

## **Comparative evaluation of two ventilator circuits during noninvasive ventilation (NIV) with Helmet: a bench study**

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## Abstract

### Purpose

The aim of this study was to compare helmet-NIV (non invasive ventilation), in terms of patient-ventilator interaction and performance, using two different circuits for connection: a double tube circuit (with one inspiratory and one expiratory line) and a standard circuit (an Y piece connected only to one side of the helmet, closing the other side).

### Methods

A mannequin, connected to a test lung, set at two different respiratory rates (20 and 30 breaths/min), was ventilated in Pressure Support Ventilation (PSV) mode with two different settings, randomly applied: Pressurization time/Expiratory trigger ( $\text{Time}_{\text{press}}/\text{Tr}_{\text{exp}}$ ) 50%/25%, Default setting and  $\text{Time}_{\text{press}}/\text{Tr}_{\text{exp}}$  80%/60%, Fast setting, through a helmet. The helmet was connected to the ventilator randomly with the double and the standard circuit.

Patient-ventilator interaction was evaluated measuring: Inspiratory trigger delay ( $\text{Delay}_{\text{trinsp}}$ ), Expiratory trigger delay ( $\text{Delay}_{\text{trexp}}$ ), Pressurization Time ( $\text{Time}_{\text{press}}$ ), Time of synchrony ( $\text{Time}_{\text{syn}}$ ). The performance was analyzed measuring: Trigger pressure drop, Inspiratory Pressure-Time Product (PTPt), Pressure Time Product at 300 ms and 500 ms (PTP 300 and PTP 500 respectively) and Pressure Time Product 500 ms expressed as percentage of an ideal PTP500 (PTP500 index).

### Results

At both respiratory rates and ventilator settings helmet-NIV with the double tube circuit showed better interaction, with shorter  $\text{Delay}_{\text{trinsp}}$ ,  $\text{Delay}_{\text{trexp}}$  and  $\text{Time}_{\text{press}}$  and longer  $\text{Time}_{\text{syn}}$  ( $p < 0.01$ ) compared to the standard circuit ( $p < 0.01$ ). Moreover, the helmet performance was significantly improved by the double tube circuit as shown by higher PTP 300, PTP500 and PTP 500 index ( $p < 0.01$ ).

### Conclusions

Compared to the standard circuit, helmet-NIV with the double tube circuit showed a significantly better patient-ventilator interaction associated with a significantly better performance and a lower rate of wasted effort at 30 breaths/min .

**Keywords**

Non invasive ventilation, Patient-ventilator interaction, Helmet, Ventilator circuits

## Introduction

Non invasive ventilation (NIV) is an effective technique to treat patients with acute respiratory failure (ARF). Although many factors can influence NIV success [1], tolerance is a crucial determinant of NIV outcome [2, 3] depending on both patient-ventilator interaction and the interface used [4, 5].

The helmet is a relatively new interface, proposed as alternative to the facemask to deliver NIV, since it reduces the incidence of some of the most common facemask side effects (i.e. pain at the nasal bridge, skin ulceration and necrosis, conjunctive inflammation, interface intolerance); therefore it is more tolerated than the facemask and requires fewer discontinuations, allowing a prolonged application [6, 7]. However, several studies have clearly demonstrated that the helmet is less efficient than the facemask in terms of gas exchange improvement [6, 7], patient-ventilator interaction [8, 9] and inspiratory effort reduction [9-11]. These drawbacks are directly related to the helmet physical characteristics, such as the large inner volume and the highly compliant material, determining an initial pressure dissipation prolonging the time needed to reach the preset level of pressure support (PS) [12].

In the last years, many efforts have been performed to improve helmet-NIV and several models of helmet with different designs and materials are now available for the clinical use [12]. Moreover ventilators technological improvements, such as specific softwares for NIV and new ventilator modes as NAVA [13] and various levels of inspiratory and expiratory triggers [14], have also been proposed to minimize the impact on patient-ventilator interaction of both air leaks and helmet intrinsic characteristics.

A poorly investigated aspect during helmet-NIV is the role played by the circuit connecting the helmet to the ventilator. In several studies [6-9] the helmet has been connected to the ventilator through a double tube circuit (one inspiratory and one expiratory line, connected to the two specific inspiratory and expiratory ports of the helmet) (Fig 1-a). However, in the clinical practice, the

interface is often connected to the ventilator through a standard circuit, connecting the Y piece only to one side of the helmet and occluding the other side, thereby realizing a single port circuit (Fig 1-b). Even if the helmet was originally designed to be connected to the ventilator through a double circuit there are no published preclinical testing of this circuit, nor a formal contraindication to the use of a standard circuit; we have personally observed the use of a single circuit in several ICUs across Europe, probably for simplicity. Knowing that the supposed improper use of these clinical devices is unfortunately widespread, we think useful to formally investigate if the kind of circuit used really plays a role in interaction during helmet-NIV.

