

Respiration by Tracheal Insufflation of Oxygen (TRIO) at High Flow Rates in Apneic Dogs

Kenji URATA, Kazufumi OKAMOTO and Tohru MORIOKA

Tracheal insufflation of oxygen (TRIO) is a technique in which oxygen is introduced into the trachea at a constant flow rate via a catheter advanced to the level of the carina. We studied the effects of flow rates (0.5, 1.0, 1.5 and 2.0 $l \cdot kg^{-1} \cdot min^{-1}$) on arterial blood gases during TRIO in 6 apneic dogs. The constant flow was administered through the tip of a catheter (I.D. 2.0 mm) advanced to a site of 1 cm above the carina. After 30 min of TRIO, the mean Pa_{CO_2} at the flow rates of 0.5, 1.0, 1.5 and 2.0 $l \cdot kg^{-1} \cdot min^{-1}$ were 88 ± 20 , 76 ± 20 , 64 ± 23 and 52 ± 18 mmHg, respectively. CO_2 elimination increased as the flow rates increased from 0.5 to 2.0 $l \cdot kg^{-1} \cdot min^{-1}$.

Based on the above study, we examined the effects of TRIO at a flow rate of 3 $l \cdot kg^{-1} \cdot min^{-1}$ in another 5 apneic dogs. TRIO, at a flow rate of 3 $l \cdot kg^{-1} \cdot min^{-1}$, was able to maintain normocarbia over 4 hr. The mean Pa_{O_2} and Pa_{CO_2} at 4.0 hr were 465 ± 77 and 41 ± 4 mmHg. Although the mechanism of pulmonary gas exchange during TRIO is unclear, our study is the first to document that normocarbia can be maintained by high-flow TRIO in apneic dogs. (Key words: apnea, artificial respiration, constant-flow ventilation, respiratory arrest, tracheal insufflation of oxygen)

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Sudden respiratory arrest is a life-threatening emergency, especially in patients with upper airway abnormalities for whom effective mask ventilation or endotracheal intubation cannot be performed. Emergency tracheostomy or cricothyroidotomy may be attempted. However, these procedures are associated with serious complications¹. In addition, percutaneous transtracheal jet ventilation, which may serve as an alternative procedure, requires special equipment².

Tracheal insufflation of oxygen (TRIO) is a technique in which oxygen is introduced into the trachea at a constant flow rate

via a catheter advanced to the level of the carina³. We have recently shown that TRIO combined with external cardiac compressions can maintain adequate oxygenation and CO_2 removal in dogs during cardiac arrest⁴.

Based on the gas transport theory of high-frequency ventilation (HFV) proposed by Slutsky et al.^{5,6}, adequate CO_2 elimination can be achieved if the jet of gas is advanced further into the lungs simply by increasing gas flow during TRIO. To examine this hypothesis, we studied the effects of TRIO at high-flow rates (0.5, 1.0, 1.5 and 2.0 $l \cdot kg^{-1} \cdot min^{-1}$) on gas exchange in anesthetized and paralyzed dogs. The final objective of this study was to clarify whether TRIO could maintain normal blood gases for several hours in apneic dogs.

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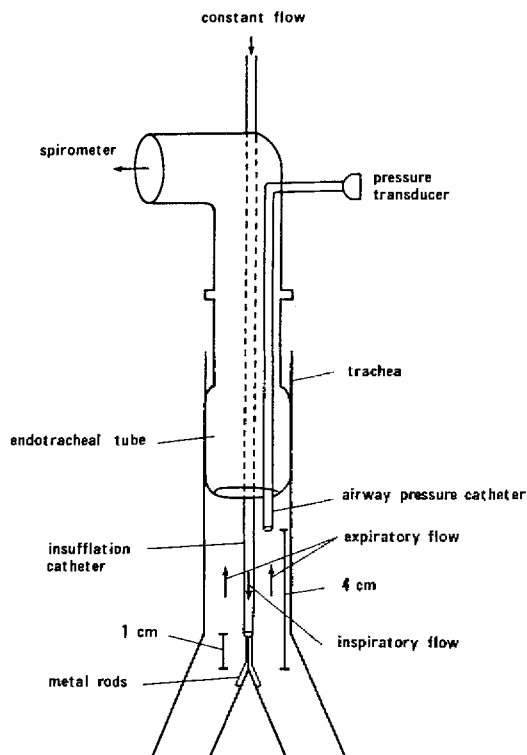


Fig. 1. Schematic diagram of experimental setup.

