Review

A review investigating the flutter's effects in people with bronchiectasis

Flutter's effect in pulmonary function and sputum clearance in bronchiectasis

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Key words:
- Flutter
- Bronchiectasis
- Sputum
- Pulmonary function

Abbreviation List
ABPA: Allergic Bronchopulmonary Aspergillosis
ACBT: Active Cycle of Breathing Techniques
AIDs: Acquired Immune Deficiency Syndrome
BC: Breathing Control
ELTGOL: Expiration with the Glottis Open in the Lateral Posture
FEV_1: Forced Expiratory Volume in One Second
$FEF_{25\%-75\%}$: Forced Expiratory Flow between 25% and 75%
FRC: Functional Residual Capacity
IC: Inspiratory Capacity
PEFR: Peak Expiratory Flow Rate
PEP: Positive Expiratory Pressure
RCTs: Randomised Controlled Trials
RV: Residual Volume
TLC: Total Lung Capacity

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ABSTRACT. BACKGROUND: Bronchiectasis is characterised by the production and retention of large volumes of secretions. These secretions could cause recurrent infections, among other complications. Chest physiotherapy aims to assist in the clearance of airway secretions and may include the flutter device. The objectives of this review are to investigate the effects of the flutter in terms of pulmonary function and sputum clearance in people with bronchiectasis. **METHODS:** MEDLINE, Cochrane Library, PubMed, CINAHL, PEDro and AMED databases were searched using subject-headings and keywords. The studies selected were those with a randomised-controlled design in which the flutter was given as one of the treatment approaches, in subjects with bronchiectasis. Inclusion and exclusion criteria were applied to the identified studies and all the relevant data was extracted and collected in a data collection sheet. The quality of these studies was assessed by two reviewers using PEDro as the quality assessment tool. **RESULTS:** Initially, eleven studies were identified. Six studies involving 96 participants met the inclusion criteria and were reviewed. A meta-analysis was not performed due to the heterogeneity of the data in the studies. Two studies concluded in favour of the flutter in terms of sputum clearance and one study showed positive or similar results in the pulmonary function while the rest of the studies had similar or negative results when compared to control and other interventions. **CONCLUSIONS:** Based on the sparse literature, the flutter device could be considered as a physiotherapy treatment option for bronchiectasis. ***Pneumon 2014, 27(4):307-314.***

INTRODUCTION

Respiratory pathologies such as bronchiectasis can impair the lungs' normal mechanisms and thus, excess amounts of secretions are produced and retained. This can lead to bacterial colonisation and lung infection[1,2]. As a result of the infection, further damage to the lungs' tissue, inflammation and other complications such as hypoxia and haemoptysis could occur[3]. Such complications could potentially lengthen the patient's stay in the hospital, increase the number of treatments required and the medication needed[4-6]. Consequently, there could be a reduction in the patient's quality of life and an increase in healthcare costs.

Physiotherapy aims to reduce the retention of secretions and improve pulmonary function. The flutter is a physiotherapy modality that could be used for these purposes as it is easy to use, encourages independence[7,8] and some studies reported higher preference compared to other modalities[9,10]. A number of studies have investigated the effects of the flutter and returned contradictory results, therefore a comprehensive review is necessary in order to draw conclusions as to the effectiveness of this modality. This review will consider the efficacy of the flutter in terms of pulmonary function and sputum expectoration in bronchiectasis.

BACKGROUND INFORMATION

Bronchiectasis is a chronic respiratory disease that is pathologically characterized by abnormal and permanent dilated airways[2,3]. Diverse aetiologies are accountable for this disease. Some of them include infections (eg. Pneumonia and Tuberculosis), cystic fibrosis, primary ciliary dyskinesia, ABPA (allergic bronchopulmonary aspergillosis), immunodeficiency (eg AIDs) and bronchial obstruction (eg. tumour and foreign body). These conditions obstruct the airflow and impair the mucus clearance by weakening or damaging the muscular and elastic components of airways' walls, instigating changes such as inflammation, oedema and fibrosis. Additionally, further damage to the tissues is caused by the immune system in an attempt to fight the infection and subside the inflammation[2,3].