The aim of this bench study was to compare helmet-NIV with both these circuits in terms of ventilator performance and patient-ventilator interaction (assuming the simulator as a patient).

### **Materials and methods**

This study was performed at the Respiratory Mechanics Laboratory (Ventil@b) of the Catholic University in Campobasso (Italy) between November 2010 and March 2011.

NIV was applied to a mannequin (Laerdal Medical AS, Stavanger, Norway), connected to an active test lung (ASL 5000, Ingmar Medical, Pittsburgh, USA) set to breath at two respiratory rates (RR), 20 and 30 breaths/min, through an helmet (Starmed Castar, Mirandola, Italy). The mannequin was connected to the ASL through the trachea with a 5 cm plastic tube having the same diameter of a 70 kg's adult man trachea (about 2 cm).

The following simulator settings remained unchanged throughout the study: (1) single-compartment model; (2) resistance 4 cmH<sub>2</sub>O/l/s; (3) compliance 60 ml/cmH<sub>2</sub>O; (4) the simulator inspiratory time is 640 ms at RR 20 and 430 ms at RR 30; (5) inspiratory muscle pressure (P<sub>mus</sub>) – 6 cmH<sub>2</sub>O with a semi-sinusoidal waveform (rise time of 15%, inspiratory hold of 5%, and release time of 25%).

Helmet-NIV was delivered in Pressure Support Ventilation (PSV) [pressure support (PS)=12 cmH<sub>2</sub>O and positive end-expiratory pressure (PEEP)= 8 cmH<sub>2</sub>O], with an ICU ventilator (Puritan Bennet 840, Covidien, USA), at two ventilator settings, randomly applied: the default setting – DS (Time<sub>press</sub>/Tr<sub>exp</sub> 50%/25%) and the fast setting – FS (Time<sub>press</sub>/Tr<sub>exp</sub> 80%/60%), where the Time<sub>press</sub> is the rise time to reach the preset level of PS and the Tr<sub>exp</sub> is the flow percentage threshold at which the expiratory valve opens, the inspiratory phase ends and expiration starts.

The helmet was placed on the mannequin and connected to the ventilator with the double tube circuit and the standard circuit, randomly applied. The presence of air leaks was eliminated by tightening the soft helmet collar to the mannequin neck.

The airflow (V') delivered by the ventilator to the helmet during the inspiratory phase was measured with a pneumotachograph (Fleisch n.2, Metabo, Epalinges, Switzerland) positioned at the distal end of the inspiratory limb of the double circuit and at the Y-piece with the standard circuit. The V'signal integrated on time was used to obtain the inspiratory tidal volume (VT) and to measure the mechanical inspiratory and expiratory time. The airway pressure (Paw) was measured by a pressure transducer with a differential pressure of  $\pm 10$  cmH<sub>2</sub>O (Digima Clic-1, KleisTEK, ICU-Lab System, Italy), placed distally to the pneumotachograph. All these signals were acquired, amplified, filtered, digitized at 100 Hz, recorded on a dedicated personal computer, and analyzed with a specific software (ICU lab 2.3, KleisTEK Advanced Electronic System, Italy ).

V', VT, Paw and Pmus were displayed on line on the computer screen. The signals obtained with the ASL were transmitted to a PC host via 10/100 MBit Ethernet, sampled and processed in real time by a specific software (Lab View, Ingmar Medical, Pittsburgh, USA).

The amount of tidal volume delivered to the simulator during its active inspiration (i.e. while  $P_{mus}$  is negative) is the neural tidal volume ( $V_{Tneu}$ ) and was calculated as the volume generated from the onset of  $P_{mus}$  negative deflection to its return to baseline.

Patient-ventilator interaction was evaluated determining:

- Inspiratory trigger delay ( $Delay_{trinsp}$ ), calculated as the time lag between the onset of  $P_{mus}$  negative swing and the start of the ventilator support (i.e.,  $Paw$  positive deflection);
- Expiratory trigger delay ( $Delay_{texp}$ ), assessed as the delay between the offset of the inspiratory effort and the offset of the mechanical insufflations (i.e., Flow deflection);
- Pressurization time ( $Time_{press}$ ), defined as the time necessary to achieve the preset level of pressure support;
- Time of synchrony ( $Time_{syn}$ ), defined as the time during which  $P_{mus}$  and  $Paw$  are in phase (ideally 100%);
- Wasted efforts (WE), ineffective inspiratory efforts not assisted by the ventilator.