Methods

Eleven adult dogs of mixed breed, weighing between 8.0 and 12.0 kg, were anesthetized with sodium pentobarbital ($25 \text{ mg}\cdot\text{kg}^{-1}$ IV). The animals were restrained in the supine position on a V-shaped board and tracheostomized. Catheters were placed in a femoral vein for intravenous drug administration and in an artery for monitoring blood pressure and blood sampling. The arterial line was connected to a pressure transducer (P231D, Gould Statham) and the systemic arterial pressure was continuously recorded on a polygraph (RM-6200, Nihon Kohden). Lead II of the ECG was monitored continuously. Body temperature was monitored with a rectal thermister (MGA-III, Nihon Kohden) and maintained within the normal range using a fluid-filled heating pad.

A single-lumen polyethylene catheter (2.0 mm I.D. and 2.7 mm O.D.) was used for

TRIO, as shown in figure 1. The insufflation catheter had previously been fixed to two parallel metal rods with a bifurcation. The tip of the catheter had been fixed 1 cm proximal to the bifurcation of the metal rods. This device was inserted into the trachea through the tracheostomy until the bifurcation of the metal rods reached the carina. Thus the tip of the insufflation catheter was placed 1 cm above the carina. Metal rods were used to facilitate the insertion of the catheter and to keep it stable in a fixed position. A bronchoscope was used to confirm whether the tip of the catheter was appropriately positioned. The insufflation catheter was then connected to a tube from a gas delivery system consisting of an oxygen flowmeter (The British Oxygen CO.) and a heated humidifier (MR 310, Fisher-Paykel Medical, Inc.).

A tracheostomy tube with an inflatable cuff was then inserted so that the insufflation catheter rested on the posterior surface of the trachea outside the tracheostomy tube, and was connected to a ventilator (CV-2000, McGaw Respiratory Therapy Co.). All the animals were paralyzed with a bolus injection of pancuronium bromide ($0.2 \text{ mg}\cdot\text{kg}^{-1}$ IV). Anesthesia and muscle paralysis were maintained with a continuous infusion of sodium pentobarbital ($7 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$) and pancuronium bromide ($0.15 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$).

Airway pressure was monitored through a polyethylene catheter (1.5 mm I.D. and 2.0 mm O.D.) inserted into the endotracheal tube through the side port of a tube connector. The tip of the catheter for monitoring airway pressure was placed 4 cm proximal to the carina. Then the catheter was connected to a pressure transducer (TP-200T, Nihon Kohden) for continuous recording of airway pressure on a polygraph.

Arterial blood gas tensions and pH were measured with a Corning 168 pH/blood gas analyzer. The blood gas analyzer was recalibrated immediately prior to each determination. All blood gas values were corrected for body temperature.

Experimental protocol: In 6 dogs, we studied the effects of 30 min of TRIO at

Table 1. pH, PaO₂, PaCO₂ and mean airway pressure (Paw) before and during 30 min of TRIO at 4 different flow rates

