The influence of Flutter\textsuperscript{\textregistered} VRP1 components on mucus transport of patients with bronchiectasis

Joana Tambascio\textsuperscript{a,}\textsuperscript,* , Léa Tatiana de Souza\textsuperscript{b} , Roberta M. Lisboa\textsuperscript{a} , Rita de Cássia V. Passarelli\textsuperscript{a} , Hugo Celso Dutra de Souza\textsuperscript{a} , Ada Clarice Gastaldi\textsuperscript{a}

\textsuperscript{a} University of São Paulo, Ribeirão Preto, São Paulo, Brazil
\textsuperscript{b} Centro Universitário do Triângulo, Uberlândia, Brazil

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**KEYWORDS**
Bronchiectasis; Mucus transport; Physical therapy modalities

**Summary**

Background: The Flutter\textsuperscript{\textregistered}VRP1 combines high frequency oscillation and positive expiratory pressure (PEP).

Objective: To separately evaluate the effect of the Flutter\textsuperscript{\textregistered}VRP1 components (high frequency oscillation and PEP) on mucus transportability in patients with bronchiectasis.

Methods: Eighteen patients with bronchiectasis received sessions with the Flutter\textsuperscript{\textregistered}VRP1 or PEP for 30 min daily in a randomized, crossover study. The treatment duration was four weeks with one of the therapies, one week of a “wash-out” period and followed by four more weeks with the other treatment. Weekly secretion samples were collected and evaluated for mucociliary relative transport velocity (RTV), displacement in a simulated cough machine (SCM) and contact angle measurement (CAM). For the proposed comparisons, a linear regression model was used with mixed effects with a significance level of 5%.

Results: The Flutter\textsuperscript{\textregistered}VRP1 treatment resulted in greater displacement in SCM and lower CAM when comparing results from the first (9.6 ± 3.4 cm and 29.4 ± 5.7°, respectively) and fourth weeks of treatment (12.44 ± 10.5 cm and 23.28 ± 6.2°, respectively; p < 0.05). There was no significant difference in the RTV between the treatment weeks for either the Flutter\textsuperscript{\textregistered}VRP1 or PEP.

Conclusion: The use of the Flutter\textsuperscript{\textregistered}VRP1 for four weeks is capable of altering the respiratory secretion transport properties, and this alteration is related to the high frequency oscillation component.
Introduction

Bronchiectasis is a respiratory pathway disease with diverse etiologies that is pathologically characterized by abnormal and permanent dilated airways and principally caused by the perpetuation of inflammatory processes induced by frequent bacterial infections. This results in an alteration of the ciliated epithelial lining and compromised mucociliary clearance effectiveness.

The damage to mucociliary clearance is associated with thicker mucous production and, therefore, results in less transport that favors the hypersecretory state observed in these patients; this can also exacerbate and increase secretion production periods resulting in significant repercussions for the individual.

Beyond medication and/or surgical treatment, patients with bronchiectasis also have indications for physiotherapeutic treatment, which constitutes an important part of the treatment regimen. The patients demonstrate difficulty with mucous elimination and transport and can experience benefits from respiratory physical therapy, which has the goal of increasing the removal of respiratory pathway secretions and consequently decreases blockages to improve pulmonary ventilation and gas exchange.

One of the instruments frequently used for respiratory physical therapy is the Flutter®VRP1 (VarioRaw S.A, Switzerland), which is a simple, small piece of equipment similar to a pipe that has a stainless steel ball within it and combines two techniques: positive expiratory pressure and high frequency oscillations, adjuvants for the treatment and prevention of alveolar collapse and the elimination of pulmonary secretions.

Some previous studies have demonstrated beneficial effects after the use of this device in patients with bronchiectasis. However, it is not clear if the mechanism of action is related to the combination of PEP and high frequency oscillation techniques or only one of these components.

Therefore, the present study was designed to evaluate the Flutter®VRP1 effects (VarioRaw S.A, Switzerland) on mucous transportability in patients with bronchiectasis in order to separately identify the effects of the PEP and high frequency oscillation components.

