



Expert article

Effect of inspiratory rise time on sputum movement during ventilator hyperinflation in a test lung model

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Abstract

Objectives Physiotherapists may use ventilator hyperinflation to enhance secretion clearance for intubated patients. This study investigated the effects of altering percentage inspiratory rise time (IRT) on sputum movement, ratio of peak inspiratory to expiratory flow rate (PIF:PEF ratio) and net peak expiratory flow (PEF) during ventilator hyperinflation in a test lung model.

Design Laboratory-based bench study.

Interventions Simulated sputum (two viscosities) was inserted into clean, clear tubing and connected between a ventilator and a resuscitation bag. Thirty-six ventilator hyperinflation breaths were applied for each 5% incremental increase in IRT between 0% and 20%.

Main outcome measures The primary outcome was sputum displacement (cm). Secondary outcomes included PIF:PEF ratio and net PEF. **Results** Significant cephalad sputum movement of 2.42 cm (1.59 to 3.94) occurred with IRT between 5% and 20%, compared with caudad movement of 0.53 cm (0.31 to 1.53) at 0% IRT (median sputum movement difference 3.7 cm, 95% confidence interval 2.2 to 4.8, $P < 0.001$). Incremental increases in IRT percentage produced linear enhancements in PIF:PEF ratio and net PEF for both sputum concentrations ($P < 0.001$). However, once the critical threshold for PIF:PEF ratio of 0.9 was achieved, the distance of sputum movement remained consistent for all IRT values exceeding 5%.

Conclusions Significant increases in sputum movement occurred when IRT percentage was lengthened to achieve the optimal PIF:PEF ratio, irrespective of sputum viscosity. This provides a theoretical rationale for therapists to consider this technique when treating mechanically ventilated patients. As no additional sputum movement was seen beyond the critical PIF:PEF ratio threshold, a low IRT percentage may potentially be used to achieve effective sputum movement.

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Keywords: Ventilators; Mechanical; Physical therapists; Tidal volume; Sputum; Peak expiratory flow rate; Flow bias

Introduction

Intubated patients receiving ventilatory support are at risk of sputum retention, airway occlusion and alveolar collapse, and may require physiotherapy to optimise ventilation and remove retained secretions [1,2]. Physiotherapists may use manual hyperinflation and ventilator hyperinflation to increase tidal volume and peak expiratory flow rate (PEF)

in order to recruit atelectatic areas or to enhance airway secretion clearance [1,3–5].

Estimates of PEF both manual and ventilator hyperinflation range from 27.8 l/min to 120 l/min [6–8]. These values do not approach the peak flows produced during huffing or coughing (360 to 720 l/min) [9], so cannot be said to be effective via the same propulsive method of air flow. Instead, sputum clearance via manual and ventilator hyperinflation is likely to depend upon two-phase gas liquid flow interactions, whereby air flow creates a shearing force upon the liquid surface, creating annular waves in the direction of air flow [10–12]. For net sputum movement towards the mouth

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(cephalad) to occur, the shear forces must exceed gravitational and viscous resistance, with an overall expiratory flow bias that exceeds a critical threshold. The critical thresholds suggested in published literature to date have been either a ratio between peak inspiratory flow and expiratory flow rates (PIF:PEF ratio) <0.9 in which PEF exceeds PIF by at least 10% [11,13–15], or when PEF exceeds PIF (net PEF) by 17 l/min, under laboratory conditions [16].

Savian *et al.* [7] found that PIF:PEF ratio was higher using ventilator hyperinflation compared with manual hyperinflation, with ventilator hyperinflation achieving a ratio of 1.27 (i.e. favouring inspiratory flow of air). This suggested that ventilator hyperinflation may promote caudad movement of sputum, embedding sputum into the lungs rather than towards the mouth. Findings may, in part, have been due to the ventilator hyperinflation method, which involved delivering large tidal volume breaths with a short inspiratory time. Subsequently, a bench-top ventilator hyperinflation investigation found that reducing inspiratory flow was associated with successfully achieving critical expiratory flow thresholds [17]. However, this inspiratory flow setting feature is not available on all ventilators. Other mechanical ventilation studies have suggested that reducing PIF by increasing the inspiratory:expiratory (I:E) time ratio and inspiratory rise time (IRT) may also create more favourable net PEF, PIF:PEF ratio and net cephalad sputum movement [15,18–20]. The purpose of this study was to investigate the effects of different IRT percentage settings during ventilator hyperinflation in order to identify:

- the effect of different IRT percentages on the movement of sputum, PIF:PEF ratio and net PEF during ventilator hyperinflation; and
- whether the movement of different viscosities of sputum (1.5% and 3%) was similar for each experimental condition.