		IPPV	TRIO				
			5 min	10 min	15 min	20 min	30 min
pH	0.5 l·kg ⁻¹ ·min ⁻¹	7.37±0.04	7.23±0.05**	7.18±0.08**	7.17±0.04**	7.14±0.06**	7.10±0.08***
	1.0 l·kg ⁻¹ ·min ⁻¹	7.35±0.05	7.26±0.07*	7.22±0.10*	7.19±0.14*	7.18±0.12**	7.16±0.12***
	1.5 l·kg ⁻¹ ·min ⁻¹	7.38±0.05	7.30±0.09	7.26±0.10	7.26±0.13	7.22±0.14	7.24±0.15 ⁺
	2.0 l·kg ⁻¹ ·min ⁻¹	7.37±0.05	7.35±0.06	7.32±0.08	7.33±0.08	7.32±0.11	7.31±0.11 ⁺
PaO ₂ (mmHg)	0.5 l·kg ⁻¹ ·min ⁻¹	444±57	419±51	423±35	435±22	391±39	405±44
	1.0 l·kg ⁻¹ ·min ⁻¹	460±18	458±21	446±22	452±48	423±68	423±32
	1.5 l·kg ⁻¹ ·min ⁻¹	439±39	454±24	430±15	438±27	435±51	441±29
	2.0 l·kg ⁻¹ ·min ⁻¹	448±49	449±42	436±36	447±22	453±28	446±28
PaCO ₂ (mmHg)	0.5 l·kg ⁻¹ ·min ⁻¹	43±3	60±7**	70±14**	73±13**	82±19*** ⁺	88±20*** ⁺
	1.0 l·kg ⁻¹ ·min ⁻¹	42±3	55±10*	63±16*	68±22*	71±19* ⁺	76±20* ⁺
	1.5 l·kg ⁻¹ ·min ⁻¹	42±3	51±11	56±15	58±18	64±22 ⁺	64±23 ⁺
	2.0 l·kg ⁻¹ ·min ⁻¹	42±3	47±8	49±13	48±12	49±16 ⁺	52±18 ⁺
Paw (cmH ₂ O)	0.5 l·kg ⁻¹ ·min ⁻¹	3.3±0.8	0.5±0.2*** ⁺	0.6±0.3*** ⁺	0.6±0.4*** ⁺	0.6±0.5*** ⁺	0.5±0.5*** ⁺
	1.0 l·kg ⁻¹ ·min ⁻¹	3.1±0.8	1.3±0.5*** ⁺	1.4±0.4*** ⁺	1.2±0.1*** ⁺	1.3±0.3*** ⁺	1.3±0.4*** ⁺
	1.5 l·kg ⁻¹ ·min ⁻¹	3.3±0.9	2.0±0.6* ⁺	2.0±0.6* ⁺	2.1±0.6* ⁺	1.9±0.4* ⁺	2.0±0.4* ⁺
	2.0 l·kg ⁻¹ ·min ⁻¹	3.4±0.7	3.2±1.0 ⁺	2.9±1.0 ⁺	2.8±0.7 ⁺	2.7±0.8 ⁺	2.9±0.8 ⁺

Values are expressed as mean ± SD. IPPV = intermittent positive pressure ventilation; TRIO = tracheal insufflation of oxygen. Significantly different compared with IPPV (paired t-test) *; $P < 0.05$ **; $P < 0.01$ Significantly different among the 4 different flow rates (one-way analysis of variance) ⁺; $P < 0.05$.

4 different flow rates (0.5, 1.0, 1.5 and 2.0 l·kg⁻¹·min⁻¹) on arterial blood gases. The flow rate of the insufflated oxygen was adjusted to the desired level by measuring the expired flow from the animal with a Wright respirometer (Haloscale, Ferraris Development & Engineering Co.) during the experiment. Based on the instructions for the respirometer, this device has the properties of reading a few per cent low at low flow rates (< 16 l·min⁻¹) and a few per cent high at high flow rates (> 16 l·min⁻¹)⁷. The order of flow rate administration was randomized. Before starting the initial run of TRIO, the animals were mechanically ventilated with pure oxygen at a tidal volume of 10–15 ml·kg⁻¹ and the ventilatory rate of intermittent positive pressure ventilation (IPPV) was adjusted to maintain PaCO₂ at 35 to 45 mmHg for at least 15 min. When PaCO₂ was found within the predetermined range, the ventilator was disconnected from the tracheostomy tube, and the initial run

of TRIO was started and maintained for 30 min. Arterial blood gas analysis and pH determination were obtained 5, 10, 15, 20 and 30 min after the start of TRIO.

Before starting the next run of TRIO with a different flow rate, dogs were placed on IPPV with pure oxygen at the high rate of 30 breaths·min⁻¹ for 5 min. Then the ventilatory rate was decreased to the pre-TRIO rate. Ventilation at this frequency was maintained for at least 15 min and arterial blood gas analysis were repeated until a steady state was achieved. This technique was used to return the body stores of CO₂ to approximately the baseline values before the next run of TRIO.

