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Original Article

Effects of vibratory sputum ejection as an assisted therapy for severe pneumonia patients on mechanical ventilation and the influence on respiratory function

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Abstract: Objective: The current study aimed to investigate the effects of vibratory sputum ejection (VSE), as an assisted therapy for patients with severe pneumonia, on mechanical ventilation and its influence on respiratory function. Methods: Seventy patients with severe pneumonia on mechanical ventilation were randomly divided into the experimental group (n=35) and control group (n=35). Patients in the control group received fiberoptic bronchoalveolar lavage (FBL), while patients in the experimental group underwent combined treatment of FBL with VSE. Vital signs, blood-gas parameters, respiratory function, inflammatory response, and prognosis of the two groups were compared. Results: There were no significant differences in respiratory rates, heart rates, and mean arterial pressure between the two groups 15 minutes before and 15 minutes after treatment. Levels of PaO_2, PaO_2/FiO_2, FEV1, and FVC in both groups were significantly increased after 7 days of treatment, compared with levels before treatment (all $P \leq 0.001$). Levels in the experimental group were significantly higher (all $P<0.01$). Levels of $PaCO_2$ and airway resistance decreased in both groups (all $P \leq 0.001$) and the experimental group enjoyed significantly lower levels than the control group (both $P<0.01$). Levels of C-reactive protein and procalcitonin in both groups were significantly decreased after 24 hours of treatment (all $P \leq 0.001$). The experimental group enjoyed significantly lower levels than the control group (both $P<0.01$). In the experimental group, the effective rate was significantly higher than that of the control group and 28-day mortality was significantly lower than that of the control group (both $P<0.05$). Conclusion: FBL combined with VSE for patients with severe pneumonia on mechanical ventilation can significantly reduce inflammation, contribute to the recovery of respiratory function, and improve prognosis. It is worthy of clinical promotion.

Keywords: Vibratory sputum ejection, severe pneumonia, mechanical ventilation, respiratory function, inflammatory response

Introduction

Severe pneumonia is a relatively serious respiratory disease. Many pathogenic bacteria or drug-resistant bacteria are often involved in the occurrence and development of pneumonia, leading to poor effectiveness of single-drug treatments. Additionally, this disease can induce respiratory failure and endanger patient lives. Therefore, long-term mechanical ventilation is often required. However, administration of sedatives during mechanical ventilation can cause inhibition of the cough reflex, increase airway secretion, and cause other adverse reactions, thereby damaging lung function [1, 2].

At present, fiberoptic bronchoalveolar lavage (FBL) is a reliable treatment for severe pneumonia patients on mechanical ventilation. It directly removes secretions from the trachea and improves the ventilation function of patients. However, patients with severe pneumonia on mechanical ventilation often have major thick mucus or sputum, which causes mucous/sputum scabs to block the small airways in lungs. This affects the treatment effects. Studies have found that vibratory sputum ejection (VSE) can effectively remove mucous/sputum scabs and inhibit the production of secretions in the bronchi [3]. Scholars have suggested that VSE promotes the shedding of mucus or other metabolites adhering to the surface of bronchial

mucosa via vibrating and directional tapping on the chest, thereby moving them from the small airways to the major airways. This helps to remove mucous/sputum scabs and secretions [4]. Researches have shown that VSE for patients with severe pneumonia on mechanical ventilation can better remove secretions and accelerate the recovery of body function [5]. However, the exact effects of FBL assisted with VSE for patients with severe pneumonia on mechanical ventilation remain unclear. The present study aimed to investigate the clinical effects of VSE, as an assisted therapy for the treatment of patients with severe pneumonia, on mechanical ventilation, examining its influence on respiratory function.

Materials and methods

Baseline characteristics

Seventy patients with severe pneumonia on mechanical ventilation, treated in Zhejiang Si'an International Hospital, from March 2015 to June 2017, were included in this study. Subjects were divided into two groups according to the random number table method, the experimental group (n=35) and control group (n=35). This study conformed to the principles of the Helsinki Declaration, as revised in 2013, and was approved by the Medical Ethics Committee of Zhejiang Si'an International Hospital. Informed consent was obtained from all participants and families.

