Effects of Autogenic Drainage on Sputum Recovery and Pulmonary Function in People with Cystic Fibrosis: A Systematic Review

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ABSTRACT

Purpose: To determine the effects of short- and long-term use of autogenic drainage (AD) on pulmonary function and sputum recovery in people with cystic fibrosis (CF). **Methods:** The authors conducted a systematic review of randomized and quasi-randomized clinical trials in which participants were people with CF who use AD as their sole airway clearance technique. **Results:** Searches in 4 databases and secondary sources using 5 key terms yielded 735 articles, of which 58 contained the terms *autogenic drainage* and *cystic fibrosis*. Ultimately, 4 studies, 2 of which were long term, were included. All measured forced expiratory volume in 1 second (FEV₁) and found no change. The long-term studies were underpowered to detect change in FEV₁; however, the short-term studies found a clinically significant sputum yield (≥ 4 g). **Conclusion:** AD has been shown to produce clinically significant sputum yields in a limited number of investigations. The effect of AD on the function of the pulmonary system remains uncertain, and questions have emerged regarding the appropriateness of FEV₁ as a valid measure of airway clearance from peripheral lung regions. Further consideration should be given to the use of FEV₁ as a primary measure of the effect of AD.

Key Words: airway obstruction; autogenic drainage; cystic fibrosis; outcome measures; systematic review.

RÉSUMÉ

Objet: Déterminer les effets de l'utilisation à court et à long terme du drainage autogène (DA) sur la fonction pulmonaire et la récupération de crachat chez les personnes qui ont la fibrose kystique (FK). **Méthodes:** Les auteurs ont procédé à un examen systématique d'essais cliniques randomisés et quasi-randomisés où les participants étaient des personnes vivant avec la FK qui utilisent le DA comme seule méthode de dégagement des voies aériennes (DVA). **Résultats:** Les recherches effectuées dans quatre bases de données et des sources secondaires au moyen de cinq termes clés ont produit 735 articles dont 58 contenaient les expressions « drainage autogène » et « fibrose kystique ». On a inclus finalement quatre études dont deux à long terme. Toutes les études ont mesuré le volume expiratoire maximum seconde (VEMS₁) et n'ont constaté aucun changement. Des études de longue durée n'avaient pas le pouvoir nécessaire pour détecter tout changement du VEMS₁, mais des études de courte durée ont constaté une production cliniquement significative de crachat (≥ 4 grammes). **Conclusion:** Il a été démontré, dans un nombre limité d'enquêtes, que le DA produit des volumes cliniquement significatifs de crachat. L'effet du DA sur le fonctionnement de l'appareil pulmonaire demeure incertain et des questions ont surgi au sujet de la pertinence du VEMS₁ comme mesure valide du dégagement des voies aériennes à partir des régions pulmonaires périphériques. Il faudrait envisager d'utiliser le VEMS₁ comme mesure première de l'effet du DA.

Cystic fibrosis (CF) is an inherited, life-limiting, multi-system disease that primarily affects the respiratory and digestive systems.¹ People with CF have altered pulmonary mucus composition and are prone to secretion retention in the lungs.^{2,3} This contributes to the advancement of CF lung disease as a result of chronic infection and a persistent, heightened inflammatory response that

progressively damages the structure and architecture of the smaller airways.^{3,4} Current evidence has indicated that CF lung disease originates in the small airways early in life; therefore, it is important that CF treatments aggressively target these sites to prevent irreversible lung damage.³ It is recommended that people with CF

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complete airway clearance daily to mitigate the effects of mucus retention in the lungs.^{5–7}

Autogenic drainage (AD), an airway clearance technique (ACT) recognized by the International Physiotherapy Group for CF,⁸ was developed by Jean Chevaillier in 1967,^{9–11} based on emerging theories and models of airflow in the lungs.^{9–13} Performing AD involves taking tidal volume breaths, with inspiratory pauses, using controlled inspiratory and expiratory effort, over the vital capacity of the lungs. The cycle starts in the expiratory reserve volume and moves through functional residual capacity into the inspiratory reserve volume in three defined stages. This technique has been shown to create sustained airflow that is higher than usual in the airways of the lungs.^{11,13,14} The increased airflow at low lung volumes is proposed to expedite the movement of mucus from the periphery of the lung (i.e., small airways) to the central airways and to improve ventilation, making it an appropriate treatment option given the evidence to date.^{3,11,15}

AD is a preferred ACT for many people with CF^{16,17} and is the third most used by Canadians with CF.¹⁸ The population of people with CF is aging: 60% of Canadians with CF are adults, and the median age of survival, based on the Canadian CF data registry, is now 50.9 years compared with 40.9 years a decade ago.^{19,20} Standard CF care, including daily airway clearance, is acknowledged to be burdensome.²¹ The continuous increase in life expectancy and increased focus on quality of life by health care professionals and patients alike make it imperative that we understand the effects of ACTs so they can be prescribed appropriately and used effectively. To date, no systematic review has examined the effects of AD in people with CF. The research question for our systematic review, therefore, was “What are the effects of short- and long-term use of AD on pulmonary function and sputum recovery for people with CF?”