In another 5 dogs, we studied long-term runs of TRIO. After the base-line values were determined under IPPV, the effects of TRIO at a flow rate of 3 l·kg⁻¹·min⁻¹ on arterial blood gases were investigated at 10, 20, 30, 60, 90, 120, 150, 180, 210 and 240 min after the start of TRIO. The constant

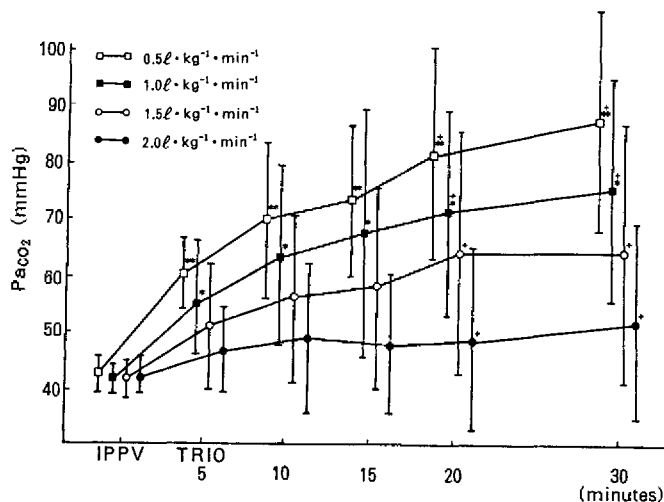


Fig. 2. Effects of 4 different flow rates on PaCO₂ during 30 min of TRIO.

Values are expressed as mean \pm SD. IPPV=intermittent positive pressure ventilation; TRIO=tracheal insufflation of oxygen. Significantly different compared with IPPV (paired t-test) *; $P < 0.05$ **; $P < 0.01$. Significantly different among the 4 different flow rates (one-way analysis of variance) +; $P < 0.05$.

Table 2. pH, PaO₂, PaCO₂, BE and mean airway pressure (Paw) during 4 hr of TRIO at 3 l·kg⁻¹·min⁻¹

	IPPV	TRIO									
		10min	20min	30min	60min	90min	120min	150min	180min	210min	240min
pH	7.39 ± 0.03	7.39 ± 0.05	7.41 ± 0.04	7.42 ± 0.04	7.39 ± 0.04	7.40 ± 0.04	7.40 ± 0.06	7.40 ± 0.02	7.39 ± 0.03	7.38 ± 0.03	7.38 ± 0.05
PaO ₂ (mmHg)	490 ± 22	506 ± 23	491 ± 37	476 ± 76	495 ± 36	494 ± 85	493 ± 35	489 ± 46	483 ± 35	495 ± 44	465 ± 77
PaCO ₂ (mmHg)	37 ± 1	37 ± 4	36 ± 4	36 ± 4	40 ± 2	39 ± 3	37 ± 4	39 ± 4	39 ± 5	38 ± 2	41 ± 4
BE (mEq·l ⁻¹)	-1.9 ± 1.8	-1.8 ± 2.5	-0.5 ± 2.0	-0.2 ± 3.2	-0.1 ± 2.3	0 ± 3.7	-0.9 ± 4.9	-0.3 ± 3.4	-0.6 ± 3.3	-1.7 ± 2.5	-0.1 ± 3.4
Paw (cmH ₂ O)	3.8 ± 0.8	5.6 ± 2.2	5.8 ± 2.0	5.6 ± 1.9	5.2 ± 2.0	5.3 ± 2.0	5.6 ± 1.8	5.1 ± 2.2	5.3 ± 1.7	4.9 ± 1.6	5.4 ± 1.9

Values are expressed as mean \pm SD. IPPV = intermittent positive pressure ventilation; TRIO = tracheal insufflation of oxygen; BE = base excess. There was no significant change with time.

intratracheal pressure monitoring and careful observation of the thorax during TRIO were carried out to ensure that the dog remained apneic throughout this experiment. The aforementioned dose of muscle relaxant was enough to prevent spontaneous breathing.

After 4 hr of TRIO, all 5 animals were sacrificed by potassium chloride (10 mEq IV). Autopsy was performed for a gross inspection of the lungs. At that time, the position of the insufflation catheter was reconfirmed to be in an appropriate position.

