Comparison of Respiratory Parameters and Plasma Cytokine Levels between Treatment with Salmeterol/Fluticasone and Ipratropium/Terbutaline/Budesonide in Mechanically Ventilated COPD Patients

Huang-Pin Wu[1,2], MD; Yu-Chih Liu[1,2], MD; Shi-Chuan Lin[2], RT; Ming-Yi Chien[2], RT; Fang-Chun Liao[2], RT; Shu-Chuan Chang[2], RT; Wen-Bin Shieh[1,2], MD

Background: It is unknown whether the bronchodilation and anti-inflammatory effects of inhaled salmeterol and fluticasone (SF) are better than those of traditionally inhaled ipratropium, terbutaline and budesonide (ITB) in mechanically ventilated patients with chronic obstructive pulmonary disease (COPD).

Methods: Nineteen stable COPD patients with respiratory failure were randomly enrolled into two groups. Patients were treated with inhaled SF delivered by a metered-dose inhaler with a spacer or with inhaled nebulized ITB. Respiratory parameters were measured for 7 days and plasma cytokine levels were measured on days 1 and 7.

Results: The kinetic curve of the rapid shallow index (RSI) from day 1 to day 7 was significant lower in the SF group than that in the ITB group. There were no significant differences in minute ventilation, intrinsic positive end expiratory pressure, and airway resistance between the ITB and SF groups from day 1 to day 7. There were no differences in plasma interleukin (IL)-6, IL-10, IL-12, and transforming growth factor-beta1 levels between day 1 and day 7 in the ITB or SF group.

Conclusions: Patients with inhaled SF treatment had a lower RSI. The effects of bronchodilators and anti-inflammation were similar between inhaled SF and ITB in COPD patients with ventilator support.

(Chang Gung Med J 2012;35:373-81)

Key words: chronic obstructive pulmonary disease, respiratory failure, ventilator, salmeterol/fluticasone

Patients with chronic obstructive pulmonary disease (COPD) may have symptoms and signs of exacerbation. An exacerbation of COPD is defined as an event in the natural course of the disease characterized by a change in the patient's baseline dyspnea, cough or sputum that is beyond normal variations.[1] Systemic corticosteroids combined with inhaled β2 agonists and anticholinergics are beneficial in the management of COPD exacerbation.[2] The impact of exacerbation is significant and symptoms

From the [1]Division of Pulmonary, Critical Care and Sleep Medicine; [2]Department of Respiratory Therapy, Chang Gung Memorial Hospital at Keelung, Chang Gung University College of Medicine, Taoyuan, Taiwan.
Received: Sep. 10, 2010; Accepted: Mar. 14, 2012
Correspondence to: Dr. Wen-Bin Shieh, Division of Pulmonary, Critical Care and Sleep Medicine, Chang Gung Memorial Hospital at Keelung. 222, Maijin Rd., Anle District, Keelung City 204, Taiwan (R.O.C.) Tel: 886-2-24313131 ext. 3173; Fax: 886-2-24335342; E-mail: binshieh@cgmh.org.tw

and lung function may take several weeks to recover to baseline values.[3] Intravenous methylprednisolone with inhaled ipratropium and terbutaline is currently widely accepted in treating ventilated COPD patients with acute exacerbations. After a patient's condition has become relatively stable with no wheezing, and little sputum production, systemic corticosteroids are changed to inhaled corticosteroids (ICS) for maintenance treatment and weaning from the ventilator. A high dose of systemic corticosteroids has well-known side effects. After stabilization of a patient with COPD stage III or IV following an exacerbation, regular treatment with ICS and long-acting inhaled bronchodilators is suggested.[2,4-6]

The pathophysiology of respiratory failure in patients with COPD is associated with many factors. The most important factor is increased airway resistance due to airway infection, with resulting dynamic hyperinflation and increased intrinsic positive end expiratory pressure (PEEP). Some parameters, such as the minute ventilation (MV), vital capacity, negative inspiratory force, and rapid shallow index (RSI), can provide important information about the potential for discontinuing ventilator support.[7] The most frequently used parameter is the RSI because it provides 4.67 of a positive likelihood ratio to predict successful ventilator discontinuation with 105/L of a threshold value.[8] It is suggested that a spontaneous breathing trial (SBT) be performed in patients with respiratory failure who have a high ventilator discontinuation potential.

