



# How Does Respiratory Rate Affect Alveolar Ventilation in Pediatric Patients?

## *Pediatric Hastalarda Solunum Hızı Alveolar Ventilasyonu Nasıl Etkiler?*

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### ABSTRACT

**Objective:** Minute ventilation is a combination of alveolar ventilation ( $V'_{alv}$ ) and dead space ventilation which is also a result of multiplication of respiratory rate (RR) by tidal volume.  $V'_{alv}$  is the volume of the air which reaches the alveoli per minute by definition. The aim of this study was to examine the effect of RR on  $V'_{alv}$  in a pediatric physiologic bench setting.

**Method:** In our study, respiratory parameters of a male child, approximately 1 year old, 78 cm in length and ideal body weight of 10 kg, were simulated. This model was ventilated in two different RR settings and with two different breathing circuits which has different dead space (DS) values. However amount of  $CO_2$  was kept same during whole bench. Static compliance, static resistance, end-tidal-carbondioxide, positive end expiratory pressure, peak inspiratory pressure, inspiratory time, expiratory-time values of each breathing circuit were taken as the mean and standard deviation of repeated measurements.

**Results:**  $V'_{alv}$  decreased from  $1.84 \pm 0.3$  L/m to  $1.63 \pm 0.5$  L/m ( $p < 0.001$ ) in the pediatric circuit and decreased from  $1.95 \pm 0.3$  L/m to  $1.83 \pm 0.5$  L/m ( $p < 0.001$ ) in neonatal circuit group.

**Conclusion:** Younger patients should be ventilated with higher RR because of their physiology. Additionally, regarding the current guidelines in pediatric mechanic ventilation, higher RR should be selected in restrictive lung disease condition. Therefore, clinicians should be more alert particularly in the younger and/or in the restrictive lung disease group regarding both the increased RR and the increased percentage of instrumental DS which results in a decreased  $V'_{alv}$ .

**Keywords:** Alveolar ventilation, dead space, respiratory rate, minute ventilation, mechanical ventilation, pediatric intensive care unit

### ÖZ

**Amaç:** Dakika ventilasyonu, alveolar ventilasyon ( $V'_{alv}$ ) ve ölü boşluk (DS) ventilasyonunun bir kombinasyonudur ve tanım olarak solunum hızının (RR) alveollere dakikada ulaşan tidal hacim ile çarpılmasının bir sonucudur. Bu çalışmanın amacı, pediatrik bir fizyolojik model ortamında RR'nin  $V'_{alv}$  üzerindeki etkisini incelemektir.

**Yöntem:** Çalışmamızda yaklaşık 1 yaşında, 78 cm boyunda ve ideal vücut ağırlığı 10 kg olan bir erkek çocuğun solunum parametreleri simüle edildi. Bu model iki farklı RR ayarında ve farklı DS değerlerine sahip iki farklı solunum devresi ile ventile edilmiştir. Ancak tüm fizyolojik modelleme boyunca  $CO_2$  miktarı aynı tutulmuştur. Statik komplians, statik direnç, end-tidal-karbondioksit, ekspirium sonu pozitif basınç, tepe inspiratuvar basınç, inspirium süresi, ekspirium süresi değerleri her solunum devresinin tekrarlanan ölçümlerin ortalaması ve standart sapması olarak alınmıştır.

**Bulgular:** Pediatrik devrede  $V'_{alv}$   $1,84 \pm 0,3$  L/m'den  $1,63 \pm 0,5$  L/m'ye ( $p < 0,001$ ), yenidoğan devresi kullanıldığında ise  $1,95 \pm 0,3$  L/m'den  $1,83 \pm 0,5$  L/m'ye ( $p < 0,001$ ) gerilemiştir.

**Sonuç:** Daha genç hastalar fizyolojileri nedeniyle daha yüksek RR ile ventile edilmelidir. Ayrıca pediatrik mekanik ventilasyonda güncel kılavuzlara göre restriktif akciğer hastalığı durumunda daha yüksek RR seçilmelidir. Bu nedenle klinisyenler özellikle yaşı küçük hastalarda ve/veya restriktif akciğer hastalığı grubunda hem artmış RR hem de  $V'_{alv}$ 'de azalma ile sonuçlanan artmış instrumental DS yüzdesi nedeni ile daha uyanık olmalıdırlar.

