The effect of intrapulmonary percussive ventilation in pediatric patients : a systematic review

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Abbreviated title

Evidence of IPV in pediatrics

Abstract

Background: Intrapulmonary percussive ventilation (IPV) is frequently used in clinical practice to enhance sputum evacuation and lung recruitment. However, the evidence in different respiratory pathologies, especially in children, is still lacking. This systematic review aims to enlist the effectiveness of IPV as an airway clearance technique in the pediatric patients.

Data sources: A systematic literature search was performed in PubMed, Web of Science and the Cochrane Library databases.

Study selection: Studies were included if the subjects suffered from a respiratory disease requiring airway clearance and the mean age of the sample was <18 y. After screening, 9 articles remained for further analysis.

Results: Three of the 9 articles examined patients with cystic fibrosis (CF). No significant differences in lung function or expectorated mucus were found compared to conventional chest physiotherapy. On the other hand, significant beneficial results were found for the treatment or prevention of atelectasis in non-CF patients using IPV. Similar results were seen when comparing therapies for neuromuscular/neurological patients. One study found that IPV reduced hospital stay and improved the clinical status of children with acute bronchiolitis compared to no physiotherapy. Severe adverse events did not occur in the included studies.

Conclusion: A limited number of studies investigated IPV in the pediatric population. Despite the heterogeneity across the studies and the small sample sizes, the results seem promising. IPV is suggested to be a safe and effective alternative for airway clearance. Future research is required to confirm these results and to further analyze the possible benefits in different respiratory pathologies.

Introduction

Respiratory physiotherapy is routinely used in different pulmonary diseases. The main goals of airway clearance techniques (ACTs) are to enhance mucus mobilization, reduce airway resistance, improve ventilation and gas exchange and to reduce work of breathing. Conventional chest physiotherapy (CPT) includes postural drainage, percussion, vibration and coughing, sometimes accompanied by tracheal or oropharyngeal suction.[1; 2] Over recent decades, new techniques have been developed, such as intrapulmonary percussive ventilation (IPV), forced expiratory technique (FET), positive expiratory pressure (PEP), oscillatory PEP, high frequency chest wall oscillations (HFCWO) and autogenic drainage (AD).[2]

Although the basic principles of ACTs are the same in adults and children, there are some physiological and pathological differences requiring different approaches. A few examples of these physiological differences in infants and young children are a more compliant chest wall, a lower functional residual capacity (FRC) and the absence of collateral ventilation, which all contribute to a higher risk for airway collapse and the development of atelectasis. The lack of voluntary cooperation will also require different methodology than the one routinely applied in adults.[2; 3]

IPV has been mentioned before as one of the more recent ACTs. One of the advantages of this technique is that active cooperation is not necessary to perform the treatment. The device provides internal thoracic percussion by delivering small bursts of high-flow air, generating airway pressures to oscillate between 5 and 35 cmH2O. This process causes the airway walls to vibrate in synchrony with these oscillations. The bursts of air at a range of 80 to 650 cycles per minute are created by the sliding Venturi body, called the phasitron.[4] IPV can be used in spontaneously breathing as well as mechanically ventilated patients. In the latter population, vital signs must be closely monitored throughout the therapy[5]. The technique is appropriate

for the treatment of mucus retention and atelectasis in respiratory diseases, such as chronic obstructive pulmonary disease (COPD), cystic fibrosis (CF) and neuromuscular diseases (NMD)[6]. Contraindications for the use of IPV are not clearly defined in the literature. In the manual of the Percussionaire® Corporation Intrapulmonary Percussive Ventilation devices, the only absolute contraindication mentioned is untreated pneumothorax, besides the lack of adequate supervision and the availability of a simpler more effective treatment[7]. In other papers untreated pneumothorax is most frequently reported[5; 8; 9], but different conditions are also mentioned as contraindications, such as hemoptysis[8; 9], rib fractures[9], increased cranial pressure[9] and active tuberculosis[8].

The physiological benefits of IPV have been described by Riffard and Toussaint (2012) and can be divided into three major effects. The first effect of IPV is the mobilization of secretions. The second effect is improvement in the recruitment of obstructed areas in the lungs, and the final effect is a measurable improvement in gas exchange.[10] Although some of the improvements in the previously mentioned parameters can be found in different studies, there is a lack of high-level evidence to support a recommendation for this therapy in the adult population with NMD, CF, COPD and patients in the post-operative phase.[4; 5; 11] In an attempt to describe the indications for IPV in different populations ,it is stated that the technique used in the pediatric population has the potential to serve as an adequate alternative to conventional CPT and highlighted the advantage of not being dependent on the active cooperation of the patient.[5] Although the level of evidence is still lacking to confirm these conclusions, the device is frequently used in clinical practice in spontaneously breathing as well as mechanically ventilated children. The purpose of this systematic review is to further investigate the current literature concerning the effectiveness and use of IPV, focusing on respiratory pathologies in the pediatric population.

Methods

This systematic review was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA)[12] statement to reduce the risk of deficient reporting.

Eligibility criteria

Clinical trials were included if they investigated the effect of IPV, the subjects suffered from a respiratory disease requiring airway clearance, the mean age of the investigated population was <18 y, and the articles were written in English. Case reports, abstracts of meetings or conferences, reviews and other articles not based on original clinical research were not considered relevant for this review and were therefore excluded. These criteria were defined a priori to draw conclusions about eligibility.

Search strategy

Since literature concerning this topic is limited, the only search term used was "intrapulmonary percussive ventilation (or ventilator)". With this search query, articles were retrieved from the PubMed, Web of Science and the Cochrane Library electronic databases. In Web of Science and the Cochrane library, the search query was refined to articles and trials, respectively. All articles through January 2018 were eligible for inclusion, and no lower limit of the publication date was predefined.

Study selection

All search results were put together in a template (template for study selection, KCE – Belgian Health Care Knowledge Centre). In the first stage, duplicates were removed and articles were screened by title and abstract. In the second stage, the content of the full texts of the

remaining studies were screened. In uncertain cases, a second reviewer got involved to determine eligibility.

Data extraction

Relevant data from the included articles were summarized in a structured table (Table 1). The following data were extracted: study design, characteristics of the subjects (including sex, age and pathology), type and duration of the intervention, outcome parameters and results.