Methods

Design

This experimental laboratory-based bench study was approved by the UCL Institute of Child Health and Great Ormond Street Hospital for Children NHS Foundation Trust Joint Research and Development Committee (Research and Development No. 13A12).

Equipment

The experimental setup was designed to emulate sputum within the adult trachea during both mechanical ventilation and ventilator hyperinflation. To achieve this, a mechanical ventilator (Servo-i Universal, Maquet, Stockholm, Sweden) was attached to a 30-cm length of transparent polyvinylchloride (PVC) tubing (RSONline, Corby, UK) with an

internal diameter of 10 mm, via a non-humidified circuit (Kimberley Clarke, TX, USA) and size 8, cuffed endotracheal tube (Portex, Minneapolis, MN, USA) [16]. The tubing, which represented the trachea, was positioned horizontally on a flat white surface using a spirit level. The remaining end of the 30-cm tube was attached to a 2-l inflatable resuscitation bag (Datex Omeda, General Electric, Madison, WI, USA), representing the lungs. This had a measured compliance of 15.5 ml/cmH₂O. All tubing was connected with plastic connectors with a negligible air leak (see supplementary material Fig. A in the online version at DOI: [10.1016/j.physio.2018.06.003](https://doi.org/10.1016/j.physio.2018.06.003)).

A mucus simulant was prepared using polyethylene oxide powder (Sentry Polyox WSR coagulant, Dow, Delaware, NJ, USA) and water to create a water-soluble resin coagulant; this has been used in a previous bench study [16]. A 1.5% solution was used to represent sputum of normal viscosity and a 3% solution represented viscous sputum, simulating that found in lung disease [16]. To create a 1.5% solution, 1.5 g of powder was mixed with 100 ml of boiling distilled water and stirred continuously on a combined hotplate with a magnetic stirrer to create a solution with consistent viscosity. An equivalent procedure using 3 g of the powder mixed with 100 ml of water was undertaken to produce the 3% solution. Both samples were coloured using red food dye to allow photographic imaging and subsequent analysis. Using a syringe, 1 ml of the sputum was injected into the middle of a new PVC tubing segment for each experiment.

Equipment for recording mucus movement and air flow

Mucus movement was captured using an 18-megapixel Cannon 600d camera, placed 40 cm above the sputum sample using a tripod perpendicular to the sputum specimen. Baseline mechanical ventilation was undertaken for 2 min, after which an image was captured during expiration. Baseline ventilation allowed the sputum to settle, providing a consistent baseline between datasets and exposing the sputum to the normal shearing forces that occur during tidal volume ventilation. Next, 36 ‘breaths’ of ventilator hyperinflation were applied and a second image was recorded during expiration.

Sigmascan Pro 5 (Stat Software Inc., London, UK) was used to evaluate the movement of simulated sputum between the end of baseline ventilation and following the ventilator hyperinflation intervention. The software measured sputum area and depth by determining the number of red pixels within each square centimeter, and calculating the movement of the sputum centre of mass from the ventilator hyperinflation.

The CO₂SMO Plus 8100 Respiratory Profile Monitor (Novamatrix Medical Systems Inc, Philips Respironics, Wallingford, CT, USA) was used to measure tidal volume, respiratory rate, PIF, PEF and peak inspiratory pressure continuously via a fixed orifice differential flow-pressure transducer. The CO₂SMO was positioned between the endotracheal tube and catheter mount, and connected to a laptop to record data (see supplementary material Fig. A in the online

version at DOI: [10.1016/j.physio.2018.06.003](https://doi.org/10.1016/j.physio.2018.06.003)). To ensure data accuracy, the CO₂SMO was calibrated prior to the experiment using a 500-ml calibration syringe (Hans Rudolph Inc., Lenexa, KS, USA) using volumes of 300 ml, 400 ml and 500 ml. Measurement within 5% of delivered volume was deemed as appropriately accurate for the study. The CO₂SMO has been validated previously over this volume range and has been used in both clinical practice and research [21,22].