All subjects met the criteria for diagnosis of severe pneumonia, according to 2001 Guidelines set forth by the American Thoracic Society [6]. Main diagnostic criteria included: Mechanical ventilation was required and vasoconstrictor had to be administrated to treat septic shock. Secondary diagnostic criteria included: Consciousness/orientation disorder; Respiratory rate ≥ 30 times/min; Multi-lobed infiltration; Oxygenation index (PaO_2/FiO_2) ≤ 250; White blood cell count less than 4.0×10^9/L; Platelet count less than 10.0×10^9/L; With azotemia (blood urea nitrogen ≥ 7 mmol/L); With hypothermia (body temperature 36°C); and With hypotension and in need of treatment of aggressive fluid resuscitation. Diagnosis of severe pneumonia was confirmed if any one of the two main criteria or any three of the secondary criteria were met.

Inclusion criteria: Patients met diagnostic criteria; Patients over 18 years of age; Patients without contraindications for VSE and FBL; Patients with complete clinical data; Patients without immune system disorders; Patients able to communicate with clear consciousness; and Patients underwent invasive mechanical ventilation and met the indications of FBL.

Exclusion criteria: Patients that dropped out of treatment or study or with aggravating conditions; Patients with poor compliance; Patients with unstable conditions; Patients with other lung diseases, such as tuberculosis or lung cancer; Patients with rheumatic diseases; Patients that were pregnant or in lactation; Patients with severe lesions in organs like the heart, liver, kidneys; and Patients with coagulation dysfunction.

Methods

All patients were given conventional treatments, such as administration of antibacterial and anti-infective agents, primary disease treatment, and warming and humidification for mechanical ventilation. The control group was treated with FBL, while the experimental group received FBL assisted with VSE [7]. The specific operations were as follows: Twenty minutes before bronchoalveolar lavage, the patients were in lateral decubitus position on the healthy side. They were treated with VSE by TC-818 vibratory sputum ejection machine (Shanghai Huanxi, China) for 15 minutes. The frequency of the machine was set individually and the direction was set as outer-to-inner and top-to-bottom mode. The above operations were performed 2 times a day. FBL was performed after back tapping was completed.

Outcome measures and efficacy evaluation

Changes in vital signs, including respiratory rate, heart rate, and mean arterial pressure, were detected and compared between the two groups 15 minutes before and 15 minutes after treatment.

Morning fasting arterial blood (2 mL, before oxygen inhalation) was collected from the radial artery in both groups before treatment and 7 days after treatment. Blood-gas parameters, arterial partial pressure of oxygen (PaO_2), partial pressure of carbon dioxide in artery ($PaCO_2$),

Table 1. Comparison of general data

Group	Experimental group (n=35)	Control group (n=35)	t/χ^2	P
Gender (n)			0.516	0.473
Male	20	17		
Female	15	18		
Age (year)	49.30±2.10	49.60±2.00	0.612	0.543
Mean duration of disease (year)	0.99±0.18	1.02±0.14	0.778	0.439
Basic diseases (n)			1.532	0.821
COPD	13	10		
Multiple organ failure	9	11		
Malignant tumor	6	4		
Stroke	5	7		
Other	2	3		
Simplified CPIS score (point)	6.88±1.79	6.91±1.62	0.074	0.942
APACHE II score (point)	24.76±5.94	25.80±5.72	0.746	0.458

Note: COPD refers to chronic obstructive pulmonary disease; CPIS refers to Clinical Pulse Infection Score; APACHE II refers to acute physiology and chronic health evaluation II.

and PaO_2/FiO_2 were measured at the two time points by blood gas analyzer (model 995, from AVL, Switzerland). Results were compared between the two groups.

Patients in both groups had pulmonary function tests (by model ST-250, from Fukuda, Japan) before and 7 days after treatment. Forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), and airway resistance (Raw) were measured. FEV1 refers to the amount of gas exhaled at the fastest speed in the first second, which is positively correlated with lung function. FVC refers to the maximum amount of air exhaled as soon as possible after a maximum inspiration, an important index for determining whether there is resistance in the respiratory tract. Both airway obstruction and prolongation of exhalation can decrease FVC. Raw refers to the pressure differences of unit flow in the airway and reflects the blockage of airways. Application of mechanical ventilation tubes can increase Raw.