Risk of bias in individual studies

The PEDro scale, based on the Delphi List, was used as a valid measure to assess the methodological quality of individual clinical trials[13]. The following items were scored: eligibility criteria, random allocation, concealed allocation, similarity of the groups at baseline, blinding of the subjects, blinding of the therapists, blinding of the assessors, > 85% follow up, intention-to-treat analysis, between-group statistical comparisons and point/variability measures. Each item was either scored with 1 (present) or 0 (not present or not reported). Non-applicable items due to the study design (e.g., similarity of the groups in an uncontrolled trial) were scored with a 0 as well. To sum the overall PEDro score of the article, the first criterion relating to external validity was not included. The total quality score of the article was rated as follows: a total score of 9-10=very high, 6-8=high, 4-5=moderate, and 0-3=low[14].

Results

Study selection

The search in the PubMed, Web of Science and Cochrane Library electronic databases resulted in 201 hits in total. After removing the duplicates, 126 records remained. Of these, 104 were discarded after the first screening of the title and abstract. The full texts of the remaining,

potentially relevant studies were screened. After this second screening, thirteen full-text articles were excluded for the following reasons: mean age of the population was >18 y, abstracts of conferences and a review. Nine articles met the eligibility criteria and were included in further analysis. These results are shown in a flowchart (Figure 1).

Study characteristics

For each study, the characteristics and main results are presented in Table 1. Of the nine included articles, four were randomized controlled trials (RCTs)[15-18], two were randomized crossover trials[19; 20], one was a prospective cohort study[21], and three were retrospective studies[15; 22; 23]; Deakins et al.[15] described an RCT as well as a retrospective study. A total of 277 participants were enrolled in the studies, with 93 subjects in the study reported in Van Ginderdeuren et al.[18] being the largest study population. The effects of IPV were described in different pathologies: CF[16; 19; 20], (suspected) atelectasis[15; 21; 23], neurological/neuromuscular disease with pulmonary complications[17; 22] and acute bronchiolitis[18]. The mean age of the subjects ranged from 121 days to 17 y. The majority of the studies used an IPV device of the Percussionaire® design[15-17; 19-21], and only two used a different kind of device: MetaNeb from Hill-rom, delivering continuous high frequency oscillations (CHFO) [22; 23], and one study did not mention the type of device[18]. CHFO is similar to IPV as they both deliver small bursts of high-flow air using the Venturi principle, and both the frequency and flow can be adapted according to the patient and type of therapy. A difference is that the exhalation orifice of the MetaNeb device offers three levels of PEP, while the IPV is an open system with minimal expiratory resistance. The MetaNeb system alternates this CHFO mode with a continuous positive expiratory pressure (CPEP) mode in repetitive cycles with nebulizing medication in spontaneously breathing patients. In mechanically ventilated patients, the CHFO mode can be applied by connecting the device with the ventilator. Since the working mechanisms of IPV

and CHFO are comparable, we chose to include the two articles using CHFO. The type of device and settings used during the therapy are listed for each study in the data extraction table (Table 1). The duration of the intervention differed from one therapy session to one year. All studies including more than one intervention group or using a crossover design comparing IPV to other ACTs (e.g., conventional CPT, AD, flutter, or HFCWO)[15-20; 22]. Only one study compared IPV and assisted autogenic drainage (AAD) to a control group not receiving respiratory physiotherapy[18]. Various outcome measures were used to assess the effects of IPV. The most frequently used outcome measures were lung function parameters[16; 17; 19; 20], oxygen saturation (SpO_2)[15; 18; 21; 23], and days of hospitalisation[16-18].

Risk of bias within studies

Each individual study's quality assessment with the PEDro scale is shown in the data extraction table (Table 1). The study by Van Ginderdeuren et al. was the only one with a very high score with a result of nine out of ten[18]. Four studies scored high on the overall score with a result of seven or six out of ten[15; 17; 19; 20], two scored moderate with a score of four or five[16; 22], and two studies scored low with a result of three out of ten[21; 23]. These last two studies did not compare results with another group or control period, resulting in a lower overall score, because criteria involving blinding, randomization, and comparison between groups could not be scored[21; 23]. The eligibility criteria and point/variability measures were present in all studies. Blinding of the therapists was not possible in any study due to the type of intervention, although four studies blinded the outcome assessors[15; 18-20].

Synthesis of results

A qualitative synthesis of the main results is provided, since a meta-analysis could not be conducted due to heterogeneity of the study design, population and outcome measures.

a. Cystic fibrosis

Three studies described the effects of IPV in CF patients[16; 19; 20]. All three combined IPV with the inhalation of albuterol compared to standard aerosol therapy with another ACT. The albuterol solution was directly delivered via the IPV device and simultaneously with the percussions in the IPV groups. Homnick et al. investigated the effects of IPV (n=8) compared to conventional CPT (n=8) in a relatively long-term trial (i.e. 180 days)[16]. They could not find an effect on lung function parameters, such as forced expiratory volume in one second (FEV1) and forced vital capacity (FVC), in either therapy regimen, and did not detect a difference between IPV and conventional CPT in days of hospitalization and antibiotic use. They reported one adverse event of minor hemoptysis potentially related to the use of IPV. Furthermore, the results of the patient satisfaction survey in the IPV group were generally positive, and all eight subjects stated they would continue the use of IPV if given the opportunity. Additionally, the randomized crossover trial by Natale et al. could not find any differences in lung function parameters between the three treatment regimens: IPV, high volume aerosol (through the IPV device with the percussion element inactivated) combined with conventional CPT, and standard aerosol combined with conventional CPT[19]. The effects on the quantity and physical properties of the expectorated mucus were similar between the types of therapy. Lastly, Newhouse et al. compared IPV to a flutter device and conventional CPT in a randomized crossover design as well[20]. They could find acute effects in FVC after 1 h for the flutter device and in FEV1 after 1 h for the flutter device and IPV, but after 4 h only the effect using the flutter device remained. No significant differences between the groups were found for either lung function or the quantity of expectorated mucus. Both Natale et al. and Newhouse et al. included stable CF patients during a short-term trial with only one session for each treatment regimen. In neither of the two latter studies were adverse events reported.