Material and methods

Patients were selected for this study if they were clinically stable with a diagnosis of bronchiectasis that was not due to cystic fibrosis, as defined by a complete clinical history, physical examination and confirmed by CT scan.

Patients were excluded from the study if they did not demonstrate a sufficient respiratory secretion quantity for the analysis or if they had developed any respiratory infection in the four weeks prior to the study or during the protocol.

This study was registered in the "Protocol Registration System — ClinicalTrials.gov" (NCT01209546) and the participating individuals were informed about all stages of the research and signed an informed consent form approved by the local ethics committee (no 6007/2007).

Protocol

The patients received Flutter®VRP1 or PEP exercise sessions daily for 30 min each day in a randomized, crossover study. Each patient received treatment with one of the therapies for four weeks, which was randomly determined by a drawing, followed by one week of a "wash-out" period and then an additional four more weeks with the other treatment modality.

The exercises were performed in the seated position, and patients were instructed to perform long and quiet expirations during the treatment. In order to evaluate the technique used by the patients and to perform the secretion collection, a physiotherapist supervised the patients twice per week. During all other days, the patients completed the exercises without supervision and were instructed to record information daily regarding the number of pauses while using the device or other relevant observations.

The Flutter®VRP1 (Flutter) protocol used the equipment without modifications. The PEP protocol used the Flutter®VRP1 device without the stainless steel ball inside and after occluding as many orifices as was necessary to produce a positive expiratory pressure equivalent to the pressure reached by patients when using the Flutter®VRP1 with the stainless ball.

Pressure was measured with a manometer connected to an orifice located in the inferior portion of the device.

Prior to completing the protocol, the participants were instructed to continue their medications according to instructions with the exception of mucolytics and were evaluated with regards to arterial pressure, cardiac frequency, partial oxygen saturation and respiratory frequency.

The respiratory secretion studied was expectorated spontaneously by the patient but always supervised by the physiotherapist.

Evaluated respiratory secretion parameters

Relative transport velocity measured on the frog palate

Frogs (Rana Catesbiana) had their palates removed following decapitation and were maintained at 4 °C for 48 h to collect the mucous. Small amounts of patient mucous were removed from a plastic tube and were submerged in ether to remove excess Vaseline and then deposited on the palate. The sample displacement was observed using a stereomicroscope with an 8× magnification lens (Carl Zeiss, Stemi1000-Germany), and the transport time was recorded with the use of a chronometer (Herweg-8904-Brazil). The results were expressed as relative transport velocity compared to the average of five experimental mucous transport velocity measurements for the frog (average of the summed velocity of the initial and final frog speeds for the experimental mucous evaluation).

Simulated cough machine transport

Analysis of the cough machine mucous transport was completed according to the model described by King et al. and adopted by the Heart Institute Precision Institute — Incor — SP. The model was composed of a
source, a solenoid valve and a simple scheme of airways, represented by a dry acrylic cylinder measuring 30 cm in length and 4 mm in internal diameter, with the three elements connected in a series. When the cough simulator machine was activated, the timing device controlled opening of the solenoid for 1 s, allowing the exit of air at 4.2 kg f/cm² of pressure, thus moving the secretion sample. Each mucous sample was tested five times and the average of these five displacements was used.

**Contact angle measurement**

The angle, in degrees, formed between the mucous and the glass surface was considered the contact angle and was measured using a goniometer with a 20° magnification lens. The glass surface used for these analyses was treated with sulphochromic acid to remove any electrical charge. The sample was evaluated five times and the average of these measurements was used.

**Statistical analysis**

To evaluate the objectives, a linear regression model with mixed effects was used (random and fixed effect) using a significance level established at 5%.

A possible sequential effect was initially evaluated and subsequently compared to the results obtained after application of the two techniques.

