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Chest physiotherapy in hospitalized patients with cystic fibrosis: a study of lung function effects and sputum production

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ABSTRACT: In order to evaluate the short-term lung function effects of high-pressure positive expiratory pressure (PEP)-mask physiotherapy (PT) in relation to PT-assisted sputum production, we studied 18 patients with cystic fibrosis (CF), hospitalized for a pulmonary exacerbation. Lung functions were measured before (a) and after PT (b) on day one (1), five (2), ten (3) and fifteen (4). Five functions improved significantly from a1 to b1, eight from a2 to b2, seven from a3 to b3, and seven from a4 to b4. Baseline (a) measurements improved only slightly, but post-PT (b) values improved more markedly from 1 to 4, and this improvement reached statistical significance for six functions; consequently, a-to-b lung function changes tended to increase from investigation 1 to 4. Eleven PT-induced lung function changes correlated to the weight of sputum produced. High-pressure PEP-mask PT therefore resulted in significant lung function improvements, and not only maintained but increased its effect in the course of the hospitalization.

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Chest physiotherapy (PT) is a traditional component of the therapeutic regimen for patients with cystic fibrosis (CF) [1–3]. PT aims at the removal of infected secretions, which not only cause atelectasis, hyperinflation and impaired gas exchange, but also contain tissue-damaging proteolytic enzymes [3, 4]. In spite of this theoretical background for the use of PT in CF patients, only a few clinical trials have so far investigated PT, and thus most evidence for its therapeutic efficacy in CF has remained anecdotal [3–5]. This situation is further complicated by the development of new and alternative PT techniques [6–9].

CF lung disease is characterized by a progressive deterioration of respiratory functions [10, 11]. Recently, several studies documented a beneficial long-term effect of PT on this lung function course [9, 12, 13]. The question of a short-term lung function benefit from PT has remained controversial; some investigators found an improvement of respiratory functions after PT [14–20], but others failed to document significant changes [21–23]. A particularly controversial issue is the contribution of PT to the lung function improvement, which is regularly observed in those patients who are hospitalized for respiratory exacerbations [2, 24]. The seemingly well-established beneficial role of antimicrobial therapy in this situation was recently challenged by a placebo-controlled trial, that remained unable to document a better lung function result for those patients treated with antibiotics than for those receiving placebo [25]. This result, indirectly, suggests that PT might be more responsible for any lung function improvement observed in hospitalized patients than generally accepted.

By combining the forced expiration technique [6] and positive expiratory pressure (PEP)-mask PT [7], we developed a high-pressure technique of PEP-mask PT, and subsequently documented a beneficial long-term effect of this technique on the lung-function status of CF patients [9]. This technique's short-term effects have so far not been investigated.

In the present study, we repeatedly measured multiple aspects of lung function before and after high-pressure PEP-mask PT in a group of hospitalized CF patients, in order to answer the following questions:

1) Does this technique result in significant short-term lung function changes?

2) Do such lung function changes, if present, correlate to PT-assisted sputum production?
3) How do PT-induced lung function changes, if observed, behave, when assessed repeatedly in the course of a hospitalization?

Methods

Eighteen CF patients, 7 males and 11 females, mean age 14.2 yrs (range 8.4–21.0 yrs), with a mean clinical score [26] of 66.2 points (range 34–93), and a mean chest radiographic score [27] of 13.2 points (range 9–20), were admitted for the treatment of a pulmonary exacerbation. The diagnosis of CF had previously been confirmed in all patients by repeatedly positive sweat tests [28].

Prior to admission, their therapeutic regimen had included an appropriate diet with pancreatic enzyme replacement, supplemental salt and vitamins, as well as chest physiotherapy. Nine patients had been on oral and five on inhaled long-term antibiotic therapy, seven used inhaled bronchodilators (salbutamol) on a regular basis. Fourteen to five days prior to admission, sputum samples were collected for bacteriological evaluation; one to six strains of *Pseudomonas aeruginosa* were identified by routine culture techniques in 17 patients, one additional strain of *Pseudomonas cepacia* in one, and one additional strain of *Pseudomonas maltophilia* in four patients. One strain of *Staphylococcus aureus* was found in nine patients, including the one without Pseudomonas colonization.

