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ORIGINAL ARTICLE

Dead space washout by intentional leakage flow during conventional ventilation of premature infants—an experimental study

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Abstract

Objective: Invasive mechanical ventilation poses a strong risk factor for the development of chronic lung disease in preterm infants. A reduction of the dead space as part of the total breathing volume would reduce the ventilation effort and thereby lower the risk of ventilator-induced lung injuries. In this experimental study, we compared the efficacy of mechanical dead space washout via uncontrolled and controlled leakage flow in their ability to eliminate CO_2 during conventional ventilation in preterm infants.

Methods: Three frequently used neonatal ventilators, operating under standard conventional ventilating parameters, were individually connected to a test lung. To maintain a constant physiological end-expiratory pCO_2 level during ventilation, the test lung was continuously flooded with CO_2. A side port in the area of the connector between the endotracheal tube and the flow sensor allowed breathing gas to escape passively or in a second experimental setup, regulated by a pump. Measurements of end-expiratory pCO_2 were taken in both experiments and compared to end-expiratory pCO_2 levels of ventilation without active dead space leakage.

Results: Following dead space washout, a significant reduction of end-expiratory pCO_2 was attained. Under conditions of uncontrolled leakage, the mean decrease was 14.1% while controlled leakage saw a mean reduction of 16.1%.

Conclusion: Washout of dead space by way of leakage flow is an effective method to reduce end-expiratory pCO_2. Both controlled and uncontrolled leakage provide comparable results, but precise regulation of leakage allows for a more stable ventilation by preventing uncontrolled loss of tidal volume during inspiration.

KEYWORDS
dead space washout, leakage flow, mechanical ventilation, preterm infant

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1 | INTRODUCTION

In preterm infants, the influence of dead space on ventilation effort is high.[1] The lower the body mass of an extremely preterm infant, the higher the requirement for high tidal volume ventilation. This is due to the relative dead space expansion by the respirator.[2] High tidal volumes are essential to overcome the mechanical dead space. Theoretically, in extreme cases concerning the smallest infants, tidal volume is less than the mechanical dead space. Therefore, gas exchange occurs with the help of turbulent flow and diffusion processes inside the airways and no longer by alveolar ventilation.[2,3] In instances involving a large dead space, high inspiratory flow and long pressure plateaus are needed for adequate CO_2 elimination.[3,4] In addition to high tidal volumes, these two factors promote ventilator-induced lung injury and bronchopulmonary dysplasia.[5,6] Therefore, reducing dead space may help improve pulmonary outcomes in mechanically ventilated preterm infants.

All ventilators for extremely small preterm infants use proximal flow measurement devices between the Y-piece connector and the endotracheal tube. These sensors not only contribute to dead space, they promote reuptake of expired gas and thereby increase alveolar CO_2.[7] Additional installations, such as end-expiratory CO_2-sensors or closed suctioning devices, further enlarge the mechanical dead space. Currently dead-space-free ventilation is technically impossible in clinical routine. Commercial dead space washout techniques are not available and due to their interferences with flow measurement and air conditioning, the diminishing of dead space through washout techniques in routine care is difficult.

The aim of this study was to evaluate the effectiveness of dead space washout using uncontrolled and controlled leakage flow.

2 | METHODS

The experimental setup of this study was influenced by an in vivo study by Claure et al.,[8] in which the authors describe a constant uncontrolled gas leakage from the endotracheal tube adapter of approximately 0.35 L/min during ventilation of preterm infants with a mean body weight of 856 g.

In our study, a test lung (Dräger Medical) simulating the lung of a 1500 g preterm infant, was tested in connection with three different ventilators: Fabian +nCPAP evolution respirator (Acutronic Medical Systems AG), Babylog® 8000 plus (Dräger Medical) (Dräger) and AVEA® standard ventilator (Vyaire Medical). All ventilators were adjusted to identical standardized ventilation settings (Table 1). The test lung was continuously flooded with 88 ml/min CO_2 to achieve constant physiological end-expiratory pCO_2 level during ventilation. Figure 1 visualizes the experimental setup.

