Pattern of ventilation during halothane anaesthesia in infants less than two months of age

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Purpose: To examine the breathing pattern of infants aged less than two months in order to understand better the effect of halothane on ventilation in infants.

Methods: The inspiratory flow waveform, the CO₂ waveform and occluded inspiratory pressure waveform were recorded at different inspired concentrations of halothane using a washout of halothane in two groups of infants undergoing elective herniorrhaphy. Data were analyzed for minute ventilation ($\dot{V}_i$) and tidal volume (V_T), parameters of timing of the breath [Total time (T_{tot}), Inspiratory time (T_i), and the ratio of the occluded to unoccluded inspiratory time (T_i^{occ}/T_i)], parameters of Amplitude of the neural output [mean inspiratory flow ($\dot{V}_T/T_i$)] and parameters of the Shape of the inspiratory breath profile [the inspiratory flow centroid (C_i/T_i), the inspiratory duty cycle (T_i/T_{tot})]. 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 (P_{MAX}) and occluded inspiratory time (T_i^{occ}) were obtained. We studied ten infants <48 wk post-conceptual age (PCA) and ten infants >48 wk. PCA Flow ($\dot{V}$), pressure (P_{ao}) and carbon dioxide tension (PCO_2) were recorded at three concentrations of inspired halothane (F_iH): 0%, 1% and 2% which corresponded to an end-tidal halothane concentration of about 0.2%, 0.8% and 1.2% respectively.

Results: In both groups $\dot{V}_i$, V_T and $\dot{V}_T/T_i$ decreased whereas dP/dt , did not, suggesting that the respiratory pump was impaired. The parameters of breath Shape did not change. Importantly the parameters of Timing showed different ten-

dencies. In infants >48 wk PCA T_i^{occ}/T_i decreased. In infants <48 wk PCA, T_i^{occ}/T_i did not change.

Conclusions: The different response in the timing parameter T_i^{occ}/T_i is consistent with a different effect of halothane on parameters of ventilatory timing in infants <48 wk PCA and this may represent a maturational effect.

Objectif: Etudier le pattern ventilatoire du nourrisson âgé de moins de deux mois afin de mieux comprendre les effets de l'halothane sur sa ventilation.

Méthodes: La forme d'onde inspiratoire, la forme d'onde du gaz carbonique et la forme d'onde de la pression d'occlusion ont été enregistrées à différentes concentrations inspirées d'halothane chez deux groupes d'enfants opérés pour herniorraphie. Ont été analysées: les données de la ventilation minute ($\dot{V}_i$) et du volume courant (V_T), les paramètres de la rythmique ventilatoire [durée totale (T_{tot}), durée de l'inspiration (T_i) et le rapport entre la respiration avec et sans occlusion (T_i^{occ}/T_i)], les paramètres de l'amplitude de la décharge neurale [débit inspiratoire moyen ($\dot{V}_T/T_i$), et les paramètres de la forme du profil inspiratoire [débit inspiratoire centroïde (C_i/T_i), le travail du cycle inspiratoire (T_i/T_{tot})]. Les voies aériennes ont été occluses en fin d'expiration et la pente des 100 msec initiales de l'occlusion (dP/dt) a été acquise simultanément à la pression maximale négative (P_{MAX}) et au temps d'occlusion (T_i^{occ}). Dix nourrissons d'âge postconceptionnel (APC) inférieur à 48 sem et dix enfants d'APC supérieur à 48 sem ont été étudiés. Le débit ($\dot{V}$), la pression (P_{ao}) et la tension du gaz carbonique (PCO_2) ont été enregistrés sous trois concentrations inspirées d'halothane (F_iH): 0%, 1% et 2% qui correspondaient respectivement à une concentration de fin d'expiration d'environ 0,2%, 0,8% et 1,2%.

