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REVIEW PAPER

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What's new in airway secretions clearance for adults? A systematic review

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ABSTRACT

Introduction. Airway clearance techniques are an essential part of routine respiratory physiotherapy, enabling bronchial secretion clearance—the mucus overproduction and retaining results in lung function deterioration and disrupts effective pulmonary rehabilitation. Several mucus clearance methods are included in the physiotherapy daily routine of patients with chronic lung conditions; nevertheless, new techniques and approaches are continuously developed.

Aim. Thus, this systematic review summarizes novel airway clearance techniques applied in patients with chronic pulmonary conditions.

Material and methods. The PubMed, Cochrane Library, and PEDro databases were searched from 2010 to 2021, and studies were selected based on eligibility criteria.

Analysis of the literature. 101 patients from five studies describing four different techniques were included. Novel techniques were non-invasive ventilation, intrapulmonary percussive ventilation, trachea vibration, and PEP-sound wave combination. Significant improvements were noted for ventilation homogeneity (NIV), saturation (NIV), respiratory rate (IPV), and diffusion capacity (VL), whereas cardiovascular function and exercise endurance did not change significantly.

Conclusion. The presented methods are considered to have similar effectiveness as well-known airway clearance techniques. However, the systematic use of presented methods in routine pulmonary rehabilitation must be preceded by in-depth investigation to provide no-bias results.

Keywords. bronchial mucus, rehabilitation, respiration

The list of abbreviations:

AD – autogenic drainage, **CF** – cystic fibrosis, **COPD** – chronic obstructive pulmonary disease, **COVID-19** – coronavirus disease 2019, **CPT** – chest physiotherapy, **FET** – forced expiratory technique, **FEV1** – forced expiratory volume in one second, **FVC** – forced vital capacity, **HR** – heart rate, **IPV** – intrapulmonary percussive ventilation, **LCI** – lung clearance index, **MEF25** – maximal expiratory flow at 25 % of the forced vital capacity, **MEF75** – maximal expiratory flow at 75 % of the forced vital capacity, **NIV** – non-invasive ventilation, **PAP** – positive airway pressure, **PEDro** – Physiotherapy Evi-

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dence Database, **PEP** – positive expiratory pressure, **RR** – respiratory rate, **SpO_2** – oxygen saturation, **TV** – trachea vibration, **VAS** – visual analogue scale, **VC** – vital capacity, **VL** – VibraLung® acoustical percussor

Introduction

Mucus expectoration is critically important in pulmonary rehabilitation, especially for patients with chronic obstructive pulmonary conditions such as Chronic Obstructive Pulmonary Disease (COPD), asthma, cystic fibrosis (CF), bronchiectasis, and more.[1-4] These diseases are characterized by chronic airway inflammation and mucus overproduction, leading to severe obstruction. Moreover, distal airway occlusion, ciliary function disorder, and often ineffective cough are key problems with proper clearing secretions, leading to lung function deterioration.[5]

Airway clearance techniques (ACTs) are an essential part of respiratory physiotherapy. These techniques allow for effective mucus evacuation and subsequently enable efficient respiratory muscle training. There are many different techniques applied depending on patients' needs, cooperation or readiness. Some of them, such as postural drainage and chest percussion, are simple and do not require much patients' involvement, but at the same time are regarding as time-consuming, often uncomfortable, and considered less effective when compared with other techniques.[6-8] Moreover, developed secretion clearance devices replaced the head-down postural drainage positions with sitting positions in many countries.[7] Routine treatment includes: (1) volitional breathing based techniques, such as forced expiratory technique (FET), active cycle of breathing technique (ACBT), and autogenic drainage (AD); (2) positive expiratory pressure (PEP) based techniques, such as PEP, Hi-PEP, and oscillating PEP; (3) oscillation based technique, such as high-frequency chest wall oscillation.[9-16] Several reviews and overviews synthesized studies on safety, effectiveness, and quality of life of patients with chronic pulmonary diseases following routinely applied ACTs protocols.[1-3] Nevertheless, respiratory rehabilitation is still developing fast because the number of patients with severe respiratory conditions is growing continuously.[17] Furthermore, nowadays, pulmonary physiotherapy is facing a high burden of COVID-19 patients and survivors, including patients with chronic pulmonary condition exacerbations.[4,18-21] Therefore, novel ACTs, including, but not limited to, methods designed especially for patients unable to use hand-held devices, are of great importance.