b. Atelectasis

In two articles, the effects of IPV on the resolution of atelectasis were investigated[15; 21]. Deakins and Chatburn conducted a retrospective study as well as an RCT[15]. They collected data from 46 mechanically ventilated children with radiographic evidence of atelectasis treated with IPV in their retrospective study. The RCT compared IPV (n=7) to conventional CPT (n=5) in a population with similar characteristics as the retrospective study. The atelectasis score (AS) significantly improved after treatment with IPV (retrospective study: 3 to 1, p<0.001; RCT: 2.3 to 0.9, p=0.026), while the AS in the CPT group showed no significant change. The AS system was based on the radiographic presence of partial or complete collapse of one or more segments/lobes, resulting in a total score ranging from 0 (complete resolution) to 4 (complete collapse of several segments/lobes). The duration of the treatment with IPV until resolution of the atelectasis was also significantly shorter compared to the CPT group. Ha et al. examined the influence of IPV treatment on the resolution of atelectasis in hospitalized children as well, using the same atelectasis scoring system[21]. They found a non-significant improvement in AS in three out of four children (2.5 to 1.25). All children had a significantly improved SpO_2 (93.3 to 95.3%, p=0.002) and clinical score (2.8 to 0.8, p=0.012) after treatment. This clinical score evaluated the presence of four symptoms: appetite deterioration, dyspnoea, mucus production and cough, with a maximum score of four. There was, however, no control group to compare these results. The retrospective study by Morgan et al. collected data from all invasively ventilated children treated with CHFO in their institution over a period of approximately 5.5 years [23]. The MetaNeb device delivering CHFO was connected with a spring-loaded T to the inspiratory limb of the ventilator circuit. They examined ventilator and gas exchange parameters before and after each CHFO episode. The most clinically relevant result found was a significant reduction in the peak inspiratory pressure (14 to 8 cmH_2O, p<0.001)

after CHFO treatment, suggesting that weaning peak pressure was possible following CHFO. Vital signs remained stable, and the therapy was well tolerated in this population. They suggested that the use of CHFO may be beneficial by improving lung compliance in pediatric patients with secretion-induced atelectasis. No complications were reported in the three studies mentioned above.

c. Neurological or neuromuscular diseases with pulmonary complications

Bidiwala et al. conducted a retrospective study comparing one year of treatment with HFCWO to a consecutive year with IPV in eight tracheostomy-dependent patients with a cognitive and developmental delay[22]. They used CHFO to deliver percussions to the ventilation. During the therapy, this CHFO mode was alternated with a CPEP mode every two to three minutes in repetitive cycles for a total of approximately ten minutes. Significant beneficial effects of CHFO compared to HFCWO treatment during the previous year were noted in all key outcome measures (mentioned as HFCWO to CHFO), i.e., reductions in the number of respiratory tract infections (15/y to 6/y, p=0.01), respiratory illnesses (32/y to 15/y, p<0.001), hospitalizations (8/y to 3/y, p=0.003), use of bronchodilators (53 episodes/y to 21 episodes/y, p<0.001) and systemic steroids (12 courses/y to 4 courses/y, p=0.003). Reardon et al. compared the use of IPV to incentive spirometry (IS, type Voldyne 2500) as the standard of care for mobilizing and clearing secretions and preventing atelectasis in 18 subjects with NMD in an RCT[17]. IPV was also successful compared to the standard use of IS in this study. The IPV group had significantly fewer hospitalization days (0 d for IPV and 8 d for IS) and antibiotic days (IPV: 0 d and IS: 44 d) and required fewer supplemental respiratory treatments, including albuterol sulfate inhalation treatments (IPV: 60 and IS: 166, p<0.001) and extra IPV sessions (IPV: 22 and IS: 172, p<0.001). The lung function parameters did not show any significant changes over the seven-month intervention period in both the IS and IPV groups.

d. Acute bronchiolitis

Van Ginderdeuren et al. (2017) performed the only study examining IPV in children hospitalized with acute bronchiolitis[18]. They evaluated the effectiveness of IPV and AAD compared to children not receiving respiratory physiotherapy during the hospitalization period in three equal groups of 31 infants. Fewer hospitalization days (IPV: 3.5 d; AAD: 3.6 d; control: 4.5 d) and a better Wang clinical severity score after the treatment were found in the intervention groups compared to the control group. The Wang clinical severity scoring system evaluates four items: respiratory rate, wheezing, retractions and general condition, with a total score ranging from 0 (best) to 3 (worst). No significant differences were found between the IPV and AAD groups. Both therapies were combined with bouncing to prevent crying and resistance to therapy, which contributed to high tolerance of both IPV and AAD.

Discussion

To provide a systematic overview, the results will first be discussed by pathology in accordance with the layout of the synthesis of results, followed by a more general discussion.

Discussion by pathology

a. Cystic fibrosis

Based on the results of the three studies including CF patients[16; 19; 20], it seems that IPV is an adequate alternative to conventional CPT, but it is not a superior technique. None of the studies found a difference between the ACTs for lung function or expectorated mucus, which were both used as outcome measures in the three studies. It should be noted that in all studies, IPV was used to inhale medication, while IPV may not be as effective in nebulizing albuterol with a standard jet nebulizer. IPV has been, in contrast to the standard jet nebulizer, poorly studied as an inhalation technique. Two studies compared these two devices on drug

deposition in the lungs[24; 25]. The first study by Reychler et al. found large differences in the aerodynamic properties between IPV and standard jet nebulization (type: SideStream®, Medic-Aid). Although the two techniques showed no significant difference in intrapulmonary deposition, the interindividual variability of the deposition with IPV nebulization was much higher. This variability contributed to their conclusion not to recommend IPV for drug delivery in the lungs.[24] A second study, comparing the same devices, noted that the amount of excreted amikacin sulphate in urine after inhalation, which reflects the drug deposition in the lungs, was six times lower with IPV nebulization compared to the standard jet nebulizer.[25] Keeping these results in mind, the effects of IPV as an ACT could have been underestimated. If IPV would have been used solely as an ACT and be preceded by standard aerosol therapy, the effects could be greater compared to conventional CPT. Despite the similar results of IPV and conventional CPT, there's a major advantage with IPV. This device can be used independently, giving the adolescent CF patient more control over a very important and time-consuming aspect of their therapy[5; 19]. Overall, IPV appears to be well tolerated by CF pediatric patients, although cautiousness is advised in patients with recurrent hemoptysis. The general quality of the three studies varied between moderate and high, but the results are based on very small sample sizes. Further research will be necessary to confirm these results. Since only stable CF patients have been studied, future research should evaluate the effects in CF patients with acute exacerbation as well. During this period of increased sputum production, the use of IPV might increase the effectiveness of airway clearance. Additionally, non-CF children with bronchiectasis have not been studied, and they may have a different response to the therapy.