Informed consent for the study was obtained from patients and parents.

Each child was hospitalized for 16 days. Antimicrobial chemotherapy was guided by the above sputum culture results and consisted of two or three antibiotics, given intravenously *t.i.d.*; dosages followed generally accepted guidelines [2]. The nutritional management was individualized; pancreatic enzymes were given in accordance to the individual pre-admission dosage. As their clinical condition allowed, the patients were encouraged to participate in physical activity. Those patients who had used bronchodilators regularly continued their medication *t.i.d.* throughout the hospitalization.

Each patient cleared his/her lung by self-administered high-pressure PEP-mask PT three times a day. This technique has been described previously [9]. Briefly, the PEP-mask (Astra Meditec, Mölndal, Sweden) is an anaesthesiology rubber mask connected to a one-way breathing valve; the outlet of this valve is equipped with an expiratory resistor, the internal diameter of which is chosen by a spirometer-assisted method [9]. While sitting upright, the patient presses the mask against his/her face, breathes in and out rhythmically for 8–10 cycles, and then performs a forced expiratory manoeuvre against the stenosis. This results in the expectoration of sputum. All patients were familiar with the method and had used high-pressure PEP-mask PT at home for a time-span of 1.8–5.3 (mean 4.5) yrs prior to the study.

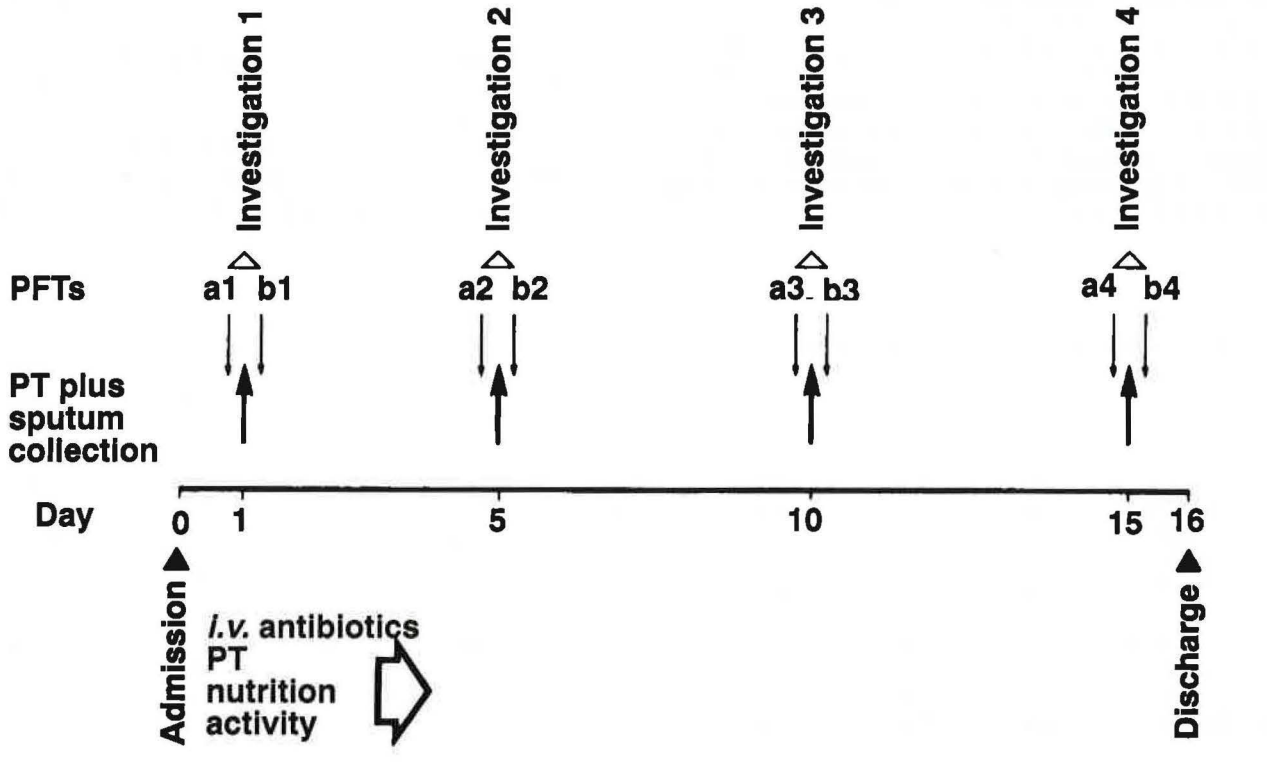

Fig. 1. – Study design. PFTs: pulmonary function tests: PT: high-pressure positive expiratory pressure (PEP)-mask physiotherapy.

The design of the study is shown in figure 1. Patients were admitted on day zero. On day one, five, ten and fifteen of the hospitalization, lung function was measured before and five minutes after the end of the morning PT session. For investigation one, two, three and four, this resulted in one pre-PT measurement "a" and one post-PT measurement "b" each (measurement a1, b1, a2, *etc.*). Bronchodilator-medicated patients inhaled their morning dose of salbutamol not later than one hour before the pre-PT measurement (a).

Pulmonary function tests (PFTs) were done in accordance with standardized guidelines [29]. A forced vital capacity manoeuvre was recorded in form of a volume-time and a maximum expiratory flow-volume curve on a pneumotachygraph spirometer (Pneumotest Junior, Jaeger, Wuerzburg, FRG), and forced vital capacity (FVC), forced expiratory volume in the first second (FEV_1), peak expiratory flow (PEF), maximum expiratory flow at 50% ($\dot{V}_{50}$) and at 25% of the remaining vital capacity ($\dot{V}_{25}$) were measured. Thoracic gas volume was measured according to the method of DuBois *et al.