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ORIGINAL ARTICLE

Intrapulmonary percussion with autogenic drainage and ventilator-associated Gram-negative infection: A pilot study

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Abstract

Background

Intrapulmonary percussive ventilation with assisted autogenic drainage physiotherapy (IPV-AADP) is a compelling form of chest physiotherapy (CPT) in mechanically ventilated critically ill patients. We evaluated the effect of IPV-AADP on the occurrence of Gram-negative infection-related ventilator-associated complications (IVACs).

Methods

Patients requiring mechanical ventilation for at least 48 hours were randomly assigned to receive either IPV-AADP, conventional CPT (CoCPT) or no CPT (NoCPT). Standard institutional prevention measures of ventilator-associated infection were guaranteed in all subjects. The study endpoint was the presence of IVACs as documented according to the Centers of Disease Control 2011 Working Group guidelines. Statistical analysis used non-parametric tests for independent samples and Fisher's exact test to compare treatment groups.

Results: Forty-five patients (24 males, 21 females) were enrolled with 15 subjects included in each study arm. IPV-AADP patients were younger (46±17 years) than CoCPT (62±18 years) and NoCPT (64±16 years) subjects (p=0.014; IPV-AADP vs. CoCPT and NoCPT) but APACHE II scores were comparable between the groups (20±8, 23±10 and 21±6 respectively for IPV-AADP, CoCPT and NoCPT subjects, p=NS). Gram-negative IVACs were diagnosed in two patients (13%) in the IPV-AADP group, seven patients (47%) in the CoCPT group and seven patients (47%) in the NoCPT group (p=0.10; IPV-AADP vs. CoCPT and NoCPT).

Conclusion

In this small pilot study, adjunctive IPV-AADP tended to decrease the occurrence of ventilator-associated Gram-negative infection as compared with CoCPT and NoCPT.

Background

CPT in mechanically ventilated patients primarily aims to facilitate clearance of airway secretions in an attempt to prevent lung atelectasis, tracheobronchial infection, and ventilator-associated pneumonia (VAP).[1,2] For this purpose, ICU physiotherapists have a large armamentarium of physical and mechanical means at their disposal. However, CPT-driven secretion management is not standardised among ICUs and varies from simply providing appropriate humidification and as-needed airway suctioning to a more complex 'multimodality' approach including percussion, manual or ventilator hyperinflation, chest wall vibrations, postural drainage, and rib-cage compression.

Intrapulmonary percussive ventilation (IPV) delivers very small bursts of tidal volume within a frequency range of 60-600 cycles/minute. By providing a convective front of gas to the distal airways, IPV provides a more homogenous distribution of alveolar ventilation, promotes alveolar recruitment, helps to 'unstick' mucus in small and middle-sized airways, and propels secretions cephalad to the central airways.[3] Encouraging results with IPV have been obtained in patients with cystic fibrosis.[4] For more than 20 years, IPV physiotherapy has replaced all other forms of CPT in our ICU. With few exceptions, this technique is routinely performed in all intubated and mechanically ventilated patients, regardless of their underlying clinical condition.

The efficacy of IPV could be enhanced by combining it with autogenic drainage. Essentially, autogenic drainage is a 'concentration intensive' respiratory self-drainage technique that explores and utilises the most optimal expiratory airflow to mobilise secretions.[5] It consists of three phases: loosening peripheral secretions by breathing at low lung volumes, collecting secretions from central airways by breathing at low to mid lung volumes, and finally expelling secretions by breathing at mid to high lung volumes. Today, it is used to treat patients with

large amounts of thick mucus. In assisted autogenic drainage, the respiratory physiotherapist uses exhaled air to remove mucus from the airways of more severely ill patients who are not capable of performing autogenic drainage independently.
Combining IPV with assisted autogenic drainage physiotherapy (IPV-AADP) might represent a more powerful form of CPT than the currently used 'multimodality' techniques for adjuvant prevention of respiratory infection in mechanically ventilated critically ill patients. We therefore assessed the effect of providing either no CPT (NoCPT), conventional CPT (CoCPT) or IPV-AADP on the occurrence of Gram-negative infection-related ventilator-associated complications (IVACs) in this population.

