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Short review

Airway clearance therapy in cystic fibrosis patients

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Abstract. Cystic fibrosis (CF) is the most common life-shortening inherited disease affecting Caucasian people. In CF, the major feature of lung disease is the retention of mucus due to impaired clearance of abnormally viscous airway secretions. Airway clearance techniques (ACTs) may significantly improve mucociliary clearance and gas exchange, thereby being of clinical benefit in reducing pulmonary complications in CF patients. ACTs include conventional chest physiotherapy, active cycle of breathing techniques, autogenic drainage, positive expiratory pressure and high-frequency chest compression. In order to suit the needs of patients, families and care-givers, ACTs need to be individually and continuously adapted.
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Key words: Airway clearance, chest physiotherapy, cystic fibrosis

Introduction

Cystic fibrosis (CF) is the most common life-shortening inherited disease affecting Caucasian people. Despite a drastic improvement in the prognosis of CF, the current median survival age is estimated of about 40 years (1, 2). Since its first description more than 50 years ago, it has been known that severe lung disease associated with chronic infection accounts for more than 80% of the CF-related mortality (3). The retention of mucus due to impaired clearance of abnormally viscous airway secretions is a major feature of lung disease in CF. CF transmembrane regulator dysfunction leads to mucus dehydration with increased mucin concentration (4). Increased mucin concentration in turn promotes hypoxemic conditions in mucus, leading to bacterial biofilm morphologic transformation (5). Infected airway secretions contain pro-inflammatory cytokines and proteases that destroy lung tissue, contributing to the development of bronchiectasis (6). Promoting airway clearance using chest physiotherapy remains a mainstay of treatment for patients with CF.

Airway clearance techniques (ACTs) have been shown to improve mucociliary clearance (7, 8). Furthermore, ACTs may decrease mucus plugging and aid the removal of secretions containing inflammatory cells and bacteria, thus improving ventilation, reducing airway obstruction and atelectasis, correcting ventilation–perfusion mismatch and decreasing the proteolytic activity in the airways (9). Accordingly, ACTs are considered as to be of clinical benefit in reducing pulmonary complications of CF and their prescription is extremely popular among the patients. ACTs currently available to treat CF patients include conventional chest physiotherapy (CCPT) or postural drainage associated with chest percussion and vibration (PD&P), active cycle of breathing techniques (ACBTs), autogenic drainage (AD), positive expiratory pressure (PEP) and its variants and high-frequency chest compression (HFCC). This overview describes the specific role of the different ACTs in

reducing the pulmonary complications of CF patients.

Conventional Chest Physiotherapy (CCPT)

CCPT was introduced in the 1950s as a standard part of CF care (10); however, until now little evidence has been provided to support its use in the clinical practice. Reisman and colleagues (11) carried out a three-year prospective study that compared the effects of CCPT on pulmonary function combined with the forced expiratory technique (FET) versus the effect of the FET alone. The authors found that combined therapy was able to reduce the annual rate of decline in respiratory function (11). In 1995, a meta-analysis of studies comparing CCPT with no physiotherapy demonstrated a significant benefit in favour of CCPT (12). In contrast, a subsequent study showed that CCPT had detrimental effects on patients by inducing hypoxic episodes (13). In addition, it has been shown that when CCPT is performed in a head-down position it can aggravate gastro-oesophageal reflux (14) and induce adverse reactions, including bronchospasm, changes in cardiac rhythm and increased intracranial pressure (15,16). Moreover, patients find CCPT so burdensome that compliance with the prescribed treatment regimen is probably less than 50% (17). Even hospitalized adolescents in a controlled setting showed significant (35%) non-adherence to a CCPT regimen (18). Currently, CCPT (modified to exclude the head-down position) should be only used in young children (less than five years old) and in patients with extremely severe lung disease who are unable to perform ACTs independently.

Active Cycle of Breathing Techniques (ACBTs) and Autogenic Drainage (AD)

In the 1990s, several self-administered ACTs were developed, including the ACBTs and AD. Both of these breathing techniques are based on increasing expiratory airflow rates to move secretions up the airways. In addition, these breathing strategies aim to improve the regularity of ventilation. ACBTs, developed by Pryor and Webber (19) at the Royal Brompton Hospital, London and originally called FET, combine forced expiration (huffing), relaxed tidal volume breathing (or breathing control) and thoracic expansion exercises. Developed in Belgium by Chevallier (20), AD utilises breathing at different lung volumes to influence the movement of mucus from different parts of the bronchial tree; at the end of the exercise a huff or cough removes the secretions from the upper airways. Some studies (21, 22) suggest that both ACBTs and AD are more effective than CCPT and may offer many advantages over CCPT. In fact, neither ACBTs nor AD causes oxygen desaturation (23, 24) or requires a care-giver, thereby promoting more independence than CCPT.