**Anahtar kelimeler:** Alveolar ventilasyon, ölü boşluk, solunum hızı, dakika ventilasyonu, mekanik ventilasyon, pediatrik yoğun bakım ünitesi

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## INTRODUCTION

The purpose of mechanical ventilation is to partially or fully support the patient's respiratory workload using a mechanical ventilator. Minute ventilation is a combination of minute alveolar ventilation ( $V'_{\text{alv}}$ ) and minute dead space ventilation, which is also a result of multiplying the respiratory rate (RR) by the tidal volume (VT).  $V'_{\text{alv}}$  is by definition the volume of air which reaches the alveoli per minute. Dead space (DS) is a combination of physiological dead space (D<sub>Sp</sub>) and instrumental dead space (D<sub>Si</sub>). D<sub>Sp</sub> is a term used to describe the region where no gas exchange occurs in the lung<sup>(1)</sup>. It is unavoidable that D<sub>Si</sub> is added to D<sub>Sp</sub> during mechanical ventilation. The lower the VT used, the more DS affects ventilation and decreases  $V'_{\text{alv}}$ . In addition, positive end-expiratory pressure (PEEP) also affects DS ventilation in physiological conditions<sup>(2)</sup>. The aim of this study was to examine the effect of RR on  $V'_{\text{alv}}$  in pediatric patients.

## MATERIALS and METHODS

The study was performed during the period from September 1-30, 2020 using B&B test lungs. In order to mimic the physiology and respiratory parameters of a healthy, male, 1-year old child, the height was chosen as 78 cm and the corresponding ideal body weight (IBW) was selected as 10 kg. Firstly, the static compliance (Cs) and static resistance (Rs) values were reached in the test lung according to the model<sup>(3)</sup>. Then the system was titrated with an amount of CO<sub>2</sub> appropriate to the patient's IBW in the amounts regulated by the Sierra Mass Flow Controller (with accuracy of  $\pm 2.0$  of full scale for 100 mL from 201-300 slpm, Sierra Instruments, California, USA) via the T-tube and CO<sub>2</sub> diffuser. The required minute CO<sub>2</sub> flow ( $V'_{\text{CO}_2}$ ) for the selected physiological model was calculated as 63 mL/m using the Brody equation [ $V'_{\text{CO}_2} = 5.56 \times (\text{PBW})^{1.05}$ ]<sup>(4)</sup>. To achieve better CO<sub>2</sub> diffusion in the physiological lung, different CO<sub>2</sub> models were tested. For the closest comparison between the natural flow-volume curve and the standard volumetric capnograph graphics loop, we selected a ring-shaped diffuser as the most appropriate. After stabilizing both the lung mechanics and end-tidal CO<sub>2</sub> (EtCO<sub>2</sub>) values on the patient model, the model was ventilated using two different breathing circuits (HAMILTON-BC8022 for pediatrics D<sub>Si</sub> and HAMILTON-BC8010 for neonates, Hamilton Medical AG, Bonaduz, Switzerland). To be able to compare the effect of RR, we reached the same minute ventilation during ventilation by using a volume-targeted, pressure-regulated mechanical ventilation mode (APV-CMV). The study design was crossover. Sequencing from opaque

envelopes prepared before each measurement was used for randomization of the measurements. When the baseline RR was lower and RR increased after crossing over, the expired VT target was decreased accordingly. Measurements were repeated five times in accordance with the crossover study design. Values for Cs, Rs, EtCO<sub>2</sub>, PEEP, peak inspiratory pressure (PIP), inspiratory time (Ti), and expiratory time (Te), and pressure support (PS) for each breathing circuit were taken as the mean and standard deviation (SD) of repeated measurements. For the measurement of EtCO<sub>2</sub> values, we used two different methods<sup>(5,6)</sup> and took the mean of these two measurement methods. After completing this first group of tests with different breathing circuits, the circuit with greater dead space was selected for the further testing. In the second group of tests, none of the parameters of the physiological lung model were changed, however RR was increased by 30% from the initial group. During all study phases, ventilation variables were measured breath-by-breath and downloaded from the ventilator's RS32 communication port using a memory card. The data was in binary form; therefore, it was converted to text files by the clinician and then transferred to a statistical analysis program. As this is a bench study, approval from the ethics committee was waived and only institutional permission was obtained.

### Statistical Analysis

The data acquired during the crossover phases were assessed for the distribution; therefore, the continuous data were expressed either in mean and SD, or median and interquartile range. The Wilcoxon test was used to analyze the data. A p-value of less than 0.05 was considered statistically significant for all comparisons.

## RESULTS

Among the respiratory circuits tested in first model, D<sub>Si1</sub> was measured as 22.5 mL and D<sub>Si2</sub> as 17.4 mL. Both D<sub>Si</sub> differences (D<sub>Si1</sub>-D<sub>Si2</sub>= $\Delta$ D<sub>Si</sub>)=14 mL were calculated. There was no statistically significant difference between the Cs values reached in both cases (Cs1=1.07 mL/cmH<sub>2</sub>O/kg, Cs2=1.1 mL/cm H<sub>2</sub>O/kg; p=0.78). However, the resistance of the smaller breathing circuit was higher than the larger one (Rs1=18.4 cm H<sub>2</sub>O/L/s, Rs2=21.9 cm H<sub>2</sub>O/L/s; p=0.012). Conversely, the  $V'_{\text{alv}}$  value measured by the smaller respiratory set was higher compared to the value measured with the larger set ( $V'_{\text{alv1}}$ =1.95 $\pm$ 0.2 L/m,  $V'_{\text{alv2}}$ =1.84 $\pm$ 0.3 L/m). As the other respiratory parameters (RR, Ti, Te, PS, PEEP, PIP) were not changed, there was no statistically significant difference between them.

