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Effect of Anesthetic Induction Regimens on Oxygen Saturation in Cyanotic Congenital Heart Disease

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The optimal induction regimen for general anesthesia in infants and children with cyanotic congenital heart disease (CCHD) should maintain or improve arterial blood oxygen saturation (Sa_{O_2}) and maintain cardiovascular stability. Both intravenous and inhalational drug regimens have been recommended for induction of general anesthesia in children with CCHD to minimize changes in oxygenation and hemodynamic variables.[1–3] However, the effects of these induction regimes on Sa_{O_2} in children with CCHD have not been compared.

Pulse oximetry is a new, noninvasive technique for measuring Sa_{O_2}. Oxygen saturation as determined by pulse oximetry correlates closely with direct Sa_{O_2} measurements.[4] Because oxygen saturation in infants and children with CCHD lies on the steep portion of the oxyhemoglobin dissociation curve,[5] pulse oximetry is a useful and sensitive noninvasive technique for estimating oxygen saturation in children with CCHD.

The purpose of this study was to investigate the effect of five anesthetic induction regimens on Sa_{O_2} during induction of anesthesia in infants and children with CCHD.

METHODS

With approval from the Committee on Human Research, 50 infants and children with CCHD presenting for elective cardiac surgery were studied. All patients were ASA Physical Status II or III, fasting and premedicated. Infants (less than 1 yr of age) were premedicated with intramuscular atropine 0.02 $mg \cdot kg^{-1}$ 1 h prior to surgery, whereas children (greater than 1 yr of age) were premedicated with pentobarbital 2 $mg \cdot kg^{-1}$ per rectum 2 h prior to surgery, and atropine 0.02 mg/kg with morphine 0.2 $mg \cdot kg^{-1}$ intramuscularly 1 h prior to surgery.

Each child was arbitrarily assigned to receive one of five induction regimens according to the discretion of the attending anesthetists: thiopental; fentanyl; ketamine; thiopental and fentanyl; or halothane. Any child considered to be unsuitable for any one of the induction regimens was excluded from the entire study. Each of the anesthetists who participated in the study administered each of the induction regimes at least once.

On arrival in the operating room, the patients were placed supine and monitored with a precordial stethoscope, blood pressure cuff, Doppler pulse detector, and electrocardiogram. A pulse oximeter probe (model N-100, Nellcor Inc., Hayward, CA) was applied to the first toe on each patient. After preoxygenation for 2 min, the patients were anesthetized with one of the above induction regimens. All induction regimens were administered intravenously except for halothane. Each intravenous agent was administered as an initial sleep dose with further increments prior to laryngoscopy. Halothane was administered with increasing inspired concentrations to a maximum of 2% (vaporizer setting). Pancuronium 0.15 $mg \cdot kg^{-1}$ was administered intravenously to facilitate endotracheal intubation in all patients. Ventilation was controlled manually. After intubation, the end-tidal P_{CO_2} was measured continuously from the distal end of the endotracheal tube (Puritan-Bennett® CO_2 analyzer). Ventilation was adjusted to maintain an end-tidal P_{CO_2} between 30 and 35 mmHg. Positive end-expiratory pressure was avoided.

During the period of study, Sa_{O_2}, heart rate, and systolic blood pressure were measured simultaneously at five intervals: 1) air (before induction of anesthesia while breathing room air); 2) preinduction (following 2 min of preoxygenation); 3) postinduction (1, 3, and 5 min after completion of induction of anesthesia); 4) laryngoscopy; and 5) postintubation at 30 s, 1, and 2 min.

The "air" measurements were recorded while the patients were breathing room air. All subsequent measure-

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TABLE 1. Demographic Data

	Thiopental	Fentanyl	Ketamine	Thiopental Fentanyl	Halothane
Age (yr)	3.1 ± 0.8	2.5 ± 0.6	4.0 ± 1.6	3.1 ± 0.6	2.2 ± 0.7
Weight (kg)	11.8 ± 1.6	11.1 ± 1.6	13.5 ± 2.7	11.6 ± 1.4	9.3 ± 1.2
Number of patients with:					
TOF	5	4	6	6	6
TGA	2	3	2	1	1
Misc	3	3	2	3	3
Number of infants	4	4	3	1	5
Number of patients with previous palliative surgery	6	7	5	4	4

Data are mean ± SE.