METHODS

Identification of studies

The protocol for our systematic review was registered with PROSPERO (registration no. CRD42014007118). We included randomized controlled trials (RCTs) or quasi-randomized clinical trials investigating the effects of AD, as described by Chevaillier,^{9,11,22} as the sole ACT for people with CF. We excluded studies if AD was combined with another ACT, if a modified method of AD was used, or if they investigated people who had received or were awaiting lung transplantation, because very poor lung function and increased respiratory rate make it unlikely that participants were able to properly perform AD.

Outcome measures

The outcome measures were pulmonary function (forced vital capacity [FVC], forced expiratory volume in

1 s [FEV₁], and forced expiratory flow between 25% and 75% of forced vital capacity [FEF_{25–75}]) and sputum recovery (dry or wet weight or volume of expectorated secretions). Pulmonary function values are used in CF research and clinical practice as primary outcome measures;^{23–25} amount of expectorated sputum is a clinically relevant measure routinely used in clinical trials on airway clearance in CF.^{6,7}

Information sources

We searched five electronic databases—CINAHL (1982–2015), PEDro (1929–2015), the Cochrane Library (1993–2015), EMBASE (1974–2015), and MEDLINE (1966–2015)—and the clinical trials registry at <http://www.clinicaltrials.gov>. The reference lists of documents identified by the screening process were also searched by hand. Any author with two or more publications in the list of eligible articles was searched by name in each database to determine whether any additional publications met the screening criteria. We reviewed abstracts from the North American Cystic Fibrosis Conference and the European Cystic Fibrosis Conference from 2008 to 2015 in the online editions of *Pediatric Pulmonology* and the *Journal of Cystic Fibrosis*, respectively. We also reviewed all available online newsletters (2003–2009) from the International Physiotherapy Group for Cystic Fibrosis (IPGCF) at <http://www.cfwf.org/ipg-cf/>. We examined the reference list of the Canadian Cystic Fibrosis Foundation’s document “Methods of Airway Clearance Questions and Answers,”²⁶ along with the AD section of the IPGCF’s “Physiotherapy for People with Cystic Fibrosis: From Infant to Adult.”⁸ Finally, we searched Google (December 2014) and Google Scholar (2014) using the terms *autogenic drainage* and *cystic fibrosis*. The last search was conducted on January 2, 2015.

Search strategy

The key search terms were *autogenic drainage*, *cystic fibrosis*, *airway clearance*, *chest physiotherapy*, and *forced exhalation*. No limits were placed on date of publication, type of study, or language; when possible, however, we imposed limits to include only studies with human participants. The results were narrowed using the Boolean operator NOT and the terms *COPD* (chronic obstructive pulmonary disease), *primary ciliary dyskinesia*, and *ivacaftor*. (See online supplement.)

Study selection

Using the key search terms, the primary author searched sources; a second author verified the process. We examined the title, abstract, keywords, and, if necessary, the body of the article using the terms *cystic fibrosis* AND *autogenic drainage* OR *airway clearance* OR *chest physiotherapy*. Any article on the subject of AD and CF was retained for further evaluation. After removing non-clinical trials, we independently reviewed the remaining

articles, adhering to the guidelines set out in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.²⁷

Assessment of studies

Our assessment of bias was defined and informed by the Consolidated Standards of Reporting Trials (CONSORT) extension for non-pharmacologic treatments²⁸ and the Cochrane Collaboration Assessment of Risk of Bias of Included Studies Guideline;^{29,30} we used the PEDro scale^{31,32} to assess the quality of the methods. We independently reviewed the eligible articles, then met to discuss our findings and interpret the results using these tools. Inclusion was determined via consensus.

Data were extracted from each eligible study by the primary author and verified by a second author. An abbreviated version of the Cochrane Collaboration data extraction form for intervention reviews of RCTs and non-RCTs guided this process.³⁰ If data were noted to have been collected but were not reported, we contacted the corresponding author to request the information.