One target in weaning is to reduce the ventilator setting to a PEEP ≤ 5 cmH_2O.[9] It has been reported that inhaled fluticasone propionate reduces airway resistance in ventilator-dependent patients with COPD.[10] It is unclear whether ICS combined with a long-acting β2-agonist (LABA) via a metered-dose inhaler (MDI) can decrease intrinsic PEEP (PEEPi) in patients using ventilators by reducing airway resistance.

Plasma interleukin (IL)-6 levels in COPD patients have been shown to decrease after recovery from exacerbations or after 7 days of treatment.[11,12] Plasma transforming growth factor-beta1 (TGF-β1) levels have been shown to be inversely correlated with the forced expiratory voume in 1 second (FEV1) (% predicted) and forced vital capacity (FVC) (% predicted) in COPD patients.[13] Greatly increased numbers of macrophages are seen in the airways and lungs of COPD patients compared with healthy people. Activated macrophages produce IL-12. In COPD patients, circulating CD4 T cells produce IL-10 less frequently than in healthy subjects.[14] The biomarkers in COPD seem to have been investigated less extensively than the markers in asthma. Whether ICS can reduce systemic inflammatory biomarkers is unclear,[15] so testing old and new biomarkers should be attempted in COPD patients.

In clinical practice, physicians have two choices of therapy in mechanically ventilated COPD patients. One is nebulized budesonide, ipratropium and terbutaline. The other is inhaled fluticasone and salmeterol. It is unknown which therapy is better. Thus, we designed a prospective randomized study to evaluate the 7-day effects of combined salmeterol and fluticasone treatment (SF group) given by MDI compared with combined nebulized ipratropium, terbutaline and budesonide treatment (ITB group) in patients with COPD using ventilators. The purpose of this study was to find the better inhalation therapy by comparing the weaning rate, respiratory parameters and systemic biomarkers in these 2 groups.

METHODS

Participants

Stable intubated COPD patients admitted to our medical intensive care unit (ICU) because of acute exacerbation and respiratory failure with ventilator use (pressure support mode) and a PEEP ≥ 8 cmH_2O were continuously enrolled from July 2007 to June 2009. Clinical stability was defined by the following criteria: (1) absence of hyperthermia or hypothermia; (2) stable hemodynamics (mean arterial blood pressure between 90 and 65 mmHg); (3) a conscious and cooperative state; and (4) no use of respiratory depressant medication. Patients were excluded if they had pneumonia, a tracheostomy, cancer, uncontrolled arrhythmia, trauma, use of systemic steroids or a history of upper abdominal surgery. Clinical characteristics were recorded, including the Acute Physiology and Chronic Health Evaluation (APACHE) II score, gender, age, and days of ventilator use. Informed consent was given by each patient or their family. All participants were monitored for 30 days. This study was approved by our institutional review board (95-1207B).

Treatment protocol

All patients were treated with intravenous methylprednisolone 40 mg every 12 h and nebulized ipratropium 0.5 mg / terbutaline 5 mg tid beginning with admission to the medical ICU. After patients had no wheezing for 2 days, they were then randomly divided into the SF and ITB groups without use of intravenous methyprednisolone. We waited for 2 days to confirm there was no active brochoconstriction. Treatment in the SF group was changed to salmeterol 25 μg / fluticasone 250 μg (GlaxoSmith) 2 puffs bid which were administered with an MDI adapted to the inspiratory limb of the ventilator circuit using an Aerovent spacer (Monaghan Medical Corporation, NY, U.S.A.). Treatment in the ITB group was changed to nebulized ipratropium 0.5 mg tid, terbutaline 5 mg tid, and budesonide 1 mg bid. The day the patients were prescribed either of the two inhalation therapies was set as day 1.