Fasting venous blood (5 mL) was collected from the elbow before treatment and 24 hours after treatment in both groups. Blood samples were centrifuged for 5 minutes at 3,500 r/min for serum separation, then stored at -20°C. Levels of inflammatory factors, including C-reactive protein (CRP) and procalcitonin (PCT), were detected by ELISA before and 24 hours after treatment. They were then compared between the two groups. All test operations were performed according to manufacturer instructions for the ELISA kit (Shanghai Boyan, China).

Therapeutic effects of the two groups were evaluated and recorded [8]. Markedly effective: Clinical symptoms, such as fever, cough, and pulmonary encephalopathy, disappeared. Blood gas levels returned to normal after treatment. Imaging results indicated recruitment maneuvers and no inflammation in the lungs. Effective: The patient's clinical symptoms were significantly relieved and blood gas levels were significantly improved after treatment. Imaging showed that partial recruitment maneuvers were gained and inflammatory lesions were significantly reduced. Ineffective: The patient's clinical symptoms and blood gas levels were not improved, or worse after treatment. Imaging showed that no recruitment maneuvers were gained and inflammatory reaction was not improved or even aggravated. Clinical effective rate = (number of markedly effective cases + number of effective cases)/total number of cases * 100%.

Statistical analyses

Data obtained in this study were analyzed using SPSS software version 20.0. Measurement data are expressed as mean ± standard deviation ($\bar{x}$ ± sd). Data conforming to normal distribution was compared by paired t-test (within groups before and after treatment) and independent sample t-test (between two groups), denoted by t. Count data are expressed as cases/percentage (n/%) and compared by Chi-squared test and likelihood ratios. *P*-values of <0.05 indicate statistical significance.

Results

Baseline characteristics

Clinical baseline data, such as gender, age, mean duration of disease, basic diseases, simplified clinical pulmonary infection scores, and acute physiology and chronic health evaluation

Table 2. Comparison of vital signs ($\bar{x}$ ± sd)

Group	Time	Respiratory rate (times/min)	Heart rate (times/min)	Mean arterial pressure (mmHg)
Experimental group (n=35)	15 min before treatment	20.54±7.01	94.96±17.24	81.37±15.62
	15 min after treatment	19.11±5.98	97.13±18.04	83.42±14.69
t		0.918	0.514	0.566
P		0.362	0.609	0.574
Control group (n=35)	15 min before treatment	20.60±6.97	94.89±18.02	81.44±15.81
	15 min after treatment	19.15±6.02	96.25±17.96	83.50±14.26
t		0.931	0.316	0.572
P		0.355	0.753	0.569

Table 3. Comparison of blood-gas parameters ($\bar{x}$ ± sd)

Group	Time	PaO_2 (mmHg)	$PaCO_2$ (mmHg)	PaO_2/FiO_2
Experimental group (n=35)	Before treatment	60.99±8.21	47.27±8.17	280.44±20.69
	After 7 d of treatment	89.04±9.70$^{**,\#\#\#}$	30.36±7.95$^{**,\#\#\#}$	382.56±24.62$^{**,\#\#\#}$
Control group (n=35)	Before treatment	61.23±8.30	46.98±8.24	281.25±20.73
	After 7 d of treatment	76.51±9.95$^{\#\#\#}$	41.50±7.65$^{\#\#\#}$	350.60±23.55$^{\#\#\#}$

Note: Compared with the control group, $^{**}P<0.01$; compared with before treatment within group, $^{\#\#\#}P\leq0.001$. PaO_2: arterial partial pressure of oxygen; $PaCO_2$: partial pressure of carbon dioxide in artery; PaO_2/FiO_2: oxygenation index.

Table 4. Comparison of respiratory function ($\bar{x}$ ± sd)

Group	Time	FEV1 (L)	FVC (L)	Raw (cmH_2O)
Experimental group (n=35)	Before treatment	1.36±0.27	1.87±0.38	22.33±1.01
	After 7 d of treatment	2.60±0.52$^{**,\#\#\#}$	2.81±0.56$^{**,\#\#\#}$	11.96±0.54$^{**,\#\#\#}$
Control group (n=35)	Before treatment	1.38±0.20	1.70±0.44	23.02±0.98
	After 7 d of treatment	2.18±0.63$^{\#\#\#}$	2.12±0.60$^{\#\#\#}$	15.88±0.69$^{\#\#\#}$

Note: Compared with the control group, $^{**}P<0.01$; compared with before treatment within group, $^{\#\#\#}P\leq0.001$. FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; Raw: airway resistance.