**Results**

There were 30 patients that were selected to participate in the study; six of these did not demonstrate any secretion during the analysis protocol and six experienced respiratory tract infections during the activity period. Therefore, 18 patients participated in and completed the protocol. Of the 18 patients, 13 were female and five were male with an average age of 51.7 ± 18.4 years. In regards to pulmonary function, one participant demonstrated values within normal ranges (VEF1/CVF > 0.7 and VEF1 of 95%) and 17 demonstrated airway obstruction (VEF1/CVF < 0.7), with three with VEF1 varying from 81 to 83%, nine with VEF1 varying from 62 to 77%, four with VEF1 varying from 31 to 47% and one with VEF1 of 29%.

The average positive expiratory pressure achieved by the patients was 15.7 cmH₂O, with a range of 4–32 cmH₂O. **Table 1** shows the results of the relative transport velocity (RTV), displacement in simulated cough machine (CSM) and contact angle measurement (CAM) for each treatment and week. The initial statistical analysis demonstrated that there was no sequential effect in the treatment of the patients, and the results were analyzed comparing the initial values between the PEP and Flutter VRP1 groups.

In regards to the relative transport velocity, there was no statistically significant difference between the treatment weeks or type of treatment (Fig. 1). When the displacement in the simulated cough machine was evaluated, there was increased displacement for the values obtained in the fourth week (12.44 ± 10.5 cm) compared to those obtained in the first week (9.6 ± 3.4 cm).

<table>
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<th>Variable</th>
<th>Average</th>
<th>DP</th>
<th>Week</th>
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*p < 0.05.

[Table 1: Description of the RTV, CSM and CAM for each treatment (Flutter and PEP) and week.]

[**Fig. 1** Graphical representation of the relative transport velocity values in the first and fourth weeks of Flutter and PEP therapy.]
of Flutter therapy ($p < 0.05$). There was no difference when the displacement values were compared between the PEP therapy treatment weeks (Fig. 2).

In regards to the contact angle measurement (CAM), there was a decrease in the values obtained in the first ($29.39 \pm 5.7^\circ$) when compared with the fourth week ($23.28 \pm 6.2^\circ$) when using the Flutter therapy ($p > 0.05$). There was no difference in the contact angle values when comparing between treatment weeks f PEP (Fig. 3).

**Discussion**

In this study, the relative transport velocity on a frog palate (RTV), the displacement on a simulated cough machine (SCM) and the contact angle measurement (CAM) of respiratory secretions were measured in patients with bronchiectasis that received oscillating positive expiratory pressure treatment (Flutter therapy) and positive expiratory pressure (PEP therapy) via the use of the Flutter™VRP1 device. The protocol included four weeks of treatment with one of the therapies, one week of a “wash-out” period and four additional weeks with the other treatment modality.

The results revealed a decreased contact angle and increased displacement of expectorated secretions submitted at the end of the fourth week of Flutter therapy treatment.

On the other hand, the use of PEP therapy, which, in this protocol, had the purpose of differentiating the two components involved in the Flutter™VRP1 mechanism (oscillation + PEP) but also constitutes one type of physical therapy technique for secretion removal (PEP or EPAP), did not reveal any changes in the properties of respiratory secretion transport during the same period.

To our knowledge, this is the first study that has demonstrated an improvement in respiratory secretion transport after exercises with Flutter™VRP1 in patients with bronchiectasis. The increased displacement measured by coughing and a reduced contact angle can be attributed to thixothropic flow, a property of mucous that results in reduced viscosity when submitted to oscillation. This effect had been demonstrated by App et al. (1998) and Ramos et al. (2009) in patients with bronchiectasis and cystic fibrosis, respectively.

Early use of oscillation equipment to aid in secretion removal came from experimental studies in dogs that demonstrated better secretion transport after oral or thoracic oscillations with the greatest effect in the 13–15 Hz frequency band. With the Flutter™VRP1, *in vitro* studies have obtained decreased mucus rigidity that is more easily transported through airways after the application of high frequency oscillations, resulting in the hypothesis that these oscillation frequencies may be capable of breaking the macromolecular bonds in the mucus.