Aim

This review aims to look through novel ACTs to summarize their usefulness in everyday pulmonary physiotherapy practice.

Material and methods

Search strategy

A systematic search of PubMed, the Cochrane Library, and Physiotherapy Evidence Database (PEDro) databases was undertaken for years from 2010 to 2021 to look for records involving the phrase "airway clearance techniques" and additional phrases: "novel"; "new"; "state of the art"; "chest physiotherapy"; "chronic pulmonary condition".

Inclusion and exclusion criteria

After duplicates removal, the retrieved publications were screened critically and independently by authors. Publications were included if they mentioned innovative airway clearance techniques in adults, discussed secretion clearance effectiveness, were classified as the randomized controlled study, cohort study, or observational study, and have been written in English or Polish. Publications were excluded if they did not have enough quantitative data in the results section and mentioned only commonly known airway clearance techniques, such as the active cycle of breathing technique, autogenic drainage, positive expiratory pressure, oscillating positive expiratory pressure, and high-frequency chest wall oscillation.

If the information presented in the title, abstract, or keywords suggested the publication might contain data relevant for this review, the full version of the article was downloaded for further investigation. The study exclusion decision was made based on all authors' opinions, and publications not meeting the inclusion criteria were excluded from the analysis.

Study quality appraisal

Extracted data included study design, population (sample size, age, disease), the study's aim, applied protocols (method, therapy duration, individual settings), and results, especially mucus secretion analysis. The primary focus was to check the actual impact of the applied method on mucus secretion. Therefore, from the final analysis, we excluded the studies that did not mention sputum/mucociliary clearance quantitative information (e.g., sputum wet/dry weight, ventilation improvement etc.). The methodological quality assessment was performed using the PEDro scale designed for randomized studies. The tool contains eleven questions scored one point each regarding the applicability of the trial (criterion 1), internal validity (criteria 2-9), and presence of statistical data (criteria 10-11).[22, 23]

Analysis of the literature

Quality appraisal results

The results of the quality assessment are presented in Table 1.

Table 1. The PEDro scale quality assessment results

Study	Rodriguez et al. [24]	Stanford et al. [25]	Paneroni et al. [26]	Kamimura et al.[27]	Wheatley et al. [28] (part I)	Wheatley et al.[28] (part II)
Eligibility Criteria	Yes	Yes	Yes	Yes	Yes	Yes
Randomly Allocated	Yes	Yes	Yes	Yes	Yes	Yes
Concealed Allocation	Yes	Yes	Yes	Yes	Yes	Yes
Similar Groups at Baseline	Yes	Yes	Yes	No	No	No
Blinding of Subjects	Yes	No	No	No	No	No
Blinding of Therapists	No	No	No	No	No	No
Blinding of Assessors	Yes	Yes	No	No	No	No
Data from > 85% of Subjects	Yes	No	Yes	No	Yes	Yes
Intention to Treat	No	Yes	Yes	Yes	Yes	Yes
Statistical comparision	Yes	Yes	Yes	No	Yes	No
Measures of Variability	Yes	Yes	Yes	Yes	Yes	No
Final score	9/11	8/11	8/11	5/11	7/11	5/11

The studies included in the analysis ranged from 5 to 9 on the PEDro scale with a median score of 7. The manuscript authored by Wheatley et al. reported two different studies' designs; therefore, it was divided for improved study quality evaluation.[28] All reported publications scored particularly poorly in blinding of subjects, therapists, and assessors. However, usually, physiotherapeutic interventions requiring patients' commitment need to be carefully explained, and often the proper training should be provided before the intervention, which limits blinding possibilities.

