The role of positive expiratory pressure (PEP) in physiotherapy of patients with cystic fibrosis. Comparison with oscillating positive expiratory pressure (OPEP)

Rola podwyższonego ciśnienia wydechowego (PEP) w fizjoterapii chorych na mukowiscydozę. Studium porównawcze z PEP generującym oscylacje (OPEP)

Teresa Orlik A,E,F, Anna Wyka-Wojeńska A,D
Rehabilitation Department, Institute of Mother and Child, Warsaw, Poland, Zakład Usprawniania Leczniczego, Instytut Matki i Dziecka, Warszawa, Polska

Abstract

Physiotherapy plays a very important role in cystic fibrosis. Its basic aim is to regularly clear bronchial passages of mucus which is responsible for exacerbation of bronchoalveolar symptoms. Positive Expiratory Pressure (PEP) and Oscillating Positive Expiratory Pressure (OPEP) are among the most commonly used bronchi clearance methods. It is not entirely clear which technique should be applied in what situations and whether these techniques are similar to other drainage techniques in terms of effectiveness. The aim of this study is to review the literature and analyse the effectiveness of both techniques, to summarise the existing evidence and to point to gaps in the knowledge about this issue.

Key words: PEP, OPEP, physiotherapy, cystic fibrosis

Streszczenie

Fizjoterapia odgrywa bardzo istotną rolę w mukowiscydozie. Jej podstawowym celem jest systematyczne oczyszczanie oskrzeli z zalegającej wydzieliny odpowiedzialnej za rozwój choroby oskrzelowo-płucnej. Do jednych z częściej stosowanych metod oczyszczania oskrzeli należą technika podwyższonego ciśnienia wydechowego (Positive Expiratory Pressure – PEP) i oscylacyjnego podwyższonego ciśnienia wydechowego (Oscillatory Positive Expiratory Pressure – OPEP). Nie do końca jest jasne, którą z technik powinno się stosować i w jakich sytuacjach oraz, czy wymienione techniki są porównywalne pod względem efektywności z innymi technikami drenażowymi. Celem niniejszej pracy jest przegląd piśmiennictwa i na tej podstawie analiza skuteczności obu technik, podsumowanie istniejących dowodów, a także podkreślzenie luk w funkcjonującej wiedzy na ten temat.

Słowa kluczowe: PEP, OPEP, fizjoterapia, mukowiscydoza.
Introduction

Cystic fibrosis (CF) is an inherited autosomal recessive genetic disease of white race. It is caused by mutations of the gene located on the long arm of chromosome 7, i.e. Cystic Fibrosis Transmembrane Conductance Regulator (CFTR), which serves as a chloride channel. The damaged function of CFTR resulting from the mutation leads to disorders of the transport of Cl ions through cell membranes of respiratory epithelium and excessive absorption of \( \text{Na}^+ \) and water in a cell. This, in turn, leads to lower hydration and thickness of cilia of the epithelium, production of thick and sticky mucus and to disorders of mucociliary clearance, particularly in the respiratory system [1]. Cystic fibrosis is a chronic progressive disease with various clinical symptoms. Changes in the respiratory system usually determine the development of the disease as well as the quality and length of life.

Physiotherapy plays a very important role in cystic fibrosis. Its aim is to regularly clear bronchial passages of thick, sticky mucus which accumulates in air passages. It was proved that regular physiotherapeutic procedures, commonly known as drainage procedures, reduce the number of exacerbations of bronchoalveolar symptoms, and, in this manner, help to slow down the disease progression and to maintain proper lung function for as long as possible [2,3]. For many years, it has been highlighted that better prognosis and quality of life of patients with cystic fibrosis depend on the improvement of complex treatment methods, including more and more efficient physiotherapy procedures [4-6].

Intensive development of physiotherapy in cystic fibrosis was mainly connected with developing and modifying methods of clearing airways which would serve as an alternative to postural drainage (also known as gravity assisted drainage) with manual chest percussion or vibration. In the 1960s and 1970s, this type of drainage was a popular method of clearing bronchi in Europe. Owing to multidirectional scientific research, traditional bronchi clearance methods were gradually replaced with modern, more efficient methods in which various tools supporting airway clearance were used. The research which exerted the greatest influence on the development of physiotherapy in cystic fibrosis mainly regarded negative effects of gastroesophageal reflux on the respiratory system and the fact that reflux was stimulated during postural drainage [7-9]. Getting to know a key role of mobilisation of mucus in effective bronchi clearance and identifying the meaning of autotherapy for patients’ independence as well as assessing the effects of this process were also significant [10].

