Ventilatory depression by halothane in infants and children

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The purpose of this study was to extend previous observations of a greater decrease in tidal volume in infants than in children during halothane anaesthesia. We analyzed the inspiratory flow waveform recorded during spontaneous ventilation in: infants, two to six months of age, and children, one to five years of age. In addition we analyzed the CO_2 signal and the pressure waveform during an occluded inspiration. The pressure generated during the initial 100 msec of inspiratory occlusion, an index of respiratory drive, was analyzed to give some insight into the aetiology of the age-related differences. In 15 infants and 15 children, Flow $(\dot{V})$, pressure (Pao) and PCO_2 were recorded at three concentrations of inspired halothane (FiH): 0%, 1% and 2% which correspond to an endtidal halothane concentration of about 0.3%, 0.9% and 1.3% respectively. Data were analyzed for minute ventilation $(\dot{V}i)$ and parameters of timing (Total time (Ttot), Inspiratory time (Ti)), the amplitude of the neural output (mean inspiratory flow (VT/Ti), tidal volume (VT)) and the shape of the inspiratory breath profile (the inspiratory centroid flow (Ci/Ti), the inspiratory duty cycle $(Ti/Ttot))$. In some, the airway was occluded at end expiration and the slope of the initial 100 msec of occlusion (dP/dt) together with the maximal negative pressure (PMAX) were measured. Estimates of respiratory mechanics E'rs $(PMAX/VT)$ and $(VT/Ti)/(dP/dt)$ were obtained. The VT and Ttot decreased with increasing FiH in both infants and children $(P < 0.05)$. The $PETCO_2$ increased in both groups and the % increase was greater in infants. The parameters of breath shape were unchanged. Infants experienced a decrease in $\dot{V}i$ as FiH increased $(P < 0.01)$. In children the parameters of breath amplitude VT/Ti and dP/dt did not change with halothane administration but, in infants, VT/Ti and dP/dt showed opposite dependencies on FiH; VT/Ti decreased whereas the dP/dt increased with increasing FiH. The E'rs was higher in infants $(P < 0.05)$. The $(VT/Ti)/(dP/dt)$ decreased as FiH increased in infants $(P < 0.05)$. We conclude that there are age-related changes in the ventilatory response to halothane.

Cette étude vise à parachever des observations précédentes selon lesquelles, sous anesthésie à l'halothane, le volume courant du nourrisson diminue plus que celui de l'enfant. Nous avons analysé la forme d'onde du débit inspiratoire enregistrée pendant la respiration spontanée chez des nourrissons âgées de deux à six mois et chez des enfants âgés d'un à cinq ans. En outre, nous avons analysé le tracé du CO_2 et la forme de d'onde de la pression pendant l'occlusion des voies respiratoires en inspiration. La pression générée pendant 100 msec d'occlusion représentant un index de l'effort respiratoire, a été analysée dans le but d'obtenir un aperçu de l'étiologie de la variation causée par l'âge. Chez 15 nourrissons et 15 enfants, le débit $\dot{V}$, la pression (Pao) et la PCO_2 sont enregistrés à trois différentes concentrations d'halothane inspiré (FiH): 0%, 1% et 2%, correspondant respectivement à une concentration téléexpiratoire d'halothane d'environ 0,3%, 0,9% et 1,3%. Sont mesurés la ventilation minute $(\dot{V}i)$, les paramètres temporels (durée totale (Ttot), durée inspiratoire (Ti)), l'amplitude de la décharge neuronale (débit inspiratoire moyen (VT/Ti), le volume courant $(VT))$ et la forme du profil inspiratoire (le débit moyen centroïde (Ci/Ti), le cycle inspiratoire $(Ti/Ttot))$. Chez certains, les voies aériennes sont occluses en fin d'expiration et la courbe des 100 msec initiales qui suivent l'occlusion (dP/dt) de même que la pression négative maximale (PMAX) sont mesurées. On évalue la mécanique par l'élastance du système respiratoire (E'rs) avec le rapport $(PMAX/VT)$ et son efficacité par le $(VT/Ti)/(dP/dt)$. Le VT et le Ttot diminuent avec l'augmentation de la FiH tant chez les nourrissons que chez les enfants $(P < 0,05)$. La $PETCO_2$ augmente dans les deux groupes mais cette augmentation est plus importante chez les nourrissons. Les paramètres de la courbe respiratoire sont inchangés. Les nourrissons subissent une baisse de $\dot{V}i$ avec l'augmentation de la FiH $(P < 0,01)$. Chez les enfants les paramètres de l'amplitude VT/Ti et le dP/dt ne changent pas avec l'administration de l'halothane, mais chez les nourrissons, le VT/Ti et le dP/dt ont une dépendance à la FiH opposée. L'E'rs est plus élevée chez les nourrissons $(P < 0,05)$. Le $(VT/Ti)/(dP/dt)$ diminue chez le nourrisson avec l'augmentation de la FiH $(P < 0,05)$.