Characteristic of included studies

The summary of database search results is presented in Figure 1. A systematic search of databases identified 4521 records. After duplicates removal, 3841 records were screened based on the title, abstract and key words, and 3798 articles were excluded. 34 full articles were evaluated, and subsequently, 5 articles were included for the review. The reasons of 29 articles exclusion were: (1) lack of information about the sputum secretion (24 publications); (2) lack of any quantitative information about sputum/mucociliary clearance (4 publications); (3) study design (1 publication).

All included publications were randomized studies, 4 randomized crossover studies, and 1 randomized controlled trial.

Reviewed publications recruited 101 patients: 67 diagnosed with CF, 22 with bronchiectasis, 6 with bronchial asthma, 5 with COPD, and 1 with chronic bronchitis. The age of participants ranged from 17 to 93 years. The number of male participants was 52 and female participants 49. The rehabilitation for most individuals was performed either by patients alone at home (n=44) or organized as ambulatory treatment (n=46). Only one publication reported inpatients intervention (n=11).[28]

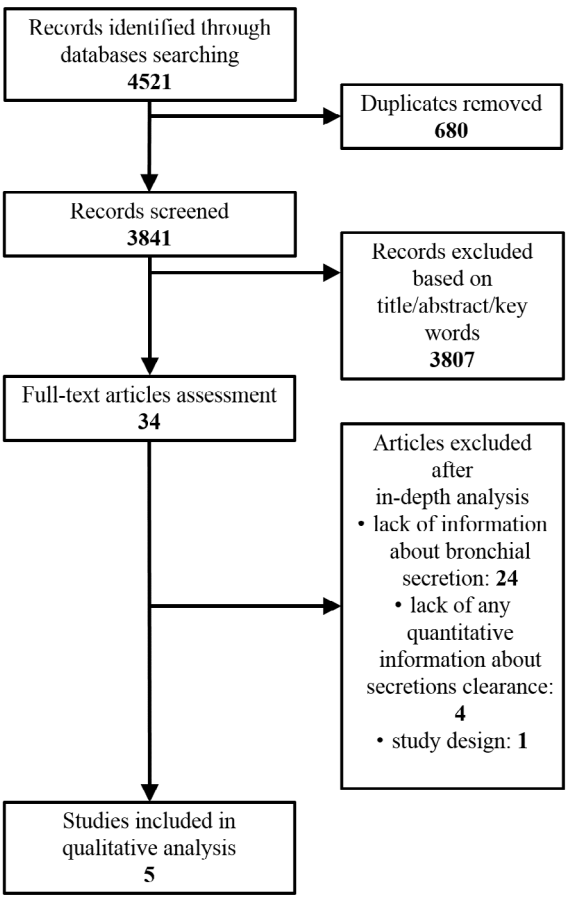

Fig. 1. Flow chart with summary of database search

The summary, including study design, aim, material and methods, results, and key findings, is presented in Table 2.

Techniques description

Five included studies reports four novel airway clearance techniques: non-invasive ventilation (NIV), in-