   b. *Atelectasis*

All three studies showed beneficial effects indicating resolution of the atelectasis and/or improvement in clinical status, assuming IPV may be effective in the treatment of atelectasis[15; 21; 23]. It should be noted that Ha et al. studied only one group of patients who all received IPV during hospitalization and it can therefore not be concluded that the improvements are due solely to the effect of IPV[21]. Mechanical ventilation is associated with a higher risk of developing atelectasis, as a result of impaired mucociliary transport and ineffective cough[26]. This emphasizes the importance of adequate airway clearance strategies in the pediatric ICU to prevent prolonged mechanical ventilation and ICU stay.[23] Morgan et al. described this importance and despite the link between CHFO and the improvement in lung compliance in patients with secretion-induced atelectasis as their key finding, no references were made in their methodology or results regarding the presence or resolution of atelectasis in their population[23]. Both the study by Ha et al. and Morgan et al. are the two studies with the lowest overall quality with scores of three out of ten. Therefore, it is important to bear in mind the possible bias in these studies. Deakins and colleagues, on the other hand, scored high on the PEDro scale, which strengthens their results. The prospective study by Deakins and Chatburn was the only one in this population to compare IPV to another ACT, namely, conventional CPT[15]. In contrast to the results of the studies with CF patients, IPV appeared to be more effective than CPT for the treatment of atelectasis.

c. Neurological or neuromuscular diseases with pulmonary complications

Patients with neurological and neuromuscular diseases are prone to develop respiratory infections due to hypoventilation, cough impairment, aspiration, and other issues; which are caused by respiratory and upper airway muscle weakness and thoracic/spinal deformities[27]. IPV could play an important role in the prevention of these pulmonary complications in this

population. Both Bidiwala et al. and Reardon et al., showed beneficial effects in most outcome measures over specific periods of time (1 y and 7 m, respectively)[17; 22]. Fewer hospitalizations and a reduction in the use of respiratory drugs when treated regularly with IPV compared to standard physiotherapy were key findings in both articles. A few advantages of IPV, particularly for this population, are that IPV is independent of inspiratory muscle strength, in contrast to IS, and that the device may be used in the sitting position which implies that patients do not have to be treated in bed, in contrast to conventional CPT. In the two included studies, no adverse events were related to the use of IPV. A preliminary report by Birnkrant et al. discussed a case with a cardiac AV block and hypoxemia during IPV in a 16-y-old patient with Duchenne muscular dystrophy, which was most likely caused by mucus plugging after mobilizing secretions to the proximal airways[28]. To prevent such events, IPV should be combined with manual or mechanical cough assist in patients with insufficient expiratory muscle strength to expectorate mucus. The physiotherapy sessions in the study by Bidiwala et al. and Reardon et al. were both accompanied with cough assist if indicated. Although IPV in patients with neurological/neuromuscular diseases seems more effective than other ACTs, the results are based on heterogeneous and small samples, with only a moderate score of four out of ten on the PEDro assessment scale for the retrospective study by Bidiwala et al. The risk of bias in the RCT by Reardon et al. is more limited, since each item on the scoring list was adequate apart from the items concerning blinding.

d. Acute bronchiolitis

Although Van Ginderdeuren and colleagues were the only ones who evaluated IPV in subjects with acute bronchiolitis, their study had the largest sample size and scored the highest on the PEDro quality assessment[18]. Therefore, we can consider their results to be of sufficient value.

Their key finding was that both IPV and AAD were able to reduce days of hospitalization and improve clinical status according to the Wang score. A recent review by Roqué et al. could not find any benefits of CPT in children or infants with acute bronchiolitis[29]. All twelve studies included in their review used conventional CPT or passive expiration techniques as ACTs. Thus, Van Ginderdeuren et al. were the first to study IPV and AAD in this population and were also the first to report beneficial effects of respiratory physiotherapy. One of the limitations is that the results were based on a population with mild-to-moderate bronchiolitis, which may not be representative of children with either very mild (for whom no hospitalization is required) or severe bronchiolitis.

General discussion

After a systematic review of the literature, the main finding was that IPV appears to be a safe and effective technique for airway clearance in pediatric patients. The most promising results were found in patients with atelectasis, neurological and neuromuscular diseases and acute bronchiolitis. In those pathologies, significant beneficial results were found supporting the use of IPV for mobilizing secretions and recruiting obstructed areas of the lungs. No significant differences were found in clinically stable CF patients compared to conventional CPT, indicating the technique is an adequate alternative. The latter finding is in accordance with the review by Schechter et al., who concluded that airway clearance is proven to be beneficial in CF patients, but no ACT appears to be superior[26]. It is suggested that the technique to be used should be individually evaluated in agreement with the patient. Concerning the other previously mentioned populations, the review by Schechter et al. reports a probable benefit of ACTs in NMD, cerebral palsy and atelectasis in mechanically ventilated patients, but in contrary to our findings, they stated that ACTs have minimal to no benefits in children with

bronchiolitis. This discrepancy could be explained by the difference in techniques used in the clinical trials included in the review. Arguments for using IPV over another technique can be that no voluntary cooperation is necessary, which is especially of interest in young children and infants or mechanically ventilated patients[6]. For older children, such as CF adolescents, the technique may offer more independent treatment[5].