Résultats: Dans les deux groupes, $\dot{V}_i$, V_T , et $\dot{V}_T/T_i$ ont diminué alors que dP/dt n'a pas changé, ce qui suggère une défec-tuosité de la pompe respiratoire. Les paramètres de la forme respiratoire n'ont pas changé. Il est important de noter que pour les paramètres de la rythmique, les tendances différentes se sont avérées différentes. Chez les nourrissons >48 sem d'APC, T_i^{occ}/T_i a diminué. Chez les nourrissons d'APC <48 sem, T_i^{occ}/T_i n'a pas changé.

Key words

ANAESTHESIA: paediatric;

ANAESTHETICS, INHALATIONAL: halothane;

VENTILATION: anaesthetics, effects of.

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Conclusion: *Cette différence de réponse des paramètres de la rythmique Ti^{occ}/Ti est cohérente avec la différence des effets de l'halothane sur les paramètres de la synchronisation respiratoire chez les nourrissons <48 sem d'APC et peut représenter une conséquence de la maturation.*

Numerous studies have reported that perioperative respiratory morbidity in infants correlates inversely with age.¹⁻⁷ The aetiology of the increased risk for postoperative apnoea is probably multifactorial and is thought to be due to an effect of the general anaesthetic agents since its incidence may be lower in infants receiving awake regional anaesthesia.⁸ It has been suggested that the immaturity of the infant's respiratory system may predispose the infant to excessive respiratory depression.^{2,5} Obstructive apnoea has been suggested as an aetiology.⁹ Some favour the notion of a central depression of ventilation since the incidence of the apnoea of prematurity correlates with the maturation of the brainstem auditory evoked potential.¹⁰ Others suggest that respiratory stimulants such as caffeine may decrease the incidence of postoperative apnoea.³ Implicit in these hypotheses is the notion that general anaesthetic agents have an effect on the ventilatory control centre and/or the activation of its motoneurons and that recovery from this effect is delayed, predisposing to postoperative apnoea. Indeed, in previous studies we found that the infant had greater respiratory depression during halothane anaesthesia than did children.^{11,12}

Recent concepts in the control of ventilation propose that mechanisms generating respiratory rhythm and pattern are separate and determined by different neural and physiological events.¹³ Therefore parameters of ventilatory control may be described in terms of Amplitude (reflecting an intensity of neural output), Timing (reflecting the switching between inspiratory and expiratory phases of the respiratory cycle) and Shape of the flow and occluded pressure waveforms. If postoperative apnoea were due to a residual effect of anaesthetic agents on ventilatory control then, at measurable concentrations of the agent, such an analysis might give some insight into which aspect of ventilatory control is perturbed by the anaesthetic agent. The following study applies such an analysis to examine the breathing pattern intraoperatively during halothane anaesthesia in infants less than two months of age.

Methods

Patient preparation

Informed consent was obtained from the parents of patients and the study was approved by the Montréal

Children's Hospital Ethics Committee on Human Experimentation. Definition of the age at risk for postoperative apnoea often reflects institutional bias.¹⁴ In our institution infants <48 wk post conceptional age (PCA) are considered to be at higher risk for apnoea. Therefore the infants studied were grouped by age as <48 wk PCA or >48 wk PCA.

We studied 12 infants <48 wk PCA (45.6 ± 1.91 wk PCA, range 44 to 48 wk, 4.8 ± 0.78 kg, 0.265 ± 0.026 m²) and infants >48 wk PCA (53.6 ± 4.4 wk PCA, range 48 to 60 wk PCA, 6.61 ± 1.2 kg, 0.313 ± 0.036 m²) undergoing elective herniorrhaphy. All patients were ASA class 1 or 2 and were free of cardio-respiratory disease. Patients were not premedicated. A history of broncho-pulmonary dysplasia and/or neurological disease were exclusion criteria.

Anaesthesia was induced with atropine ($20 \mu\text{g} \cdot \text{kg}^{-1}$) and thiopentone $3 \text{ mg} \cdot \text{kg}^{-1}$ iv and tracheal intubation was facilitated with succinylcholine ($2 \text{ mg} \cdot \text{kg}^{-1}$). Tracheas were intubated with an uncuffed endotracheal tube (ETT) (id 3.0 to 3.5 mm). 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 cmH₂O. Therefore, when data were being collected gentle pressure was applied in the submental area to minimize the leak.