PEP Mask

Several self-administered devices have been used in clinical settings to aid airway clearance in CF patients, including PEP mask and HFCC. The PEP mask, developed in Denmark in the late 1970s as an alternative to CCPT (25), is the simplest and least expensive of the airway clearance devices. Using a face mask or mouth-piece, the patient exhales through an expiratory resistor. This generates positive pressure in the airways, which in turn stabilises the peripheral airways, while air is pushed through collateral ventilation pathways into distal lung units beyond retained secretions (26). Many studies support that PEP is at least or more effective than CCPT. Otherwise, patients with severe dyspnea may be unable to maintain the breathing control necessary for an effective PEP treatment. Research on the effectiveness of PEP was recently summarized by Cochrane review (27) concluding that there was no clear evidence that this device was better than other forms of physiotherapy, although patients tended to prefer PEP mask over CCPT.

High-Frequency Chest Compression (HFCC)

HFCC has been shown to improve mucociliary clearance by producing a transient increase in expiratory flow and cough-like shear forces and decreasing

the viscoelasticity of mucus (28,29). These reports led to the development of the HFCC vest. The Vest Airway Clearance System, manufactured by Hill-Rom, is fifth-generation technology from the innovators of HFCC and consists of an air-pulse-generating compressor attached to an inflatable vest, which is worn by the patient over the thorax. When the compressor is turned on, the pressure in the vest increases and decreases between five and 25 times per second, thereby applying high-frequency oscillations to the patient's chest wall. This technique may assist patients in moving retained secretions from smaller airways to larger airways, from which they can more easily be removed by coughing.

To date, several studies have been published on the acute and long-term effects of HFCC in CF patients. Recently in a cross over study, we have compared the acute effect of HFCC and PEP mask in 23 CF adult patients hospitalised for a pulmonary exacerbation (30). In our study, we did not find any difference in pulmonary function and sputum production outcomes between the two ACTs. Similarly, previous studies carried out in young adults with CF did not find any difference between acute effects of HFCC, PEP and PD (31) and between medium term (7 to 14 days) effects of HFCC and CCPT (32). In a random cross-over trial Kluft et al. (33) demonstrated that significantly more sputum was expectorated during HFCC than during CCPT, as determined by both the wet and dry measurements. By contrast, in a recent study Phillips et al. (34) found that HFCC was less effective than ACBTs in terms of an increase in respiratory function and sputum weight. Interestingly, a long-term non-randomised study (35) showed that the rate of decline in pulmonary function was significantly decreased during the HFCC treatment period compared with CCPT. Lastly, recent reports in large groups of CF patients (36,37) showed that one- and three-year treatment programmes with HFCC were equivalent in terms of clinical outcomes compared to CCPT. As a whole, taken together these studies indicate that HFCC therapy can be a reliable alternative to CCPT in clearing secretions from the airways of patients with CF. Moreover, this treatment is usually well tolerated, although some patients – especially those with end-stage lung disease – may complain of discomfort or pain from the inflated vest.

Conclusions

Treatments to enhance the clearance of airway secretions are crucial to the management of CF lung disease. ACTs can facilitate the expectoration of tenacious secretions that would otherwise accumulate in the airways. There is evidence from short-term, but not long-term, trials about the benefit of ACT over no treatment. However, there is no consensus about which ACT is the most effective. Traditionally, chest physiotherapy relied on postural drainage combined

Table 1. ACTs. Comments

Technique		Comments
Passive	CCPT	Infant and young children; subjects unable to actively participate; patients with extremely severe lung disease. Time consuming. Problems: discomfort and pain, hypoxemia, arrhythmias, gastroesophageal reflux.
	HFCC	Patients without caregivers unable to actively participate. Problems: sense of constriction and inability to inspire. Not recommended in end stage disease, head, neck and chest injuries, active haemorrhage. High cost.
Active	ACBTs	Not required any equipment; it can be taught at very young age; less tiring in severely compromised patients.
	AD	Useful in subjects with bronchial hyperreactivity because it avoids coughing and airway closure. It requires motivation and concentration, difficult to teach in children.
	PEP Mask	Useful to increase lung volume. Time saving, more acceptable for the patient. Not recommended in subjects with severe dyspnea.

with percussion and forced expirations, although there is evidence that CCPT is at least as effective as other forms of ACTs. However, this kind of chest physiotherapy is time-consuming and sometimes uncomfortable for patients, who tend to prefer self-administered treatments. Among the self-administered techniques, ACBTs, PEP and AD require continuous active participation by the patient, while HFCC using the Vest System allows the patient to be passive and may be useful both in fatigued patients and in patients without a care-giver. In conclusion, CF is a multi-systemic disease with a high degree of variability in lung impairment and it is likely that specific airway clearance regimens may be required (Table 1). Therefore, ACTs need to be individually and continuously adapted to suit the needs of patients, families and caregivers. Randomised clinical studies are needed to examine the long-term effects of ACTs on exercise tolerance, quality of life and survival of CF patients.

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