Reduction of Endotracheal Tube Connector Dead Space Improves Ventilation: A Bench Test on a Model Lung Simulating an Extremely Low Birth Weight Neonate

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BACKGROUND: The reduction of instrumental dead space is a recognized approach to preventing ventilation-induced lung injury in premature infants. However, there are no published data regarding the effectiveness of instrumental dead-space reduction in endotracheal tube (ETT) connectors. We tested the impact of the Y-piece/ETT connector pairs with reduced instrumental dead space on CO_2 elimination in a model of the premature neonate lung. METHODS: The standard ETT connector was compared with a low-dead-space ETT connector and with a standard connector equipped with an insert. We compared the setups by measuring the CO_2 elimination rate in an artificial lung ventilated via the connectors. The lung was connected to a ventilator via a standard circuit, a 2.5-mm ETT, and one of the connectors under investigation. The ventilator was run in volume-controlled continuous mandatory ventilation mode. RESULTS: The low-dead-space ETT connector/Y-piece and insert-equipped standard connector/Y-piece pairs had instrumental dead space reduced by 36 and 67%, respectively. With set tidal volumes (V_T) of 2.5, 5, and 10 mL, in comparison with the standard ETT connector, the low-dead-space connector reduced CO_2 elimination time by 4.5% ($P < .05$), 4.4% ($P < .01$), and 7.1% (not significant), respectively. The insert-equipped standard connector reduced CO_2 elimination time by 13.5, 25.1, and 16.1% (all $P < .01$). The low-dead-space connector increased inspiratory resistance by 17.8% ($P < .01$), 9.6% ($P < .05$), and 5.0% (not significant); the insert-equipped standard connector increased inspiratory resistance by 9.1, 8.4, and 5.9% (all not significant). The low-dead-space connector decreased expiratory resistance by 6.8% ($P < .01$) and 1.8% (not significant) and increased it by 1.4% (not significant); the insert-equipped standard connector decreased expiratory resistance by 1.5 and 1% and increased it by 1% (all not significant). The low-dead-space connector increased work of breathing by 4.7% ($P < .01$), 3.8% ($P < .01$), and 2.5% (not significant); the insert-equipped standard connector increased it by 0.8% (not significant), 2.5% ($P < .01$), and 2.8% ($P < .01$). CONCLUSIONS: Both methods of instrumental dead-space reduction led to improvements in artificial lung ventilation. Negative effects on resistance and work of breathing appeared minimal. Further testing in vivo should be performed to confirm the lung model results and, if successful, translated into clinical practice. *Key words: ventilator-induced lung injury; bronchopulmonary dysplasia; very low birthweight infants; instrumental dead space; endotracheal tube connector.* [Respir Care 2016;61(2):155–161. © 2016 Daedalus Enterprises]

Introduction

Ventilator-induced lung injury is considered an important causative factor in the pathophysiology of bronchopulmonary dysplasia (BPD) in premature infants.[1] Limiting ventilator-associated lung overdistention/damage is a well-recognized approach for the prevention of BPD, but

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the best means of prevention is yet to be developed.[2,3] In extremely premature infants who require ventilation support, the instrumental dead space is relatively large, sometimes at or even exceeding the tidal volume (V_T).[4] To achieve adequate alveolar ventilation, a clinician must use a higher V_T, which increases the risk of both ventilator-induced lung injury and BPD as a result of lung overdistention with large V_T values. Another approach to this problem is to accept higher blood P_{CO_2} levels, which permits the use of a smaller V_T. This permissive hypercapnia approach has yielded improved BPD rates,[5,6] clearly demonstrating that V_T and/or breathing frequency reduction is a reasonable approach to BPD prevention. However, researchers question whether these higher P_{CO_2} levels are safe for other organs, especially the brain.[7]

The benefits of reducing instrumental dead space or mitigating its effects are well-recognized and discussed in the literature.[8,9] Multiple approaches to reduce instrumental dead space and/or its effects on patients have been proposed;[3,8-15] these suggestions even include using lung assist with extracorporeal CO_2 removal.[16] However, trimming the endotracheal tube (ETT) seems to be the only widely accepted method.[17] The most recent advance in this field was validation of high frequency oscillator ventilation as a method capable of reducing BPD.[18]

Another simple solution has been proposed: a low-dead-space ETT connector.[19] However, there is no published research regarding the effects of the low-dead-space connector. In addition, upon examining the connections between the standard endotracheal tube connector and the low-dead-space connector and a Y-piece, the author noted that the Y-piece itself has significant instrumental dead space, which is not eliminated by using the low-dead-space connector. Thus, the author designed an insert to further reduce the instrumental dead space of the entire conduit that is formed by the Y-piece and the ETT connector.

