Short-acting barbiturate sedation: effect on arterial pH and $PaCO_2$ in children

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One hundred and fifteen unpremedicated children, induced with thiamylal, a short-acting thiobarbiturate, administered rectally (25 mg·kg^{-1} body wt) or intravenously (6 mg·kg^{-1}) had arterial pH of 7.36 ± 0.03 and $PaCO_2$ of 40 ± 4 mmHg. In 22 children over two years of age, the use of fentanyl (1.2 ± 0.7 μg·kg^{-1}) in addition to the thiamylal did not change blood gas data compared to those children over two years receiving only barbiturates (pH 7.36 vs 7.36, $PaCO_2$ 41 vs 40 mmHg). Children with cyanotic congenital heart disease showed similar pH and $PaCO_2$ to acyanotic children following administration of the short-acting barbiturate. Thiobarbiturates, given in a titrated fashion under direct observation, have clinically small effects on arterial pH and $PaCO_2$ in paediatric patients.

Short-acting barbiturates are extensively used as induction agents for general anaesthesia. Rectally administered barbiturates have been used in children to induce anaesthesia, but the ventilatory effects of rectally administered barbiturates in these children have been assessed only by respiratory rate changes or the incidence of apnoea.[1–3] No studies in children have examined the effects of the short-acting barbiturates on arterial pH and $PaCO_2$. We frequently use rectal or intravenous thiobarbiturate induction of anaesthesia prior to placement of percutaneous intravenous and arterial catheters, and here report arterial blood gases when thiamylal has been administered to paediatric patients to show the effects on ventilation of a thiobarbiturate administered rectally or intravenously. Use of rectal thiamylal (25–30 mg·kg^{-1}), augmented by intermittent intravenous doses, allowed placement of intravenous and arterial catheters in a monitored induction area prior to intubation and surgery in the operating room.

Thiamylal is a thiobarbiturate which has a rapid onset and short duration of action equivalent to thiopentone.[4–6] This thiobarbiturate is available at lower cost at our institution than thiopentone or methohexitone. This paper reports our experience with thiamylal given intravenously and/or rectally in a large group of paediatric patients presenting for major surgical procedures. Patient care was not altered for study purposes. Data were collected prospectively from our standard monitoring procedures.

Key words
CARBON DIOXIDE: blood levels, drug effects; ANAESTHESIA: pediatric; ANAESTHETICS, INTRAVENOUS: thiamylal, thiobarbiturate.

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Methods

Our usual clinical practice involves induction with thiamylal and placement of percutaneous intravenous and arterial catheters followed by determination of a baseline arterial blood gas. Data for this report were collected in unpremedicated children (ASA physical status Class I–III) induced with thiamylal who had arterial catheters placed for monitoring during anaesthesia for non-emergency surgery, as described below. In an induction area with full resuscitative equipment an aqueous solution of ten per cent thiamylal (25 to 30 mg·kg^{-1}) was administered rectally to those children aged seven months to six years. Children with cyanotic heart disease received the same dose as acyanotic patients. Rectal thiamylal was not given to children < 6 months of age, to those who were emergency cases with "full stomachs," to those with gastroesophageal reflux, to those with difficult or limited airway accessibility or to those with suspected or known hypovolaemia. An intravenous catheter was placed with local anesthesia after the onset of sleep (failure to respond to voice or light touch) in the children who received rectal thiamylal; infants < 6 months and children > 7 years had intravenous catheters placed with local anaesthesia while awake. Children breathed room air or 5 L·min^{-1} O_2, at the discretion of the staff anaesthetist. Supplements of intravenous thiamylal (1–3 mg·kg^{-1}) and fentanyl (1 μg·kg^{-1}) were given as decided by the staff anaesthesiologist to

maintain anaesthesia during percutaneous placement of an arterial catheter with local anaesthesia.

Once the arterial catheter was securely taped, we drew blood anaerobically to analyze pH, $PaCO_2$, PaO_2.* This baseline sample, prior to intubation and surgery, was drawn two to five minutes following arterial catheterization when the child was undisturbed and sleeping. Apnoea, hiccoughs, coughing, laryngospasm or other problems following thiamylal use were recorded. The data were analyzed in four groups determined by our limitations for rectal thiamylal administration as reported above: Group 1 received only rectal thiamylal; Group 2 received rectal thiamylal induction and supplemental intravenous thiamylal; Group 3 only received thiamylal intravenously; Group 4 received thiamylal and supplemental intravenous fentanyl. Group 3 included infants aged three days to 11 months (n = 14) and older children (>1 yr) who did not receive fentanyl (n = 17). The data have been reported separately for the infants (less than 1 yr) and the older children in Group 3. All children who received supplemental intravenous fentanyl were >2 years of age.

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TABLE I Type of surgery

Surgery	*No. patients*
Congenital heart defects – cyanotic	18
Congenital heart defects – acyanotic	40
Orthopaedic	26
Major abdominal or thoracic	21
Craniofacial reconstruction	7
Craniotomy	3

Preoperative arterial blood gas values are not routinely obtained at CHMC in paediatric patients without pulmonary symptomatology. Seventy per cent of our patients were too young to cooperate with arterial cannulation while awake and all were concerned about being "hurt." We felt these considerations precluded arterial cannulation while these patients were awake and we were thus unable to directly compare pre- and post-sedation blood gases.