Methods

The study was approved by the Health Research Ethics Committee of the University Hospital Brussels (B.U.N. 14320084389). Oral informed consent to initiate the study was obtained from the patient's next-of-kin. Mechanically ventilated medical, surgical and/or trauma patients with negative tracheobronchial cultures were consecutively enrolled. Exclusion criteria for the study were: presence of lung infiltrates, ventilation for less than 48 hours, community-acquired or plain aspiration pneumonia, nosocomial or healthcare-acquired infection, immunosuppressive disease, neutropenia, any form of immunosuppressive therapy including steroids, worse short-term prognosis, or a contraindication for IPV-AADP (i.e. undrained pneumothorax, post sternotomy or thoracotomy, rib fractures). During the study, all patients were ventilated in the pressure-controlled mode (Evita XL, Dräger Medical). Inspired oxygen fraction and positive end-expiratory pressure (PEEP) were adapted to obtain a PaO2 ≥60 mmHg. Inspiratory pressure aimed at tidal volumes of 6-8 ml/kg and was limited at 30 cm H_2O. Patients were randomly assigned according to a computer-steered permuted block design to receive NoCPT, CoCPT or IPV-AADP treatment. CoCPT consisted of expiratory chest wall percussion and vibration, positioning, rib springing, aerosol therapy, and airway suctioning. The NoCPT group underwent passive mobilisation, aerosol therapy and tracheobronchial aspiration. Aerosols contained 4 ml hypertonic saline 3% and occasionally ipratroprium bromide, and were administered three times daily by metered-dose inhalators connected to a spacer. Closed suction was performed for no longer than 15 seconds using pressures ranging from 90-120 mmHg. IPV-AADP and CoCPT were performed by two dedicated and skilled respiratory therapists. Sessions were delivered twice daily for 20 minutes, also during the weekend. During CPT, continuous intravenous analgosedation with remifentanil and propofol was provided in doses to obtain a -4 to -5 sedation level on the Richmond Agitation-Sedation Scale. IPV was delivered by switching the patient from the ventilator to a high-frequency pulse generator (Bird IPV 2 Percussionaire®, Sand Point, Idaho, USA) using pulsatile percussions between 80 and 350 cycles per minute. Gas was delivered at adjustable pressure through a non-gated sliding venturi connected to the endotracheal tube. A pressure-controlled tidal volume breath was insufflated at regular time intervals to ensure adequate CO_2 elimination. FiO_2 and PEEP levels were kept identical to those used on the ventilator. For assisted autogenic drainage, gentle bimanual compression was progressively exerted on the patient's thorax and maintained at a level where secretions could be 'heard and felt'. Subsequently, IPV-generated expiratory flow was used to expel the collected secretions. At the end of each IPV-AADP session, endotracheal suction was performed.
In all three groups, identical standardised measures for prevention of ventilator-associated tracheobronchitis or pneumonia were undertaken: ventilation with at least 5 cm H_2O PEEP, no routine change of ventilator circuits, humidification using a heat-moisture device, semi-recumbent body positioning at an angle of at least 25°, continuous maintenance of endotracheal tube cuff pressure at 30 cm H_2O, periodic verification of residual gastric volume, daily dental hygiene, oral cleaning with 1% chlorhexidine every eight hours, a strict sedation protocol aiming at minimal sedation according to a dedicated sedation score and ensuring daily 'wake-up' calls. All patients received H2-blockers until adequate enteral nutrition was achieved. Specific types of endotracheal tubes (e.g. subglottic aspiration, silver-coated) or cuff material (e.g. polyurethane) were not used. Patients received no selective digestive decontamination treatment.
Study endpoint was a documented Gram-negative IVAC. IVACs were defined according to the Centres of Disease Control 2011 Working Group guidelines.[6] Briefly, on or after calendar Day 3 of mechanical ventilation and within two calendar days before or after the onset of worsening oxygenation, patients had to have either fever >38°C or a white blood cell count ≥12,000/mm^3 or ≤4000/mm^3 and a new antimicrobial agent started for at least four days. Additionally, the following criteria had to be met: at least one purulent respiratory secretion specimen collected from the lungs, bronchi, or trachea containing ≥25 neutrophils and ≤10 squamous epithelial cells per low power field (or corresponding semi-quantitative results) and a positive Gram-negative culture (qualitative, semi-quantitative or quantitative) of sputum, endotracheal aspirate or bronchoalveolar lavage fluid. IVACs were considered early-onset when they were diagnosed during the first four days of mechanical ventilation and categorised as late-onset after four days. Statistical analysis used non-parametric tests for independent samples and Fisher's exact test to compare treatment groups.