II scores, of the two groups were not statistically significant (all P>0.05). Thus, the two groups were comparable. See **Table 1**.

Vital signs

There were no significant differences in respiratory rates, heart rates, and mean arterial pressure, 15 minutes before and 15 minutes after treatment, between the two groups (all P>0.05). See **Table 2**.

Blood-gas parameters

There were no significant differences in blood gas levels between the two groups before treatment (all P>0.05). After 7 days of treatment, levels of PaO_2 and PaO_2/FiO_2 in the two groups were significantly increased (all P≤0.001). The experiment group enjoyed higher levels than the control group (both P<0.01). Levels of $PaCO_2$ were significantly decreased in both groups (both P≤0.001), while $PaCO_2$ in the experimental group was significantly lower than that in the control group (P<0.01). See **Table 3**.

Respiratory function

There were no significant differences in respiratory function indexes between the two groups before treatment (all P>0.05). After 7 days of treatment, levels of FEV1 and FVC in the two groups were significantly increased (all P≤0.001). Levels in the experimental group were higher than those in the control group (both P<0.01). Raw levels were significantly decreased in both groups (both P≤0.001), while the experimental group enjoyed significantly lower levels than the control group (P<0.01). See **Table 4**.

Table 5. Comparison of inflammatory factors ($\bar{x}$ ± sd)

Group	Time	CRP (mg/L)	PCT (μg/L)
Experimental group (n=35)	Before treatment	78.89±8.45	28.33±2.89
	After 24 h of treatment	36.72±7.17$^{**,###}$	15.31±2.36$^{**,###}$
Control group (n=35)	Before treatment	77.97±9.02	28.40±2.75
	After 24 h of treatment	68.34±6.05$^{###}$	20.55±3.09$^{###}$

Note: Compared with the control group, **P<0.01; compared with before treatment within group, $^{###}$P≤0.001. CRP: C-reactive protein; PCT: procalcitonin.

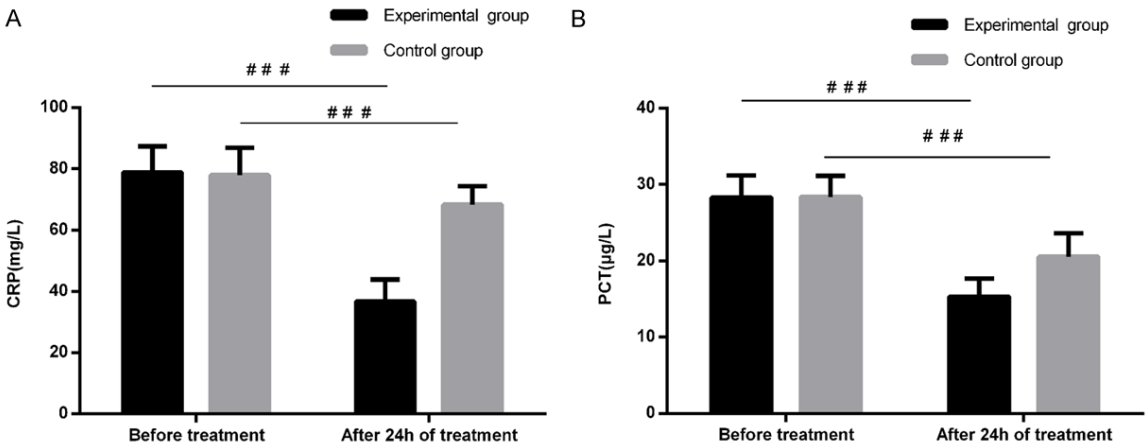

Figure 1. Comparison of inflammatory factors. A: Comparison of C-reactive protein, B: Comparison of procalcitonin; compared with before treatment within group, $^{###}$P≤0.001. CRP, C-reactive protein; PCT, procalcitonin.