Blood gas data were compared to published normal values of pH and $PaCO_2$ for awake infants, children and adults.[7–10] Mean values (±SD) for all patients and for the subgroups were compared to these published normals by Student's two-tailed t-test. Values of $p < 0.05$ were considered significant.

Results

Information from one hundred and fifteen children was collected; the age range of patients was three days to 20 years (mean 5.2 yrs ± 5.1). No premature infants were studied. The type of surgery is listed in Table I. The doses of thiamylal and fentanyl, method of administration and arterial pH, $PaCO_2$ and PaO_2 are summarized in Table II. Published normal values are tabulated in the lower section of this table. Since FiO_2 was not uniform for the entire group, statistical analysis of PaO_2 data was not done. The mean values for all patients showed a small increase in $PaCO_2$ and decrease in pH compared to the published normals. Statistical analysis showed pH significantly decreased from published normal values for infants,[7,8] children,[9] and adults[10] ($p < 0.01$). $PaCO_2$ was increased from published normal values for awake infants and children ($p < 0.01$) but not different from adult normal values ($p > 0.05$).

The reference values for infants[7] aged 3 to 24 months

TABLE II Total drug doses (mean ± SD)

Thiamylal route administered	*n*	*Age yr*	*Thiamylal mg·kg⁻¹*		*Fentanyl μg·kg⁻¹*	*Arterial blood gases*		
			Rectal	*IV*	*IV*	*pH*	*$PaCO_2$ mmHg*	*PaO_2 mmHg*
Rectal only	13	2.9 ± 2.5	27 ± 5	—	—	7.35 ± 0.03*	41 ± 3*	86 ± 23
Rectal and IV	49	3.1 ± 2.2	30 ± 4	6 ± 4	—	7.36 ± 0.03*	39 ± 4*	95 ± 46
IV only								
infant	14	0.4 ± 0.4	—	11.9 ± 4.1	—	7.38 ± 0.03*	41 ± 4*	110 ± 64
child	17	10.2 ± 4.7	—	5.2 ± 2.8	—	7.39 ± 0.02	39 ± 4*	90 ± 15
IV and IV fentanyl	22	10.3 ± 5.5	—	6.7 ± 4.6	1.2 ± 0.7	7.36 ± 0.04*	41 ± 4*	109 ± 38
TOTAL	115	5.2 ± 5.1	17 ± 15	6.0 ± 4.7	—	7.36 ± 0.03*	40 ± 4*	97 ± 43
Published normal values:								
Infants[7,8]						7.40 ± 0.03	34 ± 4	
Children[9]						7.39 ± 0.01	37 ± 2	
Adults[10]						7.40 ± 0.01	39 ± 2	

*$p < 0.01$ compared to published normal values tabulated above for infants and children.

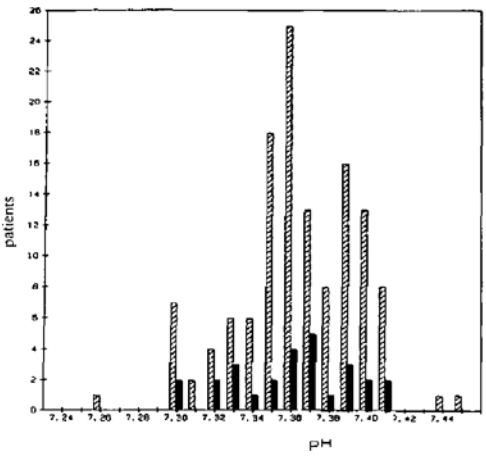

FIGURE 1 pH distribution following thiamylal induction. ▨ = all patients. ■ = cyanotic patients.

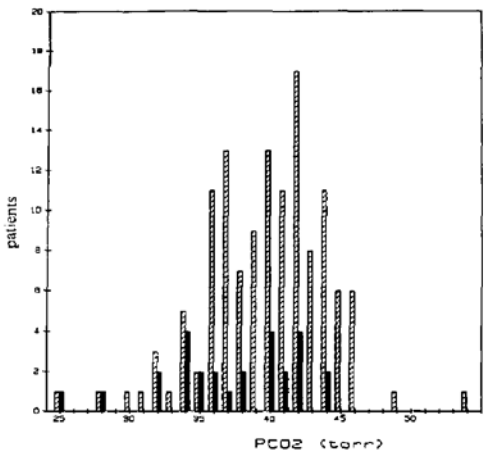

FIGURE 2 $PaCO_2$ distribution following thiamylal induction. ▨ = all patients. ■ = cyanotic patients.

used arterialized capillary samples for pH and $PaCO_2$ and showed no difference between crying and quiet infants. Healthy full-term newborns show arterial values of pH 7.37 and $PaCO_2$ 36 mmHg by seven days of age.[8] The normal reference for children[9] reports results for arterial samples from 42 healthy subjects aged 7 to 19 years. Figures 1 and 2 show the distribution of pH and $PaCO_2$ values in our patients.