Leakage flow for dead space washout was performed under two conditions. In the first experimental setup, uncontrolled leakage flow was established using a thin leakage tube connected to a perforation in the endotracheal tube connector (Figure 1). Since the flow resistance of a tube depends on both diameter and length, the leakage tube used could be shortened to produce a leakage flow of 0.35 L/min on average. A second setup tested the effect of a controlled leakage flow of 0.342 L/min, generated by a SP 100 EC pump (Schwarz Precision GmbH + Co. KG), connected via a shorter leakage tube to the endotracheal tube connector perforation. This controlled leakage flow resulted from the fixed pump capacity (0.4 L/min) and the flow resistance of the leakage tubes used. Controlled and uncontrolled leakage flow was measured by a red-y compact meter GSM (Vögtlin Instruments GmbH). The selected leakage flows washout approximately 0.5 ml dead space in 0.1 s. Thus, a significant CO_2 washout should be achievable even at high ventilation frequencies.

Breathing gas in the area between the Y-piece and the leakage opening, i.e., in the area of the flow sensor, is continuously diluted by the leakage flow. An end-expiratory pCO_2 measurement in this area would therefore be distorted. For this reason, pCO_2 monitoring was also installed in the area between the leakage opening and the "patient" in this study.

Measurements of end-expiratory pCO_2 were taken under conditions of uncontrolled and controlled leakage as well as without leakage. To document a stable situation, the end-

TABLE 1 Ventilation settings used for all ventilators during the study

Ventilation rate	**40 min^{-2}**
Inspiratory time	0.5 s
Peake inspiratory pressure	20 mbar
Positive end expiratory pressure	5 mbar
Tidal volume	10 ml
Inspiratory flow of the ventilator	7 l/min

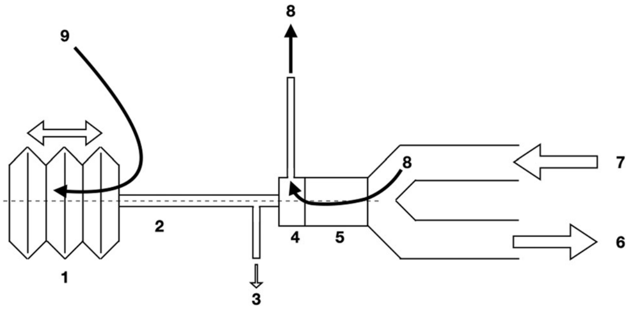

FIGURE 1 Diagram of the test setting with (1) conventionally ventilated test lung, (2) endotracheal tube, (3) end-expiratory measurement of pCO_2, (4) endotracheal tube connector, (5) Flow sensor, (6) expiratory limb of ventilation tubes, (7) inspiratory limb of ventilation tubes, (8) leakage flow through the leakage tube for dead space washout, (9) continuously CO_2 flooding of the test lung. Arrows indicate direction of airflow within the circuit. The double arrow symbolizes the movement of the test lung, the remaining arrows symbolize the direction of flow of the respiratory gas at the corresponding points

expiratory pCO_2 was measured 1 min after each change in leakage. Twenty measurements of each experimental condition were recorded per ventilator model. Measurements were statistically analyzed by performing one- and two-way analyses of variance using MedCalc® version 18.11.3. Pairwise posthoc analysis in the one-way analysis of variance was performed using Student-Newman-Keuls test.

As the experiments did not involve animal or human subjects, an ethical review was not needed.

3 | RESULTS

A total of 180 measurements were recorded, with an equal number of testing for each ventilator.

Using the Babylog® respirator the mean end-expiratory pCO_2 (95% confidence interval [CI]) without leakage during conventional ventilation was 51.5 mmHg, 95% CI (50.9, 52.1). The end-expiratory pCO_2 with uncontrolled leakage was 43.9 mmHg, 95% CI (43.3, 44.5) and with controlled leakage 43.3 mmHg, 95% CI (42.7, 43.9). Therefore, an uncontrolled leakage equates to a 14.7% reduction of pCO_2 by dead space washout and a controlled leakage leads to a reduction of 15.9%.

With the Fabian ventilator, the end-expiratory pCO_2 without leakage during conventional ventilation was 38.3 mmHg, 95% CI (37.7, 38.8). The end-expiratory pCO_2 with uncontrolled leakage was 32.8 mmHg, 95% CI (32.2, 33.3) and with controlled leakage 32.2 mmHg, 95% CI (31.6, 32.7). Dead space washout resulted in a reduction of pCO_2 by 14.4% with uncontrolled leakage and 15.9% with controlled leakage.