Nous concluons qu'il existe, sous halothane, des changements de la réponse ventilatoire en relation avec l'âge.

In a previous study during mask halothane anaesthesia we observed a 64% reduction in tidal volume (VT) in infants compared with a 47% reduction in VT in children.[1] The purpose of this study was to investigate further the ventilatory effects of halothane in these age groups by examining the inspiratory flow waveform and the CO_2 waveform during spontaneous ventilation and the pressure waveform generated during an occluded inspiration. This study involved a reexamination of a group of children previously reported in protocol 1 of reference #2. Since ventilatory control has been conceptualized in terms of (1) the timing of the respiratory cycle, (2) the amplitude of the neural respiratory drive and (3) the shape of the intra-breath flow profiles, we analyzed the inspiratory flow waveform obtained during spontaneous breathing in parameters of timing, amplitude and shape of the inspiratory flow waveform. In addition, in a subset of patients we analyzed the pressure waveforms obtained during an occluded inspiration for parameters of the amplitude of the neural output and simple parameters of respiratory mechanics.

Methods

Patient preparation

Informed consent was obtained from the patients and the study was approved by the Montreal Children's Hospital Ethics Committee on Human Experimentation. We studied 15 infants (15.1 ± 6.3 wk, range 9 to 29 wk, 6.7 ± 0.9 kg, 0.351 ± 0.032 m²) and 15 children (2.4 ± 1.2 yr, range 1 to 4.5 yr, 14.3 ± 4.0 kg, 0.596 ± 0.12 m²) undergoing elective herniorrhaphy, orchidopexy, hydrocelectomy or hypospadias repair. All patients were fasted, ASA class 1 and were free of cardio-respiratory disease. Patients were not premedicated. Prematurity was an exclusion criterion.

Anaesthesia was induced with halothane. Intravenous atropine was given (20 μg · kg⁻¹) during the inhalational induction. The tracheas of all subjects were intubated, without the use of muscle relaxants, with an uncuffed endotracheal tube (ETT) (Id 3.5 to 5.0 mm). Four patients, two from each group, required thiopentone (5 mg · kg⁻¹) to facilitate tracheal intubation. (Since 20 min elapsed between thiopentone administration and data collection we assumed that any effect of thiopentone on ventilation was minimal.) Anaesthesia was maintained with halothane in air:oxygen (FiO_2 0.4). During positive pressure mechanical ventilation an air leak was detected from around the uncuffed ETT at 12 cmH_2O. Therefore, when

data were being collected gentle pressure was applied in the submental area to minimize the effect of the air leak.

Anaeasthesia was delivered with a Mapleson D circuit. The rate of fresh gas flow was 9 L · min⁻¹. To reduce errors in gas concentration profiles caused by air dilution, PCO_2 and halothane concentrations were measured in samples obtained from the tip of the ETT through a distal sample port (Sheridan Catheter Corp., Argyle, NY).[3]

Intraoperative analgesia was provided by caudal block (1 ml · kg⁻¹, 0.25% bupivacaine with epinephrine 1:200,000) placed following induction of anaesthesia and before surgical incision. No patient moved with surgical incision nor were there clinically detectable changes in vital signs during surgery. All patients were monitored with pulse oximetry and values were greater than 97% in all patients at all FiH.

Three infants received an ilioinguinal field block (0.25% bupivacaine) in lieu of a caudal block. These three patients, like those receiving caudal blockade, showed no evidence of response to noxious stimuli intraoperatively and arrived in the recovery room sleeping. No patient required opioids in the recovery room.

In each patient, body temperature (rectal) was maintained within 0.5°C of the post-induction temperature. In children, rectal temperature was 35.8 ± 0.6°C and in infants it was 36.5 ± 0.5°C.

Signal measurement

As previously reported[2] we measured airway pressure (Pao) through a side port in the ETT connector using a piezoresistive differential pressure transducer (Microswitch #162PC01D, Honeywell, Scarborough, Ontario) referenced to atmosphere. Flow ($\dot{V}$) was measured by a heated Fleisch pneumotachograph (#0 in infants and #1 in children). The pressure drop across the pneumotachograph was measured with another piezoresistive differential pressure transducer (Microswitch #163PCO1036). The dead spaces of the #0 and #1 pneumotachographs with connections were 15 ml and 49 ml, respectively. Calibration of the pneumotachographs for O_2 was performed against a rotameter. Volume (V) calibration was performed with a precision 100 ml syringe and the gas mixture used for the study. Pressure was calibrated with a pressure manometer.

