The Effects of Apparatus Dead Space on P_{aCO_2} in Patients Receiving Lung-Protective Ventilation

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BACKGROUND: Lung-protective ventilation using tidal volume (V_T) of 4–6 mL/kg (predicted body weight) reduces mortality (compared with traditional V_T) in patients with acute respiratory distress syndrome and acute lung injury. Standardized use of lower V_T can result in respiratory acidosis and has raised new concerns about the appropriate configuration of the ventilator circuit, especially in regard to the dead space (V_D) of the apparatus. We hypothesized that, with a patient receiving lung-protective ventilation, the removal of all apparatus dead space from the circuit would reduce P_{aCO_2} and allow a reduction in minute ventilation. METHODS: All the studied patients met the American-European consensus-conference criteria for acute respiratory distress syndrome/acute lung injury, were receiving a lung-protective ventilation strategy, were > 18 years of age, and were hemodynamically stable. We prospectively tested 3 different ventilator-circuit configurations, in random sequence, for 15 min each: (1) standard hygroscopic heat-and-moisture exchanger (HME) with 15-cm flexible tubing, (2) 15-cm flexible tubing only, (3) no HME or flexible tubing. V_T, respiratory rate, positive end-expiratory pressure, and fraction of inspired oxygen were maintained constant throughout the study, and exhaled CO_2 was measured continuously. Physiologic dead space (V_D/V_T) was calculated using the Enghoff modification of the Bohr equation. RESULTS: Seven patients were studied. Removal of the HME from the circuit significantly decreased V_D/V_T (by approximately 6%) and P_{aCO_2} (by approximately 5 mm Hg). Removal of both the HME and flexible tubing from the circuit reduced V_D/V_T by an additional 5%, and P_{aCO_2} by an additional 6 mm Hg. With both circuit-configuration changes, minute ventilation fell from a mean of 11.51 L/min to 10.35 L/min, and pH increased from 7.30 to 7.38. Carbon-dioxide production did not change significantly. CONCLUSION: In patients receiving lower-V_T ventilation, removing all the apparatus V_D from the ventilator circuit reduces P_{aCO_2} and increases pH, at a lower minute ventilation. This information will help guide ventilator-circuit configuration for patients receiving lung-protective ventilation. *Key words: acute respiratory distress syndrome, ARDS, dead space, lung-protective ventilation, mechanical ventilation, hypercapnia.* [Respir Care 2006;51(10):1140–1144. © 2006 Daedalus Enterprises]

Introduction

First described in 1967, acute respiratory distress syndrome (ARDS) is a difficult disease to manage and is associated with high mortality.[1] Furthermore, laboratory and clinical research suggests that the use of a conventional tidal volume (V_T) (10–12 mL/kg) may result in ventilator-induced lung injury, which contributes to poor outcome.[2] A recent large prospective randomized study found that the use of lower V_T (6 mL/kg predicted body weight versus conventional V_T of 12 mL/kg) reduced mortality from 39.8% to 31%.[3] This lower-V_T method is known as lung-protective ventilation.

With the increased use of lung-protective ventilation in adult patients with ARDS/acute lung injury (ALI), new interest has arisen over the most efficacious configuration for the ventilator circuit. Of particular interest is the question of whether the dead space (V_D) of the apparatus in a standard ventilator circuit (such as the flexible tubing and heat-and-moisture exchanger [HME]) significantly affects the total V_D and ventilation requirements in patients with

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Carl R Hinkson RRT presented a version of this paper at the 51st International Respiratory Congress of the American Association for Respiratory Care, held December 3–6, 2005, in San Antonio, Texas.

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ARDS/ALI. When V_T is in the 8–12 mL/kg range, apparatus V_D may not be an important factor in determining total ventilatory requirements, but this may not be the case during low-V_T ventilation. In addition, patients with ARDS have severe gas-exchange impairment, including compromised CO_2 elimination, which makes normalizing the P_{CO_2} difficult or impossible in many cases.[4] We hypothesized that the removal of all apparatus V_D from a ventilator circuit during lung-protective ventilation would reduce P_{aCO_2}, increase pH, and allow a reduction in minute ventilation ($\dot{V}_E$).