Anaesthesia was delivered via a Mapleson D circuit with a rate of fresh gas flow of $9 \text{ L} \cdot \text{min}^{-1}$. The PCO₂ and halothane concentrations were measured at the distal end of a Sheridan[®] uncuffed endotracheal tube via a sample distal port (Sheridan Catheter Corp, Argyle, NY).

There was no evidence of atypical plasmacholinesterase activity since either spontaneous ventilation or reactive movement was observed at the time of turning for insertion of the caudal block in all patients. Analgesia was provided by intraoperative caudal block ($1 \text{ mg} \cdot \text{kg}^{-1}$ bupivacaine 0.25% with epinephrine 1:200,000) placed following induction of anaesthesia and before surgical incision. No patient showed evidence of response to painful stimuli intraoperatively. 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 <48 wk PCA infants rectal temperature was $36.3 \pm 0.12^\circ\text{C}$ and in >48 wk PCA infants it was $36.5 \pm 0.15^\circ\text{C}$.

Infants <48 wk PCA were monitored overnight with an apnoea monitor and a saturation monitor.

Signal measurement

In the same manner as previously reported, airway pres-

sure (Pao) was measured through a side port in the ETT connector using a piezoresistive differential pressure transducer (Microswitch #162PCO1D, Honeywell, Scarborough, Ontario) referenced to atmosphere.^{12,15} Flow ($\dot{V}$) was measured by a heated Fleisch pneumotachograph (#00 in <48 weeks PCA infants and #0 in the >48 wk PCA infants.). The pressure drop across the pneumotachograph was measured with piezoresistive differential pressure transducer (Microswitch #163PCO1036). Calibration of the pneumotachographs for oxygen was performed against a rotameter. Volume calibration was performed by integrating the flow signal obtained from the emptying of a precision 100 ml syringe filled with 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 monitor displays an average halothane concentration instead of separate inspiratory and expiratory concentrations when the respiratory rate exceeds 60 bpm. The end-tidal halothane concentrations at FiH 2% reported as an average value therefore overestimated the end-tidal value. Accuracy of the CO_2 with gas analyzers was checked periodically with known concentrations of CO_2 with halothane respectively.

A valve with 2 ml dead space (Hans Rudolph #2384B) was positioned between the pneumotachograph and the fresh gas inlet to allow interruption of the circuit during expiration, in order that the next inspiration could be occluded. Even with rapid respiratory rates, the airway could be occluded reliably 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%. An FiH 2% was maintained for 20 min, after which data were sampled. The FiH was then decreased to 1% and maintained for ten minutes after which data were collected. Thus, the protocol used a washout of halothane. Although 10 to 20 min may not represent a true pharmacological steady state, we considered it a reasonable compromise between the time constraints imposed by pharmacological and ethical considerations. Ventilation was assisted between periods of data collection.

At the end of surgery, halothane was discontinued and data were recorded until arousal (spontaneous movement) at which point the behavioural response necessitated that the tracheas be extubated. Pre-emergence occlusion data were collected at FETH 0.3%. The last minute before arousal were taken as the pre-emergence spontaneous ventilation FiH 0% data.

During data collection the surgeons were careful not to interfere with abdominal excursions. Two representa-

tive data files of 45 sec duration were collected at FiH 2% and 1% and 0%. The FETH corresponding to FiH 0%, 1% and 2% in >48 wk PCA infants were $0.19\% \pm 0.01$, $0.83\% \pm 0.01$, and $1.24\% \pm 0.04$ respectively. In <48 wk PCA infants the values were $0.21\% \pm 0.02$, $0.87\% \pm 0.03$, and $1.24\% \pm 0.04$. (Because of the inter-group differences, which were not statistically different, in the end-tidal concentrations between comparable doses of halothane, the halothane dose will be identified subsequently by the inspired level of FiH.)