* [30] in a constant-volume, whole-body plethysmograph (Body-Test, Jaeger, Wuerzburg, FRG). Vital capacity (VC), residual volume (RV) and total lung capacity (TLC) were calculated. Post-PT (b) measurements of $\dot{V}_{50}$ and $\dot{V}_{25}$ were calculated based both on the actual FVC and on absolute volume taken from the pre-PT (a) measurement (Isovol-$\dot{V}_{50}$ and Isovol-$\dot{V}_{25}$). Results of all PFTs were expressed as percentage of predicted normal values, as based on routine reference standards [31, 32].

The sputum cleared by high-pressure PEP-mask PT between PFTs a and b in investigation one, two, three and four was collected and weighed.

For statistical evaluation of the results, analysis of variance, the t-test and regression analysis by the least squares method were used, with p=0.05 as the limit of significance. In order to avoid the mathematical influence of a variable baseline situation, all lung function changes were quantified, like the measurements themselves, in percentage of predicted, and not in percentage of baseline values.

Results

On clinical criteria, the respiratory status of all patients improved markedly from hospital admission to discharge.

Lung function measurements at investigation one, two, three and four are summarized in table 1. Pre-PT (a) measurements are statistically compared to post-PT (b) values in table 2. Expiratory volumes and flow rates tended to increase, and RV/TLC tended to decrease from a to b in all four PT investigations; these changes reached statistical significance for several functions in each of the four investigations.

Measurements a1 and b1 are statistically compared to values a2, a3, a4 and b2, b3, b4, respectively, in table 3. Pre-PT (a) expiratory volumes and flow rates tended to increase throughout the hospitalization, but this increase only reached statistical significance for a minority of functions. Post-PT (b) expiratory volumes and flow rates increased, and post-PT RV/TLC decreased more markedly when compared longitudinally, and these changes reached statistical significance for a majority of functions. The maximum mean difference between pre-PT (a) and post-PT (b) measurements occurred in investigation four for 6 functions, in investigation three for 4 functions, and in investigation two and one for 1 function each. Thus, the PT-induced a-to-b PFT changes tended to increase throughout the hospitalization.