The effectiveness of the mucocilary clearance is affected by the structure, movement and number of the cilia in the airways in addition to the mucus volume and rheological properties. In Bronchiectasis, bronchial dilation, inflammation and scarring negatively affect the function of the mucociliary clearance. The neutrophils elastase, macrophages and other by-products of inflammation (cytokines, nitric oxide and free radicals) or bacteria, damage the structure of the cilia and thus its function. Additionally, inflammation and fibrosis result in thick and sticky mucus hypersecretion, which further damages the cilia and thus compromise the mucosiliary clearance[1,3]. Moreover, the retained secretions form a good medium for infectious pathogens to colonise, leading to a vicious cycle of tissue inflammation, recurrent infections, damage and dilation of the airways[11,12].

Common symptoms instigated from the above impairments include daily productive cough lasting for months, dyspnoea and fatigue[2,3].

The treatment options vary and depend on the severity of the patients. These include antibiotics, smoking cessation, immunisation, bronchodilators, surgery, lung transplant and physiotherapy to aid in sputum clearance[1,3].

Physiotherapy Treatment

With increasing mortality rates[34], the issues of cost-effective management of airway clearance and patient independence have become more significant to healthcare professionals, especially respiratory specialists and physiotherapists[13].

"Traditional" chest physiotherapy involves postural drainage combined with chest percussions or vibrations. These techniques are time consuming and may require assistance which may encourage noncompliance and dependency[14]. Moreover, it can cause hypoxaemia in severe cases and aspiration from gastroesophageal reflux[15]. More recent techniques have been developed to improve the treatment efficacy and achieve patient's autonomy, such ACBT (active cycle of breathing techniques), PEP (positive expiratory pressure) mask and Flutter[2].

Flutter and its Physiological Effects

The flutter is a handheld, pipe-shaped device with a mouthpiece and a perforated cover at either ends and contains a high-density stainless-steel ball resting in a cone inside it. This device is small thus easily carried and used even by children[8,12,17].

The Flutter's effects occur during expiration. As the ball in the flutter rolls and moves up and down it produces an opening and closing cycle. This results in the creation of oscillations in expiratory pressure and airflow. These oscillations or vibrations are felt when the oscillation frequency approaches the resonance frequency of the respiratory system and the oscillations are maximised[8,16]. These vibrations are responsible for the three advantages of the flutter:

Firstly it vibrates the airways resulting in loosening off the sputum from the walls. Secondly, it raises the endobronchial pressure intermittently during expiration. This maintains the airways' patency and reduces their collapsibility during expiration, thus, sputum can move upwards without getting trapped. Lastly, it hastens the airflow during expiration, enabling the sputum to move up the airways to be coughed out or swallowed[8,16].

The frequency can be altered by changing the angle of the stem inclination[3,8,16], but reaching oscillation frequencies between 10 to 20Hz is important for the flutter to work effectively, as these frequencies are similar to those in the human pulmonary system. However, these frequencies might vary in different people as they depend on factors such as lung volume and severity of airway obstruction.

METHODS

A literature search was undertaken to find randomised control trials (RCTs) that examined the effects of the flutter in bronchiectasis. MEDLINE, Cochrane Library, PubMed, CINAHL, PEDro and AMED databases were used to optimise the search[18]. An example of the electronic search strategy used can be found in Table 1.

Equilibrium is needed between research sensitivity and relevance, therefore both subject-headings search and keywords search, in the titles and abstracts, were used[19]. In addition, synonyms, related terms, variant spellings and truncation were utilised. Bibliographic and citation searching was employed, in order to obtain the maximum number of suitable articles and to reduce bias from other authors' interpretations. The variety in search terms was utilized with the purpose of maximising the results and of ensuring that no study relevant to the review was missed. The inclusion and exclusion criteria can be seen in Table 2.