The majority of tools, including the ones available on the Polish market, work in the system of Positive Expiratory Pressure (PEP) and Oscillating Positive Expiratory Pressure (OPEP). The application of PEP improves ventilation in broncholi, reduces the symptom called “bubble trap” and increases the Functional Residual Capacity (FRC) [2,11-13]. In turn, vibrations lead to easier clearance of thick, sticky mucus from bronchial wall, and expirations made by the device increase the expiratory flow for a short time, which makes it easier to push mucus towards central bronchi [14,15].

Despite the fact that PEP and OPEP have been in use for over 30 years, it is still not entirely clear which technique should be used in what situations, and whether these techniques are similar to other drainage techniques in terms of effectiveness. The aim of this study is to review the literature and analyse the effectiveness of both techniques on the basis of this review, to summarise the existing evidence and to point to gaps in the knowledge about this issue.

Do PEP and OPEP produce measurable therapeutic effects compared to other drainage techniques?

PEP

In a cross-over study on 9 patients in a stable state, Lannefors et al. applied 3 different methods of clearing bronchi [16]. These methods included: 1) postural drainage with thoracic expansion exercises and Forced Expiration Technique (FET), 2) PEP mask and FET, 3) physical exercise on a cycloergometer and FET. While assessing the effectiveness of these techniques on the basis of the amount of mucus cleared, the authors did not find any statistically significant differences between these regimes. A similar study was conducted by Mortensen et al. [17]. The authors concluded that postural drainage with FET was as effective as PEP with FET in tracheobronchial clearance in patients with cystic fibrosis.
In the study by Darbee et al. [18], two methods were compared, i.e. PEP and High-Frequency Chest Wall Oscillation (HFCWO). The effects of both techniques on arterial blood oxyhemoglobin saturation ($\text{SaO}_2$) and selected spirometric indices were assessed. The authors revealed that HFCWO and PEP were equally effective. As far as $\text{SaO}_2$ is concerned, the results were unequivocal. In several patients with respiratory failure and low values of $\text{SaO}_2$, an unacceptable decrease in $\text{SaO}_2$ levels was noted during the therapy with HFCWO. The authors concluded that the patients may benefit more from PEP during an acute phase of the pulmonary exacerbation.

McIlwaine et al. carried out research in which they compared out-patients treated with PEP technique with those who underwent postural drainage with chest percussion technique [19]. The study participants were paired on the basis of similar values of forced expiratory volume in 1 second (FEV$_1$) up to 15% difference, gender and age (up to 3-year difference). Patients who performed less than 85% of the recommendations (assessment based on the questionnaire) were excluded from the study. Thirty-six patients participated in the whole study that lasted 1 year. A significant increase in forced expiratory volume in 1 second (FEV$_1$) and forced vital capacity (FVC) was noted in the PEP group. McIlwaine et al. concluded that PEP is a better method for maintaining lung function in patients with cystic fibrosis compared to postural drainage with chest percussion.

**OPEP**

The majority of studies on the effectiveness of OPEP were conducted with the use of Flutter VRP1. Orlik carried out a comparative analysis of the effectiveness of selected physiotherapeutic methods in 21 in-patients [6]. She compared 5 airway clearance techniques, i.e. postural drainage with chest percussion, postural drainage with percussion and squeezing, Active Cycle of Breathing Technique (ACBT), Flutter as well as Flutter with relaxation. It was revealed that the largest amount of mucus was removed by coughing in patients undergoing ACBT and Flutter with relaxation technique. No statistically significant differences were found between the values of peak expiratory flow (PEF) and $\text{SaO}_2$ measured before and after the application of any drainage technique.

In their randomised crossover study, Pryor et al. compared OPEP with Flutter and ACBT [20]. The authors did not note a significant improvement in lung function or oxygenation in the examined patients. A significant increase in the amount of mucus cleared was noted in the study participants who underwent ACBT. The authors concluded that there were no significant differences between the application of Flutter and ACBT.

App et al. carried out research that focused on the effectiveness of autogenic drainage compared to OPEP with Flutter [21]. The study included 17 patients with cystic fibrosis. No significant differences were noted between the values of FVC and FEV$_1$ and the amount of mucus cleared during the study. However, thickness and stickiness of mucus were reduced more with the use of Flutter than during autogenic drainage. The authors concluded that the vibrations applied with certain frequency produced by Flutter may reduce the stickiness of mucus to the bronchial wall.