When comparing the first PFT measurement of the hospitalization (a1) to the last one (b4), there was a statistically significant increase of FVC ($p<0.001$), FEV_1 ($p<0.001$), FEV_1/FVC ($p<0.001$), PEF ($p<0.01$), $\dot{V}_{50}$ ($p<0.05$), Isovol-$\dot{V}_{50}$ ($p<0.001$), $\dot{V}_{25}$ ($p<0.05$), Isovol-$\dot{V}_{25}$ ($p<0.001$), and VC ($p<0.001$), as well as a statistically significant decrease of RV/TLC ($p<0.02$).

The typical lung function course is illustrated in figure 2 by the example of FVC.

Time used for PT between PFTs a and b ranged from 21–88 (mean 47.5) min. In investigation one, PT resulted in the production of 37±14 g of sputum

Table 1. – The lung function measurements

	a1	b1	a2	b2	a3	b3	a4	b4
FVC % pred	63±17	68±15	64±18	70±16	64±20	71±17	66±20	73±16
FEV_1 % pred	45±18	48±16	46±16	49±15	48±19	51±17	49±19	52±18
FEV_1/FVC %	42±17	45±15	43±15	46±15	45±18	48±16	45±18	48±17
PEF % pred	70±15	72±13	74±14	81±29	76±15	78±12	75±17	80±17
$\dot{V}_{50}$ % pred	30±18	32±19	31±18	33±19	34±22	35±21	34±24	37±24
Isovol-$\dot{V}_{50}$ % pred	see above	36±21	see above	40±21	see above	42±24	see above	45±25
$\dot{V}_{25}$ % pred	17±9	18±11	17±10	19±10	18±10	20±11	18±12	20±13
Isovol-$\dot{V}_{25}$ % pred	see above	24±14	see above	26±14	see above	28±15	see above	28±16
VC % pred	66±16	71±15	66±16	71±14	67±18	74±16	68±19	74±18
TLC % pred	117±17	119±20	115±18	117±19	116±20	118±21	119±19	120±18
RV/TLC %	54±13	52±13	53±14	51±13	53±16	50±14	54±15	51±13

Values are mean±SD. FVC: forced vital capacity; FEV_1: forced expiratory volume in one second; PEF: peak expiratory flow; $\dot{V}_{50}$, $\dot{V}_{25}$: maximum expiratory flow at 50% and 25% remaining vital capacity, respectively; VC: vital capacity; TLC: total lung capacity; RV: residual volume; Isovol-$\dot{V}_{50}$, Isovol-$\dot{V}_{25}$: $\dot{V}_{50}$ and $\dot{V}_{25}$: measurements based on absolute volume from pre-physiotherapy measurments.

Table 2. – Statistical comparison of a to b measurements

	a1 *versus* b1	a2 *versus* b2	a3 *versus* b3	a4 *versus* b4
FVC % pred	p<0.001	p<0.001	p<0.001	p<0.001
FEV_1 % pred	NS	p<0.01	NS	p<0.05
FEV_1/FVC %	NS	p<0.01	p<0.01	p<0.01
PEF % pred	NS	NS	NS	NS
$\dot{V}_{50}$ % pred	NS	NS	NS	NS
Isovol-$\dot{V}_{50}$ % pred	p<0.05	p<0.001	p<0.02	p<0.01
$\dot{V}_{25}$ % pred	NS	p<0.01	p<0.05	NS
Isovol-$\dot{V}_{25}$ % pred	p<0.001	p<0.001	p<0.001	p<0.001
VC % pred	p<0.001	p<0.01	p<0.001	p<0.001
TLC % pred	NS	NS	NS	NS
RV/TLC %	p<0.02	p<0.05	p<0.01	p<0.05

NS: not significant. For abbreviations see legend to table 1.