Only, RCTs were included, as such types of studies

TABLE 1. Search Terms for MEDLINE database

Search ID	Search Terms for MEDline Database
S1	(MH "flutter device") OR (MH flutter)
S2	AB flutter OR "flutter device"
S3	TI flutter OR "flutter device"
S4	AB "oscillating device*" OR "positive expiratory pressure device*" OR "oscillating positive expiratory pressure device*" OR "airway* clearance technique*"
S5	TI "oscillating device*" OR "positive expiratory pressure device*" OR "oscillating positive expiratory pressure device*" OR "airway* clearance technique*"
S6	**S1 OR S2 OR S3 OR S4 OR S5**
S7	(MH "lung disease*")
S8	(MH bronchiectasis)
S9	AB "lung disease*" OR bronchiectasis OR "bronchi dilation" OR "chronic sputum production disease*"
S10	TI "lung disease*" OR bronchiectasis OR "bronchi dilation" OR "chronic sputum production disease*"
S11	**S7 OR S8 OR S9 OR S10**
S12	AB sputum OR mucus OR phlegm OR secretion* OR "lung function" OR "lung airway*" OR "airway* obstruction"
S13	TI sputum OR mucus OR phlegm OR secretion? OR "lung function" OR "lung airway*" OR "airway* obstruction"
S14	**S12 OR S13**
S15	AB human* OR people*
S16	(MH "clinical trial*")
S17	AB "clinical trial*" OR trial* OR experiment*
S18	AB randomised OR "randomised controlled" OR "randomised control trial" OR randomly
S19	**S15 OR S16 OR S17 OR S18**
S20	***S6 AND S11 AND S14 AND S19***

After evaluating their titles and abstracts 8 articles were found.
S: search, AB: abstract, MH: medical heading, TI: title.

TABLE 2. Criteria.

Inclusion Criteria	Exclusion Criteria
Population:	***Population:***
People diagnosed with bronchiectasis Any degree of disease severity Randomised controlled trials (RCTs)	People diagnosed with pathologies other than bronchiectasis Studies with non-RCT designs Studies done on animals
Intervention:	***Intervention:***
The flutter group used the device for a minimum of 5 minutes per treatment session	The flutter group used the device for less than 5 minutes per treatment session
Comparison:	***Comparison:***
Comparison with control or other treatments	–
Outcome:	***Outcome:***
At least one validated outcome measure of lung function, sputum removal or airways clearance: Pulmonary function tests: Forced expiratory volume in one second (FEV_1), Forced vital capacity (FVC), Forced expiratory flow between 25% and 75% ($FEF_{25-75\%}$), Peak expiratory flow rate (PEFR) Expectorated secretions (dry/ wet weight, or volume)	Absence of any validated outcome measure of lung function, sputum removal or airways clearance (eg Auscultation)

RCTs: Randomised controlled trials, FEV_1: forced expiratory volume in one second, FVC: forced vital capacity, $FEF_{25-75\%}$: forced expiratory flow between 25% and 75%, PEFR: peak expiratory flow rate.

incorporate a thorough methodology[20]. Animal studies were excluded since the objective of this review is to assess the effects of the flutter on humans. Moreover, the minimum treatment duration of using the flutter during each session was set at 5 minutes, as this is the minimum recommended treatment period by the manufacturer (Vario-Raw S.A., Aubonne, Switzerland).

The retained secretions could cause airway obstruction[22]. Therefore, by using the flutter, more sputum would potentially be expectorated, minimizing the obstruction and thus increase the airflow. Spirometry and peak expiratory flow rate (PEFR) are simple and reliable outcome measures for pulmonary function, therefore they were included in this review[21]. However, auscultation is too subjective to be considered a reliable outcome measure[21], thus it was excluded. Although sputum quantity is not very sensitive to small changes, it has been recommended as a suitable and practical outcome measure[21].