Of the 277 included patients in all nine studies, only one adverse event of minor hemoptysis occurred. Therefore, IPV is considered safe in spontaneously breathing and mechanically ventilated children and infants, although the presence of a skilled supervisor is advised as proposed by the manufacturers of the Percussionaire® Corporation. IPV is not considered to be associated with a higher risk for GOR in infants. Van Ginderdeuren et al. were the first to evaluate the number of reflux episodes (RE) during IPV treatment in children with suspected GOR, and they even found a reduction of RE compared to a control period.[31] The results of an earlier systematic review summarizing the evidence concerning the relation between ACTs and the incidence of GOR were inconclusive, respiratory physiotherapy either aggravated GOR or had no effect. The therapies mainly focused on conventional CPT and positioning with a head-down tilt.[32]

Although the results of this review seem promising, they should be interpreted with caution. It is important to emphasize that only a limited number of studies were found with small sample sizes for the majority of the studies. The included populations were heterogeneous across the different trials, and the assessed outcome measures differed considerably, making it difficult to compare results. Since various outcome measures have been used, no meaningful conclusions can be drawn as to which parameters are the most affected by IPV. Lung function parameters have been most frequently used, but no significant changes were found in the four studies[16; 17; 19; 20]. This finding could be due to a lack of sufficient sensitivity to assess the

acute effects of respiratory therapy[33]. Additionally, one of the main limitations, especially for the pediatric population, is that young children or children with a cognitive delay are not able to correctly perform the respiratory maneuver needed for a lung function test, such as spirometry. Sputum quantity has also been used in two studies, without finding any significant results[19; 20]. This outcome measure is not considered to be accurate and reliable, since sputum production can both be over- or underestimated[34] and cannot be collected from young and/or uncooperative children. Oxygen saturation has often been assessed in these studies to evaluate IPV, but there have been inconsistent results. Two studies showed significant changes[21; 23], while two others did not report any differences[15; 18]. Although pulse oximetry is simple to perform in any population, the low sensitivity and specificity question the utility of this assessment for the evaluation of ACTs[34]. General clinical characteristics, such as days of hospitalization[16-18], use of medication[16; 17; 22], clinical scoring lists[18; 21] and number of respiratory infections[17; 22], appear to be more affected by IPV. These parameters could be sensitive to the effects of respiratory physiotherapy in long-term trials, but since they have only been used in two or three studies, no clear conclusions can be made. In a review by Marques et al., Computer Aided Lung Sound Analysis (CALSA) has been proposed as a potentially convenient and reliable measure for the evaluation of respiratory physiotherapy[34]. Digital lung sounds can provide objective information about regional changes in the airways and could easily be achieved in uncooperative patients. CALSA has already shown the potential to detect significant changes after airway clearance therapy in several recent small studies[35-38], but IPV has not yet been evaluated with CALSA.

The little research concerning IPV in pediatric patients, together with the heterogeneity across these studies, prevent us from drawing any definite conclusions. Despite the promising results, further research evaluating the effectiveness of IPV in children is required to overcome

these limitations. Larger clinical trials with sufficient quality are important to specify for which respiratory conditions IPV is indicated and what effects can be expected. Thoughts should be given to which outcome measures are appropriate to evaluate respiratory physiotherapy and which are applicable in uncooperative subjects. A combination of conventionally used outcome measures and more recent technologies is advised to study either acute changes or long-term effects. Furthermore, future research will need to focus on a wider range of pathologies in the pediatric population, besides the ones discussed in this review. To date, no studies have been found investigating IPV in populations such as children with CF with acute exacerbation, non-CF bronchiectasis, severe acute bronchiolitis, bronchopulmonary dysplasia and primary ciliary dyskinesia.

Conclusion

The aim of this systematic review is to enlist previous research concerning the use of IPV in pediatric patients. In summary, it is considerable that IPV is a safe and effective technique for airway clearance. Studies comparing IPV to standard respiratory physiotherapy showed similar or even greater effects. According to the results of the included studies, the best effects were found in patients with atelectasis, neurological/neuromuscular disease and acute bronchiolitis. A schematic overview of the conclusions is given in Table 2. These conclusions should be interpreted with caution since the limited number of studies included in this review are heterogeneous and based on small sample sizes. Future research is required to overcome these limitations and to focus on a wider range of pediatric respiratory pathologies. Another interesting aspect for future research could be the use of recent, potentially more sensitive outcome measures, for example CALSA, to assess the effects of IPV.

References

1. Dulock HL. 1991. Chest physiotherapy in neonates: A review. AACN Clin Issues Crit Care Nurs. 2(3):446-452.

2. Walsh BK, Hood K, Merritt G. 2011. Pediatric airway maintenance and clearance in the acute care setting: How to stay out of trouble. Respiratory Care. 56(9):1424-1440.

3. Oberwaldner B. 2000. Physiotherapy for airway clearance in paediatrics. European Respiratory Journal. 15(1):196-204.

4. Vargas F, Bui H, Boyer A, Salmi L, Gbikpi-Benissan G, Guenard H, Gruson D, Hilbert G. 2005. Intrapulmonary percussive ventilation in acute exacerbations of copd patients with mild respiratory acidosis: A randomized controlled trial. Critical care (london, england).9(4):R382-389. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/072/CN-00561072/frame.html. doi:10.1186/cc3724.

5. Riffard G, Toussaint M. 2012. Indications for intrapulmonary percussive ventilation (ipv): A review of the literature. Revue Des Maladies Respiratoires. 29(2):178-190.

6. Langenderfer B. 1998. Alternatives to percussion and postural drainage. A review of mucus clearance therapies: Percussion and postural drainage, autogenic drainage, positive expiratory pressure, flutter valve, intrapulmonary percussive ventilation, and high-frequency chest compression with the thairapy vest. J Cardiopulm Rehabil. 18(4):283-289.

7. Ipv ® users manual. 2008. Percussionaire® Corporation Intrapulmonary Percussive Ventilation.

8. Procedure – intrapulmonary percussion ventilation. 2014. UTMB RESPIRATORY CARE SERVICES.

9. Douglas L. The usage of intrapulmonary percussive ventilation. California Thoracic Society.

10. Riffard G, Toussaint M. 2012. Intrapulmonary percussion ventilation: Operation and settings. Revue Des Maladies Respiratoires. 29(2):347-354.

11. Antonaglia V, Lucangelo U, Zin WA, Peratoner A, De Simoni L, Capitanio G, Pascotto S, Gullo A. 2006. Intrapulmonary percussive ventilation improves the outcome of patients with acute

exacerbation of chronic obstructive pulmonary disease using a helmet. Crit Care Med. 34(12):2940-2945.

12. Moher D, Liberati A, Tetzlaff J, Altman DG, Grp P. 2009. Preferred reporting items for systematic reviews and meta-analyses: The prisma statement (reprinted from annals of internal medicine). Physical Therapy. 89(9):873-880.

13. de Morton NA. 2009. The pedro scale is a valid measure of the methodological quality of clinical trials: A demographic study. Aust J Physiother. 55(2):129-133.