Table 6. Comparison of clinical efficacy and prognosis

Group	Markedly effective (n)	Effective (n)	Ineffective (n)	Effective rate (n, %)	28 d mortality (n, %)
Experimental group (n=35)	19	12	4	31 (88.57)	2 (5.71)
Control group (n=35)	14	10	11	24 (68.57)	8 (22.86)
χ^2				4.158	4.200
P				0.041	0.040

Inflammatory factors

There were no significant differences in CPR and PCT between the two groups before treatment (both P>0.05). After 24 hours of treatment, levels of CPR and PCT in the two groups were significantly decreased (all P≤0.001). Levels in the experimental group were lower than those in the control group (both P<0.01). See **Table 5** and **Figure 1**.

Clinical efficacy and prognosis

Clinical effective rates of the experimental group were significantly higher than those of the control group. Moreover, 28-day mortality was significantly lower than that of the control group. Differences between the two groups were statistically significant (both P<0.05). See **Table 6**.

Discussion

Severe pneumonia is a pulmonary inflammatory reaction induced by pathogens. It is characterized by rapid respiratory rates, low body temperatures, pulmonary oxygenation dysfunction, and other clinical manifestations. This disease has a high rate of disability and death and is difficult to treat [9]. Mechanical ventilation is helpful for patients with severe pneumonia to get through hypoxemia, due to the commonly

poor effectiveness of routine antibiotic drugs on hypoxemia during treatment [10]. With the rapid development of medical technology, application of FBL for treatment of patients with severe pneumonia, along with mechanical ventilation, can directly identify lesions, remove sputum, and improve ventilation function. However, FBL does not help with the removal of mucus/sputum scabs and mucus in the small airways in lungs [11]. Scholars have reported that VSE can effectively reach the lesions and remove mucus/sputum scabs and mucus in small airways, such as the bronchi, maintaining airway function in the body [12]. Other studies have found that VSE has a significant effect in the treatment of ventilator-associated pneumonia [13]. A clinical study showed that VSE for patients with chronic obstructive pulmonary disease could not only maintain airway patency, but also effectively enhance the comfort of patients, improve clinical efficacy significantly, and shorten mechanical ventilation times to a great extent, thereby facilitating the recovery of body function [14]. However, application of VSE for patients with severe pneumonia on mechanical ventilation has rarely been reported. Its safety has not been clearly described. Results of this study show that there were no significant differences in respiratory rates, heart rates, and mean arterial pressure, 15 minutes before and 15 minutes after treatment, between the two groups. This indicates that the combination of FBL with VSE for patients with severe pneumonia on mechanical ventilation will not pose a threat to patient lives. Furthermore, the operation is easy to master.

Studies have shown that alveolar oxygenation dysfunction and abnormal blood gas levels, accompanied by different degrees of airway resistance and significant reduction in lung compliance, are the main obvious clinical manifestations of severe pneumonia. Timely removal of mucus/sputum scabs and mucus in small airways with effective movement from small airways to major airways for facilitating FBL is the key in treating severe pneumonia [15]. One study found that application of the VSE machine for pulmonary alveolar proteinosis could significantly reduce the frequency of dyspnea. Imaging results showed a significant reduction in bilateral pulmonary infiltration and significant improvements in blood gas indexes and respiratory function [16]. Another study showed that FBL assisted with VES for patients with severe pneumonia in intensive care units could significantly reduce the areas of infiltrative shadows in bilateral lung fields, expand the diffusion area of the lungs, and further improve ventilation function of the body [17]. Results of this study showed that levels of PaO_2, PaO_2/FiO_2, FEV1, and FVC in the two groups were significantly increased after 7 days of treatment, compared with levels before treatment. Levels in the experimental group were significantly higher than those in the control group. Levels of $PaCO_2$ and Raw decreased in both groups and levels in the experimental group were significantly lower than those in the control group. Present results suggest that VSE could significantly improve blood gas levels and respiratory function of patients with severe pneumonia on mechanical ventilation. The reason may be that the directional tapping by VSE machine can not only loosen mucus or mucus/sputum scabs in small airways due to the force perpendicular to the body's surface, but also promote the discharge of mucus or sputum in the bronchi by horizontal force, thus maintaining airway patency, promoting recruitment maneuvers, improving lung compliance, raising levels of PaO_2/FiO_2, and accelerating the recovery of respiratory function [18].