With the AVEA® respirator the end-expiratory pCO_2 without leakage during conventional ventilation was 59.7 mmHg, 95% CI (59.1, 60.3). The end-expiratory pCO_2 with uncontrolled leakage was 51.9 mmHg, 95% CI (51.3, 52.5) and with controlled leakage 50.0 mmHg, 95% CI (49.4, 50.5). The reduction of pCO_2 by dead space washout using uncontrolled leakage was 13.1% and with controlled leakage 16.3%.

Averaged across all ventilators, end-expiratory pCO_2 without leakage with conventional ventilation was 49.8 mmHg (*SD* 9.0). End-expiratory pCO_2 with uncontrolled leakage was 42.8 mmHg (*SD* 8.0) and with controlled leakage was 41.8 mmHg (*SD* 7.5).

The reduction in pCO_2 by dead space washout was 14.1% with uncontrolled leakage and 16.1% with controlled leakage. In the posthoc analysis, the difference in mean values was not statistically significant.

Tabular and Graphical representation of the results are shown in Table 2 and Figure 2, respectively.

4 | DISCUSSION

Our study has shown the enormous influence of technical dead space on the ventilation of small preterm infants. With identical CO_2 supply and uniform ventilation settings, significant differences in

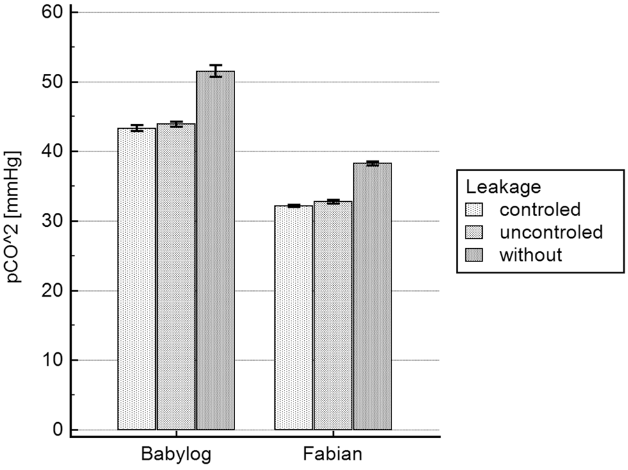

FIGURE 2 Graph of mean end expiratory pCO_2 values with controlled, uncontrolled and without leakage, averaged over all ventilators used. Error bars represents the 95% confidence intervals of the means

TABLE 2 mean end-expiratory value and corresponding change in percent of pCO2 of three types of ventilator, following leakage flow

Ventilator	Leakage	Mean end-expiratory pCO2	95% Confidence interval	Change in %
Babylog® 8000 plus	without	51.5 mmHg	(50.9, 52.1)	–
	uncontrolled	43.9 mmHg	(43.3, 44.5)	−14.69%
	controlled	43.3 mmHg	(42.7, 43.9)	−15.85%
Fabian + nCPAP evolution	without	38.3 mmHg	(37.7, 38.8)	–
	uncontrolled	32.8 mmHg	(32.2, 33.3)	−14.7%
	controlled	32.2 mmHg	(31.6, 32.7)	−15.9%
AVEA® standard ventilator	without	59.7 mmHg	(59.1, 60.3)	–
	uncontrolled	51.9 mmHg	(51.3, 52.5)	−13.1%
	controlled	50.0 mmHg	(49.4, 50.5)	−16.3%

end-expiratory pCO_2 of the tested machines have been shown. This can only be explained by corresponding differences in the technical dead space of the machines. Furthermore, it could be shown that the existing technical dead space in all machines can be washed out by the leakage flow. Both the uncontrolled and the controlled leakage methods delivered comparable results. For all three ventilators used, the mean pCO_2 could be reduced by approximately 15% with both leakage methods. Thus, the reduction in pCO_2 was not dependent on the ventilator. This universal reduction in pCO_2 is comparable to the results of Claure et al.[8]