Quality Assessment:

The quality assessment of the retrieved studies was performed by two reviewers with the use of the PEDro scale. This was done to reduce bias from the reviewer's interpretation of the studies and to aid in determining the strength of the conclusions[23].

Initially, 11 studies were found in the databases. After removal of duplicates and their evaluation against the criteria, six studies were selected and reviewed.

A data collection sheet was formed, based on the recommendations of Higgins and Deeks (2008)[25] and other systematic reviews[26,27], to standardise the data extraction process and improve the validity of this review's findings[24]. It was evaluated by two reviewers and piloted on four RCTs prior to the study in order to increase the reliability of this review. The methods, results and quality of the included studies are summarised in Table 3.

Further important results:

Guimaraes et al (2012)[28] found that the flutter showed superiority in reducing the pulmonary hyperinflation (as there was a more pronounce reduction in inspiratory capacity (IC) and total lung capacity (TLC) compared to the other groups). Moreover, both flutter and ELTGOL groups improved the functional residual capacity (FRC), the residual volume (RV) and total lung capacity.

In addition, in Thomson et al (2002)[9] study neither of the techniques produced any adverse effects on peak expiratory flow or breathlessness. However, flutter proved in this study to have a higher level of patient acceptability, which agrees with the findings from Eaton et al (2007)[10] study.

TABLE 3. Summary of selected papers.

Authors (Date)	Sample Size and Condition	Outcome measures used	Comparisons	PEDro Score	Results
Guimaraes et al (2012)[28]	10 Stable Bronchiectasis	FEV_1, FVC, $FEF_{25-75\%}$, Sputum weight	Control, ELTGOL	7/10	Mean Sputum weight: ELTGOL group (0.38 g) vs flutter group (0.15 g) vs control group (0.14 g) No statistically significant difference (p>0.05) in the lung function tests: FEV_1 (% change): Flutter group (+1.60 %) vs ELTGOL group (+2.20%) vs control group (+1.40%) FVC (% change): Flutter group (+2.44 %) vs ELTGOL group (+0.96 %) vs control group (+0.20%) $FEF_{25-75\%}$ (% change): Flutter group (+4.50 %) vs ELTGOL group (+6.00 %) vs control group (+0.43%)
Figueiredo, Zin and Guimaraes (2012)[29]	8 Stable Bronchiectasis	Sputum volume	Sham flutter	6/10	Statically and clinically significant increase (p<0.05, 95% CI) in the flutter group (28 mL±5.4 mL) vs sham group (19.6 mL±3.6 mL)
Eaton et al (2007)[10]	36 Stable Bronchiectasis	Sputum volume	ACBT with or without PD	5/10	Increase but statistically insignificant (p>0.05) in the flutter group (7.9 mL±11.4 mL) and the ACBT group (7.3 mL±9.6 mL) vs ACBT-PD group (12.6 mL±15.9 mL)
Tsang and Jones (2003)[30]	15 Exacerbation of Bronchiectasis	Sputum weight, FEV_1, FVC, PEFR	Breathing Control (BC) with or without PD	4/10	No statistically significant difference in all the outcome measures (p>0.05) Sputum wet weight: PD-BC group (34.99 g±34.65 g), Flutter-BC group (13.96 g±12.60 g) and the BC group (19.48 g±18.97 g) FVC: Flutter-BC group (0.17 L±0.06 L) vs PD-BC group (0.16 L±0.22 L) vs BC group (0.07 L±0.02 L) FEV_1: Flutter-BC group (0.05 L±0.02 L) vs PD-BC group (0.04 L±0.05 L) vs BC group (0.06 L±0.12 L)
Antunes et al (2001)[31]	10 Stable Bronchiectasis	Sputum weight, PEFR	CRP (Conventional respiratory physiotherapy)	3/10	No significant difference between the ACBT and flutter for any outcome Average gross sputum weight: Flutter group (7.2 g±2.30 g) vs CRP group (6.3 g±0.74 g) Dry sputum weight: Flutter group (0.28 g±0.28 g) vs CRP group (0.16 g±0.06 g) Mean PEFR: Flutter group (15.75 L/min ±54.75 L/min) vs CRP (22.25 L/min ±25.5 L/min)
Thompson et al (2002)[9]	17 Stable non-CF bronchiectasis	Sputum weight	ACBT with PD	3/10	No significant difference between the ACBT-PD and flutter groups for any outcome Median daily sputum: ACBT-PD group (26.6 g) vs Flutter group (23.4 g) Difference between the groups in Median weekly sputum: 7.64 g