The ventilator performance with the two helmet circuits was evaluated in terms of:

- Trigger pressure drop ( $\Delta P_{trigger}$ ), defined as the pressure drop generated by triggering the ventilator;
- Inspiratory pressure-time product (PTPt), defined as the area under the  $Paw$  curve relative to time between the onset of inspiratory effort and mechanical assistance (Fig. 2);
- Pressure-time product at 300 and 500 ms (PTP 300 and PTP 500), defined as the speediness of pressurization and the ventilator capacity to maintain the preset pressure within the first 300 ms and 500 ms, respectively (Fig. 2);
- PTP500 index, expressed as percentage of the ideal PTP, that is unattainable since it would imply a  $\Delta P$  trigger of zero and an instantaneous pressurization of the machine.

### Statistical analysis

All data are expressed as mean  $\pm$  SD. The analysis of variance (ANOVA) for repeated measures was used to detect significant differences between the different experimental conditions. When significant differences were detected, post-hoc analysis was performed using the Bonferroni test; p-values  $< 0.05$  were considered as statistically significant.

### Results

As showed in Figure 3, at both respiratory rates and ventilator settings tested, Delay<sub>trinsp</sub> (sec) and Delay<sub>trexp</sub> (sec) were significantly shorter with the double tube than with the standard circuit ( $p < 0.01$ ). At DS and RR 30 the Delay<sub>trinsp</sub> (sec) did not show statistically significant differences.

The Timepress (sec) with the double tube circuit was always shorter than with the standard circuit ( $p < 0.01$ ), except than at FS and RR 30 ( $p = 0.1$ ). A shorter Timepress indicates a better pressurization.

The Timesyn (sec) with the double tube circuit was longer than with the standard circuit in all the tested conditions ( $p < 0.01$ ), the difference was not statistically significant at DS and RR 30 (Fig. 4).

In the matter of the ventilator performance, at RR 20, with the double circuit we observed shorter  $\Delta P_{trigger}$  (cmH<sub>2</sub>O) and PTPt (cmH<sub>2</sub>O·s) values compared to the standard circuit, at RR 30 the situation was opposite (table 1). Of note at RR 30, at DS, with the standard circuit there was a WE/cycled effort ratio of 1 to 1: this means we observed a WE after each successfully triggered inspiratory effort, therefore about the 50% of cycles were wasted. At the same respiratory rate, at



FS, the standard circuit allowed a statistically better performance (in terms of  $\Delta P_{\text{trigger}}$  and  $PTP_t$ ) than the double circuit in our bench study condition.

Figure 5 depicts  $PTP_{300}$  ( $\text{cmH}_2\text{O}\cdot\text{s}$ ) and  $PTP_{500}$  ( $\text{cmH}_2\text{O}\cdot\text{s}$ ) values, that were always significantly higher with the double tube than with the standard circuit ( $p<0.01$ ); accordingly, the calculated  $PTP_{500}$  index was higher with the double then with the standard circuit, although this difference was statistically significant only at DS, at both RR (59% vs 51% at RR 20 and 57% vs 54% at RR 30,  $p<0.05$ ).

$VT$  and  $VT_{\text{neu}}$  values were significantly higher with the double tube circuit compared to the standard circuit ( $p<0.001$ ; table 1). At DS and RR 30 these values were higher with the standard circuit.

WE never occurred with the double circuit, irrespective of RR and ventilator settings; with the standard circuit, at DS and RR 30, WE accounted for 50% of the overall breaths.

## Discussion

The results of the present study suggest that during helmet-NIV, beyond the kind of helmet and the applied ventilator settings, the optimal choice of the circuit plays a major role in improving patient-ventilator interaction. Compared to the standard circuit with a Y-piece, a double tube circuit showed both a significantly better patient-ventilator interaction (shorter inspiratory and expiratory delays and longer time of synchrony) and a significantly higher ventilator performance.

As reported in the introduction, helmet is not an easy interface compared to facemask, therefore clinicians necessitate to apply various strategies to minimize its drawbacks and optimize its potentiality. The goal is to improve NIV tolerance, since this means to ameliorate patient's comfort and prolong time of continuous NIV application [6-7]. Thus it is possible to improve gas-exchange,

reduce the work of breathing and the risk of infections related to invasive mechanical ventilation [12-15-16].