In literature, different options for active dead space washout have been described: (1) Active washout with pump-injected flow, the benefit of which is a complete washout of dead space.[9] However, this technique requires special tubing and poses the risk of an uncontrolled overextension of the lung in the event of tubal occlusion. (2) The split flow technique, described by our own research group mainly that washes out the dead space of the flow sensor and the endotracheal tube connector or the connected closed suctioning device, but not the dead space of the endotracheal tube.[10] It provides the advantage that no pump is required, but requires additional large diameter split flow tubes. (3) Dead space washout with uncontrolled leakage flow, which has comparable efficacy to the split flow technique, due to identical location of the perforation in the endotracheal tube connector.[8] A major disadvantage is that uncontrolled inspiratory leakage reduces ventilation. During inspiration, the leakage flow increases due to pressure, resulting in less inspiratory volume reaching the lungs. During expiration, the leakage flow is then correspondingly lower. This also reduces the efficacy of the dead space washout and explains the somewhat lower effectiveness of uncontrolled leakage in comparison to controlled leakage, as described in this paper. As controlled and uncontrolled leakage flows were chosen based on values used in the study conducted by Claure et al,[8] further analyses would need to be made to determine the impact of leakage settings outside of these values.

Despite the availability of various techniques, mechanical dead space washout has not yet established itself in practice. This can be attributed to two fundamental problems associated with the procedure: a need for breathing gas conditioning and its potential negative impact on accurate flow measurements. In the methods described by Dassieu et al.[9] and Wald et al.,[10] fresh breathing gas is introduced into the dead space, which is partially inhaled by the patient. Therefore, the washout stream must be conditioned to have the same properties in terms of O_2 content, temperature and humidity. The split flow technique partially avoids this problem by diverting some breathing gas from the main stream in the technical dead space, making the main stream and split flow initially identical in terms of O_2 concentration, temperature and humidity. However, to maintain these equal conditions, heating of the breathing hose is still required.[10] With the utilization of leakage flow, breathing gas conditioning requirements are eliminated. A leakage flow, on the other hand, has no effect on the temperature or humidity of the respiratory gas flowing into the patient's lungs. The use of the leakage flow thus eliminates the need for respiratory gas treatment.

In neonatology, expiratory tidal volume is used in flow measurement to gauge delivered tidal volume. Every additional washout flow increases the expiratory flow, while leakage reduces it. As a result, the expiratory tidal volume is either significantly over- or underestimated, respectively. In principle, a flow sensor can be calibrated to a washout flow.[11] To enable such calibration, the washout flow should remain virtually constant; however, without a pump, such flows fluctuate greatly over the course of the breathing cycle in response to pressure changes. With controlled leakage flow through a pump, the leakage flow is always the same regardless of the pressure variations during inspiration and expiration. Due to the constant control, an accurate calculation of the tidal volume is possible. The required calibration to a constant washout flow corresponds to a zero value shift. Therefore, the quality of the tidal volume measurement remains unchanged. The influence of the leakages frequently occurring in neonatology, on the measurement of the tidal volume, thus remains unchanged.

A limitation of the present study was the type of test lung available; settings were therefore chosen as would be used for a 1500 g child. In contrast, the patients in the study by Claure et al.[8] had an average weight below 1000 g. However, only the tidal volume depends on patient weight, not the technical dead space that can be washed out. It can therefore be assumed that the effects shown would be even more impressive in smaller children with lower tidal volumes.

5 | CONCLUSION

Washout by leakage flow can significantly reduce end-expiratory pCO_2 levels and thereby minimize the adverse effects associated with mechanical dead space. Controlled leakage is not only as effective as uncontrolled leakage flow, it also allows for a more stable ventilation by preventing the uncontrolled loss of tidal volume that occurs during inspiration when leakage is not controlled. The results of this in vitro study give no information about its clinically relevance, therefore, additional clinically studies are required.

AUTHOR CONTRIBUTIONS

Martin Schöber: data curation (lead); investigation (lead); writing—review & editing (equal). **Bettina Bohnhorst**: supervision (equal); writing—review & editing (equal). **Natalee Annon-Eberharter**: visualization (equal); writing—original draft (equal); writing—review & editing (lead). **Martin Wald**: conceptualization (lead); methodology (lead); writing—original draft (lead); writing—review & editing (equal).

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CONFLICTS OF INTEREST

Martin Wald has been a consultant for the companies Fritz Stephan GmbH and medin Medical Innovations GmbH and has given paid lectures for Medtronic Österreich GmbH during the past 3 years. He has also organized workshops sponsored by the above companies. All other authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The raw data from the in vitro simulations are available upon request. Please contact the corresponding author.

ETHICAL STATEMENT

no animals or humans were involved in the experiments, and no ethical review was required.

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