14. Teasell R, Foley N, Salter K, Bhogal S, Jutai J, Speechley M. 2009. Evidence-based review of stroke rehabilitation: Executive summary, 12th edition. Top Stroke Rehabil. 16(6):463-488.

15. Deakins K, Chatburn RL. 2002. A comparison of intrapulmonary percussive ventilation and conventional chest physiotherapy for the treatment of atelectasis in the pediatric patient. Respir Care. 47(10):1162-1167.

16. Homnick DN, White F, de Castro C. 1995. Comparison of effects of an intrapulmonary percussive ventilator to standard aerosol and chest physiotherapy in treatment of cystic fibrosis. Pediatr Pulmonol. 20(1):50-55.

17. Reardon CC, Christiansen D, Barnett ED, Cabral HJ. 2005. Intrapulmonary percussive ventilation vs incentive spirometry for children with neuromuscular disease. Arch Pediatr Adolesc Med. 159(6):526-531.

18. Van Ginderdeuren F, Vandenplas Y, Deneyer M, Vanlaethem S, Buyl R, Kerckhofs E. 2017. Effectiveness of airway clearance techniques in children hospitalized with acute bronchiolitis. Pediatr Pulmonol. 52(2):225-231.

19. Natale JE, Pfeifle J, Homnick DN. 1994. Comparison of intrapulmonary percussive ventilation and chest physiotherapy. A pilot study in patients with cystic fibrosis. Chest. 105(6):1789-1793.

20. Newhouse PA, White F, Marks JH, Homnick DN. 1998. The intrapulmonary percussive ventilator and flutter device compared to standard chest physiotherapy in patients with cystic fibrosis. Clin Pediatr (Phila). 37(7):427-432.

21. Ha TKY, Bui TD, Tran AT, Badin P, Toussaint M, Nguyen AT. 2007. Atelectatic children treated with intrapulmonary percussive ventilation via a face mask: Clinical trial and literature overview. Pediatrics International. 49(4):502-507.

22. Bidiwala A, Volpe L, Halaby C, Fazzari M, Valsamis C, Pirzada M. 2017. A comparison of high frequency chest wall oscillation and intrapulmonary percussive ventilation for airway clearance in pediatric patients with tracheostomy. Postgrad Med. 129(2):276-282.

23. Morgan S, Hornik CP, Patel N, Williford WL, Turner DA, Cheifetz IM. 2016. Continuous high-frequency oscillation therapy in invasively ventilated pediatric subjects in the critical care setting. Respir Care. 61(11):1451-1455.

24. Reychler G, Keyeux A, Cremers C, Veriter C, Rodenstein DO, Liistro G. 2004. Comparison of lung deposition in two types of nebulization - intrapulmonary percussive ventilation vs jet nebulization. Chest. 125(2):502-508.

25. Reychler G, Wallemacq P, Rodenstein DO, Cumps J, Leal T, Liistro G. 2006. Comparison of lung deposition of amikacin by intrapulmonary percussive ventilation and jet nebulization by urinary monitoring. J Aerosol Med. 19(2):199-207.

26. Schechter MS. 2007. Airway clearance applications in infants and children. Respiratory Care. 52(10):1382-1391.

27. Perrin C, Unterborn JN, Ambrosio CD, Hill NS. 2004. Pulmonary complications of chronic neuromuscular diseases and their management. Muscle Nerve. 29(1):5-27.

28. Birnkrant DJ, Pope JF, Lewarski J, Stegmaier J, Besunder JB. 1996. Persistent pulmonary consolidation treated with intrapulmonary percussive ventilation: A preliminary report. Pediatr Pulmonol. 21(4):246-249.

29. Figuls MRI, Gine-Garriga M, Rugeles CG, Perrotta C, Vilaro J. 2016. Chest physiotherapy for acute bronchiolitis in paediatric patients between 0 and 24 months old. Cochrane Database of Systematic Reviews. (2).

30. Gajdos V, Katsahian S, Beydon N, Abadie V, de Pontual L, Larrar S, Epaud R, Chevallier B, Bailleux S, Mollet-Boudjemline A et al. 2010. Effectiveness of chest physiotherapy in infants hospitalized with acute bronchiolitis: A multicenter, randomized, controlled trial. PLoS Med. 7(9):e1000345.

31. Van Ginderdeuren F, Kerckhofs E, Deneyer M, Vanlaethem S, Buyl R, Vandenplas Y. 2016. Influence of intrapulmonary percussive ventilation in upright position on gastro-oesophageal reflux in infants. Pediatr Pulmonol. 51(10):1065-1071.

32. Van Ginderdeuren F, Kerckhofs E, Deneyer M, Vanlaethem S, Vandenplas Y. 2015. Influence of respiratory physiotherapy on gastro-oesophageal reflux in infants: A systematic review. Pediatr Pulmonol. 50(9):936-944.

33. Jones PW, Agusti AG. 2006. Outcomes and markers in the assessment of chronic obstructive pulmonary disease. Eur Respir J. 27(4):822-832.

34. Marques A, Bruton A, Barney A. 2006. Clinically useful outcome measures for physiotherapy airway clearance techniques: A review.: Physical Therapy Reviews. p. 299-307.

35. Dinis JaOAaPCaCGaRJaMA. 2013. Automatic wheeze and respiratory phase detectors to evaluate respiratory physiotherapy in lrti: A preliminary study.

36. Ntoumenopoulos G, Glickman Y. 2012. Computerised lung sound monitoring to assess effectiveness of chest physiotherapy and secretion removal: A feasibility study. Physiotherapy. 98(3):250-255.

37. Adachi S, Nakano H, Odajima H, Motomura C, Yoshioka Y. 2016. Lung sounds in children before and after respiratory physical therapy for right middle lobe atelectasis. PLoS One. 11(9):e0162538.

38. Marques A, Bruton A, Barney A, Hall A. 2012. Are crackles an appropriate outcome measure for airway clearance therapy? Respir Care. 57(9):1468-1475.