Results

Forty-five patients (24 males, 21 females) were enrolled with 15 subjects included in each study arm. Demographic characteristics, admission diagnosis and culture results for

Table 1. Patient characteristics and microbiology.

Gender	Age	Admission diagnosis	Microbiology
CoCPT			
F	82	Liver abscess	
F	83	Urosepsis	
M	63	Haemorrhagic shock	
F	47	Necrotising fasciitis	
M	48	Tetanus	
M	40	Cardiogenic shock	*P. vulgaris; S. marcescens*
M	80	Intracranial bleeding	*E. coli; P. mirabilis*
M	54	Peritonitis	
M	80	Intracranial bleeding	*E. coli; M. morganii*
M	67	Peritonitis	
M	51	Intracranial bleeding	*E. coli*
M	76	Peritonitis	
F	69	Cardiac arrest	*E. coli*
M	22	Head trauma	*K. pneumoniae*
M	67	Stroke	
NoCPT			
F	70	Intracranial bleeding	*K. pneumoniae*
F	80	Epiglottitis	*P. aeruginosa*
M	35	Polytrauma	*E. coli*
F	76	Sepsis	
M	73	Haemorrhagic shock	
M	60	Osteomyelitis	
M	74	Sepsis	*P. aeruginosa*
F	49	Intracranial bleeding	*E. coli; K. pneumoniae*
F	77	Sepsis	*E. coli*
F	50	Polytrauma	
M	82	Head trauma	
F	73	Polytrauma	
M	57	Meningitis	
M	73	Encephalitis	
F	33	Intracranial bleeding	*H. influenzae*
IPV-AADP			
F	65	Intracranial bleeding	
M	61	Intracranial bleeding	
M	38	Cardiac arrest	
M	21	Polytrauma	
M	63	Cardiogenic shock	*E. cloacae*
M	36	Encephalitis	
F	29	Intracranial bleeding	
F	71	Intracranial bleeding	
M	53	Cardiac arrest	
F	60	Hepatic encephalopathy	
F	69	Peritonitis	
F	34	Status epilepticus	
F	26	Cardiac arrest	
F	39	Intracranial bleeding	
F	31	Encephalitis	*E. cloacae*

CoCPT = conventional chest physiotherapy; NoCPT = no chest physiotherapy; IPV-AADP = intrapulmonary percussive ventilation with assisted autogenic drainage physiotherapy; M = male; F = female.

all treatment groups are depicted in *table 1*. The majority of patients (49%) had primary cerebral pathology or were admitted after reanimation. Before the start of the study, six CoCPT, six NoCPT and four IPV-AADP patients received antibiotic treatment (p=NS between groups). IPV-AADP patients were younger (46±17 years) than CoCPT (62±18 years) and NoCPT (64±16 years) subjects (p=0.014; IPV-AADP vs. CoCPT and NoCPT) but APACHE II scores were comparable between the groups (20±8, 23±10 and 21± 6 respectively for IPV-AADP, CoCPT and NoCPT subjects, p=NS). Gram-negative IVACs were diagnosed in two patients (13%) in the IPV-AADP group, seven patients (47%) in the CoCPT group and seven patients (47%) in the NoCPT group (p=0.10; IPV-AADP vs. CoCPT and NoCPT). Time from start of the study till occurrence of a Gram-negative IVAC ranged from 4-11 days. Early-onset IVAC was detected in four NoCPT patients, one CoCPT-treated subject and in no IPV-AADP patients (p=NS between groups). Appropriate antibiotics were prescribed to treat all documented IVACs. Survival was not different between the groups and unrelated to the identified Gram-negative microorganism. Clinical or device-related adverse events were not reported with any form of CPT.