The analogue signals of $\dot{V}$ and Pao were low-pass filtered at 45 Hz (8-pole Bessel 902LPF, Frequency Devices, Haverhill, MA) and digitized at 100 Hz with a 12-bit analog-to-digital converter (DT2801-A, Data Translation, Marlborough, MA). Data acquisition and analysis were performed on a 386 personal computer using the ANADAT-LABDAT[®] software package (RHT-InfoDat, Montreal, Quebec).

Data analysis

The $\dot{V}$ and PCO_2 signals obtained during spontaneous breathing were smoothed using a triangular window 0.1 sec wide. 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 $\dot{V}$ following an offset correction designed to avoid drift in $\dot{V}$. The delay in the PCO_2 signal caused by the finite aspiration rate of the analyzer ($50 \text{ ml} \cdot \text{min}^{-1}$) was measured by applying a step CO_2 input to the analyzer and found to be 2.05 sec. The PCO_2 signal delay was compensated for by shifting the PCO_2 signal by the delay time. Irregular breaths involving sighs or coughs were discarded.

From the $\dot{V}$ signal we determined the parameters of breath Amplitude: minute ventilation ($\dot{V} = 60 \cdot \text{Vt}/\text{Ttot}$), tidal volume (Vt) and mean inspiratory flow (Vt/Ti), breath Timing: total cycle time (Ttot) and inspiratory time (Ti), and breath Shape: the inspiratory duty cycle (Ti/Ttot) and the inspiratory flow centroid (Ci/Ti). [The mathematical equation used to calculate Ci/Ti is given in reference 15. This quantity reflects the skewness of the flow waveform. A symmetrical inspiratory flow profile would have a Ci/Ti of 0.5. A $\text{Ci}/\text{Ti} < 0.5$ would indicate an inspiratory flow profile skewed to the left with the flows in early inspiration being greater than those in late inspiration. Since Ci/Ti involves integrating flow over the whole of inspiration, it is relatively noise insensitive.] Tidal volume (Vt) was determined as the total excursion in V. Finally, end-tidal PCO_2 (PETCO_2) was obtained as the highest value of the smoothed expiratory PCO_2 signal from each breath.

In ten infants >48 wk PCA and ten infants <48 wk PCA the occluded pressure waveform was obtained at

different F_iH . The breath amplitude parameter dP/dt was derived from the occluded Pao waveforms. The dP/dt , a correlate of $P_{0.1}$, was obtained as the slope of the line fit (by linear regression) to the first 100 msec of the occluded inspiration.^{12,16,17} The coefficient of determination for the regressions was >0.97 . Values for dP/dt at all F_iH were obtained from at least three occluded pressure waveforms.

Finally, the ratio between the occluded and unoccluded inspiratory times (Ti^{occ}/Ti) was determined, where Ti^{occ} is the occluded inspiratory time defined as the time taken for Pao to decrease to its minimum value from baseline.

Because age related differences in control ventilatory volume parameters correlate well with BSA, $\dot{V}_i$ and V_T/Ti were normalised to BSA.¹¹ Therefore one would expect the F_iH 0% values for $\dot{V}_i$ and V_T/Ti to be similar. The V_T was normalized to body weight.

Statistical analysis

Mean parameter values obtained at F_iH 1% and 2% were compared with the pre-emergence (F_iH 0%) values by Dunnett t test for repeated measures.¹⁸ Two way ANOVA for Repeated Measures was performed on the data for Ti^{occ}/Ti . The difference in the sample was statistically significant ($P = 0.0465$). Inter-group differences for F_iH 0% were assessed with an unpaired t test. A P value of 0.05 was considered statistically significant.

Results

A total of 27 patients were studied. Minute ventilation for all patients studied are presented in Figure 1. In two patients in the <48 wk PCA group and one patient in the >48 wk PCA group spontaneous ventilation could not be established at an F_iH 2% and $PETCO_2$ 70 mmHg. In an additional four patients in the >48 wk PCA group satisfactory occlusions could not be obtained. These seven patients were represented in Figure 1 but were excluded from statistical analysis. Details of the demographic ventilatory parameters in the three patients for the F_iH 0% are given in Table I.

There was no difference between groups in any ventilatory parameter in the pre-emergence value.