The first strategy to apply is the use of an optimized ventilator setting. In this study, the choice of specific PS and PEEP values as well as  $\text{Time}_{\text{press}}$  and  $\text{Tr}_{\text{exp}}$  was based on the results of studies investigating the use of specific ventilator settings to enhance ventilator performance with helmet, thus improving patient-ventilator interaction. Vargas and coll. [14] showed that increasing by a 50% both PS and PEEP levels and using the highest pressurization rate can significantly improve patient-ventilator interaction during helmet-NIV. In a bench study Costa and coll. [17] evaluated patient-ventilator interaction during PSV delivered with three different interfaces (endotracheal tube, facemask and helmet). The authors concluded that an appropriate choice of ventilator settings can improve patient-ventilator interaction during helmet-NIV, especially at high respiratory rates. In particular, the use of a fast setting can significantly reduce some of the helmet limitations in terms of patient-ventilator interaction.

Moreover, new NIV-dedicated ventilator softwares have been introduced in the clinical use: they consent to improve ventilator performance and so patient-ventilator interaction, thanks to a specific algorithm designed to compensate air-leaks. New ventilation modes have also been investigated, such as the NAVA (Neurally Adjusted Ventilatory Assist), in order to improve patient-ventilator interaction during NIV, as recently demonstrated by Cammarota and coll. [13].

The success of NIV depends also on the kind of helmet. In the last years, many technological efforts have been performed to improve helmet features in terms of design, material and application systems, since it has been demonstrated [13] that the specific helmet physical characteristics may significantly affect patient-ventilator interaction, suggesting that different helmets determine different ventilator performance, even if specific ventilator settings are applied.

In the real-life clinical practice the way of connecting the helmet and the ventilator can be different among various ICUs. To our best knowledge, the present is the first study investigating this practical aspect related to helmet-NIV: the optimal circuit connecting the helmet to the ventilator and its influence on ventilator performance and patient-ventilator interaction during NIV. This element can play an important role in determining failure or success of NIV.

We decided to perform a physiologic bench study, mimicking a normal subject (with normal compliance and normal resistances) in order to define only the limitations of the interface and the ventilator setting, including the circuit, thus eliminating all the other possible variables altering the results.

In our study, during helmet-NIV, the use of a double tube circuit showed a better patient-ventilator interaction compared to the standard circuit, as demonstrated by shorter Delaytrinsp and Delaytrexp, faster Timepress and higher Timesyn, an important parameter to evaluate patient-ventilator interaction. The observed differences between the two circuits did not reach statistical significance at the DS; however, it is noteworthy that DS is not the optimal ventilator setting for NIV, especially at high respiratory rates, that dramatically reduce Timesyn during helmet-NIV.

Using the double tube circuit we observed higher PTP 300, PTP 500 and PTP 500 index, indicating a faster speediness of pressurization and a better capacity of the ventilator to maintain the preset pressure within the first 300 and 500 ms, respectively.

During helmet-NIV with the double tube circuit both patient-ventilator interaction and ventilator performance parameters were better, suggesting that interaction and performance are strongly linked and are critical for NIV success.

Further analyzing performance, at RR 20 we observed shorter  $\Delta P_{\text{trigger}}$  and PTPt values with the double tube circuit; the situation was opposite at RR 30, due to the fact that at this RR a WE/cycled effort ratio of 1 to 1 was observed.

Despite the helmet is nowadays considered a suitable alternative to the facemask for delivering NIV, it is well known from the literature that during helmet-NIV asynchronous phenomena are more likely to be produced compared to NIV with the facemask, with a significant worsening of patient-ventilator interaction [8-11], especially at elevated respiratory rates [17]. This suggests that the helmet should not be used in patients with COPD exacerbations, at high risk of patient-ventilator asynchrony and should be used with specific settings in patients with restrictive disease [14-17]. WE are common asynchronous phenomena during mechanical ventilation and, and in the present study, at RR 30 with DS we observed a WE/cycled effort ratio of 1 to 1. Moreover the absence of WE with the double tube circuit demonstrates the positive influence of the optimal circuit on patient-ventilator interaction and ventilator performance, as WE generate patient's discomfort, gas exchange deterioration, work of breathing increase and rise for risk of NIV failure [12-17].

It is noteworthy that better interaction and performance determined significantly higher VT and VTneu values with the double tube circuit compared to the standard circuit at both RR and ventilator settings, except at RR 30 with DS, but of note, this condition was altered by the presence of WE, that make the analysis unreliable. On the basis of our results we suggest the use of a double tube circuit to connect the helmet to the ventilator during helmet-NIV.