Intervention

The baseline ventilation was delivered in pressure-regulated volume control mode with positive end expiratory pressure of 5 cmH₂O, I:E time ratio of 1:2 and IRT of 5%. These settings were considered to be consistent with routine clinical care [23,24]. A baseline tidal volume of 370 ml during mechanical ventilation was applied. This volume was calculated using the ARDSNet protocol for a targeted 6 ml/kg of predicted body weight [25] using the average UK height [26]. Ventilator hyperinflation was delivered by increasing tidal volume until peak airway pressure reached 40 cmH₂O, in line with previous clinical studies [4,27,28]. During testing of the experimental setup, this volume was calculated to be between 550 and 700 ml. To provide a consistent minute volume, the respiratory rate was reduced to 8 bpm when IRT percentage was also changed. This reduction was similar to previous clinical studies, and prevented the impact of elastic recoil and airway flows that would have occurred with a higher minute volume [7,28].

IRT was manipulated using IRT percentage control, as this was the most straightforward option to modify IRT in this volume control mode. IRT was set at either a 0%, 5%, 10%, 15% or 20% interval for 36 consecutive breaths. Ventilator hyperinflation breaths started immediately after respiratory rate and IRT percentage were altered. Each experiment was completed three times for each of the 10 experimental conditions, with new tubing and sputum injection used for each experimental condition. The experiment was conducted by a physiotherapist who had specialised within the respiratory field for approximately 8 years.

Data analysis

The CO₂SMO respiratory monitor was programmed internally to deploy brief automatic calibration ‘purges’ at regular 2-min intervals; during these purges, respiratory measurements were not possible (approximately 2 to 3 s). Data from the CO₂SMO were examined and calibration purge intervals were excluded. Non-parametric tests were used to analyse the datasets for each experiment. The comparison of sputum movement across the range of IRT percentages was analysed using Kruskal Wallis analysis of variance (ANOVA), and comparison between sputum viscosity types was calculated using Mann–Whitney U-test. To determine whether there was a difference in PIF, PEF, PIF:PEF ratio and net PEF

Table 1
Experimental settings.

	Baseline ventilation	Experiment settings
Ventilator mode	PRVC	PRVC
V _T (ml)	370	550 to 700
Respiratory rate (bpm)	15	8
PEEP (cmH ₂ O)	5	5
I:E ratio	1:2	1:2
Inspiratory rise time (%)	5%	0%, 5%, 10%, 15%, 20%
Inspiratory rise time (s) ^a	0.2	<0.1, 0.35, 0.75, 1.13, 1.5
Length of ventilation	2 min	36 breaths
PAP (cmH ₂ O)	25	40
Mucus viscosity	1.5% and 3%	1.5% and 3%

I:E ratio, inspiratory:expiratory ratio; PAP, peak airway pressure; PEEP, positive end expiratory pressure; PRVC, pressure regulated, volume controlled; V_T, tidal volume.

^a Estimated number as variable dependent upon ventilator gas flow acceleration, and time is required to accelerate and deliver gas flow even when inspiratory rise time percentage is set at 0%.

between IRT ranges, the Kruskal Wallis ANOVA was used with post hoc analysis where appropriate. Spearman’s rank test was used to ascertain any correlation between PIF:PEF ratio and net PEF with IRT percentage. The level of significance was set at $P < 0.05$ and, where appropriate, the data are displayed as median with interquartile range or mean and standard deviation with 95% confidence interval.

Results

Management of data

Each dataset was examined and measurements affected by the purging process were removed. Six to seven breaths were required to reach a steady state at the pre-determined ventilator hyperinflation levels; these were excluded from the data analysis. On average, 29 ventilator hyperinflation breaths per experiment were used for statistical analysis. The experimental settings are displayed in Table 1.

