.8 ± 2.9§ (4)	0.86 ± .06 (3)

* Numbers of determinations in parentheses.
† Calculated from arterial plasma concentration.
‡ Represents PA_{co_2}.
§ $P < .01$ from control value.
¶ $P < .05$ from hyperventilation value.

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group were excluded on this basis. Over a wide range of Pa_{CO_2}'s (>42 torr), the change in IOP was less than 3 torr. The mean ± SD calculated slopes of this response (IOP/Pa_{CO_2}) were 0.05 ± 0.19 for isoflurane and 0.14 ± 0.11 for halothane ($P > .10$).

Elimination of nitrous oxide produced small (2 torr) but consistent decreases in IOP in 3 patients. Administration of pentobarbital to one patient intravenously in the preanesthetic period produced no effect on IOP. Similarly, administration of *d*-tubocurarine to two anesthetized patients had no effect on IOP.

Discussion

When patient sedation and cooperation were lacking, IOP during isoflurane or halothane anesthesia was significantly decreased. However, in cooperative, relaxed pediatric patients no significant reduction in IOP occurred following induction of anesthesia. It should be emphasized that with each anesthetic studied, the magnitude of IOP decrease during anesthesia was small, and IOP's tended to reach a common value (16 to 17 torr). This pressure probably represents a maximal change, as evidenced by failure of a paralyzing dose of *d*-tubocurarine to effect further lowering of IOP's in two patients. This is in agreement with the report of Drucker.[6]

While there are no reported studies of isoflurane for comparison, previous studies during halothane anesthesia have disclosed decreases in IOP ranging from 18 to 33 per cent.[2,3,7] These are several possible explanations for these differences. Control measurements depend on patient relaxation, sedation, and cooperation. Straining, blinking, excitement, or anxiety increases IOP, while heavy sedation decreases IOP. We found that meperidine and/or pentobarbital produced more sedation than chloral hydrate. We believe that the most important factor in evaluating anesthetic effects on IOP is the accuracy of the awake IOP measurement.

Since the children we studied ranged from infants to young adults, we did not attempt to quantitate relative anesthetic depth on an individual basis. Anesthetic requirements (MAC) in adults have been reported for isoflurane[8] and halothane[9] to be 1.16 and 0.76 vol per cent, respectively. Mean calculated alveolar concentrations in our patients were roughly equivalent to these values. However, anesthetic requirements for infants and children have been shown to be considerably (20 per cent) higher than those for adult patients.[9] Our patients received additional anesthesia with nitrous oxide which more than offset this difference. No correlation between depth of anesthesia and IOP was found in either the isoflurane group or the halothane group when alveolar anesthetic concentrations varied almost twofold.

The addition of pentobarbital or the combination of pentobarbital and meperidine resulted in significant similar increases in Pa_{CO_2} to more than 57 torr in seven of 13 patients during isoflurane and halothane anesthesia. Duncalf *et al.*[10] showed that inhalation of CO_2 by dogs anesthetized with halothane increased both IOP and cerebrospinal fluid pressure. Although they could not demonstrate a definitive relationship between IOP and cerebrospinal fluid pressure, a slight decrease in IOP occurred during hyperventilation. It is interesting that the slope of CO_2 response in their animals is similar to our findings. Our observations of CO_2 effects during isoflurane and halothane anesthesia are in agreement with results reported by Schettini *et al.*[11] and indicate that the effects of moderate hypo- and hypercarbia, as usually encountered in clinical practice, have little influence on IOP.

TABLE 4. Effects of Pa_{CO_2} on IOP in 22 Children during Isoflurane and Halothane Anesthesia*

	Number of Patients	ΔPa_{CO_2}† (torr)	ΔIOP (torr)	$\frac{\Delta IOP}{\Delta Pa_{CO_2}}$
Isoflurane	15	18.0 (19–67)	0.1 (−6 to +6)	0.05 ± 0.19
Halothane	7	22.4 (20–62)	3.0 (−6 to 0)	0.14 ± 0.11

* Values represent means ± SD (or ranges).
† All values showed changes in $Pa_{CO_2} > 6$ torr.

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