TOF = tetralogy of Fallot. TGA = transposition of the great arteries. Misc = miscellaneous lesions (see "Results").

ments were recorded while the patients were breathing 100% oxygen (except, of course, for the halothane group, which breathed 98–99% oxygen).

Statistical significance ($P < 0.05$) was determined using analysis of variance and the Student-Newman-Keuls test for the Sa_{O_2}, heart rate, and systolic blood pressure data, and the Fisher exact test for comparing the number of specific cardiac lesions, the number of palliative shunts, and the number of infants among the five groups.

RESULTS

Fifty patients were divided into five groups of equal size (table 1). There were no significant differences in age and weight among the five groups. Cyanotic cardiac lesions were classified as tetralogy of Fallot (TOF), transposition of great arteries (TGA), and miscellaneous (misc). The miscellaneous group included ventricular septal defect with pulmonary and/or tricuspid valve disease and other complex cyanotic cardiac lesions. There was no significant difference in the number of each of the cyanotic lesions among the five groups. There were no significant differences in either the number of infants or the number of patients with previous palliative surgery among the five groups (table 1). Previous palliative surgery included atrial septostomy and aorto–pulmonary shunts. Thirty patients were receiving chronic cardiovascular drug therapy including digoxin, Aldactazide,® and propranolol prior to surgery. There was no significant differences in the number of the patients taking these drugs among the five groups.

TABLE 2. Total Doses of Induction Agents

	Thiopental	Fentanyl	Ketamine	Thiopental Fentanyl	Halothane
Dose	5.7 ± 0.5	42.1 ± 8.0	2.1 ± 0.4	3.7 ± 0.5	0.5–2.0
Unit	$mg \cdot kg^{-1}$	$\mu g \cdot kg^{-1}$	$mg \cdot kg^{-1}$	$mg \cdot kg^{-1}$	%*
Dose				6.2 ± 1.1	
Unit				$\mu g \cdot kg^{-1}$	

Data are mean ± SE.
* Inspired concentration, vaporizer setting.

The total dose of each intravenous agent administered includes the initial sleep dose plus any further incremental doses administered prior to laryngoscopy (table 2). In the group anesthetized with halothane, the inspired concentration (vaporizer setting) was increased in 0.5% increments to 2% during induction of anesthesia. Thereafter, it was decreased to 1.0% for the remainder of the study.

The awake values for Sa_{O_2} did not differ significantly among the five groups of patients (fig 1). The standard errors of the means were similar for each mean value shown in figure 1. Standard error bars for halothane and fentanyl only were included for clarity. Sa_{O_2} increased significantly following the preinduction (preoxygenation) measurement and at all measurements after induction of anesthesia when compared with the awake measurements breathing room air (fig 1). Sa_{O_2} measurements did not differ significantly among the five groups at any time.

Heart rate increased significantly ($P < 0.05$) in the ketamine and halothane groups (table 3). In the ketamine group, heart rate increased significantly at 1 min postinduction and at all subsequent measurements when compared with the air and preinduction measurements. In the halothane group, heart rate increased significantly at laryngoscopy and at all subsequent measurements when compared with the measurements at 1, 3, and 5 min postinduction. Heart rate did not differ significantly among the five groups at any time.

Systolic blood pressure remained unchanged compared with baseline measurements, with two exceptions (table 4). In the thiopental group, systolic blood pressure increased significantly after laryngoscopy when compared with the 5-min postinduction measurement. In the halothane group, systolic blood pressure decreased signifi-