Observed sputum movement

The Kruskal Wallis ANOVA detected a significant difference between IRT percentage groups ($P < 0.05$), but further analysis showed no significant differences in sputum movement between groups for any IRT between 5% and 20% (Fig. 1). Significant cephalad sputum movement of 2.42 cm (1.59 to 3.94) occurred for IRT of 5% or more, across both sputum viscosities, compared with caudad movement of 0.53 cm (0.31 to 1.53) at 0% IRT across both viscosities, (median sputum movement difference 3.7 cm (95% confidence interval 2.2 to 4.8, $p < 0.001$). Sputum of normal viscosity consistently moved significantly further than viscous sputum for all ventilator hyperinflation settings (Table 2). The median difference in sputum movement between viscosities of 1.5% and 3% was 2.31 cm (1.61, 2.96, $P = 0.004$).

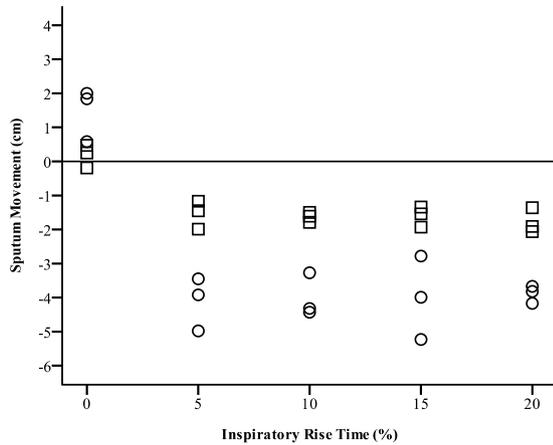


Fig. 1. Sputum movement plotted against change in inspiratory rise time during ventilator hyperinflation with 1.5% (circle) and 3% (square) sputum viscosities. The ‘0’ reference line denotes no movement in either direction. Negative movement indicates cephalad movement towards the mouth.

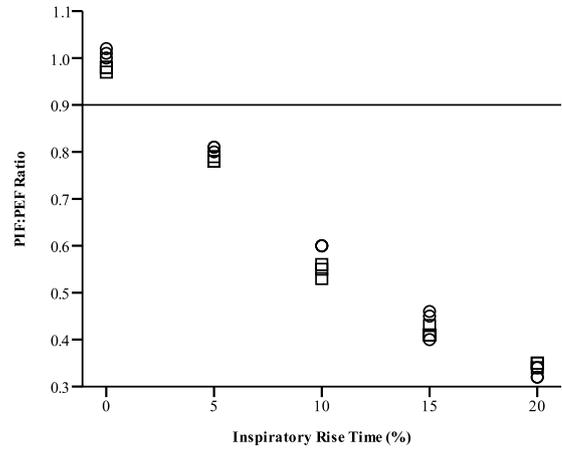


Fig. 2. Peak inspiratory to expiratory flow rate (PIF:PEF) ratios plotted against change in inspiratory rise time during ventilator hyperinflation with 1.5% (circle) and 3% (square) sputum viscosities. The reference line at 0.9 describes the PIF:PEF threshold below which net sputum movement is expected.

PIF:PEF ratio and net PEF

As IRT increased systematically between 0% and 20%, PEF did not change significantly ($P = 0.151$), but PIF reduced significantly for both sputum viscosities as IRT percentage increased ($P < 0.001$) (Table 2). Consequently, there was a strong, negative correlation ($r = -0.982$, $P < 0.001$) between mean PIF:PEF ratio and the increased IRT percentage for both sputum samples during ventilator hyperinflation. PIF:PEF ratio dropped below the theoretical critical threshold of 0.9 for cephalad sputum movement between 0% and 5% IRT, and then decreased further for each subsequent 5% increase in IRT, suggesting that mucus movement would be linearly enhanced by increasing IRT percentage (Fig. 2). For both spu-

tum viscosities, there was a significant difference ($P < 0.01$) in PIF:PEF ratio when IRT differed by more than 10%.