Table 2. Summary of reviewed manuscripts

Author	Rodriguez et al.[24]	Stanford et al. [25]	Paneroni et al. [26]	Kamimura et al.[27]	Wheatley et al. [28]
Study design	RCT	RCS	RCS	RCS	RCS
Tested technique	NIV-bilevel PAP	NIV	IPV	Cervical trachea vibration (TV method)	Sound waves + PEP (VibraLung® Acoustic Percussor-VL)
Aim	To investigate NIV efficacy as ACT in comparison to standard treatment	To investigate NIV efficacy as ACT in comparison to standard treatment	To investigate IPV efficacy as ACT in comparison to standard treatment	To investigate TV method efficacy as ACT in comparison to standard treatment	To investigate efficacy of VL as ACT in comparison to standard treatment
Population	Experimental group: 16 patients with CF 8M, 8F 28±11 y Control group: 16 patients with CF 8M, 8F 33±9 y	14 patients with CF 7M, 7F 35.5±17.1 y	22 patients with bronchiectasis 12M, 10F 64.4±8.9 y	12 patients: bronchial asthma=6, COPD=5, chronic bronchitis=1) 5M, 7F 54–93 y	Study I: 10 outpatients with CF 7M, 3F 25–34 y Study II: 11 inpatients with CF 5M, 6F 17–29 y
Treatment design	Setting: home treatment Duration: 12 weeks Frequency: 2 sessions (60 min)/day Experimental group: – Inhalation of bronchodilators and hypertonic saline 7% for 10 minutes – Autogenic drainage for 15 minutes – NIV – bilevel PAP (expiratory pressure 10 cm H_2O, inspiratory pressure 20 cmH_2O); 2 minutes breathing – Huffing (FET technique) Full cycle was repeated during 60 minutes Control group: – Inhalation of bronchodilators and hypertonic saline 7% for 10 minutes – Autogenic drainage for 15 min – PEP – 10 breaths through PEP face mask (10–20 cm H20) – Huffing (FET technique) Full cycle was repeated during 60 minutes	Setting: out-patient Duration: 2 days (1 day experimental treatment – 1 day control treatment) Frequency: 2 sessions (30 min)/day Experimental treatment: – 10 NIV breaths –settings determined individually – 4 'huffs' or coughs Control treatment: – usual ACT – 4 'huffs' or coughs	Setting: out-patient Duration: 2 days (1 day experimental treatment – 1 day control treatment) Frequency: 1 session (30 min)/day Experimental treatment: – IPV session in sitting position: 3 active cycles (2 phases low pressure–high frequency; 1 phase high pressure–low frequency) – Cough after each cycle Control treatment: – Combination of forced expiration postural drainage (prone, right-lateral decubitus, left–lateral decubitus), percussion and vibration (10 minutes each position) – Cough after each position	Setting: home treatment Duration: 12 weeks (4 weeks–experimental treatment – 4 weeks washout period – 4 weeks standard treatment) Frequency: 2 sessions (5 min)/day Experimental treatment: electronic larynx applied to cervical trachea to generate transcutaneous vibration at 80 Hz Control treatment: oscillating PEP (Acapella ®) standard treatment	Study I Setting: out-patient Duration: 2 days (1 day experimental treatment – 1 day control treatment) Frequency: 1 session (20 min)/day Experimental treatment: VibraLung breathing with sound waves (PEP + sound waves) Control treatment: VibraLung breathing without sound waves (PEP) Study II Setting: in-patient Duration: 12 days Frequency: 4 sessions (30 min)/day Experimental treatment: HFCWO 2 sessions/day + Vibralung breathing 2 sessions/day Control treatment: HFCWO 4 sessions/day
Outcome measures	1. Sputum: LCI (before and after completing the study) 2. Pulmonary function: FEV1, FVC [%] (before and after completing the study) 3. Exercise endurance: 6MWT [m]	1. Sputum: 24-h sputum wet weight [g]; 2. Pulmonary function: FEV1, FVC [l], MEF25, MEF75 [l/s], SpO_2[%], WoB and EoC 3. Treatment satisfaction: VAS [points]	1. Sputum: sputum wet and dry weight [g] 2. Cardiopulmonary function: SpO_2 [%], HR [beats/min], RR [breaths/min] 3. Dyspnea: VAS [%] 4. Sensation of phlegm encumbrance: VAS [%] 5. Discomfort: VAS [%]	1. Sputum: expectoration difficulty recorded daily – VAS 2. Pulmonary function: FEV1 [%], VC [%] 3. QoL: SGRQ, SF–36	Study I&II 1. Sputum: wet weight [g], pellet weight [g], dry weight [g] 2. Pulmonary function: FVC [l]; FEV1 [l]; FEV1/FVC [%]; SpO_2 [%]; DM/V_c 3. Cardiovascular function: HR [beats/min], stroke volume [ml]