ACBT: Active cycle of breathing techniques, BC: Breathing control, CI: Confidence Interval, CRP: Conventional Respiratory Physiotherapy (Postural drainage with percussions and vibrations), ELTGOL: Expiration with the Glottis Open in the Lateral Posture, FEV_1: Forced Expiratory Volume in One Second, FVC: Forced Vital Capacity, $FEF_{25-75\%}$: Forced Expiratory Flow between 25% and 75%, PEFR: Peak Expiratory Flow Rate, PD: Postural Drainage, %: percentage.

DISCUSSION

The studies which addressed the inclusion criteria were all included in this review, regardless of their quality due to the scarcity of the literature. Only three studies were rated as good quality (> 5/10). Therefore, the results from the other three studies need to be used with caution.

The differences in the methodologies, demographic characteristics and outcome measures made a meta-analysis inappropriate to do, therefore, the studies are discussed separately.

Pulmonary Function

In Tsang and Jones (2003)[30] study, the flutter group showed improved or similar results in pulmonary function when compared to breathing control (BC) and postural drainage groups. This could be because the sample was too small to show significant improvement. Furthermore, the subjects in Tsang and Jones (2003)[30] had an acute exacerbation and thus antibiotics were given. This might had masked a significant improvement in the lung function. Nonetheless, the vibrations produced by the flutter, prevent the airways from collapsing[12]. This could have improve the ventilation and thus, the pulmonary function seeing in the flutter group compared to the other groups.

On the other hand, Antunes et al (2001)[31] found that conventional physiotherapy was more beneficial than the flutter device, in regards to the PEFR score. It is possible that the time required for the displacement of secretions with the flutter needed to be longer for significant amount of secretions to move to the central airways and coughed out.

Guimaraes et al (2013)[28] found an improvement in the flutter group when compared with control group. However, the ELTGOL (expiration with the glottis open in the lateral posture) group showed a bigger change in FEV_1 and $FEF_{25-75\%}$. Nonetheless all the results among the three interventions were statistically insignificant. This could be attributed to the small sample size (ten patients) used and the single treatment session of 15 minutes offered in this study[28].

Sputum quantity

Figueiredo, Zin and Guimaraes (2012)[29] and Antunes et al (2001)[31] found an increase in sputum expectoration in the flutter group. The statistical improvement in sputum removal in Figueiredo, Zin and Guimaraes (2012)[29] study could be attributed to the fact that the flutter showed a great reduction in total and peripheral airway resistance which lead to reopening of the airways and better distribution of the ventilation and mucus clearance (improving the lung mechanics).

Guimaraes et al (2013)[28] and Eaton et al (2007)[10], showed similar or negative results when compared the flutter group to the control or other interventions. This could be because of the limitations of collecting the sputum, such as swallowing it rather than expectorating it, which reduces its quantity[29]. Another reason could be because ELTGOL promotes the narrowing of the airways and consequently the increase in the gas-liquid interaction, favouring the dynamic drag of the secretions towards the central airways. However, the flutter could alter the sputum rheology (reduce viscosity) favouring the already impaired mucocilary clearance mechanism. In addition, during flutter intervention bronchial secretions have to move against gravity while during the ELTGOL the patient experienced the two lateral positions which could have accelerated the airway clearance with the use of gravity[28].