Similarly, there was a strong, positive correlation between net PEF and the increase in IRT percentage ($r = 0.972$, $P < 0.001$) for both sputum viscosities. The theoretical net PEF threshold of greater than 17 l/min was achieved when IRT percentage increased to 10% or more, suggesting that mucus movement would be linearly enhanced in relation to IRT percentage as long as IRT exceeded 10% (Fig. 3). There was a significant difference in net PEF when IRT percentage increased by more than 10% for both sputum viscosities ($P < 0.01$).

Table 2
Sputum movement and airflow measurements captured at different inspiratory rise times using 1.5% and 3% sputum viscosities.

IRT	Sputum viscosity (%)	PEF (l/min) Mean (SD)	PIF (l/min) Mean (SD)	PIF:PEF ratio Mean (SD)	PEF-PIF Mean (SD)	Sputum movement (cm) Median (IQR)
Baseline ventilation	1.5	49.30 (3.52)	44.65 (2.32)	0.91 (0.03)	4.64 (1.80)	
	3	51.24 (2.85)	47.49 (1.43)	0.92 (0.05)	3.75 (2.47)	
0%	1.5	63.13 (1.25)	63.77 (1.38)	1.01 (0.03)	-0.64 (1.69)	+1.47 (1.21 to 1.92)
	3	72.23 (1.97)	70.52 (1.43)	0.98 (0.03)	1.71 (2.30)	+0.18 (0.03 to 0.36)
5%	1.5	64.72 (1.04)	52.14 (0.42)	0.81 (0.01)	12.57 (0.99)	-4.12 (-4.45 to -3.69)
	3	71.40 (1.71)	55.56 (0.47)	0.78 (0.02)	15.54 (1.75)	-1.54 (-1.72 to -1.31)
10%	1.5	63.57 (1.19)	38.11 (0.28)	0.60 (0.01)	25.45 (1.20)	-4.01 (-4.38 to -3.80)
	3	74.02 (2.42)	40.49 (0.25)	0.55 (0.02)	33.54 (2.44)	-1.63 (-1.70 to -1.56)
15%	1.5	68.39 (6.16)	29.69 (0.54)	0.44 (0.03)	38.70 (5.67)	-4.00 (-4.61 to -3.39)
	3	73.16 (2.74)	30.49 (0.19)	0.42 (0.02)	42.68 (2.68)	-1.60 (-1.74 to -1.44)
20%	1.5	76.97 (2.36)	24.96 (0.21)	0.32 (0.01)	52.01 (2.31)	-3.89 (-4.00 to -3.75)
	3	71.79 (3.33)	24.68 (1.36)	0.34 (0.01)	47.11 (2.47)	-1.78 (-1.99 to -1.64)

IQR, interquartile range; IRT, inspiratory rise time; PIF, peak inspiratory flow; PEF, peak expiratory flow; PIF:PEF ratio, peak inspiratory flow:peak expiratory flow ratio; PEF-PIF, peak expiratory flow-peak inspiratory flow; SD, standard deviation.

The movement of sputum towards the endotracheal tube is denoted by a descending, more negative value, and caudad movement is indicated by an ascending, positive value.

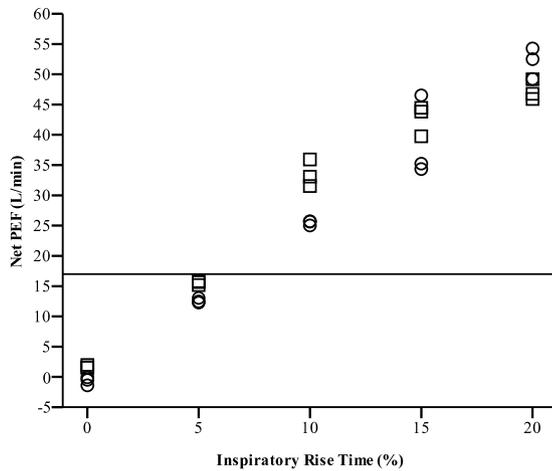


Fig. 3. Net peak expiratory flow (PEF) plotted against change in inspiratory rise times during ventilator hyperinflation with 1.5% (circle) and 3% (square) sputum viscosities. The reference line at 17 l/min describes the threshold above which net sputum movement is predicted.