App et al. (1998), in a similar protocol (four week, crossover study), evaluated respiratory secretions after using the Flutter™VRP1 device or autogenic drainage techniques in patients with cystic fibrosis. The authors reported reduced viscosity and increased calculated ciliary transport and cough treatment transport indices after using the Flutter™VRP1.

Previously, in cystic fibrosis, Konstan et al. (1994) evaluated the effectiveness of Flutter™VRP1 device by comparing the results with conventional respiratory physical therapy techniques (voluntary cough or postural drainage) and reported a greater sputum expectorated volume with the use of the Flutter™VRP1 device. However, in the same year, Pryor et al. (1994) compared results of the use of the Flutter™VRP1 device and an active respiration cycle and observed a greater expectorate volume with the active respiration cycle.

In regards to patients with bronchiectasis, some previous studies have studied the effectiveness of the Flutter™VRP1 in relation to the expectorate secretion volume, relative velocity on the frog palate, displacement in the simulated cough machine, contact angle and respiratory secretion viscosity. However, studies by Antunes (2001) and Valente (2004) did not demonstrate beneficial results after the use of the Flutter™VRP1.
Pires et al. (2004), in a case study with results from only one patient and only three therapy sessions, observed improved ciliary transport, cough transport and respiratory secretion viscosity after the use of the same equipment compared to thoracic percussion.

Ramos et al. (2009) have already demonstrated decreased respiratory secretion viscosity after the use of a Flutter® VRP1 for only one day. However, the viscosity alteration did not demonstrate improved transport indices for ciliary or cough transport, which, in reality, leaves doubts about the clinical effectiveness of the device. Those results confirm the findings of Valente et al. and the present study, neither of which observed acute effects from Flutter® VRP1 therapy either after a single 40-min session or after one or two weeks of therapy (present study).

It is likely that our results are related to the fact that we employed the technique daily during the four weeks of proposed treatment, whereas others have studied the effects with a maximum of only four Flutter® VRP1 sessions in bronchiectasis patients.

Although we did not evaluate respiratory secretion viscosity, our results indirectly suggest physical property changes due to the fact that use of the Flutter® VRP1 device over a four week period was capable of modifying secretion properties, as demonstrated by the decreased contact angle and improved cough transport. These alterations favor secretion removal in these patients with damaged mucociliary transport that use coughing as a primary clearance mechanism.

The lack of changes in the relative transport velocity, representative of ciliary transport function, is consistent with previous work and may be related to the fact that the relative transport velocity in our samples was within the normal range, varying from 1.0–1.1.

Another hypothesis is that patients with chronic hypersecretion initially have mucociliary transport damage, but with changes in cough transport. With disease progression, the cough transport also becomes damaged. It is possible that the changes induced by the Flutter® VRP1 exercises promote a partial reversion of these alterations, thereby demonstrating improved cough transport but not improved ciliary transport.

PEP therapy, as previously mentioned, also represents a secretion removal technique and, in this study, was used to isolate the mechanisms used by Flutter® VRP1 therapy that correlated with the improvement in respiratory secretion transport. However, the lack of significant results for this technique implies that the four week period was not enough to modify the secretion transport properties. In other words, the factor that was capable of influencing transport properties is more related to the oscillation technique that the Flutter® VRP1 offers than with positive expiratory pressure.

The average attained expiratory pressure during this protocol was 15.7 cmH₂O with a range of 4–32 cmH₂O. We believe that this variation did not interfere with our results because the positive expiratory pressure level used was similar to that produced by the Flutter® VRP1. This strategy was used to separately identify the involved mechanisms in the selected equipment. Moreover, the authors that evaluated the Flutter® VRP1 device with controlled expiratory pressures did not find significant results between transport index values.

These results allow us to conclude that the use of the Flutter® VRP1 device for four weeks is capable of modifying respiratory secretion transport properties and that this alteration is more closely related to the high frequency oscillation component of the treatment.

Conflict of interest
None declared.

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