The $\dot{V}_i$ decreased in both groups such that at F_iH 2% the decrease in the <48 wk PCA group was 77% and in the >48 wk PCA group it was 81%. The $PETCO_2$ increased such that at F_iH 2% the proportional increase in infants <48 wk PCA was 133% and in those >48 wk PCA it was 134%. The pattern of breathing was shallow. The V_T decreased 62% in the infants >48 wk PCA and 65% in the infants <48 wk PCA (Figure 2).

The Ti decreased 82% (Figure 2) in the <48 wk PCA group however the overall T_{tot} did not change. In con-

FIGURE 1 The $\dot{V}_i$ for all patients at F_iH 0%, 1% and 2% are shown. PCA had no effect on the values of $\dot{V}_i$.

trast in the >48 wk PCA group both T_{tot} and Ti decreased ($P < 0.05$). The ratio Ti^{occ}/Ti did not change in infants <48 wk PCA whereas in those >48 wk PCA it was decreased (Figure 3).

The shape parameters Ti/T_{tot} and Ci/Ti were unchanged in either group. The pre-emergence value for Ti/T_{tot} was 0.44 ± 0.02 in infants <48 wk PCA and did not change with halothane administration. In infants >48 wk PCA the pre-emergence value was 0.46 ± 0.02 and did not change with halothane administration. The Ci/Ti in infants <48 wk PCA was 0.48 ± 0.0 and an F_iH 0% whereas in infants >48 weeks PCA was 0.49 ± 0.01 . The Ci/Ti did not change in either group with halothane administration. The Amplitude parameters V_T/Ti and dP/dt showed different dependencies with halothane concentration (Figure 4). The V_T/Ti decreased $\dot{V}_i$ in both groups ($P < 0.05$) whereas the dP/dt did not change with halothane administration.

Discussion

The effect of halothane on ventilation in infants >48 wk PCA is similar to that reported previously, in that at F_iH 2%, the infants experienced a 20% decrease in $\dot{V}_i$ ($P < 0.05$) and 40% decrease in V_T ($P < 0.01$).^{11,12} Both the decrease in $\dot{V}_i$ and the rapid shallow pattern of respiration predisposed to CO_2 retention and the infants >48 wk PCA experienced an increase in $PETCO_2$. As in our previous study the parameters of breath Amplitude dP/dt and V_T/Ti showed opposite dependencies with F_iH . The values of dP/dt were similar to those previously reported in infants.³

TABLE 1 Demographic data of the three infants who experienced apnoea at FiH 2% ventilatory parameters for the pre-emergence period (FiH 0%) are given, where *deviation $\geq$ one SD from group mean and †deviation $\leq$ two SD from group mean.

Patient	Birth age (wk)	PCA (wk)	Temp °C	F _{ET} H %	V _i L·m ⁻² ·m ⁻¹	V _T ml·kg ⁻¹	T _{tot} sec	T _i /T _{tot}	P _{ET} CO ₂ mmHg	dP/dt cm·sec ⁻¹	T _i ^{occ} /T _i
1	29	45	35 ⁹	0.13	6.2	6.1	0.5	0.45	51.6*	122	1.11*
2	33	46	36 ²	0.29	9.5*	4.9	0.9	0.49	40.7	179*	0.99*
3	Term	60	36 ⁹	0.18	4.8	7.7	1.3	0.44	46.7	38†	1.41

FIGURE 2 The change in $\dot{V}_i$, $P_{ET}CO_2$, $\dot{V}_T$ and T_{tot} during halothane anaesthesia are shown. Intragroup statistical differences from the pre-emergence (FiH 0%) value are indicated ($P < 0.05$).

Postconceptional age made no obvious difference to the $\dot{V}_i$ at any concentration of FiH (Figure 1). There was no difference between groups in the response to halothane for $\dot{V}_i$, $\dot{V}_T$ and $P_{ET}CO_2$ (Figure 2).