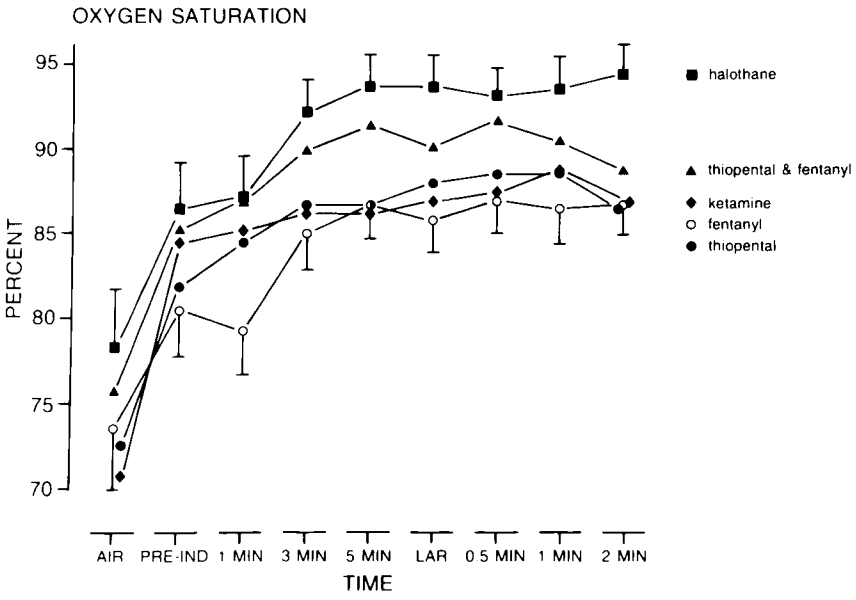

FIG. 1. Oxygen saturations during the period of study for the five groups. Data are mean ± SEM. Time axis: Air = awake control measurements; Pre-Ind = preinduction following preoxygenation; 1 min, 3 min, 5 min = intervals postinduction. LAR = laryngoscopy; 0.5 min, 1 min, 2 min = intervals postintubation.

cantly 5 min postinduction when compared with the awake measurement.

DISCUSSION

The optimal induction regimen for patients with CCHD should maintain or improve Sa_{O_2} and maintain cardiovascular stability. Although ketamine is recommended for induction of anesthesia in patients with CCHD,[1] all five induction regimens in this study were equally effective in maintaining or improving Sa_{O_2}, heart rate, and systolic blood pressure. Ketamine is recommended for induction of anesthesia in patients with CCHD because of its cardiovascular stability.[1] Previous studies reported that ketamine did not alter heart rate, blood pressure, or intracardiac shunt in children with CCHD either prior to surgical repair[6] (breathing spontaneously) or after surgical repair (ventilated).[7] In the present study, ketamine maintained heart rate and systolic blood pressure.

Fentanyl is effective for induction of anesthesia in children with CCHD because systolic blood pressure and cardiac output remain unchanged. Theoretically, fentanyl will also decrease oxygen consumption.[8] Hickey *et al.*[9] reported no significant changes in either pulmonary or systemic hemodynamics in ventilated infants after cardiac surgical repair during fentanyl anesthesia. In a further study, Hickey and Hansen[10] found a significant increase in transcutaneous oxygen tension following induction of anesthesia with fentanyl in children with CCHD. The results of our study are in agreement with their findings and indicate that induction of anesthesia with fentanyl and 100% oxygen is associated with an increase in Sa_{O_2} in patients with CCHD.

TABLE 3. Heart Rate during Induction of Anesthesia

	Thiopental	Fentanyl	Ketamine	Thiopental Fentanyl	Halothane
Air	144 ± 9	149 ± 9	145 ± 11	139 ± 10	132 ± 4
Preinduction	148 ± 10	143 ± 7	146 ± 12	129 ± 9	131 ± 8
Postinduction					
1 min	148 ± 11	144 ± 10	157 ± 10*	137 ± 8	125 ± 6
3 min	145 ± 10	143 ± 8	159 ± 11*	130 ± 9	124 ± 6
5 min	144 ± 9	140 ± 8	159 ± 10*	133 ± 8	126 ± 5
Laryngoscopy	149 ± 8	146 ± 9	159 ± 10*	134 ± 7	146 ± 5†
Postintubation					
30 s	152 ± 8	143 ± 9	161 ± 10*	142 ± 8	147 ± 5†
1 min	148 ± 8	146 ± 9	163 ± 11*	136 ± 7	145 ± 5†
2 min	147 ± 8	142 ± 10	164 ± 11*	136 ± 9	144 ± 6†

Data are mean (beat/min) ± SE.
* $P < 0.05$ compared with air and preinduction.
† $P < 0.05$ compared with 1, 3, and 5 min postinduction.