Weaning guide

Weaning was performed according to the general weaning guidelines of our department of respiratory therapy.[16] Briefly, respiratory therapists screened for the following weaning criteria daily:

1. Mean blood pressure greater than 65 mmHg
2. Heart rate less than 140 beats per minute
3. SpO_2 greater than 92%
4. PEEP less than 8 cmH_2O
5. FiO_2 less than 35%
6. Pressure-support mode ventilation with pressure less than 10 cmH_2O

Patients meeting the criteria entered a 2-h SBT. The SBT was stopped for the following reasons:

1. Respiratory rate greater than 35 breaths/min for more than 5 min
2. Saturation of less than 90% for more than 30 s despite 50% FiO_2 with O_2 supplementation
3. A 20% decrease or increase in heart rate for more than 5 min
4. Persistent systolic blood pressure over 180 or less than 90 mmHg on repeated measurements
5. Diaphoresis or paradoxical movement of the abdomen for 5 min

If patients passed the SBT successfully, extubation was performed. Successful weaning was defined as no requirement for reintubation or non-invasive positive pressure ventilation.

Measurements of respiratory parameters

Respiratory parameters including static PEEPi, airway resistance, MV, and RSI were measured daily at 12:00 noon for 7 days before an attempt at spontaneous breathing. Static PEEPi and airway resistance were measured by an Evita® 2 dura ventilator (Draeger Medical, Inc., Lubeck, Germany).

Measurement of plasma cytokine levels

Plasma was obtained from 2 ml of whole blood after centrifugation at 12:00 noon on day 1 and day 7 before the medication was inhaled. Samples were stored at –80°C until use. Plasma levels of IL-6 and TGF-β1 were measured using human enzyme-linked immunosorbent assay (ELISA) kits (R & D Systems, Minnesota, U.S.A.). Plasma levels of IL-10 were measured using an ELISA kit (Pierce Biotechnology, Illinois, U.S.A.). Plasma levels of IL-12 were measured using an IL-12p40 ELISA kit (Becton Dickinson, CA, U.S.A.).

Statistical analysis

Statistical analyses were done using the Statistical Package for the Social Sciences (SPSS) software V17.0.0 for Windows (IBM, Corp., New York, U.S.A.). Continuous variables are represented as means ± standard deviation. Categorical variables were compared using the chi-Square test. The Mann-Whitney test was employed to compare differences in continuous variables and changes in the cytokine levels after 6 days between the SF and ITB groups. The Wilcoxon signed-ranks test was used to compare the differences in plasma cytokine levels between day 1 and day 7. The differences in sequential data of respiratory parameters between the SF and ITB groups were compared by generalized estimating equations which account for correlation within subjects.[17] The dependent variables were respiratory parameters and the predictor was the patient group. A p value less than 0.05 was considered statistically significant.

RESULTS

Nineteen patients were enrolled in this study. There were no differences in age, sex, APACHE II score, height, and body weight on day 1 between the

two groups (Table). There were no significant differences in the MV, PEEPi, airway resistance, or RSI between the ITB and SF groups from day 1 to day 7 (Fig. 1). The 7-day kinetic curve of the RSI in the SF group was significantly lower than that in the ITB group ($p = 0.022$). The kinetic curves of the MV, PEEPi, and airway resistance did not differ between the ITB and SF groups. There were no differences in plasma IL-6, IL-10, IL-12, and TGF-beta1 levels between day 1 and day 7 in the ITB and SF groups (Fig. 2). The changes in plasma IL-6, IL-10, IL-12, and TGF-beta1 levels after 7 days did not differ between the ITB and SF groups.