Halothane and PCO_2 were measured with a Nellcor N-2500 Multi-function Pulse Oximeter with Agent Analyzer (Nellcor Inc., Hayward, CA). The accuracy of the CO_2 analyzer and the halothane analyzer was checked periodically with a known concentration of CO_2 and halothane. The Nellcor analyzer displays an average halothane concentration instead of separate inspiratory and expiratory concentrations when the respiratory rate exceeds 60 bpm. Since most babies breathed more rapidly

than 60 bpm at FiH 2%, the end-tidal halothane concentrations at FiH 2% in infants were reported as an average value which therefore overestimated the end-tidal value. A two-way valve with an inflatable balloon in the inspiratory limb (Hans Rudolph #2384B) was positioned between the pneumotachograph and the fresh gas inlet to allow interruption of the circuit during expiration, so that the next inspiration could be occluded. Even with rapid respiratory rates, the airway could reliably be occluded at end expiration.

The signals $\dot{V}$, Pao and PCO_2 were recorded during spontaneous breathing at three levels of inspired halothane concentration (FiH): 2%, 1% and 0%. Anaesthesia was induced with 2% FiH and maintained for 20 min, after which data were sampled. The Fi was then decreased to 1% and maintained for ten minutes after which data were collected. Ventilation was assisted between periods of data collection. In infants, the expired to inspired halothane ratio is reported to be 0.7 at eight minutes,[4] therefore although 10 to 20 min may not have represented a true pharmacological steady state, we considered it a reasonable compromise between the time constraints imposed by pharmacological and ethical considerations.

At the end of surgery, halothane was discontinued and data were recorded continuously until arousal (spontaneous movement) at which point the behavioural response necessitated that the tracheas be extubated. The last 30 sec before arousal were taken as the pre-emergence (FiH 0%) value. The FETH corresponding to pre-emergence, (Fi 0%), FiH 1% and FiH 2% in children were 0.32% ± 0.06, 0.86% ± 0.04, and 1.23% ± 0.13 respectively. In infants, the values were 0.28% ± 0.12, 0.91% ± 0.20 and 1.41% ± 0.30. (Since this FETH value of 1.41% in infants represented an average rather than an end-tidal value it overestimated the end-tidal value).

During data collection the surgeons interrupted their dissection so as not to interfere with chestwall excursion. Two data files were taken for FiH 2% and 1% and one data file was taken for FiH 0%.

Data analysis

A detailed description of the data analysis is given in reference #2. The beginning and end of inspiration and expiration were identified from the zero crossing points of the $\dot{V}$ signal. Volume (V) was obtained by numerical integration of $\dot{V}$. Irregular breaths involving sighs and coughs were discarded.

From the $\dot{V}$ signal we determined the parameters of breath amplitude: minute ventilation ($\dot{V}i = 60 \cdot V_T/T_{tot}$), tidal volume ($V_T$) and mean inspiratory flow (V_T/T_i), breath timing: total cycle time (T_{tot}) and inspiratory time (T_i), and breath shape; the inspiratory flow centroid (C_i/T_i) and the inspiratory duty cycle (T_i/T_{tot}). (The math-

ematical equation used to calculate C_i/T_i is given in reference #2. This quantity reflects the skewness of the flow waveform. A symmetrical inspiratory flow profile would have a C_i/T_i of 0.5. A $C_i/T_i < 0.5$ would indicate an inspiratory flow profile skewed to the left with the flows in early inspiration being greater than those in late inspiration. Since C_i/T_i involves integrating flow over the whole of inspiration it is relatively noise insensitive.) Finally, end-tidal PCO_2 ($PETCO_2$) was obtained as the highest value of the smoothed expiratory PCO_2 signal from each breath.

In six infants and 11 children the occluded pressure waveform was obtained at different FiH. The pressure generated 100 msec into an occluded inspiratory effort (P0.1) has been used in the past as an index of respiratory drive.[5-8] In the present study we used, as a correlate of P0.1, the slope of the initial 100 msec of the occluded Pao waveform (dP/dt), obtained by linear regression. This quantity reflects essentially the same phenomena as P0.1 (indeed, if Pao increases linearly from baseline then $dP/dt = 10 \times P0.1$), but is less noise-sensitive than P0.1 because it uses all the data in a 100 msec interval rather than a single point at the end of the interval. The coefficient of determination for multiple measures of dP/dt was 9.2 ± 0.6%. Because of the rate of arousal following cessation of halothane administration, only single values of dP/dt were obtained for the pre-emergence value.