RESULTS

We retrieved a total of 735 unduplicated articles (see Figure 1). Of these, 58 met the preliminary selection criteria; 49 were then excluded because they were not RCTs (33), used AD in combination with another treatment (4), contained umbrella terms that did not include AD (5), used modified AD (breathing at self-selected lung volumes;²² 3), or were old abstracts and data of interest were unobtainable (4). Of the 49 excluded studies, 28 were review articles. A total of 9 publications, including one abstract, were reviewed; 5 of these were excluded because they investigated the German method of AD—"modified AD"²² (2)^{33,34}—or because there was insufficient data to compare effects (3).^{35–37} Two of these studies appeared very promising,^{36,37} but the authors did not respond to our request to share their data.

Characteristics of studies

Four publications^{6,16,38,39} were ultimately included in our systematic review (see Table 1). There were 54 participants in total, aged 9–42 years, with an average FEV₁ of 59% predicted (range 45%–74%). The studies were published between 1992 and 2010; the most recent examined long-term AD use, whereas the older studies investigated single treatment sessions. The studies compared the effects of AD with at least one commonly used ACT. We found heterogeneity across studies with respect to how the AD technique was taught and assessed, as well as in treatment duration. None of the studies used an objective method to assess participants' AD technique or their adherence to treatment.

Critical Analysis

For risk-of-bias assessments, see the online supplement. Studies varied from having a low risk of bias¹⁶ to an unclear risk of bias when the methods were not

described in sufficient detail to allow categorization.^{38,39} One study had a moderate risk of bias resulting from incomplete data reporting,⁶ because the authors reported collecting data at baseline and at 6 and 12 months, but the 6-month data were not included in the article. The quality of each study was good, ranging from 6 to 8 on the PEDro scale (Table 2).^{31,32,40}

Effect of intervention

All studies compared AD with different ACTs, but none found between-group differences in FEV₁. To further evaluate the effects of AD on the outcomes of interest for this review, we isolated data specific to AD from each larger comparative study and created four data subsets of outcome measures for AD alone. These subsets presented pretest and posttest results with no control group⁴¹ and were used to inform the results of this systematic review (see Table 1). Because the number of participants in each study who were using AD was low (10–17) and the methodologies varied, meta-analysis was not possible.

The only outcome common to all four studies was FEV₁, which did not change significantly after AD. McIlwaine and colleagues¹⁶ found a predicted mean change in FEV₁ of less than 1% after 1 year of AD in adolescents, and Pryor and colleagues⁶ found a non-significant change in mean FEV₁ of –0.04 L over 12 months in an adult AD group. The authors of the long-term studies reported inadequate power to detect a change in FEV₁ because of a large number of participant withdrawals.^{6,16} The short-term studies also found non-significant differences in mean FEV₁ percent predicted before and after AD in people who were not having an exacerbation.^{38,39} These short-term studies did not discuss power calculation and sample size, but all had small participant numbers, which suggests they may have been underpowered.

FVC was reported in three studies.^{16,38,39} Giles and colleagues³⁹ and McIlwaine and colleagues¹⁶ reported a non-significant change of 2% or less after AD over the short and long term, respectively, and Pflieger and colleagues³⁸ reported significant improvement in mean FVC (5% predicted) after a single AD session. McIlwaine and colleagues, the only group to report FEF_{25–75%}, found a non-significant mean change of –1.91% over 1 year.¹⁶

Short-term studies by Pflieger and colleagues³⁸ and Giles and colleagues³⁹ found a clinically significant yield of sputum (≥ 4 g/session wet weight).³⁷ This minimal clinically important difference was based on the work of Osman and colleagues,³⁷ who assessed sputum expectoration in a single airway clearance session in people with CF. Participants in Pflieger and colleagues³⁸ study, whose baseline sputum production was >20 mL per day, expectorated an average of 36 (SD 25) g over 80 minutes, whereas Giles and colleagues³⁹ reported that participants expectorated an average of 14 (SD 3) g over 60 minutes.

Figure 1 Flow diagram.

IPGCF = International Physiotherapy Group for Cystic Fibrosis; NACFC = North American Cystic Fibrosis Conference; ECFC = European Cystic Fibrosis Conference; CPGCF = Canadian Physiotherapy Group for Cystic Fibrosis; AD = autogenic drainage; CF = cystic fibrosis; CPG = Clinical Practice Guideline.