Table 3. – Longitudinal statistical comparison of measurements

	a1 *versus*			b1 *versus*		
	a2	a3	a4	b2	b3	b4
FVC % pred	NS	NS	NS	p<0.05	p<0.05	p<0.01
FEV_1 % pred	NS	NS	p<0.02	p<0.01	NS	p<0.01
FEV_1/FVC %	NS	p<0.05	NS	NS	p<0.01	p<0.01
PEF % pred	NS	NS	NS	NS	p<0.001	p<0.02
$\dot{V}_{50}$ % pred	NS	p<0.05	NS	NS	NS	p<0.02
Isovol-$\dot{V}_{50}$ % pred	NS	p<0.05	NS	NS	p<0.05	p<0.01
$\dot{V}_{25}$ % pred	NS	NS	NS	NS	NS	NS
Isovol-$\dot{V}_{25}$ % pred	NS	NS	NS	NS	p<0.05	NS
VC % pred	NS	NS	NS	NS	p<0.05	NS
TLC % pred	NS	NS	NS	NS	NS	NS
RV/TLC %	NS	p<0.05	NS	NS	p<0.01	NS

NS: not significant. For abbreviations see legend to table 1.

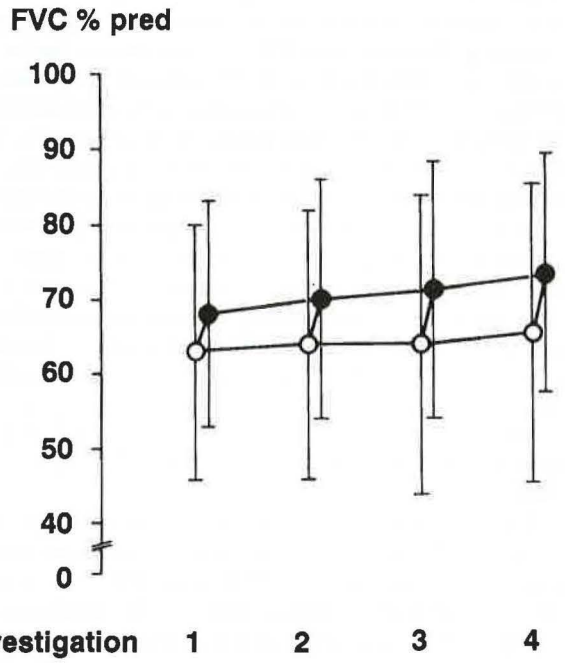

Fig. 2. – Longitudinal development of forced vital capacity (FVC) (mean±SD). Circles are pre-PT (a) measurements, dots stand for post-PT (b) values. PT: high-pressure positive expiratory pressure (PEP) mask physiotherapy.

(range 17–66 g); in investigation two, the amount of sputum produced was 35±15 g (range 8–66 g); in investigation three this was 31±15 g (range 6–56 g), and in investigation four 35±19 g (range 7–77 g).

Some lung function changes correlated significantly to the amount of sputum produced. Delta-FVC correlated to sputum production in investigation three (r=0.745, p<0.001) and four (r=0.691, p<0.01), delta-FEV_1 to sputum production in investigation one (r=0.734, p<0.001), two (r=0.472, p<0.05) and three (r=0.511, p<0.05), delta-FEV_1/FVC to sputum production in investigation three (r=0.603, p<0.01), and four (r=0.600, p<0.02), and delta-VC to sputum production in investigation three (r=0.762, p<0.01) and four (r=0.474, p<0.05). A further such correlation was found for delta-RV/TLC in investigation two (r=0.473, p<0.05), and three (r=-0.762, p<0.001). When correlating all sputum weights produced by all patients in all four PT investigations to the pooled PT-induced lung function changes, there was a statistically significant correlation for delta-FVC (r=0.434, p<0.001), delta-FEV_1 (r=0.303, p<0.02), delta-FEV_1/FVC (r=0.347, p<0.01), delta-VC (r=0.361, p<0.01), and for delta-RV/TLC (r=-0.374, p<0.01). In summary, there was a statistically supported tendency for bigger PT-induced lung function changes to occur in those patients with a higher PT-assisted sputum production.