A possible explanation is that, using a standard circuit, both the inspiratory and the expiratory flows are forced to pass through the Y piece of the circuit, probably generating turbulences that may increase resistances inside the passage, thus inducing alterations in patient-ventilator interaction. These drawbacks can be reduced with the application of a double tube circuit, since in this case the inspiratory and the expiratory flows pass through different limbs, probably avoiding turbulences and their negative consequences.

Finally, several important limitations of the present study must be addressed. First, we tested only one kind of helmet and one ventilator, thereby our results cannot be generalized to all the devices

present on the market, although major differences are unlikely, because of similar design of the inspiratory and expiratory ports in the various devices clinically used. Another limitation is that we performed a bench physiological study, not a clinical study on critically ill patients, neither a bench study testing different respiratory system mechanics conditions to simulate clinical sceneries. Finally, the design of our study does not allow to investigate CO<sub>2</sub> elimination, although it would be interesting to investigate if the two different circuits have an impact on CO<sub>2</sub>-rebreathing because of the increased expiratory resistance with the standard circuit.

### **Conclusions**

In order to correctly apply helmet-NIV it is important to consider that, beyond the kind of helmet and the ventilator settings, also the optimal choice of the circuit plays a major role in improving patient-ventilator interaction. Compared to the standard circuit with a Y-piece, with a double tube circuit we observed both a significantly better patient-ventilator interaction, with shorter inspiratory and expiratory delays, a longer time of synchrony, the absence of WE and a better ventilator performance, suggesting that this kind of circuit should be preferred in the clinical practice.

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### Figure notes

**Fig1-a** Schematic representation of a helmet connected to a ventilator through the double tube circuit.

**Fig1-b** Helmet connected to the ventilator through a standard circuit: the Y piece is connected only to one side of the helmet, the other side is occluded.

**Fig2** Inspiratory pressure-Time product (PTPt), Pressure-Time Product at 300 and 500 ms (PTP 300 and PTP 500) on the Pressure-Time trace.

**Fig 3** Inspiratory trigger delay ( $\text{Delay}_{\text{trinsp}}$ ), pressurization time ( $\text{Time}_{\text{press}}$ ) and expiratory trigger delay ( $\text{Delay}_{\text{texp}}$ ) at 20 and 30 breaths/min, with two ventilator settings (DS=Default setting [ $\text{Time}_{\text{press}}/\text{Tr}_{\text{exp}}$  50%/25%]; FS=Fast setting [ $\text{Time}_{\text{press}}/\text{Tr}_{\text{exp}}$  80%/60%]).  
Black columns correspond to the double tube circuit, grey columns to the standard circuit.  
Double circuit vs Standard circuit:  $p < 0.05 = *$ ;  $p < 0.01 = **$

**Fig4** Time of synchrony ( $\text{Time}_{\text{syn}}$ ) at 20 and 30 breaths/min, with two ventilator settings (DS=Default setting [ $\text{Time}_{\text{press}}/\text{Tr}_{\text{exp}}$  50%/25%]; FS=Fast setting [ $\text{Time}_{\text{press}}/\text{Tr}_{\text{exp}}$  80%/60%]).  
Black columns correspond to the double tube circuit, grey columns to the standard circuit.  
Double circuit vs Standard circuit:  $p < 0.05 = *$ ;  $p < 0.01 = **$

**Fig5** Pressure-time product at 300 and 500 ms (PTP 300 and PTP 500) at 20 and 30 breaths/min (RR20 and RR30) with two ventilator settings (DS=Default setting [ $\text{Time}_{\text{press}}/\text{Tr}_{\text{exp}}$  50%/25%]; FS=Fast setting [ $\text{Time}_{\text{press}}/\text{Tr}_{\text{exp}}$  80%/60%]).  
Black columns correspond to the double tube circuit, grey columns to the standard circuit.  
Double circuit vs Standard circuit:  $p < 0.05 = *$ ;  $p < 0.01 = **$