Results	Experimental group 1. LCI pre 10.2±2.37; post 9.2±2.55 2. FEV1% pre 43±12; post 41±12 FVC% pre 64±12; post 61±16 3. 6 MWT pre 553±69; post 559±95 Control group: 1. LCI pre 9.69+2.5; post 9.76+2.5 2. FEV1% pre 55±15; post 54±13 FVC% pre 78±13; post 78±12 3. 6 MWT pre 539±55; post 553±77 Experimental vs control: 1. LCI* (p=0.01) 2. FEV1 (p=0.52), FVC (p=0.25) 3. 6MWT (p=0.76)	Experimental vs control treatment: 1. Sputum: Exp. 48.1±30.8; Ctr. 49±29.4; p=0.84 2. Pulmonary function: no significant difference in FEV1, FVC, MEF25, MEF75, EOC and WoB; SpO2*: Exp. 95.7±2.3; Ctr. 94±2.5; (p=0.004) 3. Treatment satisfaction: no significant difference	Experimental vs control treatment: 1. Δ Sputum: wet weight = 3.0 g (p=0.58); dry weight = –0.31 g (p=0.26) 2. Δ Cardiopulmonary function: SpO_2 = 0.6 (p=0.35); HR = –0.4 (p=0.82); RR* = –1.6 (p=0.047) 3. Dyspnea: Exp. pre 35%±29%; post 23%±20% (p=0.004)* Ctr. pre 33%±27%; post 27%±26% (p=0.09) 4. Sensation of phlegm encumbrance: Exp. pre 47±35%; post 27±32% (p=0.001) Ctr. pre 48±1%; post 37±35% (p=0.03) 5. Discomfort: Exp. 23±17%; Ctr. 40±27% (p=0.03)*	Experimental treatment: 1. Sputum: expectoration difficulties decreased during usage 4/12 patients 2. Pulmonary function: FEV1% pre 66.8%; post 66.3% (p=0.7334); VC% pre 87.5%; post 89.6% (p=0.1294) 3. QoL: SGRQ pre 48.4; post 54.1 (p=0.4238); SF–36: PCS pre 31.3; post 39.9 (p=0.1099); MCS pre 51.9; post 49.5 (p=1.000); RCS: pre 41.3; post 34.6 (p=0.5693) Control treatment: 1. Sputum: expectoration difficulties decreased during usage 5/12 patients 2. Pulmonary function: FEV1% pre 69.2%; post 67.1% (p=0.6089); VC% pre 90.7%; post 88.9% (p=0.0957) 3. QoL: SGRQ pre 54.2; post 49.9 (p=0.4238); SF–36: PCS pre 36.0; post 36.9 (p=0.8501); MCS pre 50.0; post 51.5 (p=0.2095); RCS: pre 50.1; post 51.4 (p=0.5186) Device preference and effectiveness: 6 patients rated TV method and 5 patients rated Acapella® as more effective; VAS: Exp. 60 (20–80); Ctr. 50 (20–100) p=0.9257	Study I: 1. Sputum: wet weight: Exp. 10.5; Ctr. 10.0 (p=0.25); dry weight: Exp. 0.58; Ctr. 0.67 (p=0.57) pellet weight: Esp. 5.9; Ctr. 4.4 (p=0.25) Experimental treatment: 2. Pulmonary function: FVC: pre 4.1; post 4.0 (p=0.25) FEV1: pre 2.6; post 2.5 (p=0.13) FEV1/FVC: pre 61; post 61 (p=0.71) SpO_2: pre 97; post 98 (p=0.41) DM/V_C: pre 0.72; post 0.76 (p=0.04)* 3. Cardiovascular function: HR: pre 89; post 88 (p=0.24) Stroke volume: pre 43; post 39 (p=0.38) Control treatment: 2. Pulmonary function: FVC: pre 4.1; post 4.0 (p=0.38) FEV1: pre 2.6; post 2.7 (p=0.43) FEV1/FVC: pre 64; post 64 (p=0.59) SpO_2: pre 98; post 98 (p=0.59) DM/V_C: pre 0.68; post 0.72 (p=0.28) 3. Cardiovascular function: HR: pre 95; post 89 (p=0.02)* Stroke volume: pre 38; post 32 (p=0.16) Study II: results reported as supplementary figures, no quantitative data provided
Key findings	NIV significantly improved ventilation homogeneity and has similar effectiveness as PEP. NIV is safe in long–term application	NIV significantly improved oxygen saturation. NIV has similar effectiveness in sputum clearance as standard treatment but the study is unpowered (small number of participants)	IPV presented similar to CPT effectiveness in airway clearance, oxygen saturation, and heart rate. IPV significantly improved breathing and was better tolerated by individuals	The TV method presented similar to oscillating PEP effectiveness in promoting sputum expectoration and quality of life improvement, but the study is unpowered (small population, lack of objective airway clearance results e.g. sputum weight)	The single intervention of the VL presented similar to PEP effectiveness in sputum expectoration and ventilation parameters. The VL seems to promote diffusion whereas PEP improves cardiac function