Discussion

Through the years, CPT has become an integral part of the multidisciplinary approach to critically ill ventilated patients. However, there is a dearth of high-level evidence to support any particular CPT technique.

Studies that assessed the usefulness of CPT in ICU patients mainly evaluated mortality rate or clinical outcomes such as incidence of VAP, ventilator-free days, or length of ICU and hospital stay. All relevant prospective and controlled studies are summarised in *table 2*. Ntoumenopoulos et al. studied 46 mechanically ventilated trauma patients (22 CPT and 24 controls). CPT consisted of twice-daily lung hyperinflation and postural drainage. Patients in both groups received routine nursing care, including at least two-hourly patient turning and airway suctioning. CPT was not associated with a reduced incidence of VAP according to clinical and radiological criteria.[7] The same investigators presented another study in 60 critically ill mechanically ventilated medicosurgical patients (24 CPT vs. 36 controls). Here, CPT comprised twice daily positioning, expiratory chest wall vibrations and airway suctioning. VAP occurred in 14 (39%) control patients and in two (8%) CPT subjects (OR=0.4; 95% CI 0.03-0.56; p=0.02).[8] A difference in duration of ventilation, length of ICU stay, or mortality rate was not observed in either of these studies.[6,7] Templeton and Palazzo evaluated 172 patients (87 CPT vs. 85 controls). CPT comprised twice-daily patient positioning, manual pulmonary hyperinflation with vibration, rib springing, and airway suctioning. VAP was observed in more patients receiving CPT than in control patients (35 vs. 25; p=0.13). Patients receiving CPT had significant prolongation of median time to become ventilator-free.[9] Pattanshetty and Gaude studied 101

Table 2. Prospective controlled studies of chest physiotherapy in mechanically ventilated patients.

Author (reference)	Number of patients	RPT intervention	Result
Ntoumenopoulos[7]	22 CPT 24 Controls	MLH, postural drainage; bid	No difference in VAP incidence and duration of ventilation between groups
Ntoumenopoulos[8]	24 CPT 36 Controls	Body positioning, expiratory chest wall vibrations, suction; bid	Less VAP in CPT group
Templeton & Palazzo[9]	87 CPT 85 Controls	Body positioning, MLH, rib springing, chest wall vibrations, suction; bid	Tendency for more VAP and prolonged ventilation in CPT group
Pattanshetty & Gaude[10]	50 CPT 51 Controls	Body positioning, chest wall vibrations, suction; bid	Less VAP, more successful weaning and lower mortality in CPT group; no difference in duration of ventilation or length of ICU stay
Pattanshetty & Gaude[11]	87 CPT 86 Controls	Body positioning, MLH, chest wall vibrations, suctioning; bid (controls received MLH and suction	No difference in VAP incidence between groups; prolonged duration of hospitalisation in CPT group
Patman[12]	72 CPT 72 Controls	Body positioning, MLH, suction; x6/day	No significant difference between groups for any outcome

CPT = chest physiotherapy; MLH = manual lung hyperinflation; VAP = ventilator-associated pneumonia; bid= twice daily; ICU = intensive care unit