Research has shown that severe pneumonia on mechanical ventilation is often accompanied with serious basic diseases and low immune function. Moreover, in-bed times of the patients are relatively long. Thus, their bodies are in inflammatory states [19]. Presently, CRP and PCT are sensitive and effective indicators for clinical diagnosis of infections. CRP is an acute phase protein. Its abnormal high expression will occur at the early stage of the disease. PCT is highly sensitive to diseases caused by bacterial infections. It has been widely examined for the diagnosis and prognosis of such diseases [20, 21]. Reports have shown that VSE could effectively and completely remove sputum and clear the inflammatory factors in the deep part of airway, which represents an important role in improving respiratory function, clinical therapeutic effects, and prognosis [22]. A study including 120 patients with bronchopneumonia treated by FBL combined with VSE showed that combined treatment could better remove secretions in the airways, restore airway patency, help eliminate pathogenic factors, and inhibit occurrence of inflammatory reactions, thus forming a virtuous circle [23]. This study showed

that levels of CRP and PCT in the two groups were significantly lower after 24 hours of treatment and the experimental group enjoyed significantly lower levels than the control group. Also, in the experimental group, clinical effective rates were significantly higher than those of the control group. Also, 28-day mortality was significantly lower than that of the control group, indicating that assisted treatment of VSE for patients with severe pneumonia on mechanical ventilation could significantly alleviate inflammation, achieving favorable clinical and prognostic results. The reason may be that FBL combined with VSE can effectively and completely remove pathogenic factors in the deep part of airway, thus accelerating sputum removal, improving respiratory function, and effectively clearing inflammatory factors. However, the sample size in this study was small and the time involved was relatively short. Therefore, an optimized treatment plan with a larger sample size is necessary for future studies, aiming to improve patient respiratory function and comfort levels.

In summary, combined treatment of FBL with VSE for patients with severe pneumonia on mechanical ventilation can effectively alleviate inflammatory reactions, facilitate the recovery of respiratory function, and improve prognosis. It is worthy of clinical application.

Disclosure of conflict of interest

None.

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References

[1] Kishimoto M, Yamana H, Inoue S, Noda T, Myojin T, Matsui H, Yasunaga H, Kawaguchi M and Imamura T. Sivelestat sodium and mortality in pneumonia patients requiring mechanical ventilation: propensity score analysis of a Japanese nationwide database. J Anesth 2017; 31: 405-412.

[2] Yan Y and Hu C. Influential factors for mechanical ventilation offline in patients with severe pneumonia. J Central South Univ (Med Ed) 2015; 40: 107-111.

[3] Ortín A, Jiménez R, Rebollo S, Herrera L, Moreno S, Fernández A, Galindo M, Murcia J, Tárraga L and Ojados A. Outcome of patients with initial non-mechanical ventilation management in severe pneumonia. Intensive Care Medicine Experimental 2015; 3: 1-1.

[4] Nguyen Thi Dieu T, Pham Nhat A, Craig TJ and Duong-Quy S. Clinical characteristics and cytokine changes in children with pneumonia requiring mechanical ventilation. J Int Med Res 2017; 45: 1805-1817.

[5] Eom JS, Song WJ, Yoo H, Jeong BH, Lee HY, Koh WJ, Jeon K and Park HY. Chronic obstructive pulmonary disease severity is associated with severe pneumonia. Ann Thorac Med 2015; 10: 105-111.

[6] Wu J, Jin YU, Li H, Xie Z, Li J, Ao Y and Duan Z. Evaluation and significance of C-reactive protein in the clinical diagnosis of severe pneumonia. Exp Ther Med 2015; 10: 175-180.

[7] Monsel A, Zhu YG, Gennai S, Hao Q, Hu S, Rouby JJ, Rosenzwajg M, Matthay MA and Lee JW. Therapeutic effects of human mesenchymal stem cell-derived microvesicles in severe pneumonia in mice. Am J Respir Crit Care Med 2015; 192: 324-336.