TABLE 4. Systolic Blood Pressure during Induction of Anesthesia

	Thiopental	Fentanyl	Ketamine	Thiopental Fentanyl	Halothane
Air	102 ± 5	105 ± 5	106 ± 5	94 ± 4	94 ± 5
Preinduction	102 ± 5	104 ± 6	109 ± 6	94 ± 5	91 ± 5
Postinduction					
1 min	99 ± 4	104 ± 3	113 ± 5	92 ± 5	90 ± 4
3 min	98 ± 4	103 ± 4	111 ± 7	88 ± 4	88 ± 4
5 min	96 ± 3	106 ± 5	110 ± 7	86 ± 3	81 ± 5†
Laryngoscopy	110 ± 6*	107 ± 6	113 ± 6	88 ± 3	86 ± 7
Postintubation					
30 s	108 ± 4	104 ± 6	111 ± 7	88 ± 3	89 ± 8
1 min	106 ± 3	104 ± 6	111 ± 8	90 ± 4	89 ± 8
2 min	104 ± 3	103 ± 6	113 ± 8	89 ± 5	89 ± 7

Data are mean (mmHg) ± SE.
* $P < 0.05$ compared with 5 min postinduction.
† $P < 0.05$ compared with air.

Halothane and thiopental have been used for induction of anesthesia in infants and children with CCHD.[11] Both of these drugs may cause calcium-dependent myocardial depression[12] and peripheral vasodilation.[13–15] These two latter effects may alter the degree of the right-to-left intracardiac shunt or interatrial mixing and thereby decrease Sa_{O_2}. Although halothane was associated with a decrease in systolic blood pressure (5 min postinduction, table 4), there was no corresponding decrease in Sa_{O_2}. Our data for halothane are in agreement with Hensley *et al.*,[16] who reported that Sa_{O_2} increases in children with CCHD after an inhalational induction with halothane, 70% nitrous oxide, and 30% oxygen. The results of our study also indicate that both thiopental alone and thiopental in combination with fentanyl may be used without detrimental effect on Sa_{O_2} in these patients, provided the drugs are administered in incremental doses.

Sa_{O_2} is affected by several factors in patients with CCHD: 1) the inspired fraction of oxygen; 2) the extent of right-to-left shunting or mixing; 3) oxygen consumption; 4) cardiac output; and 5) the mixed venous oxygen tension.[17] If the magnitude of the right-to-left shunt is 35% or less, Sa_{O_2} will increase when the inspired fraction of oxygen is increased.[18] In the present study, Sa_{O_2} increased in all five groups when the inspired fraction of oxygen was increased from 21% to 100% (before the induction of anesthesia). Because all of the children were heavily premedicated and well sedated, both the functional residual capacity,[19–24] and the chemoreceptor sensitivity to oxygen[25] may have decreased during the preinduction period in the unstimulated premedicated child. However, when the child was then stimulated by applying a mask to the face, he or she was suddenly aroused and ventilation may have increased, resulting in an increase in Sa_{O_2}.[26]

Our study dealt with a heterogenous population of patients with CCHD. Forty-one patients (82%) were at risk for right-to-left shunting and arterial oxygen desaturation. Although Sa_{O_2} increased significantly during induction of anesthesia with all five induction regimens, we are not able to conclude that right-to-left shunt does not increase with any of these regimens. It is possible that if the degree of right-to-left shunt had increased during induction of anesthesia, this was offset by a concomitant decrease in oxygen consumption and increase in cardiac output, both of which increase mixed venous oxygen saturation of the shunted blood.[17,27–30] The relative importance of each of these factors on Sa_{O_2} remains unclear. Out results in this heterogenous population of patients however, are in agreement with similar data‡ from a homogenous population (tetralogy of Fallot) of children in which induction of anesthesia with either intramuscular ketamine or halothane by mask resulted in similar increases in Sa_{O_2}.

Sa_{O_2} increased significantly in the nine patients with TGA (18%) anesthetized with the five induction regimens. Because of their anatomy, these patients rely on interatrial mixing of oxygenated and venous blood to provide systemic oxygen delivery. In these patients the degree of right-to-left shunt is balanced by the degree of left-to-right shunt; together, these two factors determine the degree of interatrial mixing. Arterial desaturation will occur with a decrease in the degree of interatrial mixing. However, as discussed previously in relation to right-to-left shunts, we cannot conclude that interatrial mixing *per se* was not reduced during induction of anesthesia in patients with TGA. This, again, is due to our inability to measure all of the factors influencing the Sa_{O_2}. Nevertheless, the net result of the five induction regimens is an increase in Sa_{O_2} in patients with TGA.

In summary, the results of this study indicate that all five induction regimens evaluated may be used safely during induction of anesthesia in infants and children with CCHD.

‡ Greeley WD, Bushman G, Davis DP, Reves J: unpublished data, 1986.

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