Methods

The study was conducted between September 28, 2004, and January 18, 2005, at Harborview Medical Center, which is a level-one trauma, burn, and acute-care hospital in Seattle, Washington. Patients who met the study criteria were identified during respiratory-care shift report by the study authors. Patients were selected who met the American-European consensus-conference criteria[5] for ARDS/ALI, were > 18 years of age, were on lung-protective ventilation protocol (V_T of 4–6 mL/kg predicted body weight), and were hemodynamically stable. The patients were managed according to a local protocol that is based on the ARDS Network protocol for lung-protective ventilation.[3] The University of Washington investigational review board approved the study, and informed consent was obtained from each patient's legal next of kin prior to any data collection. Patients were studied nonconsecutively.

At the time of the study, the patients were not undergoing any procedures and were reasonably calm and synchronous with the ventilator (Servo 300, Siemens/Maquet, Bridgewater, New Jersey). A respiratory monitor (CO_2SMO Plus 8100, Novametrix Medical Systems, Wallingford, Connecticut) was connected at the circuit Y-piece to measure exhaled CO_2 (volumetric capnography).[6] The device was warmed and calibrated. Three ventilator-circuit configurations were tested:

1. Standard hygroscopic HME (Humid-Vent Filter Light, Hudson RCI, Research Triangle Park, North Carolina) with an approximately 15-cm piece of flexible tubing (Tube-Flex, Puritan Bennett, Pleasanton, California)
2. Flexible tubing (approximately 15 cm) only
3. No HME or flexible tubing

The order of configuration was randomized for each patient, and the baseline configuration was the setup the patient had at the time of the study.

After 15 min on one of the circuit configurations, an arterial blood sample was drawn from an indwelling catheter, and, from the patient's exhaled gas we measured end-tidal carbon dioxide, mixed expired carbon dioxide, and carbon-dioxide production. Blood pressure, heart rate, and respiratory rate were monitored. V_T, set respiratory rate, positive end-expiratory pressure, and fraction of inspired oxygen were maintained constant throughout the study period. Then the circuit was changed to the next configuration and, after 15 min elapsed, the data gathering was repeated with that circuit configuration.

The data were analyzed using spreadsheet software (Excel, Microsoft, Redmond, Washington) and graphing software (Prism, GraphPad Software, San Diego, California). Physiologic V_D (V_D/V_T) was calculated using the Enghoff modification of the Bohr equation:[7]

$$V_D/V_T = (P_{aCO_2} - P_{eCO_2})/P_{aCO_2}$$

in which P_{eCO_2} is the mixed expired pressure of carbon dioxide.

The data are presented as mean ± standard deviation. Differences between conditions were compared using a paired *t* test with the Bonferoni correction for multiple comparisons. Differences were considered significant when $p < 0.05$. Linear regression was performed to determine the correlation coefficient between the fraction of apparatus V_D (normalized to the maximum [HME + flexible tubing]) and the mean of measured variables, with linearity confirmed with the runs test.

Results

Seven patients were enrolled in the study (Table 1). The volume of the HME was 60 mL, and that of the flexible tubing was 55 mL, for a total maximum apparatus V_D of 115 mL. Removal of the HME from the circuit decreased V_D/V_T by approximately 6% ($p = 0.01$) and decreased P_{aCO_2} by 5 mm Hg ($p = 0.007$) (Fig. 1). Removing both the HME and the flexible tubing decreased V_D/V_T by an additional 5% ($p = 0.007$) and decreased P_{aCO_2} by an additional 6 mm Hg ($p = 0.03$). Removing both the HME and the flexible tubing allowed for a $\dot{V}_E$ decrease, from a mean of 11.51 L/min to 10.35 L/min ($p = 0.02$) and increased pH from 7.30 to 7.38 ($p = 0.005$) (Fig. 2). The relationships between apparatus V_D and V_D/V_T and $\dot{V}_E$ were linear, with correlation coefficients of 0.99 and 0.94, respectively. With removal of apparatus V_D there was a trend toward increased carbon-dioxide production, but there were no significant changes in mean arterial pressure, P_{aO_2}, or heart rate (Table 2).