Similar results were obtained by the Tsang and Jones (2003)[30] study. They found that the postural drainage and the control groups expectorate more sputum than the flutter group. Perhaps the duration of the study was too short for the subjects to master the technique and perform it correctly by attaining their optimum oscillation frequency, and thus failing to maximise the flutter's effects

Although, Thompson et al (2002)[9] study found that the median daily sputum weight was slightly more in the ACBT-PD group compared to the flutter group, the median weekly sputum weights were similar. This could be because the patients had a month to practice and master the flutter technique, thus improving their sputum expectoration.

Quality of the Trials

Compliance with the interventions was unreliable in all the studies, as the subjects continued to receive their medication. However, since both groups received it, any effects the medication might have had, would have affected the subjects in both groups, thus overall the influence of the results was limited.

Random allocation enhanced the comparability of the groups in terms of the intervention as randomisation increases the similarities of the subjects in the groups. Thus, it reduces bias as it compares two otherwise identical groups[35]. Random allocation was done in all the trials. Thus, they have reduced bias and made their results more reliable.

Tsang and Jones (2003)[30], Antunes et al (2001)[31] and

Thompson et al (2002)[9] failed to take measurements of at least one of the outcome measures from more than 85% of the subjects that initially were allocated to the groups. The subjects who dropped out of the studies might have been significantly different from the remaining subjects, something which could have considerably influenced the results, thus increasing bias in these studies[32,33]. Therefore, the reliability and validity of the results in these three studies might be reduced.

All studies failed to justify the sample size used. Thus, it is questionable whether the subjects that participated in the studies represented the entire population from which they were recruited. This might lead to selection bias and the question as to whether the sample size was large enough for the flutter to have a statistically significant effect in the pulmonary function and sputum expectoration of the targeted population[32,33]. Nonetheless, it must be noted that when conducting a study with patients, it is not always possible to get the number of subjects needed to represent the entire population. In addition, it must be noted that some pathologies such as bronchiectasis are less common than others, and therefore, the sample size would be expected to be much smaller.

Limitations

One possible limitation is the fact that due to the clinical heterogeneity in the studies, such as the diverse outcome measures, a meta-analysis was not performed. Having homogenous studies is a difficult task to achieve in clinical practice as different Trusts could be using different outcome measures and protocols. Furthermore, all of the reviewed studies have small sample sizes. Small samples lack the statistical power to detect the effect of the intervention[38]. However, the difficulty in finding a larger sample size within the time frame of the study is acknowledged as it often requires a considerable amount of resources, time and finance involving a long term project and/or multiple research sites. Lastly, it must be noted that low-quality RCTs were included in this review due to the scarcity of high-quality studies. This could have compromised the strength of this review's conclusions.

Further Work

Bronchiectasis is a chronic condition with acute exacerbations, therefore, future studies should be planned to reflect clinical practice by focusing on short-term interventions during an exacerbation or long-term studies on initially stable patients. Additionally, more adequately-powered and high-quality randomised control studies comparing the flutter with other airway clearance modalities, need to be done before clinically valuable information can be gained with regard to treatment efficacy. Such studies should examine the flutter's influence on quality of life, number of respiratory exacerbations per year, number of days antibiotics were given, costs and number of physiotherapy sessions needed.

CONCLUSION

The aim of this review was to determine the effectiveness of the flutter in improving the lung function and sputum clearance in people with bronchiectasis.

In summary, there were two studies in favour of the flutter, in terms of sputum clearance and four studies showed similar or negative results. In terms of pulmonary function, one study showed negative results, one study had positive or similar results and one study had both positive and negative results when compared to the control and other interventions. Therefore, from the articles reviewed, there is some evidence to suggest that the flutter improves pulmonary function and sputum clearance in people with bronchiectasis. However, it is difficult to reach concrete conclusions and offer clinical recommendations because of the heterogeneity of the studies and the differences in their results.