Abbreviations used in table only: RCT – randomized controlled trial; RCS – randomized crossover study; M – male; F – female; y – years; FET – forced expiratory technique; EoC – Ease of sputum Clearance questionnaire; WoB – Work of Breathing questionnaire; SGRQ – St George Respiratory Questionnaire; SF–36 – The Short Form (36) Health Survey; PCS – physical component summary; MCS – mental component summary; RCS – role–social component summary; DM/V_C – functional unit of diffusion; HFCWO – high–frequency chest wall oscillation

trapulmonary percussive ventilation (IPV), cervical trachea vibration (TV method), and combination of sound waves with positive expiratory pressure (VL- VibraLung® acoustical percussor).[24-28]

NIV and IPV are well-known pulmonary rehabilitation methods applied in exacerbations of chronic respiratory conditions and acute pulmonary events.[26,29,30] NIV covers all non-invasive ventilation types, providing positive airway pressure that alleviates pulmonary exacerbation, reduces breathing work, and enhances tidal volumes, which is suggested effective in secretion mobilization.[29,31,32] IPV was initially applied to treat smoke-induced lung damage, but its ability to deliver a small burst of high-flow gas, imitating tidal volumes, was suggested to effectively clear airway secretions.[33-35] Besides, IPV promotes respiratory function and reduces hospitalization.[36]

Two remaining techniques employ airway oscillation mechanisms based on resonance effect. This effect promotes chest wall movements, and therefore secretions mobilization and airways clearance.[37] Cervical trachea transcutaneous stimulation (tracheal vibration- TV method) is normally used to generate voice after laryngectomy, but it was also suggested to augment airway oscillation, which reduce mucus viscosity, and therefore promote mucociliary clearance.[27,38,39] VibraLung® acoustical percussor is a device combining standard positive expiratory pressure (4-5 H_2O) with additional sound waves applied at various ranges of frequencies.[40] Its efficacy as an airway clearance technique is based on acoustic theory, suggesting a relationship between airway segment size and frequency applied to promote airway oscillation.