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	RR20 breaths/min		RR30 breaths/min	
	Double circuit	Standard circuit	Double circuit	Standard circuit
<b><math>\Delta P_{\text{trigger}}</math> <i>DS</i> (cmH<sub>2</sub>O)</b>	0.79±0.04*	1.29±0.01	1.76±0.02**	0.99±0.03
<b><math>\Delta P_{\text{trigger}}</math> <i>FS</i> (cmH<sub>2</sub>O)</b>	0.57±0.01**	0.78±0.02	1.52±0.06**	1.4±0.07
<b>PTPt (cmH<sub>2</sub>O·sec) <i>DS</i></b>	0.1±0.01*	0.3±0.01	0.36±0.01*	0.14±0.01
<b>PTPt (cmH<sub>2</sub>O·sec) <i>FS</i></b>	0.06±0.01**	0.1±0.01	0.25±0.02	0.29±0.01
<b>PTP 500 (% of ideal PTP 500) <i>DS</i></b>	59%*	51%	57%*	54%
<b>PTP 500 (% of ideal PTP 500) <i>FS</i></b>	67%	66%	64%	63%
<b>VT (ml) <i>DS</i></b>	768.33±6.81**	555.67±2.31	565.67±4.62**	580.67±4.73
<b>VT (ml) <i>FS</i></b>	690.67±7.51**	570.33±6.03	568.01±3.46**	368.01±3.61
<b>VT neu (ml) <i>DS</i></b>	552.01±8.68**	257.67±6.81	145.33±1.15**	200.67±4.51
<b>VT neu (ml) <i>FS</i></b>	625.33±14.22**	391.67±2.08	169.67±8.50	151.33±3.06

**Table 1** Comparison between double tube circuit and standard circuit during helmet-NIV, at 20 and 30 breaths/min, in terms of: Trigger pressure drop ( $\Delta P_{\text{trigger}}$ ), Inspiratory Pressure Time Product (PTPt), Pressure Time Product 500 ms expressed as percentage of Ideal PTP500 (PTP500 index), Tidal Volume (VT) and neural Tidal Volume (VT neu).

DS= Default setting [Time<sub>press</sub>/Tr<sub>exp</sub> 50%/25%]; FS= Fast setting [Time<sub>press</sub>/Tr<sub>exp</sub> 80%/60%].

Double circuit vs Standard circuit: p < 0.05= \*; p<0.01=\*\*



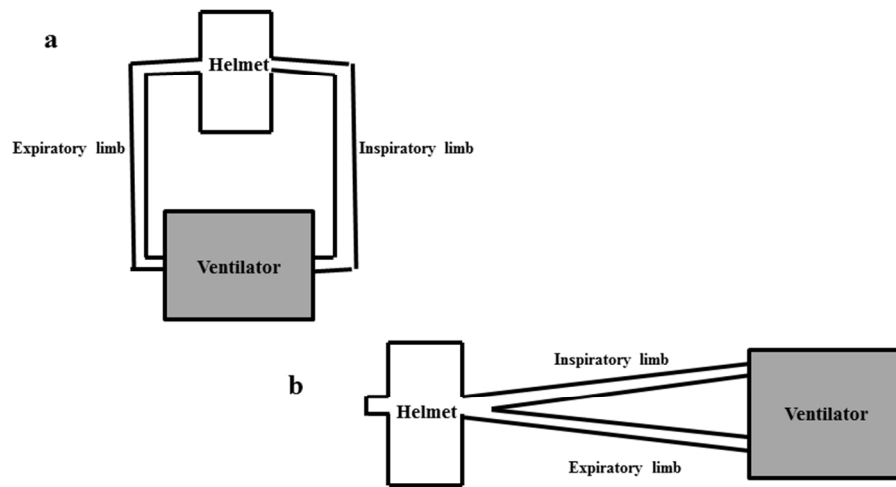


Fig1-a Schematic representation of a helmet connected to a ventilator through the double tube circuit.

Fig1-b Helmet connected to the ventilator through a standard circuit: the Y piece is connected only to one side of the helmet, the other side is occluded

254x190mm (96 x 96 DPI)