Discussion

As documented by this study, high-pressure PEP-mask PT, when applied in CF patients, results in a statistically significant short-term improvement of respiratory functions. The spectrum of measured changes indicates a PT-induced reduction of expiratory airflow obstruction and hyperinflation. Furthermore, the magnitude of PT-induced lung function changes correlated to the amount of sputum produced. Last, but not least, PT-induced lung function improvements were not only maintained but even tended to increase during the course of the hospitalization; this indicates a major contribution of PT to the overall lung function improvement that was observed from hospital admission to discharge.

A wide spectrum of routine PFTs were used for assessing the short-term effects of the investigated PT technique. While the observed PT-induced lung function changes remained small, their pattern is physiologically coherent. Expiratory volumes and flow rates tended to increase with PT, while RV/TLC decreased simultaneously. These changes indicate decreased obstruction of expiratory airflow plus decreased hyperinflation [33, 34]. Such changes are opposed to those progressive alterations of respiratory functions that characterize the deteriorating long-term course of the disease [10, 11]. Consequently, the observed short-term effects of PT are clearly beneficial; they correspond to a previously documented, beneficial long-term effect of this PT technique [9].

Almost all lung functions improved from the first (a1) to the last (b4) PFT assessment, and this improvement resembled the lung function course of hospitalized CF patients as observed in a previous investigation [24]. In contrast to previous work, however, the present study offers more insight into the contribution of PT to this overall improvement. While pre-PT (a) PFT measurements improved only discretely during the course of the hospitalization, post-PT (b) functions improved more markedly and, consequently, a-to-b lung function changes tended to increase with ongoing treatment. This suggests that PT did account for a large proportion of the overall lung function improvement observed.

In general, the beneficial effect of hospitalizations for exacerbations of CF lung disease can be attributed to antibiotics, PT, nutrition and rest [2, 24]. The last two factors are unlikely contributors to the improvement observed in the present study; patients remained active throughout the hospitalization and their nutritional regimen was adapted to their personal eating habits. Much more extensive and longer-lasting attempts at supplemental nutrition have failed to result in significant lung function improvements [35, 36]. It follows that the observed beneficial effect was caused by either antimicrobial therapy, or PT, or by the combination of both. Recently, the seemingly well-established role of antimicrobial therapy in this treatment situation was challenged by a placebo-controlled trial, that remained unable to document a better lung function result for those patients treated with antibiotics than for those receiving placebo [25]. Together with the result of the present study, this suggests that, in regard to the short-term effects of such hospitalizations, the role of antimicrobial therapy might have been over-, and that of PT underestimated. Nevertheless, a word of caution against interpreting the observed lung function changes as exclusively caused by PT seems indicated. Patients had used the same PT technique at home before being hospitalized. While, as previously observed [37], compliance could have been poor and close observation and guidance by the physiotherapists might have resulted in a markedly improved efficacy of PT, it remains unlikely that this factor alone did account for the entity of the observed changes. It follows that the lung function improvements regularly observed in hospitalized CF patients might most likely be due to a combination effect of PT and antimicrobial therapy. This hypothesis of a synergism between PT and antibiotics, however, is not proven but only suggested by the results of the present study, and therefore should be subject to further investigation.