Statistical analysis: All values are expressed as mean \pm SD. Statistical analysis for the 4 groups of flow rates were performed using a one-way analysis of variance. Comparisons between the base-line values under IPPV and the values under TRIO were analyzed with a paired Student t-test. $P < 0.05$ was considered significant.

Results

Table 1 shows the effects of 30 min of TRIO at 4 different flow rates (0.5, 1.0, 1.5 and 2.0 l·kg⁻¹·min⁻¹) on arterial blood gases

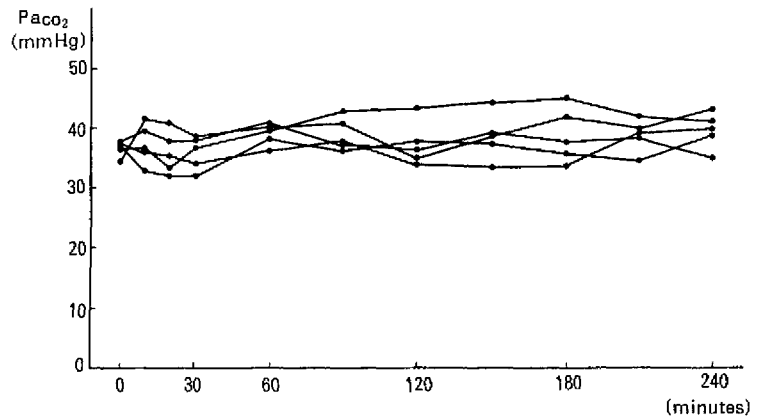


Fig. 3. Individual variations of PaCO_2 during 4 hr of TRIO at a flow rate of $3 \text{ l}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ in 5 apneic dogs.

Table 3. Hemodynamics and body temperature (BT) during 4 hr of TRIO at $3 \text{ l}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$

	IPPV	TRIO									
		10min	20min	30min	60min	90min	120min	150min	180min	210min	240min
SAP (mmHg)	184 ± 34	186 ± 36	187 ± 36	188 ± 35	187 ± 34	188 ± 29	187 ± 26	183 ± 30	183 ± 37	174 ± 39	165 ± 49
DAP (mmHg)	106 ± 14	114* ± 18	114* ± 16	117* ± 16	119** ± 14	120* ± 10	121* ± 8	120* ± 12	118 ± 18	110 ± 25	103 ± 33
MAP (mmHg)	136 ± 23	141* ± 25	143** ± 25	144* ± 24	145** ± 21	143 ± 17	143 ± 15	141 ± 17	142 ± 25	135 ± 32	126 ± 39
HR ($\text{beat}\cdot\text{min}^{-1}$)	150 ± 24	156 ± 28	156 ± 26	154 ± 25	158 ± 24	152 ± 19	154 ± 16	151 ± 17	154 ± 18	153 ± 24	148 ± 23
BT ($^{\circ}\text{C}$)	38.4 ± 0.7	38.2* ± 0.5	38.0* ± 0.6	38.0 ± 0.7	38.3 ± 0.7	38.2 ± 0.6	38.3 ± 0.8	38.1 ± 0.8	38.1 ± 0.8	38.2 ± 0.9	38.2 ± 0.7

Values are expressed as mean \pm SD. IPPV = intermittent positive pressure ventilation; TRIO = tracheal insufflation of oxygen; SAP = systolic arterial pressure; DAP = diastolic arterial pressure; MAP = mean arterial pressure; HR = heart rate; BT = body temperature. Significantly different compared with IPPV (paired t-test). *, $P < 0.05$ **; $P < 0.01$.

and mean airway pressure in 6 apneic dogs. The significant flow-dependent changes were observed in pH, PaCO_2 and mean airway pressure. As the flow rates increased, the PaCO_2 levels decreased significantly 20 min after the start of TRIO (figure 2) and the pH levels increased significantly 30 min after the start of TRIO. The mean airway pressure significantly increased 5 min after the start of TRIO as the flow rates increased, but the absolute values of mean airway pressure remained consistently low.