Previous studies have validated the mechanical models for comparing the impact of dead space in different combinations of the respiratory equipment.[20,21] These models eliminate the uncontrollable variables that are often present in living beings. The model used by Wald et al[21] is based on measurement of the CO_2 removal rate from a test lung connected to a ventilator with the equipment under the test. Using this model was especially attractive because the model permits the direct measurement of the patient-relevant parameters of the respiratory equipment.

In this study, comparative testing of 3 ETT and Y-piece setups was performed. The setup influence on CO_2 elimination time and additional mechanical parameters of the respiratory system, including resistance and work of breathing, was measured for various tidal volumes using the mechanical model.

QUICK LOOK

Current knowledge

Positive pressure ventilation in a premature newborn baby is one of the major factors responsible for the ventilator associated trauma leading to development of broncho-pulmonary dysplasia. Reduction in the instrumental dead space improves alveolar ventilation and can reduce the ventilator associated lung trauma.

What this paper contributes to our knowledge

In a lung model study, reduction of instrumental dead space at the level of the endotracheal tube adaptor results in more efficient ventilation. Changes in airway resistance were small. If confirmed in in vivo experiments, this modification could eventually lead to reduction in incidence and/or severity of broncho-pulmonary dysplasia.

Methods

This research was exempted from Institutional Review Board review by the University of Oklahoma Institutional Review Board.

I adapted the previously established mechanical model[21] to simulate the ventilator settings and parameters of a human patient on the lower end of viability, with a body weight of about 500 g. The typical parameters of larger premature infants were also studied. All experiments were performed at room temperature with no warming or humidification equipment or mode used.

Equipment and Setup

A SERVO-i ventilator (Maquet, Wayne, New Jersey) equipped with an Air Life infant isothermal breathing circuit with a 90° Y-piece (Cardinal Health, Dublin, Ohio; catalog number MR850) was used in neonatal mode. In order to exclude potential interfering variables, air filters, humidifiers, and warmers were not used. A 46-mL neonatal artificial test lung supplied with the ventilator was connected to the Y-piece of the circuit using a 2.5-mm internal diameter ETT via a 15-mm connector with standard dimensions (both from Portex/Smith Medical, Dublin, Ohio). An extra volume of 1.5 mL was added between the ETT and the artificial lung to represent the anatomical dead space. The ETT was cut to 13 cm in length. The exhalation elbow of the circuit had a custom-embedded probe of the CO_2 analyzer (Philips Monitor, Andover, Massachusetts). The CO_2 analyzer produced a sine wave of CO_2 concentration in the exhaled air on the monitor. The

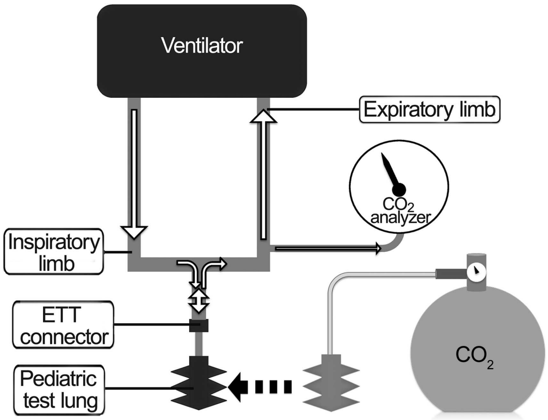

Fig. 1. Schematic of study setup.