Nonetheless, the results of this review can assist the physiotherapist when allocating services to the patients with bronchiectasis. Taking into consideration bronchiectasis is chronic and irreversible and that the physiotherapy treatment would be permanent, the cost-benefit relation and independence in the long-run could favour the use of the flutter. Furthermore, the flutter can be an option for those who prefer it or those who have difficulty in accessing other treatments at the hospital. However, it is worth noting that the conclusions reached in this review are affected by the limitations presented earlier.

REFERENCES:

1. West J. Pulmonary Pathophysiology: the Essentials. 7th ed. Lippincott Williams & Wilkins, London, 2008.
2. Welsh D, Thomas D. Obstructive Lung Disease. In: Ali J, Summer W, Levitzky M. (editors). Pulmonary Pathophysiology. 2nd ed. McGraw-Hill, London, 2004, pp. 85-104.
3. Hough A. Physiotherapy in Respiratory Care: an Evidence-based Approach to Respiratory and Cardiac Management. 3rd ed. Nelson Thornes, Cheltenham, 2001.
4. Kapur N, Masters B, Newcombe P, Chang A. The Burden of

Disease in Pediatric Non-Cystic Fibrosis Bronchiectasis. Chest 2012; 141:1018-24.

5. Chung F, Barnes N, Allen M, et al. Assessing the Burden of Respiratory Disease in the UK. Respir Med 2002; 96:963-75.
6. Weycker D, Edelsberg J, Oster G, Tino G. Prevalence and Economic Burden of Bronchiectasis. Clin Pulm Med 2005; 12:205-9.
7. Tambascio J, De Souza LT, Lisboa RM, Passarelli RDCV, De Souza HCD, Gastaldi AC. The Influence of Flutter VRP1 Components on Mucus Transport of Patients with Bronchiectasis. Respir Med 2011; 105:1316-21.
8. Hristara-Papadopoulou A, Tsanakas J, Diomou G, Papadopoulou O. Current Devices of Respiratory Physiotherapy. Hippokratia 2008; 12:211-20.
9. Thompson CS, Harrison S, Ashley J, Day K, Smith DL. Randomised Crossover Study of the Flutter Device and the Active Cycle of Breathing Technique in Non-Cystic Fibrosis Bronchiectasis. Thorax 2002; 57:446-8.
10. Eaton T, Young P, Zeng I, Kolbe J. A Randomised Evaluation of the Acute Efficacy, Acceptability and Tolerability of Flutter and Active Cycle of Breathing with and without Postural Drainage in Non-cystic Fibrosis Bronchiectasis. Chron Respir Dis 2007; 4:23-30.
11. Barker A. Bronchiectasis. N Engl J Med 2002; 346:1383-93.
12. Pryor J, Prasad SA. Physiotherapy Techniques. In: Pryor J, Prasad SA. (editors). Physiotherapy for Respiratory and Cardiac Problems: Adults and Paediatrics. 4th ed. Churchill Livingstone/ Elsevier, Edinburgh, 2008, pp. 134-217.
13. Dodd M, Webb K. Bronchiectasis, Primary Ciliary Dyskinesia and Cystic Fibrosis. In: Pryor J, Prasad SA. (editors). Physiotherapy for Respiratory and Cardiac Problems: Adults and Paediatrics. 4th ed. Churchill Livingstone/Elsevier, Edinburgh, 2008, pp. 550-90.
14. Konstan MW, Stern RC, Doershuk CF. Efficacy of the Flutter Device for Airway Mucus Clearance in Patients with Cystic Fibrosis. J Pediatr 1994; 124:689-93.
15. McIlwaine M, Wong L, Peacock D, Davidson G. Long-term Comparative Trial of Positive Expiratory Pressure Versus Oscillating Positive Expiratory Pressure (Flutter) Physiotherapy in the Treatment of Cystic Fibrosis. J Pediatr 2001; 138:845-50.
16. Lagerkvist AL, Sten GM, Redfors SB, Lindblad AG, Hjalmarson O. Immediate changes in blood-gas tensions during chest physiotherapy with positive expiratory pressure and oscillating positive expiratory pressure in patients with cystic fibrosis. Respir Care 2006; 51:1154-61.