Table 2 shows the mean values in pH, PaO_2 , PaCO_2 , base excess and mean airway

pressure before and during 4 hr of TRIO at $3 \text{ l}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$. As shown in figure 3, individual values of PaCO_2 were within the normal range throughout 4 hr of TRIO at $3 \text{ l}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$. Neither progressive respiratory nor metabolic acidosis was observed during these long runs of TRIO. Moreover, in spite of the very high flow TRIO, mean airway pressure values were not elevated since the tracheostomy remained open, allowing excess gas flow to freely escape. No pulmonary barotrauma was observed at autopsy after 4 hr of TRIO.

Table 3 shows the changes in hemodynam-

ics and body temperature during TRIO at 3 $l \cdot kg^{-1} \cdot min^{-1}$. Diastolic and systolic arterial pressures tended to increase initially after the start of TRIO, but the overall hemodynamic changes were minimal to negligible. No hemodynamic depression due to high-flow TRIO was observed.

Discussion

We have demonstrated that CO_2 elimination during TRIO increased as the gas flow rates increased and that TRIO at a flow rate of 3 $l \cdot kg^{-1} \cdot min^{-1}$ maintained normocarbia and adequate oxygenation without hemodynamic impairment for over 4 hr in apneic dogs.

The mechanisms of gas exchange during TRIO are not well known. Based on the traditional concept of pulmonary gas exchange, CO_2 elimination should not occur without intermittent tidal gas movements. Also a tidal volume greater than the dead-space volume should be indispensable in achieving effective gas exchange during artificial ventilation. However, this traditional concept of pulmonary gas exchange has been challenged by observations demonstrating that effective alveolar ventilation can occur with a tidal volume less than the dead-space volume during HFV⁸. How can gas exchange in the lungs be produced during TRIO without tidal gas movements?

With the use of the technique of apneic oxygenation^{9,10}, it is possible to maintain adequate oxygenation for prolonged periods of time. However, Pa_{CO_2} increases progressively at a rate of about 3–6 mmHg \cdot min⁻¹ with this technique. In our experiments, we did not observe increases in Pa_{CO_2} during TRIO at a gas flow of 3 $l \cdot kg^{-1} \cdot min^{-1}$. In this regard, TRIO differs appreciably from apneic oxygenation.

Burwen et al.¹¹ have proposed that gas transport during TRIO occurs in two distinct zones. Zone I is the region just distal to the catheter where gas is transported by jet flow. Zone II is the peripheral region of the lungs free from any influence of the jet flow where gas is transported by molecular diffusion. In the latter region, Burwen et

al.¹¹ have demonstrated that cardiogenic oscillations play an important role in augmenting gas transport during TRIO in animal experiments¹¹. We also commonly observed fine oscillations of airway pressure corresponding to the heart beat during TRIO. These cardiogenic oscillations might have contributed to CO_2 elimination in the peripheral region of the lungs in our apneic dogs.

Slutsky et al.^{5,6} suggested that the crucial variable in determining CO_2 elimination during HFV might be the magnitude of the gas flow rate rather than the individual values of respiratory rate and tidal volume. Based on this theory, CO_2 elimination may be enhanced by simply increasing the gas flow rates without tidal gas movements. In the present study, CO_2 elimination increased linearly with the gas flow rates increase during TRIO. These findings are consistent with the theory of HFV proposed by Slutsky et al.^{5,6}. Using the gas transport theory of Watson et al.¹², it may be deduced that increasing the gas flow rate of TRIO could cause an increase in penetration depth of the bidirectional convective streaming in airways closest to the jets as well as augmentation of the turbulent diffusivity in the downstream region¹³. It is conceivable that an increase in the gas flow of TRIO produced an enlargement of the region of zone I, resulting in an increase in CO_2 elimination in apneic dogs.

In our study, normocarbia was obtained by insufflating gas at a flow rate of 3 $l \cdot kg^{-1} \cdot min^{-1}$. Lehnert et al.¹⁴ reported that, in apneic puppies, normocarbia was obtained by introducing a constant flow into both main-stem bronchi at about 1 $l \cdot kg^{-1} \cdot min^{-1}$, namely, constant-flow ventilation (CFV). The reason why we required a gas flow of about 3 times that mentioned above to obtain normocarbia may be accounted for by the difference in the catheter position between TRIO and CFV. The tip of the catheter position in TRIO was about 3 cm closer to the mouth in comparison with that in CFV reported by Lehnert et al.¹⁴. According to the mathematical model of gas transport studied by Ingenito et al.¹⁵, such

small changes in catheter position may produce large changes in the efficacy of CO₂ elimination.