Four of the studied patients were receiving V_T of 6 mL/kg, whereas the other 3 patients were receiving 4 mL/kg. Reductions in V_D/V_T and P_{aCO_2} occurred in both groups, although the effects tended to be larger among the patients receiving 4 mL/kg. For example, comparing the maximum and minimum apparatus V_D, P_{aCO_2} fell from 68 ± 10 mm Hg to 51.7 ± 8.4 mm Hg in patients who received V_T of 4 mL/kg, whereas P_{aCO_2} fell from 59.5 ± 14.5 mm Hg to

Table 1. Baseline Characteristics

Patient Number	Age (y)	Sex	Diagnosis	V_T (mL/kg)	V_T/kg
1	19	M	Motor-vehicle accident, lung resection, ARDS, closed head injury	270	4.4
2	68	M	Motor-vehicle accident, burns to 28% of total body surface area, ARDS, rib fractures	290	4
3	59	M	End-stage liver disease, polymyositis, COPD, acute lung injury, acute renal failure, fungal bacteremia	280	4.4
4	56	F	Subarchnoid hemorrhage, toric seizure, COPD, ARDS	355	6
5	25	M	ARDS, aspiration pneumonia	465	6
6	52	M	ARDS, hepatitis C, hypertension	425	6
7	54	F	Motor-vehicle accident, C2 fracture, left rib fractures, acute lung injury	275	6
Summary	Mean age 48 ± 18	5 male 2 female		Mean 337 ± 80	Mean 5.3 ± 1

ARDS = acute respiratory distress syndrome
COPD = chronic obstructive pulmonary disease

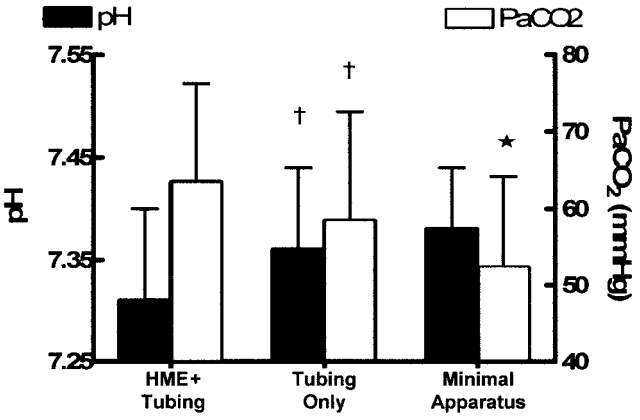

Fig. 1. Changes in pH and P_{aCO_2} with 3 ventilator-circuit configurations: (1) with both flexible tubing and heat-and-moisture exchanger (HME), (2) with flexible tubing only, and (3) with no HME or flexible tubing. * Without HME or tubing, P_{aCO_2} was significantly better ($p < 0.05$) than with tubing only. † With tubing only, both P_{aCO_2} and pH were significantly better ($p < 0.05$) than with HME plus tubing.