Table 1 Summary of Included Studies

Study	Participants	Intervention	Results for AD group
McIlwaine et al. ¹⁶ 2-y crossover trial	<i>n</i> = 36; 17 participants (9 male) did AD; mean age 14 y “Proven diagnosis of CF”; compliant with PD&P	PD&P in 5–6 positions 3–5 min with deep breathing, huff and cough 30 min BID or AD 30 min BID until patient felt all mucus was evacuated from lungs	Mean change in % predicted over 1 y: FVC 2.35 (SD 1.87; NS); FEV ₁ 0.97 (SD 2.25; NS); FEF _{25–75%} –1.91 (SD 3.75; NS). Sputum weight not tested.
Pryor et al. ⁶ 12-mo prospective RCT	<i>n</i> = 65; 13 participants (10 male) did AD; mean age 25.9 y CF diagnosed via genotype, sweat chloride, or sweat sodium, age ≥16 y, FEV ₁ ≥25%	AD, ACBT, PEP Cornet, or flutter BID in sitting; individualized frequency and length of intervention	Mean litres at 0 and 12 months: FEV ₁ 2.68 (SD 1.29) vs 2.64 (SD 1.22; NS). Sputum weight not tested.
Giles et al. ³⁹ randomized 2-day crossover trial	<i>n</i> = 10 (7 male); patients aged 12–42 y who wanted to learn a new airway clearance technique	PD&P: 7 positions ×3 min, huff and cough after each position or AD until lungs are clear	Mean % predicted, pre- vs 1 hr post-Rx: FVC 68 (SD 18) vs 67 (SD 18; NS); FEV ₁ 49 (SD 8) vs 50 (SD 8; NS). Sputum wet weight: 14 (SD 3) g.
Pfleger et al. ³⁸ randomized 5-day crossover trial	<i>n</i> = 15 (5 male); aged 9–22 y Age > 6 y, trained and cooperative with PFTs, producing >20 ml of sputum per day, from local CF clinic	Randomly assigned PEP, AD, PEP-AD, AD-PEP, coughing	Mean % predicted pre- vs 30-min post-Rx: FVC 69 (SD 21) vs 73 (SD 20; <i>p</i> < 0.05); FEV ₁ 54 (SD 20) vs 56 (SD 19; NS). Sputum wet weight: 36 (SD 25) g.

AD = autogenic drainage; CF = cystic fibrosis; PD&P = postural drainage and percussion; BID = twice a day; FVC = forced vital capacity; NS = not significant; FEV₁ = forced expiratory volume in 1 second; FEF_{25–75%} = forced expiratory flow from 25% to 75% of vital capacity; ACBT = active cycle of breathing techniques; PEP = positive expiratory pressure; post-Rx = after treatment; PFTs = pulmonary function tests.

Table 2 PEDro Scores of Included Studies

PEDro category	McIlwaine et al. ¹⁶	Pryor et al. ⁶	Giles et al. ³⁹	Pfleger et al. ³⁸
Random allocation	Y	Y	Y	Y
Concealed allocation	N	N	N	N
Groups similar at baseline	Y	Y	Y	Y
Participant blinding	N	N	N	N
Therapist blinding	N	N	N	N
Assessor blinding	Y	Y	N	Y
<15% dropouts	Y	Y	Y	Y
Intention-to-treat analysis	Y	Y	Y	Y
Between-group difference reported	Y	Y	Y	Y
Point estimate and variability reported	Y	Y	Y	Y
Total PEDro score (0–10)	7	7	6	7

Y = yes; N = no.

DISCUSSION

The clinical trials included in our review demonstrate that AD is an ACT that generates clinically significant sputum yields, but they do not show significant improvement in FEV₁ in people with CF using AD over a short- or long-term period. The short-term studies measured sputum yield, which is the direct outcome of air-

way clearance, but the long-term studies omitted the challenging task of collecting and measuring the amount of sputum that participants cleared. All studies used FEV₁ as their primary outcome measure, making two inherent assumptions: first, that FEV₁ is sensitive to the removal of mucus from the lungs and therefore reflects the effectiveness of AD as an ACT, and, second, that

FEV₁ can improve, or at least be maintained, in people who complete airway clearance and follow the usual clinical course of CF. Currently, however, people with CF experience an average annual decline in FEV₁ of 2% predicted.⁴

The short-term studies we reviewed showed that AD cleared a clinically significant amount of sputum in a single treatment session. Pflieger and colleagues³⁸ chose participants who produced copious amounts of secretions and found an improvement in their FVC. In contrast, participants in the study by Giles and colleagues,³⁹ who typically produced smaller amounts of sputum that were collected over a shorter time period, did not show an associated change in FVC after treatment. Sputum yield is considered a clinically relevant outcome measure, but its validity has repeatedly been challenged.^{6,7,42,43} Wet weight measurements of sputum may be contaminated by saliva or diminished because the person swallows mucus instead of expectorating it.⁴³ In addition, duration of the collection period can affect the sample amount.⁴³

