Comparison of Intrapulmonary Percussive Ventilation and Chest Physiotherapy*  
A Pilot Study in Patients With Cystic Fibrosis

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Study objective: To compare the intrapulmonary percussive ventilator (IPV) to chest physiotherapy (P&PD) with respect to acute changes in (1) pulmonary function and (2) sputum physical properties in patients with cystic fibrosis (CF).

Design: Randomized crossover.

Setting: Community-based CF referral center.

Participants: Nine nonhospitalized persons (range, 7 to 40 years; median, 12.4 years) with moderate to excellent Shwachman scores.

Interventions: Three treatment regimens: (1) 2.5 mg albuterol delivered via IPV (internal percussive component activated); (2) 2.5 mg albuterol delivered via IPV (internal percussive component inactivated), followed by P&PD; and (3) 2.5 mg albuterol delivered via updraft nebulizer, followed by P&PD.

Measurements and results: Outcome measures included pulmonary function testing (PFTs) and quantitative and qualitative sputum analysis. Among the three treatment groups, there were no significant differences in the change in predicted PFTs 1 h or 4 h after treatment, nor in the volume of sputum expectorated in the first 4 or in the subsequent 20 h. Among patients receiving IPV, more serious disease was associated with greater improvement in FEF25-75 1 h after treatment, but these differences disappeared by 4 h. There were no meaningful differences in viscoelastic characteristics of sputum expectorated after each treatments. Participants reported general satisfaction with no adverse effects while using IPV.

Conclusions: This initial pilot study suggests (1) stable patients with CF tolerated one treatment of IPV without adverse sequelae, and (2) IPV was as effective as standard aerosol and P&PD in improving short-term PFT results and enhancing sputum expectoration. (Chest 1994; 105:1789-93)

CF = cystic fibrosis; FEF25-75 = mean forced expiratory flow during the middle of FVC; FEV1 = forced expiratory volume in 1 s; FVC = forced vital capacity; IPV = intrapulmonary percussive ventilation; IPV-1 = Intrapulmonary Percussionator Ventilator; HVA/P&PD = high-volume aerosol delivery with the IPV device with the internal percussive component inactivated, followed by P&PD; P&PD = chest percussion and postural drainage; PEF = peak expiratory flow; PFT = pulmonary function test; STD = standard aerosol delivery followed by P&PD

The management of the pulmonary complications of cystic fibrosis (CF) focuses on the enhancement of mucociliary clearance to optimize gas exchange and minimize infections due to mucostasis. Achieving this end involves the following: (1) removing mucus from the airways with mechanical or manual chest percussion and postural drainage (P&PD) and cough; (2) increasing airway caliber with beta2-adrenergic aerosols; and (3) controlling acute and chronic infection with antibiotic therapy. Despite these therapies, the inability to adequately expectorate viscous bronchial secretions, especially from the smallest airways, remains a serious problem for persons with CF.1-3

A number of techniques have been developed to mobilize airway secretions, including vigorous cough, the forced expiration technique, the use of a positive expiratory airway pressure (PEP) mask, and exercise-stimulated deep breathing.4-8 Although none of these techniques have been shown to have a therapeutic benefit over conventional P&PD, they offer the advantage of increased patient independence, overcoming a significant barrier to compliance. This is especially true for adolescents and adults with CF.9

The intrapulmonary Percussionator ventilator (IPV-1, Perussionaire, Sand Point, Idaho) (IPV-1) was developed in 1979 and recently received US Food and Drug Administration approval for human use.10 The device (retailing for about $2,500) delivers rapid minibursts of gas mixture at 200 to 300 cycles per minute through a sliding Venturi with added continuous aerosol generation. The physiologic basis for its potential effectiveness is unknown, but it is presumed to be enhanced mucociliary clearance through bronchodilation from a combination of increased airway distending pressure and delivery of

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a bronchodilator nebulizer solution. The contribution of increased airway humidification and cough stimulation is unknown at present. The two most salient innovations provided by IPV-1 with respect to its application in CF therapy include (1) the simultaneous combination of mechanical with pharmacologic interventions (aerosols) to mobilize endobronchial secretions, and (2) the development of a patient-operated device for chest physiotherapy which may allow greater independence for the adolescent and adult with CF. To date, however, there are few published experimental studies in humans using this instrument, and none involving patients with CF.11-15

We undertook a pilot study in nine patients with CF severity grades of excellent to moderate in order to begin to assess the effectiveness of IPV-1 in facilitating mucous production and mobilization as compared with standard aerosol and chest physiotherapy.