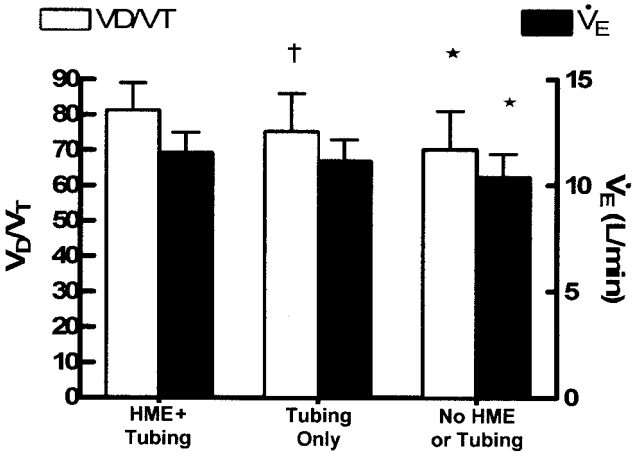

Fig. 2. Changes in physiologic dead space (which is the dead space divided by the tidal volume [V_D/V_T]) and minute volume ($\dot{V}_E$) with 3 ventilator-circuit configurations: (1) with flexible tubing and heat-and-moisture exchanger (HME), (2) with flexible tubing only, and (3) with no HME or flexible tubing. * With no HME or tubing, both V_D/V_T and $\dot{V}_E$ were significantly better ($p < 0.05$) than with tubing only. † With tubing only, V_D/V_T was significantly better ($p < 0.05$) than with HME plus tubing.

52.7 ± 15.3 mm Hg in patients who received 6 mL/kg (ie, 25% versus 17% relative change, $p = 0.007$ for difference between groups).

Discussion

ARDS/ALI is characterized by severe ventilation-perfusion mismatch, due to increased pulmonary vascular permeability and alveolar injury, leading to alveolar flooding, disruption of the hypoxic vasoconstriction response, and shunting due to collapsed alveolar units.[4] The result is severe compromise of pulmonary gas exchange, with resulting hypoxemia and hypercapnia, which is frequently resistant to conventional oxygen therapy and mechanical ventilatory support. The gas-exchange abnormality can be further demonstrated by an increase in the Enghoff modification of the Bohr V_D (physiologic V_D, V_D/V_T).[8,9] The increased V_D/V_T is believed to be due primarily to areas of shunt and low alveolar ventilation-perfusion rather than areas of high alveolar ventilation-perfusion, but the net result remains impaired CO_2 elimination, with consequent hypercapnia and respiratory acidosis, despite increased intensity of ventilatory support.[10]

Table 2. Effect of Circuit Configuration on Gas Exchange and Vital Signs*

Variable	Flexible Tubing and HME	Flexible Tubing Only	No Flexible Tubing or HME
Arterial pressure (mm Hg)	85 ± 12	81 ± 16	80 ± 13
Heart rate (beats/min)	104 ± 21	101 ± 20	95 ± 20
P_{aO_2} (mm Hg)	77 ± 17	80 ± 23	81 ± 23
$\dot{V}_{CO_2}$ (mL/min)	147 ± 56	172 ± 59	175 ± 51
f (breaths/min)	35.4 ± 6.6	34.3 ± 6.8†	31.9 ± 6.3‡

*Values are mean ± SD
†$p < 0.05$ versus no flexible tubing, no HME
‡$p < 0.05$ versus flexible tubing and HME
HME = heat-and-moisture exchanger
$\dot{V}_{CO_2}$ = carbon dioxide production

In patients who received low V_T as part of a lung-protective strategy, the apparatus V_D of the ventilator circuit may also contribute to impaired CO_2 elimination and hypercapnia. For example, the HME used in our study had a V_D of 60 mL and the flexible tubing had a V_D of 55 mL. The baseline apparatus V_D was 15 mL for the CO_2 monitor and inline suction catheter, whereas the V_T ranged from 270 mL to 465 mL, with a mean of 337 ± 80 mL. The apparatus V_D with both the HME and the flexible tubing accounted for 40.3 ± 8.5% of the V_T, and the apparatus V_D of the flexible tubing alone accounted for 21.7 ± 4.6% of V_T. The baseline apparatus V_D accounted for 4.6 ± 1.0%. Indeed, we found that removal of the HME and flexible tubing from the ventilator circuit reduced V_D/V_T, which significantly reduced P_{aCO_2} at a lower total $\dot{V}_E$. Removal of apparatus V_D was also associated with a clinically relevant increase in arterial-blood pH.