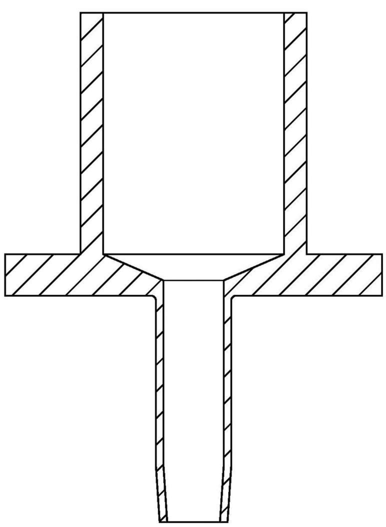

Fig. 2. Standard endotracheal tube connector.

schematic representation of the equipment setup is presented in Figure 1.

The ventilator/circuit was assembled according to the manufacturer's specifications. The full pre-use calibration and testing procedure was performed following the manufacturer's guidelines, as detailed in the user manual. The circuit compliance compensation was enabled. The ventilator was set at the volume-controlled continuous mandatory ventilation mode with PEEP of 5 cm H_2O, delivering room air at a frequency of 60 breaths/min. Inhalation time was set at 0.5 s with no inspiratory pause.

The experiment was performed with 3 different connector configurations used to link the Y-piece and the ETT: (1) standard connector that was supplied with the ETT (Fig. 2); (2) low-dead-space connector provided by Hallowell EMC, Pittsfield, Massachusetts (Fig. 3) (the connector is manufactured with a sample port, which was occluded during the experiment); (3) standard connector as supplied with the ETT, but equipped with an insert

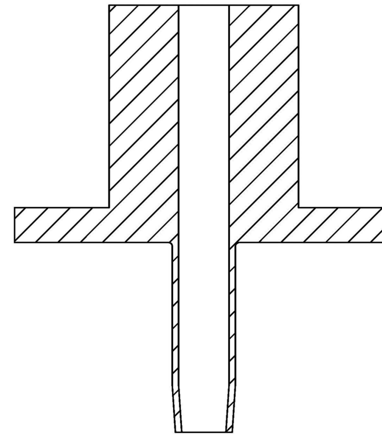

Fig. 3. Low-dead-space endotracheal tube connector.

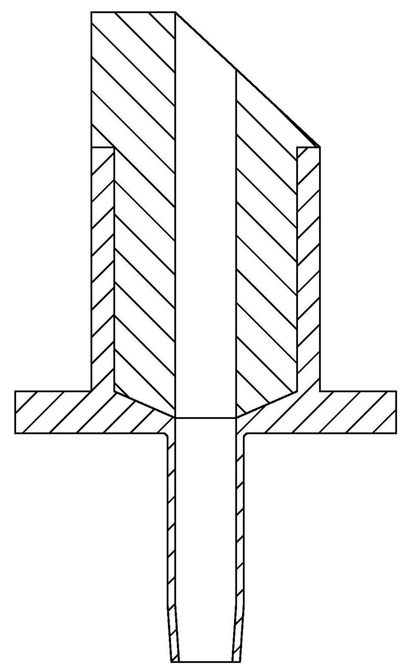

Fig. 4. Standard endotracheal tube connector with insert placed in it.

made of inert plastic with a 2.5-mm internal diameter (Fig. 4). As can be seen in Figure 4, the insert fills the excessive dead space in the standard connector in the same fashion as the low-dead-space connector. The insert also extends into the Y-piece, further reducing its dead space.

The instrumental dead space of the combinations of the Y-piece and the ETT connectors was measured geometrically. The volume of the insert-equipped standard connector was measured by the water displacement method ascribed to Archimedes.[22] The dead space of the conduit composed of the Y-piece and the standard ETT connector with insert was calculated by subtracting the insert volume from the measured dead space of the Y-piece and standard ETT connector combination.