The relationship between sputum clearance and pulmonary function remains unclear,⁷ but the significant improvement in FVC after clearance of sputum using AD should not be ignored. An increase in FVC represents an increase in the volume of air that can be exhaled from the lungs.^{44,45} This air is exhaled from the larger, central airways as well as the smaller, peripheral airways, because the manoeuvre is aimed at exhaling one's vital capacity.^{13,14} CF disease slowly progresses in the peripheral airways,³ producing a concentration of thick mucus. AD is proposed to remove this mucus and augment airflow in these small airways, which could account for the short-term improvement in FVC.^{13–15,38} The lack of improvement in FVC over the long term in the study by McIlwaine and colleagues¹⁶ may reflect the multifactorial nature of CF disease progression, and FVC may therefore only be relevant for short-term evaluation of airway clearance.

The short-term studies found no significant effect of AD on FEV₁. In contrast to FVC, FEV₁ measures airflow in the large airways.^{3,46} Because of the brief nature of the FEV₁ manoeuvre, air is exhaled primarily from the proximal airways, because the lungs empty sequentially from the central to peripheral airways. Therefore, it is not surprising that FEV₁ did not change after AD in a group of people in a non-exacerbation state, because secretions are not concentrated in the large airways where they can obstruct airflow and diminish FEV₁. The long-term studies investigated improvement of FEV₁ but did not find significant changes. Typically, the clinical course of CF results in an average annual decline in FEV₁ of 2% predicted.⁴ It is interesting that neither study reported this decline in FEV₁. Therefore, it is possible that AD may help preserve lung function over the course

of the disease, in keeping with current goals of CF disease management.⁴⁷ However, in the absence of a controlled clinical study that is adequately powered, we cannot draw a definitive conclusion about the influence of AD on the preservation of FEV₁.

FEV₁ remains the gold standard for measurement of CF disease progression,^{24,48} but its status has been challenged in recent years by new evidence that pathological pulmonary changes occur in the peripheral airways while FEV₁ remains constant.^{3,49,50} Over the long-term clinical course of CF, FEV₁ is considered a measure of irreversible damage to the large airways³ and, once it is below 30% predicted, a significant predictor of mortality.⁵¹ Improved survival and lack of deterioration in FEV₁ over time^{4,48,52–54} make reliance on FEV₁ as a primary outcome measure in clinical practice and research challenging.⁵⁵ Clinically, FEV₁ represents the influence of multiple treatments on various components of CF disease, and therefore it cannot measure the specific influence of a particular intervention, such as airway clearance, over time.^{25,55–57} Clinical trials have struggled to generate sufficient power to detect a significant change in FEV₁.^{55,56} Investigators should consider other measures and distinguish between assessing the effects of interventions and assessing CF disease progression when using such measures. In the meantime, perhaps researchers and clinicians should re-evaluate how they view FVC when assessing single-treatment interventions.

The AD interventions in the studies we reviewed were of varied duration, and AD skill and adherence were not assessed. Results were limited by small participant numbers, a lack of power to detect a change in FEV₁ (the primary outcome measure), and an unclear risk of bias in two of the four studies. Use of control groups, such as retrospective data from patients who were non-adherent to airway clearance, would have helped clarify the lack of change in FEV₁ because such patients might have shown comparatively significant declines. Finally, FEV₁ appears non-specific to the proposed effects of AD.

CONCLUSION

AD has been shown to produce clinically significant sputum yields, albeit in a small number of studies. The effect of AD on the function of the pulmonary system remains uncertain. Long-term studies did not demonstrate change in FEV₁, although these studies were all underpowered and therefore firm conclusions could not be drawn. The results do, however, contribute to current debate on the appropriateness of FEV₁ as a primary outcome measure for the effectiveness of AD, and of other ACTs, in CF treatment. Future investigations should consider innovative designs and appropriate measures when evaluating the effectiveness of physiotherapy for people with CF.

KEY MESSAGES

What is already known on this topic

Daily airway clearance is a standard of care for people with cystic fibrosis (CF). Autogenic drainage (AD) is the third most used airway clearance technique for Canadians with CF. Preliminary investigations suggest that AD can alter airflow and improve ventilation; however, the effects of AD, both short term and long term, have not been reviewed systematically.

What this study adds

AD has been shown to produce clinically significant sputum yields. The effect of AD on the function of the pulmonary system remains uncertain. The use of FEV₁ as a primary outcome measure of the direct effects of AD should be further deliberated. FVC may have clinical value in the assessment of an AD session, but more specific and sensitive measures are needed to validate long- and short-term AD effects.

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