Although we insufflated the gases at flow rates as high as 3 l·kg⁻¹·min⁻¹ into the lowest part of the trachea in apneic dogs in this study, mean airway pressure values were not elevated since the tracheostomy remained open in our animal models, allowing excess gas flow to freely escape. No hemodynamic derangement or progressive metabolic acidosis was observed during the 4 hr of TRIO, nor was pulmonary barotrauma observed in any of the dogs. However, since compliance of the human chest wall is less than that of dogs¹⁶, the airway pressure may reach dangerous levels if the same high flow rate is used on humans. In addition, this technique may produce pulmonary barotrauma and hemodynamic depression if the expiratory gas route is accidentally obstructed.

In conclusion, we have demonstrated that CO₂ elimination during TRIO increases as the gas flow rates increase, and that normocarbica can be maintained by high-flow TRIO without hemodynamic derangement over 4 hr in apneic dogs. Further studies are needed to clarify whether this technique can be used as a temporary measure to maintain the life of an apneic patient.

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References

1. Rogers LA: Complications of tracheostomy. *South Med J* 62:1496-1500, 1969
2. Klain M, Smith RB: High frequency percutaneous transtracheal jet ventilation. *Crit Care Med* 5:280-287, 1977
3. Slutsky AS, Watson J, Leith DE, Brown R: Tracheal insufflation of oxygen (TRIO) at low flow rates sustains life for several hours. *Anesthesiology* 63:278-286, 1985
4. Okamoto K, Urata K, Katsuya H, Morioka T: Effects of tracheal insufflation of oxygen (TRIO) on blood gases during external cardiac compressions in dogs under ventricular fibrillation. *J Anesth* 3:16-22, 1989
5. Slutsky AS, Drazen JM, Ingram Jr RH, Kamm RD, Shapiro AH, Fredberg JJ, Loring SH, Lehr J: Effective pulmonary ventilation with small-volume oscillations at high frequency. *Science* 209:609-611, 1980
6. Slutsky AS, Kamm RD, Rossing TH, Loring SH, Lehr J, Shapiro AH, Ingram Jr RH, Drazen JM: Effects of frequency, tidal volume, and lung volume on CO₂ elimination in dogs by high frequency (2-30 Hz), low tidal volume ventilation. *J Clin Invest* 68:1475-1484, 1981
7. Nunn JF, Ezi-Ashi TI: The accuracy of the respirometer and ventigrator. *Br J Anaesth* 34:422-432, 1962
8. Bohn DJ, Miyasaka K, Marchak BE, Thompson WK, Froese AB, Bryan AC: Ventilation by high frequency oscillation. *J Appl Physiol* 48:710-716, 1980
9. Draper WB, Whitehead RW: Diffusion respiration in the dog anesthetized by pentothal sodium. *Anesthesiology* 5:262-273, 1944
10. Draper WB, Whitehead RW: The phenomenon of diffusion respiration. *Anesth Analg* 28:307-318, 1949
11. Burwen DR, Watson J, Brown R, Josa M, Slutsky AS: Effect of cardiogenic oscillations on gas mixing during tracheal insufflation of oxygen. *J Appl Physiol* 60:965-971, 1986
12. Watson JW, Burwen DR, Kamm RD, Brown R, Slutsky AS: Effects of flow rate on blood gases during constant flow ventilation in dogs. *Am Rev Respir Dis* 133:626-629, 1986
13. Slutsky AS, Menon AS: Catheter position and blood gases during constant-flow ventilation. *J Appl Physiol* 62:513-519, 1987
14. Lehnert BE, Oberdorster G, Slutsky AS: Constant-flow ventilation of apneic dogs. *J Appl Physiol* 53:483-489, 1982
15. Ingenito E, Kamm RD, Watson JW, Slutsky AS: A model of constant-flow ventilation in a dog lung. *J Appl Physiol* 64:2150-2159, 1988
16. Bennett FM, Tenney SM: Comparative mechanics of mammalian respiratory system. *Respir Physiol* 49:131-140, 1982