In the study by Konstan et al. [22], the mass of sputum expectorated after the application of Flutter was compared to the mass of sputum expectorated in forced cough and during postural drainage with percussions and vibrations. During the session with Flutter, all the study participants coughed up significantly more mucus ($p<0.001$) than during postural drainage and forced cough technique. The authors concluded that Flutter is more effective in helping to cough up mucus than traditional techniques of clearing airways in patients with cystic fibrosis.

In her 7-month study, Orlik assessed the effectiveness of selected physiotherapeutic methods in 80 patients divided into 4 subgroups [23]. In each group, a different airway clearance technique was applied, i.e. postural drainage with chest percussion, postural drainage with percussion and squeezing, ACBT and OPEP with Flutter. The author noted a statistically significant increase in the values of all the examined spirometric indices in the ACBT group. In the OPEP group, an increase in FEV$_1$ (statistically insignificant differences) and FVC (statistically significant differences) was noted. The author concluded that forced breathing with Flutter led to an increase in lung obturation in patients with bronchial hyperresponsiveness.
Comparison of PEP and OPEP

The crossover study by Lagerkvist et al. included 15 patients with cystic fibrosis [24]. The aim of the study was to assess the effects of PEP and OPEP (Flutter) on the values of gas tensions in blood. The authors concluded that OPEP led to more favourable changes in the values of PaO$_2$ and PaCO$_2$ compared to PEP; however, these changes disappeared very quickly, i.e. within less than 10 minutes. Neither PEP nor OPEP brought about differences in spirometric values.

In their study that lasted 1 year, McIlwain et al. compared the effectiveness of PEP and OPEP (Flutter) [25]. Forty patients with cystic fibrosis were randomly assigned to one of the assessed therapies. Patients who performed less than 80% of the recommended sessions per month (assessed on the basis of the questionnaire) were excluded from the study. Thirty-two patients completed the study. The authors did not reveal statistically significant differences in lung function of patients who were treated with PEP. In turn, in the case of patients who were using Flutter, a decrease in the values of lung function indices was noted after one year, while FVC difference was statistically significant compared to PEP.

Van Winden et al. conducted a two-week randomised crossover study in which they compared OPEP with Flutter method and PEP mask method applied in clinically stable children with cystic fibrosis [26]. The PEF was measured before and after a morning physiotherapy session and patients completed a questionnaire regarding day and night cough, production of sputum and difficulty breathing. No significant differences were found between the PEF in both groups. Moreover, no differences were revealed concerning oxygenation before, during and 30 minutes after the session of clearing airways. There were no significant differences in the assessment of symptoms included in the questionnaire for either of the two therapies.

The crossover study by Borka et al. included 10 patients with cystic fibrosis [27]. Within the study, 260 procedures were performed aimed at measuring the mass of sputum expectorated. The authors concluded that PEP was more efficient than Flutter. Flutter is a useful additional tool.

Discussion

In the presented publications, the authors obtained considerably different research results. It regarded both the comparisons of PEP and OPEP with other drainage techniques and the comparisons of both methods with each other. The only exception was the comparison of PEP and OPEP with postural drainage with percussion which is treated as a conventional physiotherapy method of clearing bronchi. In 4 of the presented studies on the effectiveness of the aforementioned methods, statistically significant differences regarding the values of FEV$_1$, FVC and mass of sputum expectorated were noted, where PEP and OPEP produced better outcomes [6,21,24,25]. The application of various research procedures by different authors, e.g. comparing PEP and OPEP with various therapeutic methods (a different method in every study), and the application of different indices to assess therapy effects bring about unquestionable difficulties in drawing unanimous conclusions on measurable therapeutic effects of PEP and OPEP in patients with cystic fibrosis. The studies also differed in the length of observation periods, which lasted from one week to one year. In one work, the number of performed procedures was given instead of the length of observation period [27]. The majority of the examined groups had small populations.

Homogeneity of research groups is a significant criterion in the assessment of the effectiveness of airway clearance techniques that is often neglected in the research methodology and in the analysis of results. Due to a progressive character of cystic fibrosis, the research should include groups of patients at similar stages of the disease. Changes in lungs and bronchi in patients with cystic fibrosis at an advanced stage are so big that physiotherapy is less effective. These patients should not be included in the same study as patients with less advanced changes in lungs. For instance, in her study, Orlik suggested that while assessing the effectiveness of physiotherapeutic methods, patients with the diagnosed bronchial hyperresponsiveness should be analysed separately [23]. An interesting solution concerning the methodology of assigning patients to groups was put forward by McIlwaine et al. Patients were paired on the basis of similar values of FEV$_1$%N taking into account 15% difference [20].