Procedure

Before the experiment, the ventilator was put in standby mode. The CO_2 analyzer was switched on and warmed up for 20 min. Then the artificial lung with its additional anatomical dead space was filled with 100% CO_2 (United States Pharmacopoeia) and immediately attached to the ETT, without any agitation or disturbance. Following attachment of the artificial lung to the ETT, the ventilator was started, and the CO_2 analyzer monitor was observed for CO_2 concentration sine waves, synchronous with breaths. The time required for complete removal of CO_2 was recorded in full seconds, equal to the number of breaths. The complete removal of CO_2 out of the test lung was evidenced by a flat line at the zero mark on the monitor. Following observation of the flat line on the CO_2 analyzer monitor for 10 s, the artificial lung was manually squeezed several times to move most of the gas out to the lung, thus to ensure the absence of any residual CO_2. Each combination of connections was tested 10 times, with V_T set at 2.5, 5, and 10 mL.

In a separate run under the same conditions, we tested the effect of the connectors on the measured and calculated ventilator parameters. These parameters included end-expiratory pressure, peak airway pressure, end-expiratory flow, dynamic compliance, resistance at inspiration and expiration, and work of breathing. Each combination of connections was tested 10 times (10 breaths), with V_T set at 2.5, 5, and 10 mL. Room air was used for filling of the test lung and its ventilation. The data were downloaded from the ventilator and analyzed.

Statistical analysis was performed with a one-way analysis of variance test for independent samples with a post hoc Tukey test. The mean values of the 10 runs of each experiment were compared. An α level of <0.05 was considered significant. The calculations were performed using an online tool (http://vassarstats.net/anova1u.html, *Accessed September 18, 2015*).

Results

The instrumental dead space of the conduit formed by the Y-piece and the ETT connector was measured/calculated as 3.72 mL for the standard configuration, 2.37 mL (36% less) for the Y-piece with the low-dead-space connector, and 1.22 mL (67% less) for the combination of the Y-piece and standard connector with the insert in place.

The complete elimination of CO_2 out of the test lung was confirmed by the absence of any detectable CO_2 following a few complete squeezes of the test lung at the end of each experiment. The time required for complete elimination of CO_2 out of the artificial lung is shown in Figure 5. The insert-equipped standard connector reduced the elimination time by 13.5, 25.1, and 16.1% (all $P < .01$), compared with the standard connector alone, as measured with V_T of 2.5, 5, and 10 mL, respectively. The low-dead-space connector reduced the time by 4.5% ($P < .05$), 4.4% ($P < .01$), and 7.1% (not significant), compared with the standard ETT connector, as measured with V_T of 2.5, 5, and 10 mL, respectively.

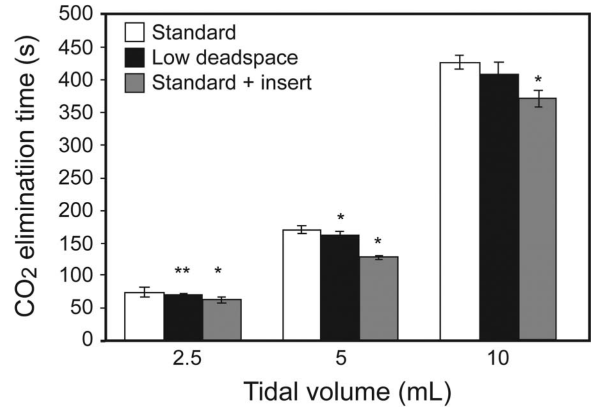

Fig. 5. The time required for complete elimination of CO_2 out of the test lung. * = $P < .01$ compared with the standard connector; ** = $P < .05$ compared with the standard connector. Whiskers denote ± SD.

Both the low-dead-space connector and the insert-equipped standard connector changed the respiratory mechanics parameters of the system, which are summarized in Table 1. Inspiratory resistance increased but reached statistical significance only with the low-dead-space connector, ventilated with V_T of 2.5 and 5 mL (up 17.8 and 9.6%). However, the corresponding increase of work of breathing was 4.7 and 3.8%, and the increase in dynamic compliance was 8.2 and 10.8%. In contrast, there was a declining trend in the expiratory resistance, which reached statistical significance with the low-dead-space connector, ventilated with V_T of 2.5 mL (down 6.8%).