The response of infants >48 wk PCA supports the notion that the principle effect of halothane on ventilatory control in these infants is on parameters of Timing. Breath timing is a measure of the rhythmicity of breathing and reflects both the intrinsic rhythmicity of the neural network of the pacemaker generating the underlying rhythm and its modulation by chemoreceptive input, neural input and pharmacologic input. von Euler modeled the inspiratory off switch mechanism as having two progressively increasing excitatory inputs which terminated inspiration when a given threshold was reached.⁹ The first was from volume-related afferent input from the pulmonary stretch receptors and the second from progressively increasing centrally generated inspiration-related activity.

The ratio T_i^{occ}/T_i assesses the relative influence of the first and is, therefore, a measure of the Hering Breuer lung inflation reflex (HBR). In the pre-emergence state it was >1.0 suggesting that pulmonary input was an

FIGURE 3 The effect of halothane on the timing parameters T_i and T_i^{occ}/T_i is shown. In infants >48 wk PCA both decreased with increasing F_{ET}H ($P < 0.05$). In infants <48 wk only the timing parameters T_i decreased.

FIGURE 4 The effect of halothane on the amplitude (drive) parameters $\dot{V}_T/T_i$ and dP/dt . The $\dot{V}_T/T_i$ decreased with halothane administration in both groups whereas dP/dt did not. Intragroup statistical differences from the pre-emergence (FiH 0%) value are indicated ($P < 0.05$).

important factor in terminating inspiration.¹⁹ This HBR remains active beyond the neonatal period. In infants up to two months of age Rabbitte *et al.*²⁰ showed a $>38\%$ prolongation of T_i during airway occlusion at end inspi-

TABLE II Demographic data for infants <48 wk PCA. Two infants experienced postoperative desaturations.

Patient	Gestational age at birth	PCA (wk)	Wt (kg)	Hg g · L ⁻¹	Apnoea intraop	Desat/Apnoea postop	Preop apnoea
1	29 wk	45	3.9	88	Y	Y	Y Remote
2	33 wk	46	3.6	113	Y	Y	Y
3	Term	46	4.5	94	N	N	N
4	Term	41	4.3	79	N	N	N
5	34 wk	43	4.7	105	N	N	N
6	Term	44	4.3	140	N	N	N
7	32 wk	46	6.1	96	N	N	N
8	Term	45	4.0	127	N	N	N
9	Term	45.5	5.8	97	N	N	N
10	Term	45	5.8	128	N	N	N
11	Term	47	5.3	118	N	N	N
12	Term	44.5	5.2	123	N	N	N

ration, a value which agrees with the pre-emergence Ti^{occ}/Ti of 1.5. In infants >48 wk PCA the ratio decreased with halothane administration. Since both Ti and T_{tot} decreased with halothane administration, this would suggest that the relative importance of the pulmonary volume-related feedback to inspiratory duration decreased and the duration of inspiration was determined primarily by centrally generated inspiration-related activity. This relative increase in the contribution of central activity to the duration of inspiration would be consistent with experimental brainstem preparations which suggest that halothane exerts on structures rostral to the brainstem to produce its characteristic tachypnea.^{21,22}

In contrast Ti^{occ}/Ti did not decrease in infants <48 wk PCA during halothane administration. This implies that pulmonary volume related feedback remained an important determinant of inspiratory duration during halothane administration. The finding that Ti and T_{tot} decreased by a lesser extent than older infants and that Ti^{occ}/Ti did not change may indicate that halothane had a different effect on central structures which influence timing parameters in infants <48 wk PCA.

The parameters of Shape Ci/Ti and Ti/T_{tot} did not change during halothane anaesthesia supporting a previous observation that breath shape is robust and relatively unaffected by halothane.^{12,15,23}