The effective elastance of the respiratory system (E'rs) was determined as the ratio of the maximal negative pressure (PMAX) to the V_T of the preceding unoccluded breath. The efficiency of the respiratory system in transforming pressure into flow was assessed with the ratio $(V_T/T_i)/(dP/dt)$.[6]

Because of the non-linear dependence of ventilation and body weight we normalized the ventilatory variables $\dot{V}i$ and V_T/T_i to body surface area so that the intergroup pre-emergence value should be similar. Tidal volume was normalized to body weight because unlike $\dot{V}i$ and V_T/T_i when normalized to body weight V_T is relatively age independent.

Statistical analysis

Group results for the various parameters are expressed as mean ± SEM. Mean parameter values obtained at FiH 1% and 2% were compared with the pre-emergence value (FiH 0%) values by Dunnett t test for repeated measures.[9] Inter-group differences were assessed with an unpaired t test. A P value < 0.05 was considered statistically significant and a P value < 0.01 was considered highly significant.

Results

The $\dot{V}i$ was not different between the two groups at the pre-emergence FiH of 0% (Figure 1a). However, whereas
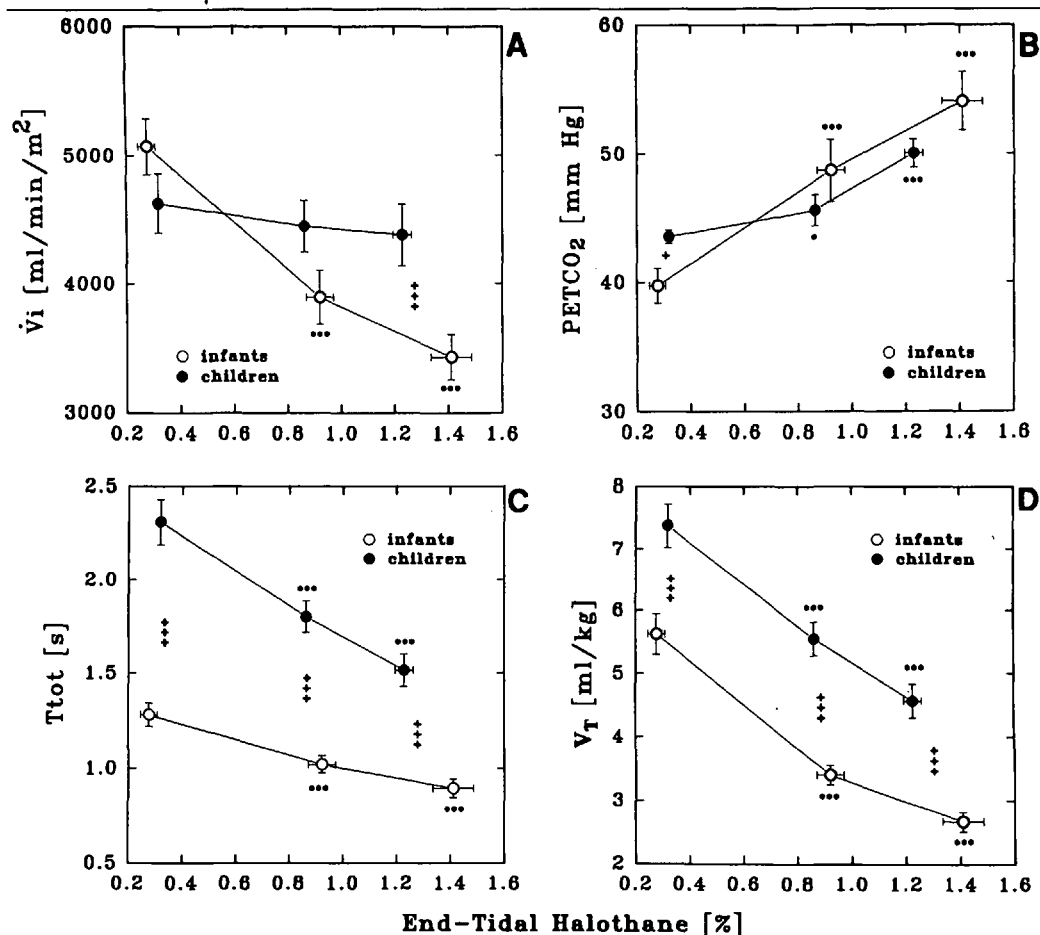
FIGURE 1 Data for V̇i(A), PETCO₂(B), Ttot(D) and VT(C) with increasing FiH (mean ± SEM) for infants (o—o) and children (●—●). Intragroup differences $*P < 0.05$, $**P < 0.01$ and intergroup differences $^+P < 0.05$, $^{++}P < 0.01$. (The FETH of 1.4% in infants represents an average, not an end tidal value. See Methods.)