Discussion

This study provides experimental support for the hypothesis that reduction of instrumental dead space leads to improvements in extremely low-birth weight neonate lung bench model ventilation. In practical terms, this means that the same level of alveolar ventilation could be achieved with less minute ventilation with the use of low-dead-space equipment. This reduction in the required minute ventilation allows the clinician to employ less harmful levels of V_T or peak inspiratory pressure and/or breathing frequency while keeping blood P_{CO_2} within the normal range. All of these parameters have been shown to directly correlate with severity of BPD.[23]

Table 1. Influence of Different Adaptors on Pulmonary Mechanics Parameters

	V_T = 2.5 mL			V_T = 5 mL			V_T = 10 mL		
	S	LD	Ins	S	LD	Ins	S	LD	Ins
Peak airway pressure, mean ± SD cm H_2O	10.25 ± 0.032	10.18 ± 0.017	10.22 ± 0.016	15.33 ± 0.046	15.28 ± 0.05	15.31 ± 0.03	26.98 ± 0.58	27.28 ± 0.07	27.29 ± 0.11
% change from S		−0.7*†	−0.3*		−0.3‡	−0.2		1.1	1.1
Inspiratory resistance, mean ± SD cm H_2O/L/s	26.35 ± 2.21	31.03 ± 2.8	28.73 ± 2.38	33.37 ± 2.5	36.57 ± 2.77	36.19 ± 2.33	41.99 ± 2.23	44.08 ± 2.65	44.48 ± 2.78
% change from S		17.8*	9.1		9.6‡	8.4		5.0	5.9
Expiratory resistance, mean ± SD cm H_2O/L/s	419.82 ± 15.63	391.22 ± 9.7	413.7 ± 10.32	404.22 ± 7.21	397.02 ± 6.71	400.14 ± 6.32	426.8 ± 7.41	432.67 ± 7.12	430.96 ± 13.54
% change from S		−6.8*†	−1.5		−1.8	−1.0		1.4	1.0
Work of breathing (ventilator), mean ± SD J/L	0.25 ± 0.007	0.27 ± 0.005	0.26 ± 0.005	0.53 ± 0.004	0.55 ± 0.009	0.54 ± 0.005	1.12 ± 0.027	1.15 ± 0.005‡	1.15 ± 0.007
% change from S		4.7*†	0.8		3.8*	2.5*		2.5	2.8*
Dynamic compliance, mean ± SD mL/cm H_2O	0.58 ± 0.012	0.62 ± 0.011	0.58 ± 0.011	0.55 ± 0.01	0.61 ± 0.018	0.57 ± 0.013	0.52 ± 0.011	0.54 ± 0.01	0.54 ± 0.008
% change from S		8.2*†	1.6		10.8*†	4.6*		3.3*	3.7*
End-expiratory flow, mean ± SD L/min	0.002 ± 0.004	0.012 ± 0.006	0 ± 0	0.007 ± 0.008	0.053 ± 0.018	0.025 ± 0.01	0.05 ± 0.02	0.115 ± 0.021	0.126 ± 0.016
% change from S		567†	−100		700*†	282‡		127*	150*
End expiratory pressure, mean ± SD cm H_2O	5.52 ± 0.009	5.49 ± 0.01	5.503 ± 0.005	5.58 ± 0.012	5.55 ± 0.013	5.56 ± 0.01	6.08 ± 0.036	6.09 ± 0.014	6.09 ± 0.014
% change from S		−0.5*	−0.3*		−0.4*	−0.4*		0.1	0.2

* Difference detected with analysis of variance testing and $P < .01$ in comparison with the standard connector.
† Difference detected with analysis of variance testing and $P < .01$ in comparison with the insert-equipped standard connector.
‡ Difference detected with analysis of variance testing and $P < 0.05$ in comparison with the standard connector.
S = standard connector
LD = low-dead-space connector
Ins = standard connector equipped with an insert

Since only one specific setup was used, the findings might be applicable only to the specific combination of equipment and parameters that was used in this study (ie, ETT cut to 13 cm, inspiratory time 0.5 s and breathing frequency 60 breaths/min). Real-life situations would include several other factors that might shape the effect of the instrumental dead-space reduction, like the air leak around an uncuffed ETT, routinely used in neonates. It is also unknown whether the effect would be clinically relevant, even if the findings were confirmed by a study with actual patients being ventilated. However, taking into consideration the anticipated benefits and the lack of likely negative outcomes associated with low-dead-space equipment, it is prudent to choose equipment combinations with lower instrumental dead space whenever possible.