Manuscripts outcomes summary

The effectiveness of secretion clearance was assessed in all included publications. Three studies discussing NIV, IPV, and VL reported sputum collection: wet weight, wet and dry weight, and wet, dry, and pellet weight, respectively. One study, examining NIV-bilevel PAP, evaluated lung clearance index (LCI), indicating ventilation homogeneity.[24-26,28] The paper investigating the TV method reported expectoration difficulty recorded daily on the Visual Analogue Scale (VAS) by patients.[27] No significant difference was detected in sputum weight (wet, dry, or pellet) for NIV, IPV, and VL methods than standard treatment regimens (CPT, PEP, and oscillating PEP). NIV-bilevel PAP (positive airway pressure) significantly reduced LCI values (p=0.01), whereas expectoration difficulties after a single treatment with the TV method decreased in 4 among 12 patients.[24,27]

Pulmonary functions

Respiratory functions were measured in all included studies. Four research reported spirometry volume (FVC, VC, FEV1) and flow (MEF25, MEF75) parameters, three studies oxygen saturation (SpO_2), one study respiratory rate (RR), and one study diffusion capacity.[24-28] No significant differences were reported for spirometry results, comparing both pre-post treatment results and experimental-control treatment results. However, two sessions of NIV significantly improved oxygen saturation (p=0.004), a single intervention of IPV reduced respiratory rate (p=0.047), and a single VL session improved diffusion capacity (p=0.04).[25,26,28]

Cardiovascular functions

Among all reviewed manuscripts, two reported the impact of selected ACT on heart rate, and one of them additionally the impact on stroke volume. Obtained results were statistically insignificant.[26,28]

Exercise endurance and dyspnea

Only one publication discussed the impact of airway clearance technique on exercise endurance, measured with a 6-minute walk test (6MWT); however, no difference between the experimental and control group was recorded. The dyspnea, measured with VAS, was also reported by just one publication, and it was significantly reduced after a single session of IPV (p=0.004).[24,26]

Users impressions and quality of life

Two manuscripts included user impressions: one discussed discomfort during treatment[26] [ref], and the other treatment satisfaction, both reported as VAS score results. Only one publication discussed the impact of applied treatment on quality of life. While treatment satisfaction and quality of life were similar for experimental and standard approaches, the discomfort during the IPV session was significantly decreased (p=0.03).[25-27]

Study limitations

This systematic review has some limitations. Firstly, the number of included studies is insufficient to draw solid conclusions. However, the authors decided to include only publications with insufficient quantitative data, especially the absence of sputum/lung clearance outcomes, and exclude studies on commonly known airway clearance techniques (ACBT, AD, PEP, oscillating PEP, HFCWO). Moreover, the final decision was based on the authors' subjective opinion, hence some of the publications could have been accidentally excluded. Secondly, the methodological quality of included studies was reduced by poor blinding of subjects, therapists, and assessors. Thirdly, occurring inconsistencies in study duration, frequency of daily intervention, and measured outcomes among all studies limited the possibilities of analysis. Nevertheless, this systematic review is an insightful investigation of the state of the art ACTs, emphasizing additionally the necessity to further study designed techniques.

Conclusion

Most of the novel methods discussed in this systematic review improved secretion clearance, and therefore lung function, but neither routine treatment nor novel technique appears to be superior. Among five, three studies investigated a single physiotherapy session, which substantially limits the diagnostic approach, but at the same time shows the immediate intervention effect. Not a single study presented a significant increase in sputum expectoration; however, it has been demonstrated that long-term application of NIV-bilevel PAP improves ventilation homogeneity, considering NIV as an efficient airway clearance technique. Moreover, just a single NIV session improves oxygen saturation and provides good preparation for subsequent pulmonary rehabilitation. Similarly, a single session of IPV significantly decreases respiratory rate and dyspnea, promoting successful respiratory training. Furthermore, patients considered IPV more comfortable when compared to standard CPT. Two oscillation-based methods presented similar efficacy to widely used ACTs, with only one significant improvement of diffusion capacity increased by VL.

Several limitations need to be addressed before these methods will be considered everyday treatment. Firstly, the number of participants should be increased. Secondly, the study duration should be increased to a long-term course of the chosen method since a single session is insufficient to draw a solid conclusion. Thirdly, many outcome measures need to be carefully revised to provide no bias information.

Although the number of limitations occurs, the presented methods' effectiveness is considered similar to well-established airway clearance techniques, suggesting the possibility to include them as a routine treatment after in-depth investigation.

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