V̇i did not change with increasing FiH in children, in infants it decreased at both FiH 1% and 2% ($P < 0.05$) (Figure 1a). The Ttot decreased in both groups ($P < 0.05$) (Figure 1c). The percentage decrease in Ttot at FiH 2% was similar in both groups: 32.4% (±19.3) in children and 28.9% (±15.2) in infants (Figure 1c). Therefore, the different responses in V̇i were due to a greater proportional decrease in VT in infants than in children (Figure 1d). The PETCO₂ increased in both groups (Figure 1b) ($P < 0.01$). In infants the PETCO₂ at FiH 2% was 54.2 ± 2.3 mmHg (range 35.7 to 72.0 mmHg). In children it was 50.1 ± 1.1 mmHg (range 40.4 to 58.1 mmHg). The increase in PETCO₂ at FiH 2% was proportionally greater in infants (136.7% ± 4.7) than in children (114.9% ± 1.9) ($P < 0.05$).

Figure 2 shows that the shape parameter Ci/Ti did not change consistently with halothane administration in either group. Neither did the Ti/Ttot change with halothane administration in infants. In children Ti/Ttot in-

creased at FiH 1% and 2% but the change did not show a consistent trend.

The pre-emergence value of VT/Ti was the same in both groups. In children neither VT/Ti nor did dP/dt changed with halothane administration (Figure 3). The VT/Ti and dP/dt showed opposite dependencies on FETH in infants. In infants VTTi decreased ($P < 0.05$). In contrast, dP/dt showed an increase at FiH 2% in infants ($P < 0.05$). At all FiH 0% dP/dt was greater in infants than in children ($P < 0.05$).

Figure 4 shows representative tracings of Pao during an occluded breathing manoeuvre in an infant under baseline conditions and during FiH 2%. The initial rate of decrease of Pao (dP/dt) is greater at FiH 2% than at FiH 1%. The total change in Pao during the manoeuvre (PMAX) is also greater at FiH 2%. However, the duration of the manoeuvre is greater at FiH 0% than at FiH 2%.
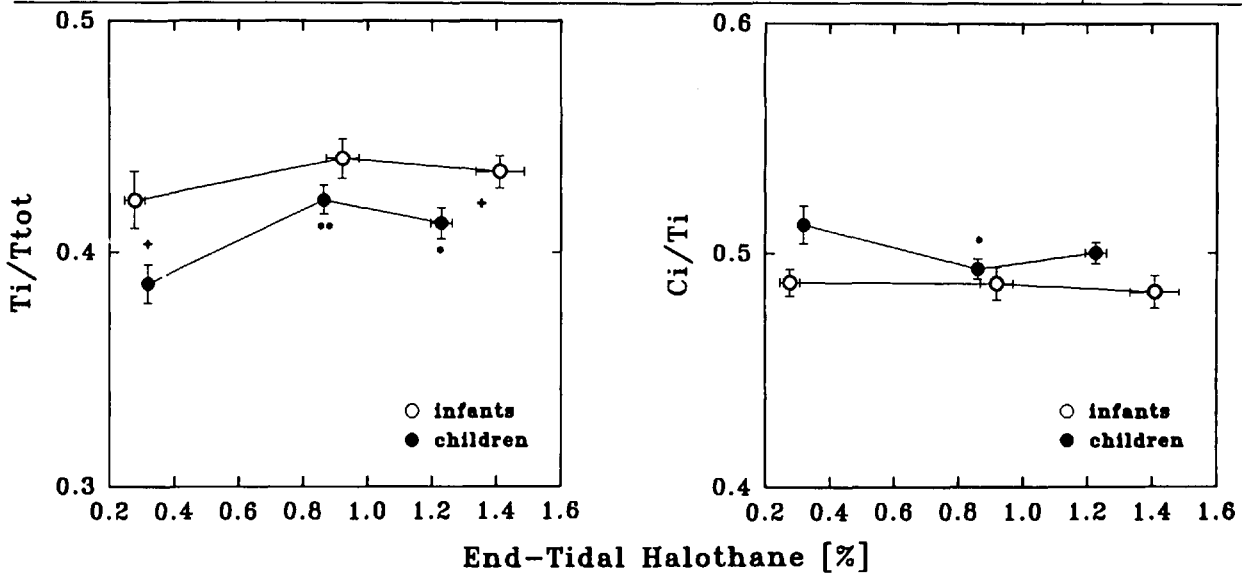
Finally, the Table gives the group values for dP/dt