Figure 1 PRISMA flowchart study selection.
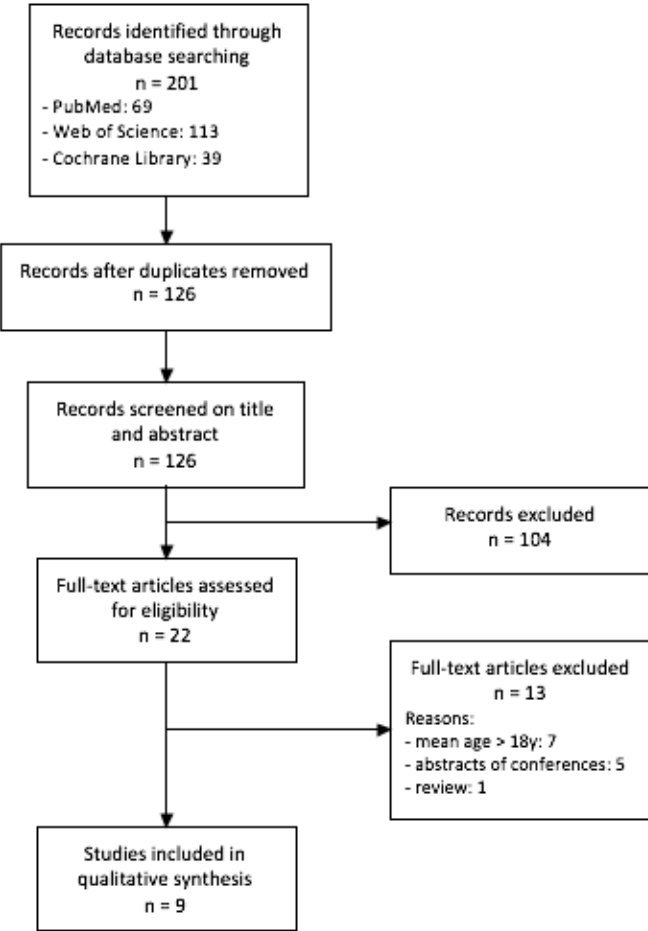
Table 1 Data extraction.

Author	Study design	PEDro score	Groups	Participants	Intervention	IPV characteristics	Intervention period	Results
Homnick et al.	RCT	5	Group 1: IPV	8 (5M/3F) subjects with CF, mean age 12 y (5-24y)	IPV, 20-30min 2x/d, with albuterol	type: Percussionator; f: 3-5 Hz; p: 10-30 cmH$_2$0	180 d	Lung function (FVC, FEV1, FEF25-75): NS change
								Anthropometrics (BMI, BW): NS change
								Satisfaction survey: subjects stated they would continue the use of IPV
								AE: 1 event of minor hemoptysis possibly related to IPV
			Group 2: CPT	8 (5M/3F) subjects with CF, mean age 10 y (5-18 y)	CPT: 20 min of percussion and postural drainage; preceded by aerosol with albuterol; 2x/d		180 d	Lung function (FVC, FEV1, FEF25-75): NS change
								Anthropometrics (BMI, BW): NS change
								AE: none reported
								IV antibiotic days: NS difference IPV compared to CPT
								Days of hospitalization: NS difference IPV compared to CPT
Natale et al.	Randomized crossover	7	1 group, 3 treatment regimens	9 (5M/4F) subjects with CF, mean age 14.6 y ±3,6	a) IPV, with albuterol	type: Percussionator IPV-1; f: 200-300 cycles/min; O$_2$ delivery pressure 1.2 psi/kg body weight	3x 1 d	Expectorated sputum: NS differences in physical properties between treatments
					b) HVA/P&PD: high volume aerosol with albuterol, followed by CPT (percussion and postural drainage)			Lung function (FVC, FEV1, FEF25-75): NS pre vs post treatment within the three regimens, NS differences between regimens, except in more severe disease IPV was correlated with a greater ↑ in FEF25-75
					c) STD: standard aerosol with albuterol, followed by CPT (percussion and postural drainage)			AE: none reported in any of the treatment regimens

Table 1 Continued.

Author	Study design	PEDro score	Groups	Participants	Intervention	IPV characteristics	Intervention period	Results
Newhouse et al.	Randomized crossover	6	1 group, 3 treatment regimens	10 (9M/1F), children with CF, mean age 17 y (9-25 y)	a) IPV: 20 min 3 d/w, with albuterol b) Flutter: standard aerosol with albuterol, followed by 15 min flutter, 3 d/w c) CPT: standard aerosol with albuterol, followed by 20 min conventional CPT, 3 d/w	type: IPV-1, percussionaire; p (10-30 cmH$_2$O) and f (3-5 Hz) individually determined to patient comfort and visible thoracic movement	3x 1 session	Sputum wet weight: NS differences between treatment regimens Lung function: FVC sign. ↑ after 1 h for flutter; FEV1 sign ↑ after 1 and 4 h for flutter and after 1 h for IPV; RV, TLC, RV/TLC, NS change; NS differences between the treatment regimens AE: none reported in any of the treatment regimens
Deakins et al.	Retrospective	7	1 group	46 subjects with atelectasis, median age 4.2 y (1 m - 15 y)	IPV, 10 min every 4-6 h, with albuterol	type: Percussionator IPV-1; f: 180-220 cycles/min; p: 15-30 cmH$_2$O	6.2 d	AS: ↓ 3 to 1 (p <0,001) AE: none reported
	RCT		Group 1: IPV	7 subjects with atelectasis, age range 7 w - 3 y	IPV, 10 min in intervals of 20 s with 5-10 s pauses, every 4 h	type: Percussionator IPV-1; f: 180-220 cycles/min; p: 15-30 cmH2O	3.1 d	AS: ↓ 2.3 to 0.9 (p = 0.026) Static compliance: NS change SpO$_2$: NS change f: NS change AE: none reported
			Group 2: CPT	5 subjects with atelectasis, age range 2 m – 14 y	CPT (percussion, clapping, vibration), 10-15 min, every 4 h		6.2 d	AS: NS change Static compliance: NS change SpO$_2$: NS change f: NS change AE: none reported

Table 1 Continued.