Discussion

To the authors' knowledge, this is the first study to investigate whether altering IRT percentage during ventilator hyperinflation can improve the expiratory flow bias and cephalad net sputum movement in ventilated patients. The main finding was that cephalad movement of sputum could be observed for all IRT values meeting or exceeding 5%, and retrograde sputum movement was likely when IRT was set at 0%. Furthermore, despite the published theoretical models predicting a linear relationship between sputum movement and PIF:PEF ratio or net PEF, once critical thresholds were achieved, no further enhancement was observed in sputum movement for any IRT values meeting or exceeding 5%. Finally, sputum of normal viscosity moved significantly further than thicker sputum for all IRT percentages, either in a retrograde direction (when IRT was set at 0%) or in a cephalad direction (when IRT was set at 5%, 10%, 15% or 20%).

Given the strong relationships between increasing IRT percentage and both PIF:PEF ratio and net PEF, sputum movement might be expected to be further enhanced with each 5% incremental increase in IRT in a systematic and predictable manner (Figs. 2 and 3). However, sputum movement appeared to plateau for all IRT values between 5% and 20%, despite conditions exceeding the threshold criteria for sputum movement (Figs. 1 and 4). Factors such as insufficient number of breaths at the full ventilator hyperinflation volume, crude measurement of sputum movement or inability of the PVC tube to represent a ciliated humidified airway may have contributed to the lack of differentiation in sputum movements between 5% and 20% IRT. However, the most likely rationale is related to the flow threshold. Annular flow occurs when air flow exceeds 6 to 20 l/min, and formation of mist flow occurs at a threshold of 150 l/min air flow or above [10,11,13,14,29]. The highest peak flow achieved during this study measured 79 l/min, well below the threshold required

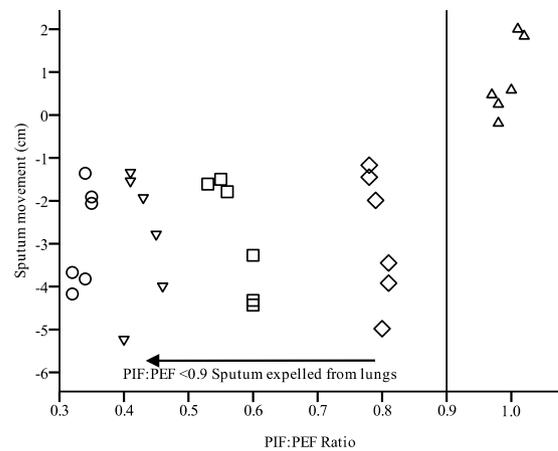


Fig. 4. Peak inspiratory to peak expiratory flow rate ratios (PIF:PEF) plotted against sputum movement during ventilator hyperinflation at the differing inspiratory rise time (IRT) percentages. The reference line at 0.9 describes the threshold above which net sputum movement is predicted. Circles represent data outcomes gathered using a 20% IRT percentage. Downward triangles represent data outcomes gathered using a 15% IRT percentage. Squares represent data outcomes gathered using a 10% IRT percentage. Diamonds represent data outcomes gathered using a 5% IRT percentage. Upward triangles represent data outcomes gathered using a 0% IRT percentage.

for mist flow. This may explain why the sputum movement did not increase continuously between 5% and 20% IRT in the manner suggested by PIF:PEF ratio and net PEF graphs. This result contrasts with the study by Kim *et al.*, which detected a linear relationship between the rate of air flow and speed of mucus movement, although they used continuous unidirectional air flow for their study [30].

Net PEF exceeded the threshold of 17 l/min when IRT was increased to 10% and above, whilst generation of PIF:PEF ratio < 0.9 occurred for all data points between 5% and 20% IRT. Comparing these two threshold requirements for two-phase gas liquid flow, it is clear that PIF:PEF ratio of 0.9 predicted mucus movement more accurately than net PEF of 17 l/min, despite similarities in the methods used by Volpe *et al.* and the current study [16]. The 17 l/min threshold has not been reproduced by any other authors. Conversely, research examining PIF:PEF ratios used the theory of fluid mechanics to provide a mathematical modelling solution applicable to multiple conditions of two-phase gas liquid flow, and therefore may be more generalisable to other settings [13,14].