FIGURE 2   Ti/Ttot and Ci/Ti for the two groups. Figures for the inspiratory duty cycle (Ti/Ttot) and the inspiratory centroid (Ci/Ti). No significant change in shape parameters occurred. Intragroup differences $*P < 0.05$ and intergroup differences $^+P < 0.05$. (The FeTH of 1.4% in infants represents an average, not an end tidal value. See Methods.)
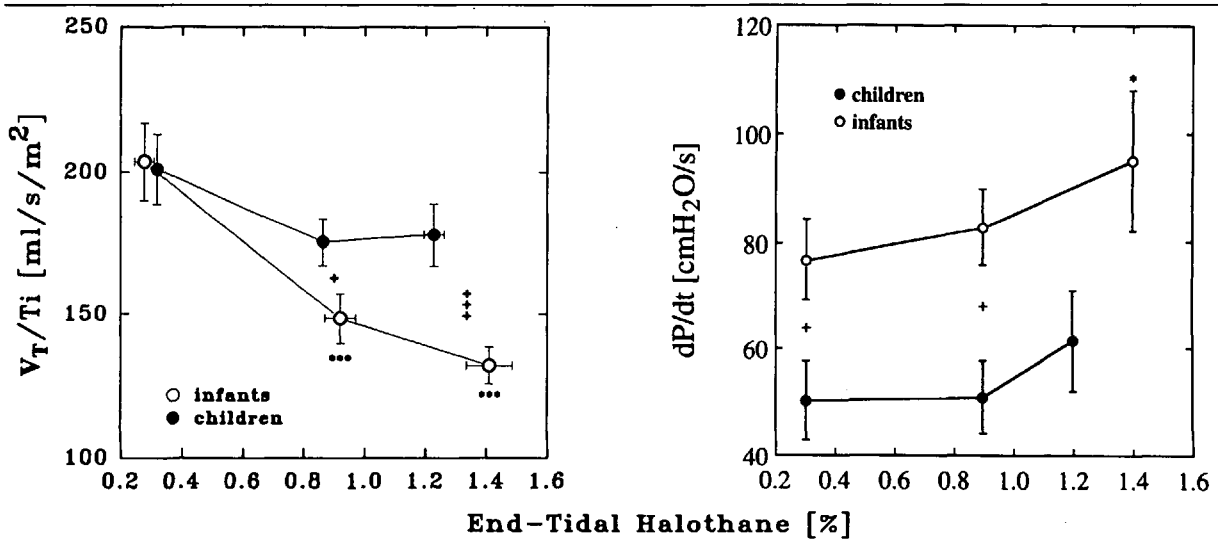

FIGURE 3   This figure shows the effect of halothane on the parameters of amplitude of the breath showing opposite dependencies on FeTH. The mean inspiratory flow (VT/Ti) decreased as FeTH increased, with infants showing a greater rate of decrease than children (Figure 3A). The increase in dP/dt (11 children (●—●) and six infants (o—o) with increasing FiH contrasts the findings of VT/Ti. Intragroup differences $*P < 0.05$ and intergroup differences $^+P < 0.05$. (The FeTH of 1.4% in infants represents an average, not an end tidal value. See Methods.)

and indices of respiratory mechanics (E's, (VT/Ti)/(dP/dt) PMAX) obtained from the occluded breathing efforts.

Discussion

Whereas there was no difference in the pre-emergence value of V̇i between the two groups as FiH increased, V̇i decreased in infants but not in children (Figure 1a). This finding supports the notion that there is a greater

respiratory depression in infants than children. This finding is magnified when halothane MAC is considered. The minimum alveolar concentration (MAC) of an inhalational agent, is age related such that halothane MAC is about 1.08% in infants and 0.91% in children.[10]

Comparison of V̇i in Figure 1a with that of Figure 2b in our previous study[2] shows that the decrease in V̇i reported in the reference #2 was due to the decrease in
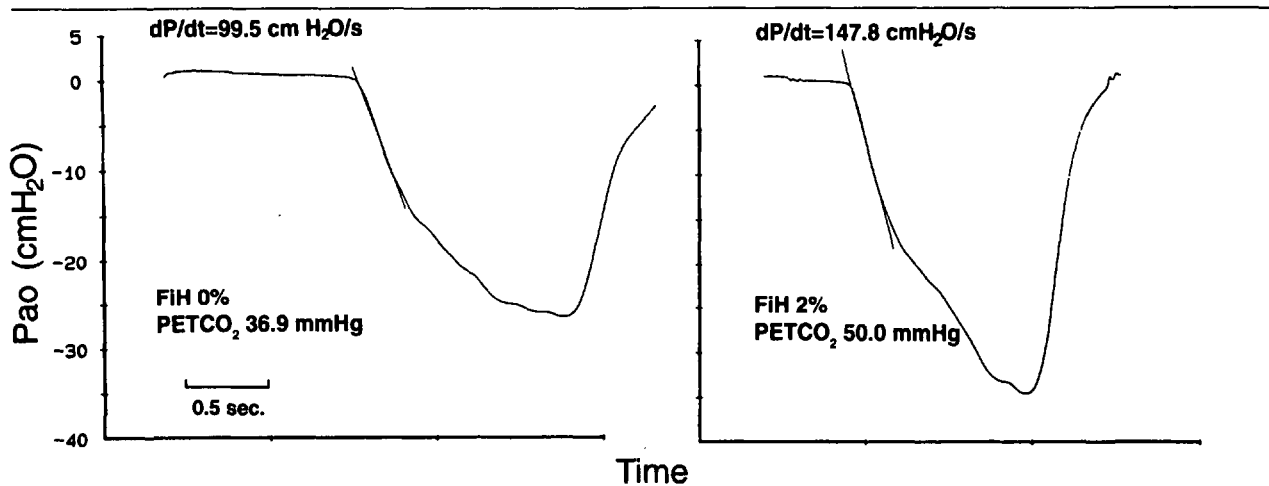
FIGURE 4   Representative tracing of Pao during an occluded breathing manoeuvre in an infant at FiH 0% and FiH 2%. Note the linearity of the pressure waveform in its initial portion. The slope (dP/dt) was determined by fitting a linear regression over the initial 100 msec of the occlusion. The PMAX at FiH 2% was -33 cmH_2O and at FiH 0% was -28 cmH_2O.