Patients on lung-protective ventilation with impaired CO_2 elimination may benefit from the removal of all possible apparatus V_D, for 3 reasons. First, removal of apparatus V_D reduces hypercapnia and increases arterial-blood pH. Second, a reduction in ventilatory demand, with an associated decrease in $\dot{V}_E$, may decrease air trapping and intrinsic positive end-expiratory pressure, with consequent reduced intrathoracic pressure, improved hemodynamics, and lower intracranial pressure. The latter is supported by observations of the effects of HMEs on ventilatory mechanics in spontaneously breathing patients.[11–13] Third, the improved CO_2 elimination may allow reducing V_T or respiratory rate, which may reduce gas trapping and ventilator-induced lung injury.

There is ongoing debate regarding the harm or benefits of hypercapnia on gas exchange and lung injury. Experimental models suggest that inhalation of CO_2 to induce hypercapnic acidosis improves P_{aO_2} in animals with normal lungs.[14,15] Inhaled CO_2 attenuated lung injury in experimental models.[16,17] In contrast, inducing hypercapnia by reducing $\dot{V}_E$ increased lung injury in rabbits treated with lipopolysaccharide.[18] In addition, the benefits of therapeutic or passive hypercapnia on gas exchange or lung injury have not been reproduced in patients with severe lung injury. A recent retrospective analysis of data from the original ARDS Network lung-protective-ventilation trial found that hypercapnia did not affect mortality in patients ventilated with low V_T (6 mL/kg) but was associated with a mortality reduction in the high-V_T group.[19] Similar to other investigators, we found no P_{aO_2} effect from manipulation of apparatus V_D and the associated changes in P_{aCO_2}.[20,21] Thus it would be premature to recommend hypercapnic acidosis as a protective or therapeutic strategy in patients with ARDS and ALI, particularly when induced by a reduction in $\dot{V}_E$.

Two other studies have examined the effects of apparatus V_D on ventilation in ARDS. Prin et al[20] studied 11 patients with ARDS. In that study the HME, which had an apparatus V_D of 100 mL, was removed when P_{aCO_2} exceeded 55 mm Hg. That study found a pH increase, from 7.20 ± 0.08 to 7.26 ± 0.06 ($p < 0.005$) and P_{aCO_2} reduction from 67 ± 9 mm Hg to 56 ± 6 mm Hg ($p < 0.003$).[20] In another study Prat et al[21] studied the effects of various-size apparatus V_D, ranging from 120 mL to 0 mL. They found a pH increase, from 7.18 ± 0.08 to 7.28 ± 0.08 ($p < 0.05$), and P_{aCO_2} reduction, from 80.3 ± 20 mm Hg to 63.6 ± 13 mm Hg ($p < 0.05$)

Our study differs from the latter 2 studies in a couple of ways. First, we did not modify the patients' ability to control their ventilation. Prin et al[20] administered cisatracurium during the study procedure, and Prat et al[21] maintained their patients' sedation level to achieve a Ramsey score of 6, resulting in a fixed $\dot{V}_E$ in both studies. In our study the patients were able to adjust $\dot{V}_E$ with the changes in apparatus V_D, and V_D removal significantly reduced $\dot{V}_E$, which may reduce air trapping and allow reduction in the intensity of ventilation. We found pH and P_{aCO_2} improvements comparable to the previous studies, despite the fact that we reduced the $\dot{V}_E$. Second, the V_T in our study (5.3 ± 1 mL/kg) was lower than in the studies by Prin et al (7.6 ± 0.6 mL/kg) and Prat et al (6.9 ± 1.8 mL/kg).

The routine removal of apparatus V_D from the ventilator circuit during lung-protective ventilation has some theoretical disadvantages. The absence of the flexible tubing can increase tension on the ventilator circuit and potentially increase the risk of inadvertent extubation. Removing the HME from the circuit necessitates the use of a more costly active heated humidifier device. However, for patients with severe gas-exchange abnormalities and associated hypercapnia and respiratory acidosis, removal of apparatus V_D offers an important clinical benefit and should be routinely considered.

Conclusion

In patients with ARDS or ALI receiving lung-protective ventilation, removing all possible apparatus V_D reduces P_{aCO_2} and increases pH, at a lower $\dot{V}_E$. We recommend a circuit with the minimum possible apparatus V_D for adults, and practice guidelines that trigger removal of V_D from the circuit.

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