17. Myers T. Positive Expiratory Pressure and Oscillatory Positive Expiratory Pressure Therapies. Respir Care 2007; 52:1308-27.
18. Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0. Hoboken NJ: Wiley-Blackwell, Chichester, West Sussex, 2008.
19. Lefebver C, Manheimer E, Glanville J. Searching for Studies. In: Higgins J, Green S. (editors). Cochrane Handbook for Systematic Reviews of Interventions. John Wiley & Sons, West Sussex, 2008, pp. 96-150
20. Kunz R, Vist G, Oxman AD. Randomisation to Protect Against Selection Bias in Healthcare Trials. Cochrane Database Syst Rev, 2007; 18:MR000012.
21. Marques A, Bruton A, Barney A. Clinically Useful Outcome Measures for Physiotherapy Airway Clearance Techniques: a Review. Phys Ther Rev 2006; 11:299-307.
22. Singh S, Hudson I. Cardiopulmonary Function Testing. In: Pryor J, Prasad SA. (editors). Physiotherapy for Respiratory and Cardiac Problems: Adults and Paediatrics, 4th ed. Churchill Livingstone/ Elsevier, Edinburgh, 2008, pp. 60-114.
23. University of York NHS Centre for Reviews and Dissemination. Systematic reviews: CRD's guidance for undertaking reviews in health care. Centre for Reviews and Dissemination, University of York, York, 2009.
24. Bettany-Saltikou J. How to Do a Systematic Literature Review in Nursing: a Step by Step Guide. McGraw-Hill/Open University Press, Maidenhead, 2012.
25. Higgins J, Deeks J. Selecting Studies and Collecting Data. In: Higgins J, Deeks J. (editors). Cochrane Handbook for Systematic Reviews of Interventions. John Wiley & Sons, West Sussex, 2008, pp. 151-86.
26. Morrison L, Agnew J. Oscillating Devices for Airway Clearance in People with Cystic Fibrosis. Cochrane Database Syst Rev 2014; 20:CD006842
27. Elkins MR, Jones A, van der Schans C. Positive Expiratory Pressure Physiotherapy for Airway Clearance in People with Cystic Fibrosis. Cochrane Database Syst Rev 2006; 19:CD003147.
28. Guimaraes F, Moco V, Menezes S, Dias C, Salles R, Lopes A. Effects of ELTGOL and Flutter VRPI on the Dynamic and Static Pulmonary Volumes and on the Secretion Clearance of Patients with Bronchiectasis. Rev Bras Fisioter 2012; 16:108-13.
29. Figueiredo P, Zin W, Guimaraes F. Flutter Valve Improves Respiratory Mechanics and Sputum Production in Patients with Bronchiectasis. Physiother Res Int 2012; 17:12-20.
30. Tsang SMH, Jones AYM. Postural Drainage or Flutter Device in Conjunction with Breathing and Coughing Compared to Breathing and Coughing Alone in Improving Secretion Removal and Lung Function in Patients with Acute Exacerbation of Bronchiectasis: a Pilot Study. Hong Kong Physiotherapy Journal 2003; 21:29-36.
31. Antunes L, Carvalho S, Borges F, Assis V, Godoy I. A Study of the Conventional Chest Physiotherapy versus Flutter® VRP1 in the Treatment of Patients Carrying Bronchiectasis. Salusvita 2001; 20:11-34.
32. Greenhalgh T. How to Read a Paper: the Basics of Evidence-based Medicine. 3rd ed. BMJ, London, 2006.
33. Hicks C. Research Methods for Clinical Therapists: Applied Project Design and Analysis. 3rd ed. Churchill Livingstone, Edinburgh, 1999.
34. Roberts H, Hubbard R. Trends in bronchiectasis mortality in England and Wales. Respir Med 2010; 104:981-5.
35. Helewa A, Walker J. Critical Evaluation of Research in Physical Rehabilitation: Towards Evidence-based Practice. W.B. Saunders, London, 2000.