Vi in infants since children show no decrease in Vi at a FiH 2%. In reference #2 we concluded that the halothane induced changes in ventilation reflected a scaling of the breath in time and/or amplitude. However, the fact that Vi, VT/Ti and dP/dt, all parameters of amplitude of neural drive, did not change during halothane administration in children suggests that, in children, the changes in ventilation during halothane administration are primarily due to an effect on timing parameters.

The parameters of timing Ti and Ttot, of the breath profile, decreased during halothane anaesthesia in both groups (Figure 1c). Animal experiments suggest that this trachypnoea is mediated by both a central and a peripheral effect of halothane.[11,12]

We analyzed the shape of the inspiratory flow wave-form, a parameter which has been relatively neglected in discussions of ventilatory control but one which does convey subtle information of the output of the respiratory centre. Neither shape parameter, Ci/Ti nor Ti/Ttot, changed consistently with increasing FiH in either age group indicating that the basic breath shape was preserved. Jonsson also found that flow pattern was preserved during halothane administration in adults and children.[13]

During halothane anaesthesia $PETCO_2$ increased in children whereas Vi was unchanged. This may indicate a greater fractional ventilation of deadspace. In fact, given the observed increase in frequency and decrease in VT, one would expect an increase in deadspace ventilation. The $PETCO_2$ increased in both groups as FiH increased but the magnitude of the increase was greater in infants supporting the notion of a greater respiratory depression in infants. Since some infants at FiH 2% breathed at

respiratory rates in excess of 60 bpm the end-expiratory plateau in the CO_2 waveform may have been inadequate to reflect the arterial CO_2 accurately and the reported CO_2 may, in fact, have underestimated the true CO_2.

The amplitude parameter dP/dt is minimally affected by the mechanics of the respiratory system since in the initial 100 msec of inspiration there is little change in flow or volume.[5] This is part of its appeal as a non-invasive index of central respiratory drive. However, one must be cautious in interpreting dP/dt solely as a parameter of the amplitude of respiratory drive. It can be affected by changes in functional residual capacity (FRC) because of the influence of lung volume on the force length characteristics of the diaphragm.[7] Since FRC decreases during halothane anaesthesia[14,15] the influence of lung volume on dP/dt must be considered.

The higher dP/dt in infants at FiH 0% may have been due to this influence of lung volume on dP/dt. Since infants maintain end expiratory lung volume at a value above that determined passively by the opposing recoils of chest wall and lung and since the active mechanisms involved are attentuated during halothane anaesthesia, it is possible that infants experienced a greater decrease in FRC during halothane anaesthesia.[15-17] The could have enhanced the force length characteristics of the infants's diaphragm. Additionally the resistive load imposed by a 3.5 mm ETT is greater than that of a 5.0 ETT and may have contributed to the higher value of dP/dt in infants at FiH 0%.

We did not measure FRC in this study and therefore cannot assess its effect on dP/dt. However, a priori, we doubt that lung volume (i.e., FRC) was a major determinant of the observed change in dP/dt during ha-