This is the first study of PT in CF patients which, in contrast to previous investigations [14, 16, 17, 20], succeeded in documenting a statistically significant interrelationship of PT-assisted sputum production and lung function improvement. While it seems reasonable to expect bigger lung function changes after the clearance of more secretions, there might be several PT-related factors which can disturb such a cause-effect relationship. Firstly, some PT techniques might mobilize but not completely remove secretions in some patients [17, 20]; moving secretions from one part of the tracheobronchial tree to another might account for erratic lung function changes. High-pressure PEP-mask PT is continued until no further sputum is produced, and thus this technique might facilitate a more complete clearance of sputum than obtained with other methods. As suggested by wheezing observed after PT [17], the second factor that might have interfered with PT-induced lung function changes in previous investigations, is bronchospasm. In the present study, bronchodilator medication before PT sessions for those patients with coexisting hyperreactive airway disease protected the airways from the mechanical irritation of PT. While this premedication thereby prevented any major interaction of bronchoconstriction and sputum-related PFT changes, it also held the theoretical risk of contributing a bronchodilator effect to sputum-related lung function changes. Therefore, a minimum interval of one hour between bronchodilator medication and pre-PT PFTs was chosen to separate a possible bronchodilator effect from PT-assisted sputum clearance and thereby effected lung function changes.

The question arises as to whether the findings of the present study are specific for the PT technique investigated, *i.e.* high-pressure PEP-mask PT. At present, different centres propagate different PT techniques. As an alternative to conventional PT (postural drainage, chest percussion and vibration, directed coughing), the forced expiration technique [6], autogenic drainage [8], conventional PEP-mask PT [7], and high-pressure PEP-mask

PT [9] have been developed. In contrast to other techniques, neither autogenic drainage nor PEP-mask PT employs postural drainage for mobilizing secretions. present, there is no clear idea whether one method is more effective than the other, and the results of comparative studies from different centres contradict each other [7, 9, 20, 38–41]. There might be several explanations for this somewhat confusing situation. Firstly, there is considerable interindividual variation in the pathophysiology of CF lung disease, and any given PT technique, that might ideally suit the needs of one particular patient, might not be equally effective in another one [3, 4]. Thus, each patient might have his/her own, individual "best" PT technique. Secondly, PT is always a complex sequence of mechanical interventions and, therefore, will depend in its efficacy on a variety of therapeutic details. Consequently, it is not suprising that a given centre tends to find its own, locally developed or modified method superior to other techniques. Thus, each centre might also have its own, individual "best" PT technique. It follows that the findings of the present study might not be strictly specific for high-pressure PEP-mask PT, but might, at least in part, apply to other properly executed techniques as well. Nevertheless, there is the need to evaluate the different techniques in comparative trials, and to find criteria for individualizing their application. Hopefully, future PT for CF patients will not be a rigid routine but rather a maximally effective intervention, carefully tailored to the specific needs of each patient.

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Physiothérapie thoracique chez les patients hospitalisés pour fibrose kystique: une étude des effets sur la fonction pulmonaire et la production de crachats. B. Oberwaldner, B. Theibl, A. Rucker, M.S. Zach.

RÉSUMÉ: Pour évaluer les effets fonctionnels pulmonaires à court terme d'une physiothérapie au moyen d'un masque PAP à haute pression en ce qui concerne la production assistée d'expectorations, nous avons étudié 18 patients atteints de fibrose kystique, hospitalisés pour une poussée pulmonaire. Les épreuves fonctionnelles ont été meusurées avant (a) et aprés (b) physiothérapie aux jours un (1), cinq (2), dix (3), et 15 (4). La fonction pulmonaire a été améliorée cinq fois de façon significative entre a1 et b1, huit fois entre a2 et b2, sept fois entre a3 et b3, et sept fois entre a4 et b4. Les mesures de base (a) ne se améliorées que légèrement, mais les valeurs après physiothérapie (b) ont été améliorées davantage entre 1 et 4, et cette amélioration a atteint une signification statistique pour six fonctions; en conséquence, les modification fonctionnelles pulmonaires de a à b tendent à augmenter de l'investigation 1 à l'investigation 4. Onze modifications fonctionnelles pulmonaires induites par la physiothérapie étaient en corrélation avec le poids d'expectoration produite. Le masque PEP à pression élevée employé pour physiothérapie entraîne dès lors des améliorations fonctionnelles pulmonaires significatives et maintient son effet, voire même l'augmente, pendant le dècours de l'hospitalisation.
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