Both types of sputum moved in the same direction in response to changes in IRT percentage. This is clinically relevant, demonstrating that sputum may behave in a similar manner over a range of viscosities and does not require different conditions in order to promote cephalad movement. The greater movement of the sputum of normal viscosity is consistent with previous studies as well as clinical practice [11,13,14,16], signifying that mucus of a lower viscosity will respond more quickly during ventilator hyperinflation interventions.

During the volume control mode, IRT percentage is the percentage of time taken to reach PIF over the respiratory cycle. Both the increase in IRT percentage and reduction of the respiratory rate will increase the calculated IRT as measured in seconds (Table 1). These figures are estimates due to ventilator variability to achieve the desired maximal flow within a pre set time [32]. Both the length of IRT (as measured in seconds) and pulmonary airway pressure will generate the resultant PIF. Although favourable PIFs were achieved at only 5% IRT during these experimental ventilator hyperinflation conditions, if respiratory rate was higher, IRT percentage may have to be manipulated further to optimise PIF.

The laboratory-based bench experimental design was chosen as it permitted proof-of-concept analysis of multiple experimental conditions. These were tested to identify methods of improving the effectiveness of ventilator hyperinflation, without the need to involve patients in the first instance. The lung model excluded physiological variations and therefore controlled for potential confounding factors that would occur in the clinical environment. However, a laboratory-based study with a fixed diameter tube and inflatable bag cannot replicate normal patient physiology exactly (i.e. multiple airway branching, dynamic airway compression, collateral ventilation, lung hysteresis, variable lung unit compliance, mucociliary escalator, non-uniform sputum viscosity, etc.). This model was unable to reproduce the layers within the airway surface liquid or the ciliary movement, and instead focused upon dry gas flow on homogenous sputum. The impact of humidity upon the viscous and elastic properties of simulated sputum has not been accounted for. Additionally, the simulated trachea was placed horizontally rather than at the 30° head up position used clinically. Consequently, the additional force required to move sputum upwards was not reproduced, potentially reducing the flow thresholds at which sputum movement occurred and/or increased the resulting sputum movement at the set IRT percentage. Due to the experimental method using a tube with an inner diameter of 10 mm, these results cannot be generalised to bronchial clearance.

This method of enhancing ventilator hyperinflation through alteration of IRT percentage provides a theoretical rationale to improve tracheal sputum clearance in clinical practice. The potential negative side effects of an inappropriately long IRT percentage could include patient–ventilator asynchrony and consequential discomfort. However, most patients requiring a volume control mode are sedated and such effects are small in magnitude, easy to identify and quick to reverse. Given that an optimal PIF:PEF ratio was achieved at a conservative IRT percentage, it should be feasible to achieve an optimal balance between patient comfort and effective sputum movement. Further analysis of PIF:PEF ratios during ventilator hyperinflation in clinical practice to ascertain whether the threshold <0.9 is achieved at a conservative IRT percentage in patients with higher lung compliance could prove useful.

This study confirms that increasing IRT percentage results in a favourable PIF:PEF ratio and increases net PEF within a test lung model through a reduction in PIF. This creates conditions that theoretically promote two-phase gas liquid flow of cephalad mucus movement and therapeutic tracheal clearance. However, once critical thresholds for sputum movement are achieved, no further net benefit is seen by increasing IRT percentage further. During this study, effective cephalad sputum movement occurred when IRT percentage was set between 5% and 20%. Therefore, clinicians are encouraged to analyse PIF and PEF outcomes generated during ventilator hyperinflation, and consider lengthening IRT percentage to optimise their treatment whilst monitoring patient comfort and synchrony.

Ethical approval: Ethical approval was not required for this laboratory-based bench study since the study did not involve human participant. The study was registered with Great Ormond Street Hospital for Children NHS Trust and University College London, Institute of Child Health Research Ethics Committee (Research and Development No. 13A12).

Conflict of interest: None declared.

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