TABLE Values for dP/dt, PMAX, (VT/Ti)/(dP/dt), E'rs obtained from the occluded breathing efforts in 11 children and in six infants

	dP/dt $cmH_2O \cdot sec^{-1}$	$PMAX$ cmH_2O	$(VT/Ti)/(dP/dt)$ $ml \cdot cmH_2O^{-1}$	$E'rs$ cmH_2O/ml^{-1}
FiH 0%				
Infants	76.82	25.85	0.95	5.22
$n = 6$	7.63	3.02	0.09	0.67
Children	50.19	25.16	2.5	3.7
$n = 13$	7.27	1.93	0.18	0.30
Intergroup	$P < 0.05$	NS	$P < 0.01$	$P < 0.05$.
FiH 1%				
Infants	82.78 (NS)	22.31 (NS)	0.86 (NS)	5.00 (NS)
$n = 6$	7.12	2.07	0.12	0.51
Children	50.77 (NS)	19.68 ($P < 0.05$)	2.47 (NS)	3.38 (NS)
$n = 13$	6.81	1.91	0.26	0.45
Intergroup	$P < 0.05$	NS	NS	$P < 0.05$
FiH 2%				
Infants	95.18 ($P < 0.05$)	20.96 (NS)	0.72 ($P < 0.05$)	6.21 (NS)
$n = 6$	12.86	2.60	0.09	1.21
Children	61.26 (NS)	17.84 ($P < 0.05$)	1.98 (NS)	3.85 (NS)
$n = 13$	9.51	1.69	0.24	0.43
Intergroup	NS	NS	$P < 0.05$	$P < 0.05$

( ) P value for Intra Group difference from FiH 0% value.

lothane administration. Firstly, although Ochiai[18] showed a dose-related reduction in the activity of the chest wall musculature during halothane administration the relationship between activity in the chest wall musculature and FRC is unknown. Secondly, to attribute the increase in dP/dt during halothane administration to a graded decrease in FRC due to a graded decrease in chestwall tone in inconsistent with the observation that the addition of neuromuscular blockade to halothane anaesthesia does not result in a further decrease in FRC.[14] Thirdly, to explain the infant's increase in dP/dt with increasing FiH to a decrease in FRC would imply that these spontaneously breathing infants, whose tracheas were intubated, were able to increase FRC as FiH decreased (see Methods). Furthermore, if infants experienced a large decrease in FRC this was not reflected by a change in E'rs (Table). Canet et al.[8] also showed a dose-related increase in P0.1 during halothane anaesthesia in adults but could not attribute the increase in P0.1 solely to a greater mechanical advantage of the diaphragm and postulated a halothane-induced increase in central respiratory drive.

Respiratory depression was greater in infants than in children during halothane anaesthesia. We think it unlikely that the decrease in V̇i in infants was due to a decrease in ventilatory drive as dP/dt did not decrease and, in fact, increased with halothane administration. In infants clearly an additional factor resulted in a decrease in V̇i and VT/Ti. The ratio (VT/Ti)/(dP/dt) decreased

with increasing FiH suggesting a mechanical inefficiency in ventilation. Derenne et al. also reported a decrease in (VT/Ti)/(dP/dt) during CO_2 rebreathing in adults during methoxyflurane anaesthesia and postulated an anaesthetic induced "hindrance to ventilation."[6] Canet[8] also postulated "a peripheral factor" to explain the decrease in ventilation and preservation of respiratory drive during halothane administration in adults. Clarification of the precise nature of this "peripheral factor" will require further study. It may be that the inherent properties of the infant's respiratory system predispose him a greater fall in VT when Ti is shortened. Tusiewicz et al. postulated that there may be an altered recruitment pattern of the respiratory motoneurons during halothane administration.[15] In addition the infants compliant chestwall may predispose to paradoxical chestwall motion during halothane anaesthesia.[15,16]

To summarize our findings, children are able to maintain V̇i at an FiH of 2%. The pattern of respiration was rapid and shallow with an increase in respiratory frequency and a decrease in tidal volume. This predisposed them to an increase in deadspace ventilation with an increase in PeTCO_2. Parameters of the shape of the intra-breath profiles did not change appreciably during halothane anaesthesia. Parameters of the amplitude of the neural respiratory output, namely VT/Ti and dP/dt, also did not change during halothane anaesthesia in children.

Infants showed a different response. Unlike children,

the $\dot{V}i$ decreased at F$_I$H 2%. The pattern of breathing was also rapid and shallow. Both the decrease in $\dot{V}i$ and the altered respiratory pattern predisposed the infant to a greater increase in P$_{ET}CO_2$. Like children, the parameters of breath shape did not change. Unlike children, the parameters of breath amplitude showed opposite dependencies on halothane concentration and V$_T$/Ti decreased whereas dP/dt increased.

Although lung volume is an important determinant of dP/dt, for the reasons stated above, we do not think that the observed increase in dP/dt in infants was due to a dose-related change in FRC during halothane administration. We speculate that respiratory drive was relatively well maintained in both infants and children during halothane anaesthesia, a notion which is supported by a previous study in infants[19] and a recent study in adults.[8] We hypothesize that the decrease in $\dot{V}i$ in infants with halothane administration was due to a mechanically impaired respiratory pump and not due to an age-related difference in respiratory control.

Acknowledgments

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