In the second group of tests, RR was increased by 30% from 30 b/min to 39 b/min. This resulted in a decrease in  $T_i$  and  $T_e$ . In addition,  $V_{Te}$  was decreased to 6.4 mL in order to compare the DS effect. By decreasing  $V_{Te}$  to lower values, we were able to keep the minute ventilation equal in both phases of the second group of tests.  $V'_{alv}$  value measured with the higher D<sub>Si</sub> ( $V'_{alv3}$ ) was  $1.63 \pm 0.5$  L/m, whereas  $V'_{alv4}$  was measured as  $1.84 \pm 0.3$  L/m while using the other circuit with smaller D<sub>Si</sub>.

## DISCUSSION

In our study, we demonstrated that the increase in RR resulted in a decrease in  $V'_{alv}$ . This is because the RR is a multiplier for  $V'_{alv}$ , which must be subtracted from the total minute ventilation. Considering the normal RR for younger children is higher than for older ones or adults, this effect will be more prominent in younger patients<sup>(7)</sup>. During ventilation with the pediatric circuit,  $V'_{alv}$  decreased from  $1.84 \pm 0.3$  L/m to  $1.63 \pm 0.5$  L/m when we increased the rate from 30 to 39. Similarly when RR was increased with the same percentage during ventilation with the neonatal circuit,  $V'_{alv}$  decreased from  $1.95 \pm 0.3$  L/m to  $1.83 \pm 0.5$  L/m. This is clear evidence of the fact that for both circuits, an increase in RR caused a decrease in  $V'_{alv}$ . Another reason for the decrease in  $V'_{alv}$  is the other multiplier of the DS ventilation, which is D<sub>Si</sub> itself. The increase in D<sub>Si</sub> values in the breathing circuit also caused a decrease in the  $V'_{alv}$  value in the model during our study. Simply by changing the D<sub>Si</sub> by keeping RR at 30,  $V'_{alv}$  decreased from  $1.95 \pm 0.2$  L/m to  $V'_{alv2} = 1.84 \pm 0.3$  L/m ( $p < 0.001$ ) in the neonatal circuit. When RR was kept at 39 b/m,  $V'_{alv}$  decreased from  $1.84 \pm 0.3$  L/m to  $1.63 \pm 0.5$  L/m ( $p < 0.001$ ). To achieve the same  $V'_{alv}$  in the model, it is necessary to increase either RR or VT, similar as the clinician would do<sup>(5,8)</sup>. However, particularly the increases in RR cannot affect  $V'_{alv}$  values linearly<sup>(9)</sup>. For this reason, clinicians should either use breathing sets with a low D<sub>Si</sub> value or avoid using fittings and heat and moisture exchanger filters that are likely to increase D<sub>Si</sub> when using a low D<sub>Si</sub> is not possible. D<sub>Si</sub> will be higher in neonatal and infant patients than in adult or adolescent populations, and the increase will be greater the smaller the patient is. In addition, younger patients should be ventilated with a higher RR because of their physiology. According to the current guidelines in pediatric mechanical ventilation, a higher RR should be selected in restrictive lung disease conditions<sup>(10,11)</sup>.

## Study Limitations

The one main limitation of this study is that rather than providing clinical data, we tested the bench settings

optimized to mimic the physiology and respiratory parameters of a healthy, male, 1-year old child. Nevertheless, these settings may help us to understand the mechanisms of real physiology with reproducibility of the specific, predefined test conditions.

## CONCLUSION

Our results demonstrated that a higher RR resulted with lower  $V'_{alv}$ . Particularly in the smaller and/or the restrictive lung disease group, clinicians should therefore be more alert in terms of both the increased RR and the increased percentage of D<sub>Si</sub> that results with a decrease in  $V'_{alv}$ .

## Ethics

**Ethics Committee Approval:** As this is a bench study, approval from the ethics committee was waived and only institutional permission was obtained.

**Informed Consent:** Informed consent is not required.

**Peer-review:** Internally peer-reviewed.

## Author Contributions

Surgical and Medical Practices: G.C., Concept: G.C., S.T., E.S., P.S., H.A., Design: G.C., M.Ç., E.S., P.S., H.A., Data Collection and/or Processing: G.C., G.A., S.T., F.S., Ö.S.S., Analysis and/or Interpretation: G.C., S.T., M.Ç., E.S., P.S., Ö.S.S., H.A., Literature Search: G.C., G.A., S.T., M.Ç., E.S., F.S., P.S., Ö.S.S., H.A., Writing: G.C., G.A., S.T., M.Ç., P.S., Ö.S.S., H.A.

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