Methods and Materials

The study was approved by the Human Use Committee of Bronson Methodist Hospital. Informed consent was obtained from all participants and the parents/guardians of those patients under 18 years old.

Participants with CF diagnosed by clinical history, physical examination, and standard plicarpine iontophoresis16 were recruited from the Cystic Fibrosis Center at Michigan State University/Kalamazoo Center for Medical Studies. Patients with a history of pneumothorax, pulmonary surgery, or with active acute respiratory infection were not eligible for the study. Severity of CF was determined for each participant prior to the start of the study using the Shwachman-Kulczycki table.17

A randomized crossover trial consisting of three treatment regimens was administered to nine participants. On day 1 of the study, each participant was assigned to a sequence of three treatments that would be randomly received during a 5-day period. The three experimental treatment groups included the following: (1) IPV—2.5 mg albuterol in 19.5 ml normal saline solution delivered via the IPV-1 with simultaneous internal pulmonary percussion (oxygen delivery pressure 1.2 psi/kg body weight at a rate of 200 to 300 cycles per minute); (2) high volume aerosol and PoPD (HVA/PoPD)—2.5 mg albuterol in 19.5 ml normal saline solution delivered via the nebulizer component of the IPV-1 (with the internal pulmonary percussion inactivated), followed by respiratory therapist-administered chest P&P; and (3) standard aerosol and PoPD (STD)—2.5 mg albuterol in 3.0 ml normal saline solution delivered via standard nebulizer, followed by manual chest physiotherapy administered by a respiratory therapist according to CF Foundation guidelines.18

Participants went without breakfast and received regularly prescribed oral medications, but did not receive home chest physiotherapy on each morning of the study. Pulmonary function testing (PFT), including forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1), peak expiratory flow (PEF), and mean forced expiratory flow during the middle half of vital capacity (FEF25-75), was administered by a pulmonary function technician unaware of the treatment regimen to be received by the participant. The best of three FVC maneuvers was obtained and recorded for each participant. The same technician and

<table>
<thead>
<tr>
<th>Participant No./ Age, yr/ Sex</th>
<th>CF Severity Score</th>
<th>CF Severity Grade</th>
<th>Mean Baseline FEV1, % pred</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/40.1/M</td>
<td>43</td>
<td>Moderate</td>
<td>38.7</td>
</tr>
<tr>
<td>2/14.3/M</td>
<td>58</td>
<td>Mild</td>
<td>37.1</td>
</tr>
<tr>
<td>3/13.3/M</td>
<td>55</td>
<td>Mild</td>
<td>78.4</td>
</tr>
<tr>
<td>4/8.1/F</td>
<td>39</td>
<td>Mild</td>
<td>34.2</td>
</tr>
<tr>
<td>5/16.5/F</td>
<td>92</td>
<td>Excellent</td>
<td>83.2</td>
</tr>
<tr>
<td>6/12.4/M</td>
<td>79</td>
<td>Good</td>
<td>74.8</td>
</tr>
<tr>
<td>7/7.4/M</td>
<td>90</td>
<td>Excellent</td>
<td>95.1</td>
</tr>
<tr>
<td>8/1.9/F</td>
<td>76</td>
<td>Good</td>
<td>80.1</td>
</tr>
<tr>
<td>9/7.9/F</td>
<td>64</td>
<td>Mild</td>
<td>71.4</td>
</tr>
<tr>
<td>Mean (SE) 14.6 (3.4)</td>
<td>68.4 (5.6)</td>
<td></td>
<td>65.9 (7.6)</td>
</tr>
<tr>
<td>Median</td>
<td>12.4</td>
<td></td>
<td>74.8</td>
</tr>
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</table>

Based on the Shwachman-Kulczycki scoring system for CF, with scores ranging from 20 to 100; larger scores indicate lower disease severity.25

1 CF severity grade is also determined by the Shwachman-Kulczycki system; a grade of excellent is assigned to scores from 86 to 100; good, 71 to 85; mild, 56 to 70; moderate, 41 to 55; and severe, less than 41.