The parameters of Amplitude V_T/Ti and dP/dt showed opposite dependencies with FiH . Whereas V_T/Ti decreased dP/dt did not change consistently with halothane administration. Interpretation of dP/dt solely as a parameter of respiratory drive is complicated by the decrease in functional residual capacity (FRC) which is associated with halothane anaesthesia^{24,25} since lung volume may affect the force length characteristics of the diaphragm and thereby the value of dP/dt . We were able

to study an infant who breathed quietly from a mask during caudal anaesthesia for bilateral hernia repair. (Since this baby was not anaesthetized the FRC would not be expected to decrease.) The infant was now 43 wk PCA (2.4 kg) and had a history of apnoea and bronchopulmonary dysplasia. During spontaneous ventilation the $\dot{V}_i$ was $10.4 \text{ L} \cdot \text{min}^{-2} \cdot \text{m}^{-1}$, $V_T = 8.6 \text{ ml} \cdot \text{kg}^{-1}$, T_{tot} was 0.8 sec. The dP/dt was $90.8 \text{ cm} \cdot \text{sec}^{-1}$.

In three patients spontaneous ventilation could not be established at an FiH 2% ($PETCO_2$ 70 mmHg). Patient 1 (Table I) was expremature born at 33 wk PCA with a diagnosis of congenital tubular acidosis and had a preoperative history of apnoea associated with gastroesophageal reflux. The pre-emergence $\dot{V}_i$ was the highest value for any patient studied and may represent a baseline $\dot{V}_i$ consistent with chronic renal tubular acidosis. Patient 2 was born at 29 wk PCA. Patient 3 was a term infant with an unremarkable preoperative history.

Two of these infants had postoperative arterial oxygen desaturation (Table II), although the relevance of the pre-emergence parameters of ventilation summarized in Table I to their postoperative course is not clear. The first apnoea in patient 1 occurred 3.5 hr after arriving in the recovery room and probably represents a continuation of his preoperative ventilatory pattern. Patient 2 had experienced apnoeas in the first week of life but had been apnoea free for six weeks prior to surgery. The trachea was extubated when the infant was awake in the operating room but he arrived in the recovery room with a saturation while breathing room air of 85%. He continued to require oxygen to maintain a saturation >95% for seven hours postoperatively. Fourteen hours postoperatively, during sleep, he desaturated to a room air saturation of 93% and required oxygen. There were no apnoeas and no comment was made on the pattern of breathing.

Investigators have suggested that the increased risk of postoperative apnoea in infants is due to an instability of the central pattern generator for breath rhythmicity.^{2,4,5} However in a large series of unanaesthetized infants and premature babies, no consistent relationship between periodic breathing and apnoea was demonstrated.²⁶ Krane reported a postoperative study of expremature infants and showed a 33% incidence of oxygen desaturation which was not consistently associated with apnoea although there was an association with an irregular respiratory pattern.⁷ Therefore the relationship between age, apnoea and postoperative desaturation remains undefined.

To summarize, the findings of this study support our previous work that in infants, $\dot{V}_i$ was decreased during halothane anaesthesia and that the shallow pattern of breathing predisposed to CO_2 retention. Parameters of breath shape were unchanged. Respiratory drive was preserved but respiratory efficiency was impaired. Importantly the parameters of breath Timing showed a striking difference between younger and older infants. Our findings are consistent with the notion that determinants of the pattern of breath Amplitude and breath Shape are independent of those influencing breath rhythmicity. This age related difference in the behaviour of the Timing parameters to halothane may represent an immaturity of the neural network of the respiratory centre.