Another finding in this study is the confirmation of complete CO_2 elimination out of an artificial lung by ventilation with V_T below dead space. This phenomenon was previously observed in vivo[4] and implied in bench tests.[21,24] This study actually demonstrated that the CO_2 elimination was complete in the bench model.

In everyday practice, in-line suction devices and end-tidal CO_2 measurement connectors could further increase the instrumental dead space. In light of these findings, attempts to eliminate their use where possible and/or to choose combinations with minimal instrumental dead space might result in similar effects. However, clinical studies are required to confirm that using the low-dead-space connector, the insert-equipped standard connector, or any other method of instrumental dead-space reduction produces the expected improvements in the BPD rate or severity.

Both the low-dead-space connector and the insert-equipped standard connector are significantly narrower than the standard ETT connector and could increase the resistance of the system. Indeed, using both connectors resulted in increased inspiratory resistance. However, the corresponding effect on ventilator work of breathing was barely significant (<5%). Surprisingly, the expiratory resistance had a trend toward reduction and even reached statistical significance with LD ventilated with V_T of 2.5 mL (6.8% less). Changes in other parameters either did not reach statistical significance or were of such a low magnitude that one would not expect any clinically relevant effect from these changes.

With the assumption that the standard ETT connector has no resistance at all and the gas flow is always laminar, the addition of the low-dead-space connector or the insert-equipped standard connector would add 15 mm (low-dead-space connector) or 20 mm (insert-equipped standard connector) to the length of the ETT, which is usually cut to no less than 10 cm. Since the resistance of a tube is directly proportional to its length, the addition of low-dead-space connectors would be capable of increasing resistance by no more than 20%. In the described experiment, the ETT was cut to 13 cm, so the highest expected addition to the resistance would be 15.4% for the insert-equipped standard connector and 11.5% for the low-dead-space connector. The observed maximal increase in inspiratory resistance was on the order of these expected values: 9.06% for the insert-equipped standard connector and 17.79% for the low-dead-space connector. However, the observation of decreased expiratory resistance contradicts this theory. This might be because the gas flow within many parts of the circuit is not laminar, but turbulent. This turbulence increases resistance to the gas flow. Therefore, one could speculate that the observed differences between the theoretically expected and measured resistances are due to changes in the turbulence of flow with the introduction of the new connectors.

Conclusions

In summary, the insert-equipped standard connector and the low-dead-space connector somewhat increase the total inspiratory resistance of the system and ventilator work of breathing but are unlikely to affect patients on full ventilatory support, since the ventilator would compensate for the changes. The lack of any observed increase in expiratory resistance indicates that expiration time would not be affected. Thus, one should not expect an increase in the risk for auto-PEEP and breath-stacking.

Increased inspiratory resistance with a corresponding increase of work of breathing, although relatively small (<5%), could affect patients during weaning from the ventilator. The significance of this effect should be further explored in an animal model and/or in clinical situations.

Although clinical use of the proposed insert may be not practical, it shows the importance of further work toward reducing instrumental dead space while ventilating an extremely small patient, like an extremely low-birth weight infant. It is also important to consider that the low-dead-space connector has been reported to be incompatible with some devices.[25]

The best known prevention for BPD is reducing the time spent on the ventilator. In intubated infants, multiple approaches to minimize ventilator-induced lung trauma have been described, but there is currently no universally effective and safe measure for BPD prevention or therapy. At the same time, BPD is a major problem affecting many infants.

Any method that reduces the incidence or severity of BPD by even a small fraction could lead to a significant number of prevented and/or attenuated cases. This study has provided experimental evidence that supports using a simple method to decrease instrumental dead space, which allows for reduced ventilator settings without compromising CO_2 elimination. Pending confirmation in the clinical setting, using this method of instrumental dead-space reduction should be expected to translate into a lower incidence and/or severity of BPD.

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