Most children received supplemental intravenous thiamylal after rectal thiamylal induction (Group 2), but arterial pH and $PaCO_2$ were not different than in those children receiving only rectal thiamylal (Group 1). The 22 patients (Group 4) who received intravenous thiamylal and fentanyl (1–2 $\mu g \cdot kg^{-1}$) had blood gas results which were not different from children who received only thiamylal; five of these patients had rectal thiamylal induction followed by supplemental intravenous thiamylal and fentanyl.

Comparison of $PaCO_2$ data for children breathing room air (mean 40 ± 4 mmHg, range 30–54 mmHg) or 5 $L \cdot min^{-1}$ supplemental O_2 (mean 39 ± 4 mmHg, range 28–45 mmHg) showed no statistical difference ($p > 0.1$). $PaCO_2$ was the same in children whether or not supplemental oxygen was used. PaO_2 levels under 65 mmHg were seen only in children with cyanotic heart disease. Eighteen children with cyanotic heart disease (mean age 2.5 ± 3.3 yrs) showed a mean pH of 7.36 ± 0.03 and $PaCO_2$ of 38 ± 4 mmHg following rectal and IV thiamylal, values similar to our acyanotic children after thiamylal. These 18 children all received supplemental O_2 following induction.

Three patients expelled the rectal medication, two had hiccoughs, and five coughed after induction. Neither apnoea nor marked bradypnea was seen in our patients, but two patients did show respiratory depression; a three-year-old with pH 7.26, $PaCO_2$ 54 mmHg and PaO_2 74 mmHg and a one-year-old infant with pH 7.31, $PaCO_2$ 49 mmHg, and PaO_2 80 mmHg.

Discussion

In 115 children presenting for nonemergency major surgery and induced with rectal and/or intravenous thiamylal, mean $PaCO_2$ remained within an acceptable clinical range. A statistically significant increase in mean $PaCO_2$ to 40 mmHg, compared to published normal values of 34 to 37 mmHg in awake infants and children was seen. Mean pH was 7.36 ± 0.03, slightly below the published normal values.[7–10] These change were of small magnitude and unlikely to cause physiologic changes in the majority of children. Similar changes have been reported with the onset of sleep,[11] or following thiopentone induction in adults.[12] Our results are consistent with those of Knill[13] in adults sedated or anaesthetized with thiopentone. We observed marked increases in $PaCO_2$ with respiratory acidosis in only two of our 115 patients (1.7 per cent). In the 22 patients over two years of age who received fentanyl (1–2 $\mu g \cdot kg^{-1}$) in addition to thiamylal, blood gases were the same as those in children receiving only thiamylal. Comparison of arterial pH and $PaCO_2$ in children breathing room air to those receiving supplemental oxygen following induction showed no difference in $PaCO_2$.

Children with cyanotic heart disease have arterial

desaturation which may affect respiratory control,[14] and may lead to exaggerated respiratory depression when these children are given narcotics and sedatives.[15] Thiamylal given rectally and/or intravenously in titrated doses under close direct observation did not cause changes in $PaCO_2$ or pH of any greater magnitude in the cyanotic compared to the acyanotic children in our series (see Figures 1 and 2).

Thiamylal is a short-acting thiobarbiturate used in the same dose as thiopentone. Swanson[4] reported anaesthetic doses and effects in several animal models and showed its similarity to thiopentone. Human pharmacologic comparisons of these barbiturates[5,6] have also shown similar dosage and anaesthetic effects with these thiobarbiturates. Data comparing these two agents in children have not been reported.

The incidence of complications after thiamylal induction in our paediatric patients was low. Apnoea or bradypnoea was not seen in our patients, but has been reported by others.[2] Although we did not observe major complications with thiamylal induction, the possibility of respiratory depression (seen in 1.7 per cent of our patients) and airway problems with coughing mandate the need for oxygen and resuscitation equipment, and personnel capable of airway management to be immediately available when this medication is used rectally or intravenously.

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Résumé

Cent-quinze enfants non prémédiqués induits avec du thiamylal, un thiobarbiturique à courte action, administré par voie rectale (25 $mg \cdot kg^{-1}$) ou par voie intraveineuse (6 $mg \cdot kg^{-1}$) avait un pH artériel de 7.36 ± 0.03 et une $PaCO_2$ à 40 ± 4 mmHg. Chez 22 enfants âgés de plus que deux ans, l'utilisation du fentanyl (1.2 ± 0.7 $\mu g \cdot kg^{-1}$) en plus du thiamylal n'a pas altéré les données de la gazométrie comparativement aux enfants ayant reçu uniquement les barbituriques (pH 7.36 vs 7.36, $PaCO_2$ 41 versus 40 mmHg). Les enfants atteints d'une maladie cardiaque congénitale cyanogène ont démontré des pH et des $PaCO_2$ identique aux enfants acyanotiques après administration du barbiturique à courte action. Des thiobarbituriques, administrés sous surveillance et titrés provoquent de faibles effets cliniques sur le pH artériel et la $PaCO_2$ chez les patients pédiatriques.