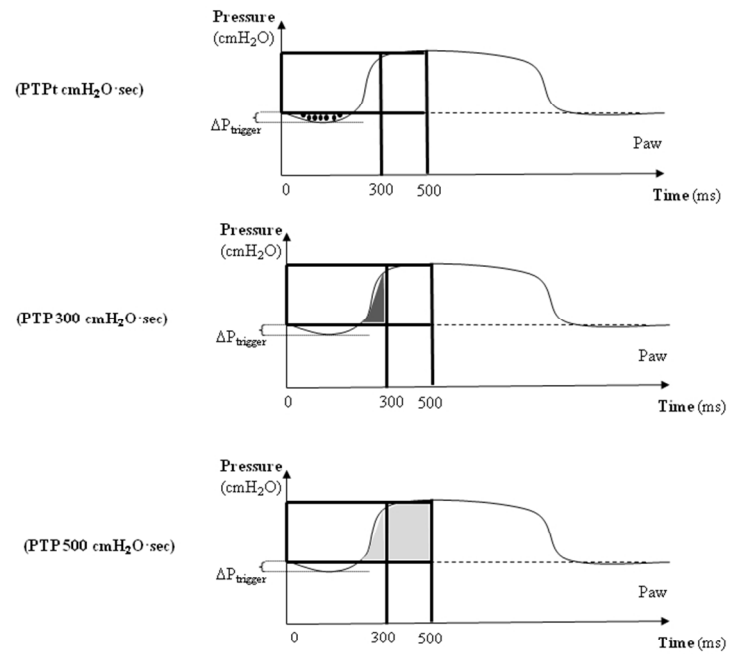


Fig. 2: Inspiratory pressure-Time product (PTPt), Pressure-Time Product at 300 and 500 ms (PTP 300 and PTP 500) on the Pressure-Time trace.  
254x190mm (96 x 96 DPI)

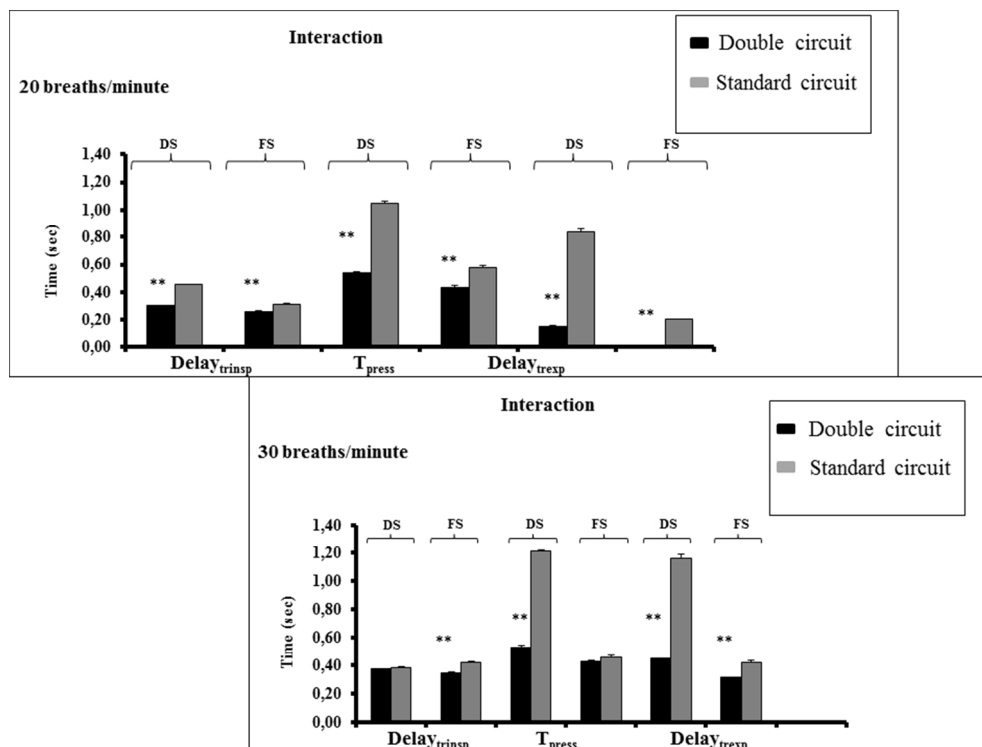


Fig. 3: Inspiratory trigger delay (Delay<sub>trinsp</sub>), pressurization time (Time<sub>press</sub>) and expiratory trigger delay (Delay<sub>trexp</sub>) at 20 and 30 breaths/min, with two ventilator settings (DS=Default setting [Time<sub>press</sub>/T<sub>rexp</sub> 50%/25%]; FS=Fast setting [Time<sub>press</sub>/T<sub>rexp</sub> 80%/60%]).

Black columns correspond to the double tube circuit, grey columns to the standard circuit.

Double circuit vs Standard circuit:  $p < 0.05 = *$ ;  $p < 0.01 = **$

254x190mm (96 x 96 DPI)