DISCUSSION

This study is the first to show that the respiratory parameters of ventilated COPD patients in the first 7 days of treatment with inhaled salmeterol/fluticasone are similar to those using conventional nebulized ipratropium/terbutaline/budesonide treatment. This suggests that salmeterol/fluticasone and ipratropium/terbutaline/budesonide provide parallel bronchodilatory effects in the airways of ventilated COPD patients. However, the kinetic curve of the RSI in patients treated with inhaled salmeterol/fluticasone was lower than that in patients with conventional nebulized ipratropium/terbutaline/budesonide. This means that patients treated by inhaled salmeterol/fluticasone could attempt a SBT earlier then those receiving ITB.

Few studies have reported on the respiratory parameters in intubated ventilated patients with COPD. Nava et al. found that inhaled fluticasone via MDI reduced PEEPi and airway resistance in ventilator-dependent COPD patients after 6 days of treatment.[10] FEV1 changes significantly underestimated the bronchodilator response compared with changes in airway resistance. In our study, the mean airway resistance was decreased on day 3 compared with that on day 1. However, statistical significance was not achieved, even though a LABA was prescribed at the same time (data not shown). The possible cause was the dose of inhaled fluticasone. A daily dose of 2000 μg fluticasone was used in Nava's study compared with 1000 μg fluticasone in our study. The findings suggest that 2000 μg might be a better dose for fluticasone in ventilator-dependent COPD patients.

After 6 days of treatment, plasma IL-6, IL-10, IL-12 and TGF-beta1 levels had not changed in either group. This suggests that inhaled fluticasone or budesonide could not inhibit systemic inflammation or promote systemic anti-inflammation in a such short period. Importantly, changes in plasma IL-6, IL-10, IL-12 and TGF-beta1 levels after 7 days of treatment did not differ between the SF and ITB groups. These findings indicate that the effects on systemic biomarkers of inhaled fluticasone 1 mg daily via MDI and 2 mg budesonide via a nebulizer were equal.

Drugs must be transformed to aerosols for delivery to the airway. There are two methods to do this. One is to nebulize a liquid drug to an aerosol, the other is to deliver a dry powder by an MDI. In clinical practice, most patients using ventilators receive

Table Clinical Characteristics of Ventilated Patients with Chronic Obstructive Pulmonary Disease on Day 1

	ITB N = 10	SF N = 9	*p* value
Age, years	81.5, 70.0-90.0	77.0, 58.0-87.0	0.18
Sex, male (%)	9 (90.0)	7 (77.8)	0.58
APACHE II score	17.5, 10.0-27.0	18.0, 14.0-31.0	0.46
Height, cm	157.0, 154.0-170.0	165.0, 135.0-172.0	0.90
Body weight, kg	46.5, 35.0-80.0	51.0, 32.0-70.0	0.68
Weaning success in 30 days (%)	4 (40.0)	5 (55.6)	0.66

Abbreviations: ITB: ipratropium, terbutaline, and budesonide; SF: salmeterol and fluticasone; APACHE: Acute Physiology and Chronic Health Evaluation.

Values are given as median and range or number (%).