adult mechanically ventilated patients. Twice-daily manual hyperinflation and suctioning were administered to 51 control patients. Fifty CPT patients additionally received positioning and chest wall vibrations. As compared with controls, CPT was associated with a highly significant decrease in VAP rate and reduced mortality (24% vs. 49%; p=0.007).[10] However, a subsequently published study by the same authors including 173 patients found no difference in VAP incidence and a longer duration of hospitalisation in the 87 subjects allocated to a similar multimodality CPT.[11] Patman et al. studied 144 mechanically ventilated patients with brain injury (72 CPT and 72 controls). Diagnosis of VAP required the presence of positive quantitative cultures obtained by non-bronchoscopic lavage. CPT consisted of six treatments (i.e. positioning, manual lung hyperinflation, and airway suctioning) in each 24-hour period. No difference was observed in VAP incidence between the groups (14 CPT vs. 19 controls; p=0.32). Although CPT tended to reduce the duration of mechanical ventilation and length of ICU and hospital stay, none of these outcomes reached statistical significance.[12] Finally, Castro et al. compared CPT consisting of at least four treatment sessions over a 24-hour period with CPT consisting of only one visit over a six-hour period in 146 patients (73 subjects in each group). CPT was similar for both periods and consisted of body positioning, manual thorax percussion, and suction. Patients undergoing intensive CPT had significantly less duration of ventilation and ICU stay, developed fewer respiratory infections, and had lower mortality.[13] However, this study compared CPT in two different hospitals. Important baseline patient characteristics such as degree of organ failure, sedation level, and coma scale were substantially or significantly different between patients which makes any valuable comparison doubtful.

Overall, the evidence emanating from these trials on the usefulness of CPT in intubated and mechanically ventilated patients is conflicting. Differences in CPT interventions, methodological quality and range of samples in these studies preclude statistical analysis of pooled results. Also, the 'multimodality' CPT applied in most studies makes it impossible to determine the effectiveness of individual treatment components. Evaluation of a potential impact of CPT on outcome variables such as ICU/hospital length of stay and mortality is most likely flawed by differences in underlying disease type and severity and concomitant comorbid disorders. In all but one[12] study, diagnosis of VAP relied on clinical, biological, and radiographic criteria, sometimes bundled in a score. However, pooled specificity and sensitivity of such assessment is low[14] and inter-observer variability in the diagnosis of VAP is extremely high.[15] Our study is the first to use a novel approach of estimating ventilator-associated infection based on documenting purulent secretions and microbiological findings but eliminating both the low specificity of chest X-ray interpretation and the variability in ordering and collecting of lower respiratory tract specimens. Although this approach was essentially designed for surveillance purposes, it is more in keeping with traditional clinical constructs of VAP.

Our study has important shortcomings and limitations. First, as a pilot project, it is heavily underpowered and thus cannot determine whether adding CPT with IPV-AADP to a standard VAP prevention program may cause fewer Gram-negative IVACs. Second, bias introduced by the heterogeneity in admission diagnoses, the incompletely documented medico-surgical patient histories, the concomitant antibiotic therapy for non-pulmonary infectious disease, the inter-individual difference in duration of stress ulcer prophylaxis and enteral nutrition policy, and the younger age of the IPV-AADP patients may have skewed the study results. Third, the high prevalence of acute cerebral pathology renders evaluation of outcome parameters such as duration of mechanical ventilation or ICU length of stay irrelevant. Fourth, it can be argued that reporting Gram-negative IVACs is an inappropriate study endpoint.

Despite being proposed as an algorithm to streamline diagnosis, the Centres of Disease Control definition of ventilator-associated conditions is found to insufficiently capture VAP.[16] Conversely, measures to decrease the incidence of VAP do not necessarily affect IVAC rates.[17] However, our study results should be interpreted within the pathogenic continuum of progressive Gram-negative tracheobronchial colonisation with bacterial growth and increasing inflammation leading to ventilator-associated tracheobronchitis and eventually VAP.[18] Ventilator-associated tracheobronchitis appears to be an important risk factor for VAP. Moreover, patients in the 'ventilator-associated tracheobronchitis phase' do benefit from targeted antimicrobial treatment in terms of more ventilator-free days and less subsequent VAP[19] Finally, the relative complexity, availability, and cost of IPV might be questioned. Yet, physiotherapists are rapidly trained to work with the device (personal experience) and any ICU involved in high-frequency ventilation can easily and safely implement IPV physiotherapy.

Conclusions

CPT combining IPV with assisted autogenic drainage tends to reduce the occurrence of Gram-negative IVACs. The limited number, heterogeneity, and baseline disease characteristics of the studied patients preclude determining whether IPV-AADP hastens recovery, shortens duration of ventilation, or improves outcome.

Disclosures

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