Author	Study design	PEDro score	Groups	Participants	Intervention	IPV characteristics	Intervention period	Results
Ha et al.	Prospective uncontrolled cohort	3	1 group	6 subjects in respiratory distress with suspicion of atelectasis, mean age 36 m $\pm$24	IPV, 10 min 2x/d	type: Impulsator; f: 150-220 cycles/min; p: 0.5-1 kPa; I/E ratio: 1/1	5 d	AS: NS change SpO$_2$: ↑ from 93.2 to 95.3% (p=0.002) Clinical score: ↓ from 2.8 to 0.8 (p=0.012)
Morgan et al.	Retrospective	3	1 group	59 (37M/22F) invasively ventilated subjects, median age 2 y (1 m – 19 y)	IPV, 10 min	type: MetaNeb, CHFO mode, f: 230 cycles/min	1-39 treatments per subject	HR: NS change; BP: NS change Ventilation parameters: PIP ↓ from 14 cmH$_2$O to 8 cmH$_2$O (p<0.001); other ventilator parameters (PEEP, exhaled Vt, airway pressure, breathing f) NS change Gas exchange parameters: FiO$_2$: ↑ from 0.35 to 0.40 (p=0.002); SaO$_2$/FiO$_2$ ↓ from 259 to 243 (p=0.003); other gas exchange parameters (PaO$_2$/FiO$_2$, PaCO$_2$, oxygen index): NS change AE: air leak in 1 subject
Bidiwala et al.	Retrospective	4	1 group, 2 treatment regimens	8 (4M/4F) tracheostomy dependent subjects with chronic illness, age 1-22 y	1st year: HFCWO, 2-3x/d 2nd year: IPV, 10 min, 2-3x/d	Type: Metaneb, 2 modes used in a cyclic manner: CHFO and CPEP	2x 1 y	# Respiratory illness: ↓ from 32/y with HFCWO to 15/y with IPV (p<0.001) # Respiratory tract infections: ↓ from 15/y with HFCWO to 6/y with IPV (p=0.01) Use of bronchodilators: ↓ from 53 episodes with HFCWO to 21 episodes with IPV (p<0.001) Use of steroids: ↓ from 12 courses with HFCWO to 4 with IPV (p=0.003) # hospitalizations: ↓ from 8 to 3 with IPV (p=0.003) AE: none reported

Table 1 Continued.

Author	Study design	PEDro score	Groups	Participants	Intervention	IPV characteristics	Intervention period	Results
Reardon et al.	RCT	7	Group 1: IPV	9 (6M/3F) subjects with NMD, median age 17 y (11-19 y)	IPV, 10-15 min 2x/d	type: Impulsator; f: 120 cycles/min; p: individually set inducing visible chest oscillations, range 20-40 cmH$_2$O	7m	Days of antibiotics: 0 Days hospitalized: 0 School days missed: 1 Pulmonary infections: 0 Lung function (FEV1, FVC, TLC, MVV, MIP, MEP): NS change Supplemental respiratory treatments: 60 extra albuterol inhalations; 22 extra IPV sessions
			Group 2: IS	9 (8M/1F) subjects with NMD, median age 17 y (14-19)	IS, 5-10 min 2x/d		7m	Days of antibiotics: 44, sign. higher than IPV with IRR = 43 Days hospitalized: 8, sign. higher than IPV with IRR = 8,5 School days missed: 5 Pulmonary infections: 3 Lung function (FEV1, FVC, TLC, MVV, MIP, MEP): NS change Supplemental respiratory treatments: 166 extra albuterol inhalations; 172 extra IPV sessions; both sign. higher than IPV group (p<0,001)
Van Ginderdeuren et al.	RCT	9	Group 1: IPV	31 (15M/16F) subjects with bronchiolitis, mean age 135 d ±132	IPV, 4 cycles of 5 min per day, combined with bouncing	type: -; f: 300 cycles/min, P: 6-10 mbar	from hospital admission until discharge	Days of hospitalization: 3.5 ±1.3; sign. ↓ than control (p=0,03), but NS with AAD Secondary outcomes: Wang score improved sign. better than control, sign. better than AAD immediately after intervention, but NS after 1 h; HR and SaO$_2$ showed NS changes
			Group 2: AAD	31 (16M/15F) subjects with bronchiolitis, mean age 121 d ±118	AAD, 20 min/d, combined with bouncing		from hospital admission until discharge	Days of hospitalization: 3.6 ±1.4; sign. ↓ than control (p<0,05), but NS difference with IPV Secondary outcome: Wang score improved sign. better than control; HR and SaO$_2$ showed NS changes
			Group 3: control	31 (13M/18F) subjects with bronchiolitis, mean age 160 d ±143	Bouncing, 20 min/d		from hospital admission until discharge	Days of hospitalization: 4.5 ±1.9; sign. ↑ than IPV and AAD Secondary outcomes: Wang score sign. less improvement than IPV and AAD; HR and SaO$_2$ showed NS changes

Abbreviations: AAD, assisted autogenic drainage; AE, adverse events; AS, atelectasis score; BP, blood pressure; BMI, body mass index; BW, body weight; CHFO, continuous high frequency oscillations; CPT, chest physiotherapy; CPEP, continuous positive expiratory pressure; f, frequency; FEF25-75, forced expiratory flow at 25-75% of vital capacity; FEV1, forced expiratory volume in one second; FiO_2, fraction of inspired oxygen FVC, forced vital capacity; HFCWO, high frequency chest wall oscillations; HR, heart rate; IPV, intrapulmonary percussive ventilation; IRR, incidence rate ratio; NS, non-significant; p, pressure; $PaCO_2$, partial pressure of arterial carbon dioxide; PaO_2, partial pressure of arterial oxygen; PEEP, positive end expiratory pressure; PIP, peak inspiratory pressure; RCT, randomized controlled trial; RV, residual volume; SaO_2, blood oxygen saturation level by invasive oximetry; sign., significant; SpO_2, blood oxygen saturation level by pulse oximetry; TLC, total lung capacity, Vt, tidal volume; #, number of.

Table 2 Key points.

- IPV is suggested to be a safe technique in spontaneously and mechanically ventilated children.
- IPV is considered to be effective for airway clearance and could be an adequate alternative to other ACT's for children with respiratory diseases in general.
- IPV appears to be superior to other ACT's in children with atelectasis neurological/neuromuscular disease and mild/ moderate acute bronchiolitis.
- Only a limited number of studies with small sample sizes investigated the effects of IPV in the pediatric population.
- Besides larger clinical trials with sufficient quality and the use of adequate outcome measures, future research should focus on a wider range of pathologies, such as children with CF with acute exacerbation, non-CF bronchiectasis, severe bronchiolitis, bronchopulmonary dysplasia and primary ciliary dyskinesia.