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References

- 1 Steward DJ. Preterm infants are more prone to complications following minor surgery than are term infants. *Anesthesiology* 1982; 56: 304-6.
- 2 Kurth CD. Postoperative arterial oxygen saturation: what to expect (Editorial). *Anesth Analg* 1995; 80: 1-3.
- 3 Welborn LG, Hannallah RS, Fink R, Ruttimann UE, Hicks JM. High-dose caffeine suppresses postoperative apnea in former preterm infants. *Anesthesiology* 1989; 71: 347-9.
- 4 Welborn LG, Ramirez N, Oh TH, et al. Postanesthetic apnea and periodic breathing in infants. *Anesthesiology* 1986; 65: 658-61.
- 5 Coté CJ, Kelly DH. Postoperative apnea in a full-term infant with a demonstrable respiratory pattern abnormality. *Anesthesiology* 1990; 72: 559-61.
- 6 Adropoulos DB, Heard MB, Johnson KL, Clarke JT, Rowe RW. Postanesthetic apnea in full-term infants after pyloromyotomy. *Anesthesiology* 1994; 80: 216-9.
- 7 Krane EJ, Haberkern CM, Jacobson LE. Postoperative apnea, bradycardia, and oxygen desaturation in formerly premature infants: prospective comparison of spinal and general anesthesia. *Anesth Analg* 1995; 80: 7-13.
- 8 Harnik EV, Hoy GR, Potolicchio S, Steward DR, Siegelman RE. Spinal anesthesia in premature infants recovering from respiratory distress syndrome. *Anesthesiology* 1986; 64: 95-9.
- 9 Kurth CD, LeBard SE. Association of postoperative apnea, airway obstruction, and hypoxemia in former premature infants. *Anesthesiology* 1991; 75: 22-6.
- 10 Henderson-Smart DJ, Pettigrew AG, Campbell DJ. Clinical apnea and brain-stem neural function in preterm infants. *N Engl J Med* 1983; 308: 353-7.
- 11 Brown KA, Bissonnette B, Holtby H, Ein S, Shandling B. Minute ventilation during mask halothane anaesthesia in infants and children. *Can J Anaesth* 1993; 40: 112-8.
- 12 Brown KA, Reich O, Bates JHT. Ventilatory depression by halothane in infants and children. *Can J Anaesth* 1995; 42: 588-96.
- 13 Feldman JL, Smith JC, Ellenberger HH, et al. Neurogenesis of respiratory rhythm and pattern: emerging concepts. *Am J Physiol* 1990; 259: R879-R886.
- 14 Fisher DM. When is the ex-premature infant no longer at risk for apnea? (Editorial). *Anesthesiology* 1995; 82: 807-8.
- 15 Reich O, Brown K, Bates JHT. Breathing patterns in infants and children under halothane anesthesia: effect of dose and CO_2 . *J Appl Physiol* 1994; 76: 79-85.
- 16 Derrene J-P, Couture J, Iscoe S, Whitelaw WA, Milic-Emili J. Occlusion pressures in men rebreathing CO_2 under methoxyflurane anesthesia. *J Appl Physiol* 1976; 40: 805-14.
- 17 Milic-Emili J, Zin WA. Relationship between neuromuscular respiratory drive and ventilatory output. In: *The Handbook of Physiology. The Respiratory System*. Bethesda, Maryland: The American Physiological Society, 1986; 631-46.
- 18 Dunnett CW. A multiple comparison procedure for comparing several treatments with a control. *Journal of American Statistical Association* 1955; 50: 1096-21.
- 19 von Euler C. On the central pattern generator for the basic breathing rhythmicity. *J Appl Physiol* 1983; 55: 1647-59.
- 20 Rabbette PS, Costeloe KL, Stocks J. Persistence of the Hering-Breuer reflex beyond the neonatal period. *J Appl Physiol* 1991; 71: 474-80.
- 21 Berkenbosch A, de Goede J, Olivier CN, Quanjer H. Sites of action of halothane on respiratory pattern and ventilatory response to CO_2 in cats. *Anesthesiology* 1982; 57: 389-98.

- 22 *Gautier H, Bonora M, Zaoui D.* Influence of halothane on control of breathing in intact and decerebrated cats. *J Appl Physiol* 1987; 63: 546–53.
- 23 *Jonsson LO, Zetterström H.* Flow pattern and respiratory characteristics during halothane anaesthesia. *Acta Anaesthesiol Scand* 1985; 29: 309–14.
- 24 *Cherniack NS, Lederer DH, Altose MD, Kelsen SG.* Occlusion pressure as a technique in evaluating respiratory control. *Chest* 1976; 70: 137–41.
- 25 *Fletcher ME, Stack C, Ewart M, et al.* Respiratory compliance during sedation, anesthesia, and paralysis in infants and young children. *J Appl Physiol* 1991; 70: 1977–82.
- 26 *Barrington KJ, Finer NN.* Periodic breathing and apnea in preterm infants. *Pediatr Res* 1990; 27: 118–21.