ATS-approved spirometer (Gould System 21, Sanyo, Compton, Calif) were used for all PFT measurements throughout the study. After pretreatment PFTs were obtained, participants were randomized to one of three treatment groups. A second respiratory technician, experienced with both P&P as well as the IPV-1, administered the assigned treatment to each participant. Upon completion of each 24-h study day, participants were asked to resume their regularly prescribed home chest physiotherapy regimens.

The PFTs were recorded as percent of predicted values, and the differences between pretherapy and posttherapy values were compared. The latter were obtained at 1 and 4 h after the initiation of treatment. In addition, all sputum expectorated was collected over two time periods: the initial 4 and subsequent 20 h after each treatment. During the first 4 h, saliva contamination was minimized by placing dental cotton in the mouth over the parotid duct before sputum expectoration.19 The quantity of sputum expectorated was determined by volume. Then this sample was stored at −70°C prior to determination of sputum physical properties.20 The second sputum sample, expectorated over the next 20 h, was collected for volume determination.

To compare the effects of standard treatment to IPV and to HVA/IPV, within-person statistical analyses were performed for both PFTs and sputum properties. For PFT comparisons, pretreatment and posttreatment PFTs were calculated as percentage of predicted, based on age-appropriate Morris et al21 or Polgar et al.22 standards for each participant during each treatment. Then the improvement in PFTs was then calculated for each participant using each treatment. Finally, the improvements obtained using the standard treatment were compared with the improvements following each of the other treatments for each participant. Similarly, physical properties of sputum expectorated following standard therapy were compared with physical properties of sputum obtained following IPV or HVA/P&P for each participant. The appropriate paired Student's t test statistic23 and p value were then inspected. In this way, each participant acted as their own control, assumptions or independence in statistical testing were not violated, and power was maximized. Furthermore, this process yields an easily interpretable result. The relationship between severity of CF disease and change from baseline PFTs after each treatment was assessed using standard least squares regression. For all tests, p values of less than or equal to 0.05 were considered significant.
RESULTS

Characteristics of the nine participants, including their severity of CF, are indicated in Table 1. The participants in this pilot study represented a wide range of ages from 7.4 years to 40.1 years old, with moderate to excellent disease severity. Participants tolerated all respiratory treatment without adverse consequences. Subjectively, participants reported no discomfort with use of IPV compared with conventional P&PD therapy.

Pulmonary function data for the three treatment regimens are shown in Figure 1. A comparison between the treatment groups (STD vs IPV and STD vs HVA/P&PD) showed no significant differences in the change from baseline in percent of predicted FPTs 1 h or 4 h after each respiratory treatment when analyzed by paired Student’s t test. Similarly, no differences were detected in the volume of sputum expectorated in the first 4 h or in the subsequent 20 h between the STD and other treatment groups (data not shown here). No direct relationship between disease severity and response to any respiratory treatment was observed, except for patients receiving IPV. In that case, more severe disease was significantly correlated with greater improvement in FEF25-75 1 h after treatment ($r^2=0.47$, $p=0.04$), but these differences disappeared by 4 h.

Overall, the respiratory treatments had little differential effects on in vitro sputum physical properties. Specifically, a comparison between the treatment groups (STD vs IPV, STD vs HVA/P&PD, and IPV vs HVA/P&PD) revealed no trends with respect to mucus hydration. However, sputum collected after IPV treatment tended to be the most rigid and elastic, while STD-generated sputum was least rigid and elastic. These differences reached statistical significance at simulated cough frequency (100 radi-}

an/s) where IPV mucus elasticity was greater than HVA/P&PD sputum ($p=0.025$), and sputum expectorated after STD was significantly less rigid than HVA/P&PD ($p=0.049$). Cough clearability of the small airways (4 mm) was significantly greater after HVA/P&PD treatment compared with STD alone ($p=0.03$), but not in the large (12 mm) model airway.

DISCUSSION

This pilot study compared a novel mechanical device, the IPV-1, with standard chest physiotherapy in ambulatory patients with CF. The IPV-1 is a lightweight, self-contained instrument that simultaneously combines two effective methods of tracheobronchial secretion mobilization: chest percussion and the delivery of an aerosolized bronchodilator solution. Facilitating clearance of mucus may allow greater small airway patency and increased expiratory flow rate, with more effective removal of retained endobronchial secretions. Thus, these theoretical capabilities make the IPV-1 an attractive device for chest physiotherapy in patients with CF and, perhaps, other obstructive lung diseases.