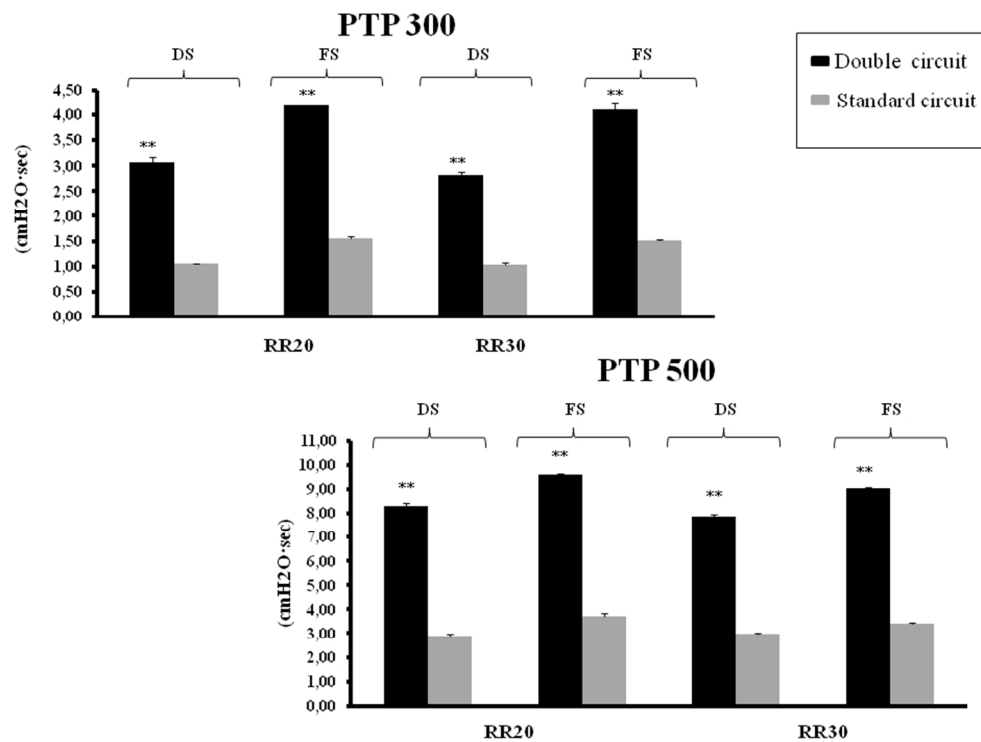


Fig. 5: Pressure-time product at 300 and 500 ms (PTP 300 and PTP 500) at 20 and 30 breaths/min (RR20 and RR30) with two ventilator settings (DS=Default setting [Timepress/Trexp 50%/25%]; FS=Fast setting [Timepress/Trexp 80%/60%]).

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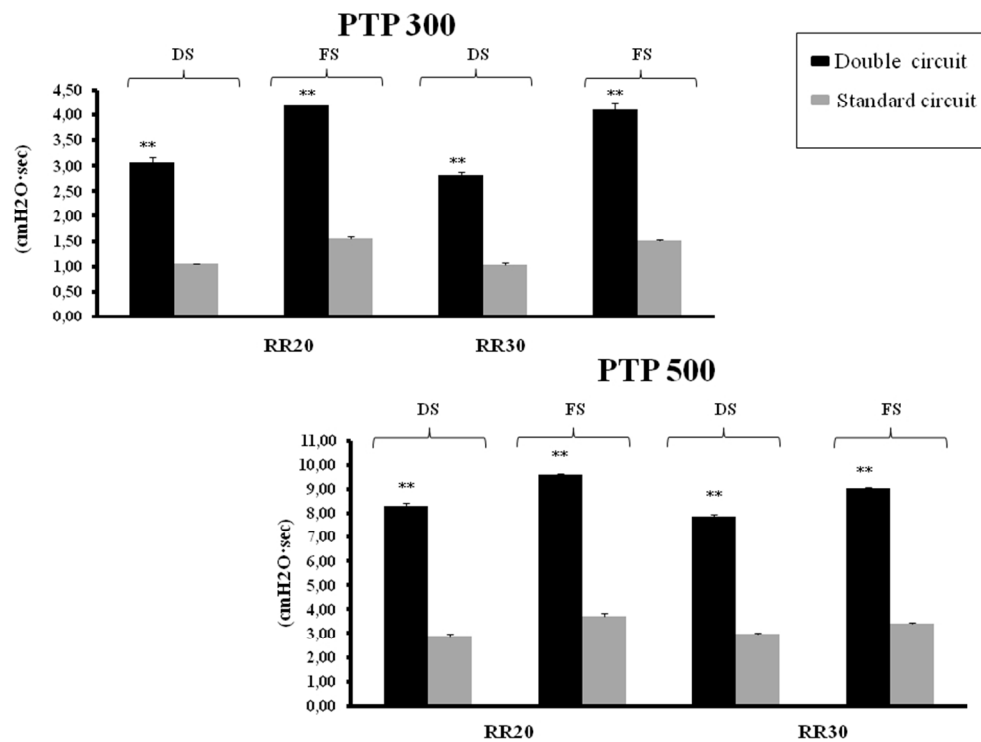


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