[8] Tagami T, Matsui H and Yasunaga H. Antithrombin and mortality in severe pneumonia patients with sepsis-associated disseminated intravascular coagulation: an observational nationwide study: reply. J Thromb Haemost 2015; 13: 680-682.

[9] Agweyu A, Gathara D, Oliwa J, Muinga N, Edwards T, Allen E, Maleche-Obimbo E and English M. Oral amoxicillin versus benzyl penicillin for severe pneumonia among kenyan children: a pragmatic randomized controlled noninferiority trial. Clin Infect Dis 2015; 60: 1216-1224.

[10] Chisti MJ, Salam MA, Smith JH, Ahmed T, Pietroni MA, Shahunja KM, Shahid AS, Faruque AS, Ashraf H, Bardhan PK, Sharifuzzaman, Graham SM and Duke T. Bubble continuous positive airway pressure for children with severe pneumonia and hypoxaemia in Bangladesh: an open, randomised controlled trial. Lancet 2015; 386: 1057-1065.

[11] Shi ZY, Qin YL, Zhu YM, Pan XJ, Zhou X, Tan XT and Liu YH. Effect of bronchoalveolar lavage by fiber bronchoscope with vibratory sputum excretion for the treatment of patients with severe pneumonia on mechanical ventilation: a prospective, randomized, controlled study of 286 patients. Chin Crit Care Med 2017; 29: 66-70.

[12] Zhou Z, Han XT, Ning FL, Wen H, Fan MY, Yuan X, Luo JY and Zhao Y. Clinical effect of pulmonary rehabilitation therapy including respiratory exercise and vibration expectoration on patients with pulmonary infection after abdominal

surgery. Chin Crit Care Med 2017; 29: 255-259.
[13] Ying LJ, Lv T, Li ZX and Lu D. Curative effect of ambroxol combined with vibratory phlegm ejection machine on ventilator associated pneumonia. Chin J Geriatr 2014; 33: 871-873.
[14] Chen M and Zhu MY. Application of vibratory PEP phlegm ejection in the pulmonary rehabilitation of patients with chronic obstructive pulmonary disease. Journal of Clinical Pulmonary Medicine 2017; 22: 1323-1326.
[15] Ohta R and Shimabukuro A. Rural physicians' scope of practice on remote islands: a case report of severe pneumonia that required overnight artificial airway management. J Rural Med 2017; 12: 53-55.
[16] Zhang PY. Nursing care of alveolar proteinosis by whole lung lavage combined with vibration phlegm ejection machine. Shanghai Nursing Journal 2013; 13: 55-57.
[17] Seki M, Fuke R, Oikawa N, Hariu M and Watanabe Y. Association of influenza with severe pneumonia/empyema in the community, hospital, and healthcare-associated setting. Respir Med Case Rep 2016; 19: 1-4.
[18] Muro F, Mtove G, Mosha N, Wangai H, Harrison N, Hildenwall H, Schellenberg D, Todd J, Olomi R and Reyburn H. Effect of context on respiratory rate measurement in identifying non-severe pneumonia in African children. Trop Med Int Health 2015; 20: 757-765.
[19] Tagami T, Matsui H and Yasunaga H. Antithrombin or thrombomodulin administration in severe pneumonia patients with sepsis and disseminated intravascular coagulation: reply to two papers. J Thromb Haemost 2015; 13: 686-688.
[20] Brunkhorst FM, Al-Nawas B, Krummenauer F, Forycki ZF and Shah PM. Procalcitonin, C-reactive protein and APACHE II score for risk evaluation in patients with severe pneumonia. Clin Microbiol Infect 2002; 8: 93-100.
[21] Porfyridis I, Georgiadis G, Vogiazianos P and Georgiou A. Late-breaking abstract: Evaluation of CRP, PCT, clinical pulmonary infection score and pneumonia severity scores for the diagnosis and prognosis of nursing home acquired pneumonia. European Respiratory Journal 2011; 179.
[22] Li W, Ding C and Yin S. Severe pneumonia in the elderly: a multivariate analysis of risk factors. Int J Clin Exp Med 2015; 8: 12463-12475.
[23] Tsai HC and Chang SC. Fatty acid binding proteins as biomarkers of disease severity and response to treatment in severe pneumonia required admission to intensive care unit. Ann Transl Med 2016; 4: 415.