There are few published studies that examine the efficacy and safety of IPV in clinical settings. In a study involving ventilator-dependent patients with adult respiratory distress syndrome, patients ventilated with the IPV-1 had significantly better oxygenation and improved carbon dioxide elimination compared with those patients receiving conventional ventilation at the same positive end-expiratory pressures and proportion of oxygen in inspired air. Prior to the current study, the efficacy of IPV was examined in six patients with CF hospitalized with acute lower respiratory tract infections at our institution. Subjective ease of sputum expectoration without perceived clinical difficulty was noted. No adverse effects of IPV were identified by the patients or the
respiratory therapists administering the IPV treatment. Therefore, the purpose of this study was to investigate the safety of one-time IPV treatment under controlled conditions in clinically stable patients with CF.

For the adolescent and adult with CF, there may be numerous benefits to use of IPV for chest physiotherapy compared with standard P&PD. Independence is a difficult developmental task for all adolescents, but it is often more challenging in the adolescent with a chronic disease such as CF. Use of the IPV may allow the adolescent more control over one important aspect of his or her CF therapy. Furthermore, one complete treatment with IPV lasts approximately 20 min, compared with 30 min for aerosol delivery followed by P&PD. This significant time savings, coupled with ease and comfort of IPV administration, may contribute not only to more effective self-management of disease, but may also foster self-esteem and a sense of mastery.

The safety of any new respiratory therapy must be assured before it can be recommended for further and more rigorous clinical trials, and certainly before clinical application. In this preliminary study, participants tolerated all respiratory treatments without adverse consequences or subjective discomfort. Furthermore, the magnitude of the differences observed herein was small and without clinical importance. This is especially reassuring as the sample size in any pilot study is limited and large or meaningful differences might not be detected, given the comparatively reduced statistical power provided. This is not the case in the current study and the results can be viewed with greater confidence.

To our knowledge, this study is the first to compare the physical properties of sputum after high-volume aerosol delivery with simultaneous IPV, high-volume aerosol followed by P&PD, and standard volume aerosol followed by P&PD. It has been demonstrated that sputum rheology potentially may be altered by hydration from externally administered moisture while the quantity and quality of airway mucus may be affected by β-adrenergic and cholinergic agents. In addition, it has been suggested that airway shear may be altered by high-frequency positive pressure as delivered by the IPV device. Therefore, we hypothesized that the use of IPV may alter sputum character and volume. However, there were no consistent or meaningful differences in sputum physical properties among the three treatment modalities despite HVA and positive pressure generated by the IPV device. These data, therefore, suggest that a single experimental treatment did not alter measured sputum physical properties.

In summary, a single IPV treatment was as effective as standard chest physiotherapy in improving acute pulmonary function and enhancing sputum expectoration in ambulatory older children and adults with excellent to moderate CF severity grades. Although this study was limited to the acute effects, it serves as an important starting point for long-term studies of efficacy and safety of IPV use in patients with CF.

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REFERENCES
1 Davis PB. Pathophysiologics of pulmonary disease in cystic fibrosis. Semin Respir Med 1985; 6:261-70
5 Hofmeyer JL, Webber BA, Hodson ME. Evaluation of positive expiratory pressure as an adjunct to chest physiotherapy in the treatment of cystic fibrosis. Thorax 1986; 41:561-54
10 Bird FM. Intrapulmonary percussive ventilation (IPV). Flying Physician 1987; 30:4-8
12 Gallagher TJ, Boysen PC, Davidson DD, Miller JR, Leven SB. High frequency percussive ventilation compared with conventional mechanical ventilation [abstract]. Crit Care Med 1985; 13:312
Sixth European Congress on Intensive Care Medicine, Barcelona, Spain, October 1992

16 Gibson LE, Cooke RE. A test for concentration of electrolytes in sweat in cystic fibrosis of the pancreas utilizing pilocarpine by iontophoresis. Pediatrics 1959; 23:545-49


18 An introduction to chest physical therapy. Bethesda: Cystic Fibrosis Foundation, 1992


23 Cooper PJ, Robertson CF, Hudson IL, Phelan PD. Variability of pulmonary function tests in cystic fibrosis. Pediatr Pulmonol 1990; 8:16-22