While analysing patients with cystic fibrosis, it is important to take into consideration an individual
reaction of a patient to a particular drainage technique. An individual reaction depends to a large extent on motivation and good knowledge of the drainage technique application. Each of the techniques can be adapted with regard to the position in which drainage is performed, number of cycles, duration of drainage, number of expirations in a cycle, length of expirations and length of intervals between cycles. Moreover, high awareness of parents or adult patients concerning the role of physiotherapy in treating cystic fibrosis is significant as it allows to control the progress of a physiotherapeutic session. An interesting and objective study assessing the cooperation of a patient while applying the recommended drainage techniques and performing all the physiotherapeutic sessions per day was conducted by McIlwaine et al. They used a questionnaire assessing to what extent the patients followed the recommendations. The patients who performed less than 80% of the recommended sessions per month were excluded from the study [20,25].

The application of oscillation aimed at making mucus less thick and sticky, and helping to clear the airways is a significant issue in physiotherapy of patients with cystic fibrosis. In this context, the application of OPEP in everyday practice is perceived as more effective than other airway clearance techniques and physiotherapeutic methods. In the aforementioned studies as well as in other PubMed publications, the authors obtained extremely different results regarding the effectiveness and role of oscillation in clearing the airways. Several authors indicated a favourable influence of oscillation by Flutter on lung function in patients with cystic fibrosis compared to other techniques of clearing the airways [28,29,30]. Other authors did not note any influence of Flutter therapy on lung function [21,22,23,31]. There was also one study which revealed that lung function in patients with cystic fibrosis worsened after the application of the therapy with the use of Flutter [20].

The reviews of Cochrane Database Syst. Rev. published in 2014, 2015 and 2017 did not provide a unanimous conclusion regarding higher effectiveness of PEP and OPEP compared to other physiotherapy techniques applied in the therapy of patients with cystic fibrosis. Only McIlwaine et al. revealed that in the studies in which the disease advancement was a basic assessment criterion, a significant decrease in the frequency of exacerbations of bronchialveolar symptoms was noted in patients applying PEP compared to those using HFCWO (The Vest) [32]. Moreover, no evidence was found that one device was better than the other [15, 32,33,].

Summary

Performing homogeneous, high-quality research assessing physiotherapeutic techniques in patients with cystic fibrosis is very difficult. Cystic fibrosis is a disease with a very changeable clinical progress with periods of stability and periods of various-intensity exacerbations of bronchialveolar symptoms. Therefore, recruiting study participants is very hard. Moreover, physiotherapy is a standard way of treating patients so conducting a blind study is impossible. This is the reason why short-term and crossover studies are the dominating types of studies assessing the effects of physiotherapy on various indices in patients with cystic fibrosis. It has to be highlighted that in the case of cystic fibrosis, which is regarded as a rare disease, carrying out high-quality studies will be often connected with the fact that the number of participants is insufficient to draw any statistical conclusions.

In the light of the fact that there are many airway clearance techniques and similar research results regarding their effectiveness, the question arises about preferable criteria of selecting a particular technique for a patient with cystic fibrosis. More and more attention is drawn to the fact that factors other than effectiveness should be taken into account while selecting a technique. The significance of patients’ independence in performing the procedures and following the rules of physiotherapy as well as patients’ preferences regarding the applied techniques are more and more often stressed. The preferences may be connected with lifestyle, patients’ beliefs concerning the best effectiveness or easy application of a given technique, or possibilities to shorten the duration of a physiotherapy session.

In Poland, there are no current studies which would assess the preferences of patients or the frequency of applying particular drainage techniques. Such multi-centre research was conducted in 2000 and the results were published in Standardy Medyczne [34]. The research revealed that Flutter was applied by 44% of the patients over 18 years of age in Poland. Taking into account my own experience as well as the diversity and easier availability of devices on
the Polish market compared to PEP devices, we may conclude that currently, the number of Polish patients using OPEP is higher. The British research revealed that the frequency of using particular airway clearing techniques differs significantly depending on a country and ranges from 6% to 23% in the case of OPEP and from 10% to 40% in the case of PEP [35].

While selecting a particular drainage device, a financial aspect is also very important. The costs of PEP and OPEP devices are comparable and range from 200 PLN to 500 PLN, while the Polish National Health Service refunds 200 PLN once in two years. Compared to the costs of The Vest, i.e. 32 000 PLN to 36 000 PLN, OPEP is more financially attractive for patients with cystic fibrosis. OPEP is a method which enables patients to be independent from their guardians. It takes less time to achieve similar therapeutic effects than other methods and is affordable. Despite contradictory research results, it can be assumed that in the near future, this method will dominate physiotherapy of patients with cystic fibrosis in Poland.

References