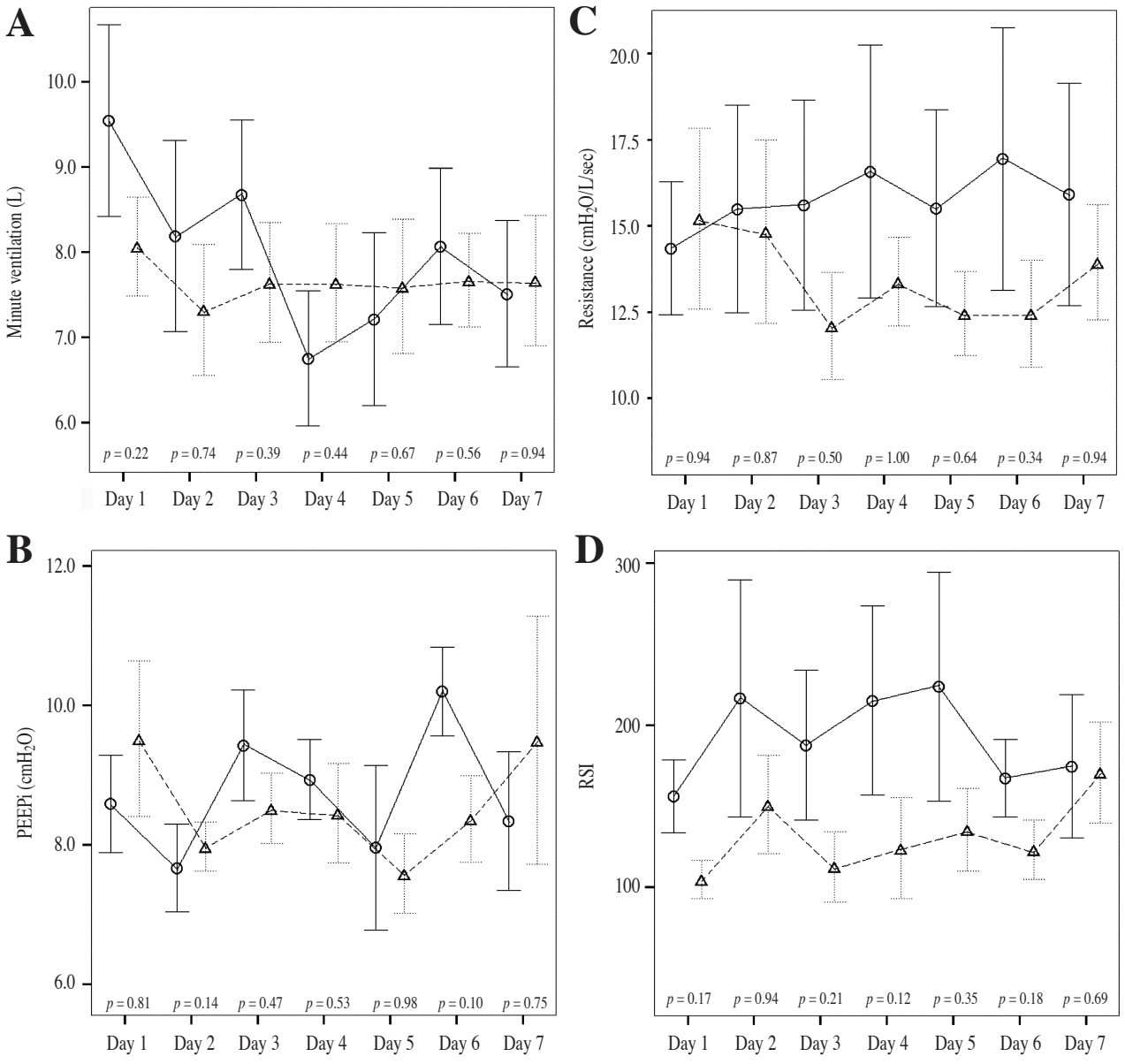

Fig. 1 There were no significant differences in the minute ventilation (A), intrinsic positive end-expiratory pressure (PEEPi) (B), airway resistance (C), and rapid shallow index (RSI) (D) between the ipratropium/terbutaline/budesonide (ITB) (circles) and salmeterol/fluticasone (SF) (triangles) groups from day 1 to day 7. Error bars show mean ± 1.0 standard error of the mean. The 7-day kinetic curve of the RSI in the SF group was significantly lower than that in the ITB group ($p = 0.022$). The 7-day kinetic curves of the MV, PEEPi, and airway resistance did not differ between the ITB and SF groups.

inhaled medication via small-volume aerosol delivery systems (nebulizer). However, a large number of clinical trials have shown that condensation in the ventilator circuit can be contaminated by a patient's secretions. The American Thoracic Society recommends that condensation be prevented from entering either the endotracheal tube or inline medication neubulizers.[18] Nebulizers are more time-consuming to use than MDIs and require equipment maintenance and cleaning for infection control.[19] Using an MDI with a spacer is an efficient method for delivering inhaled drugs to the lungs of mechanically venti-

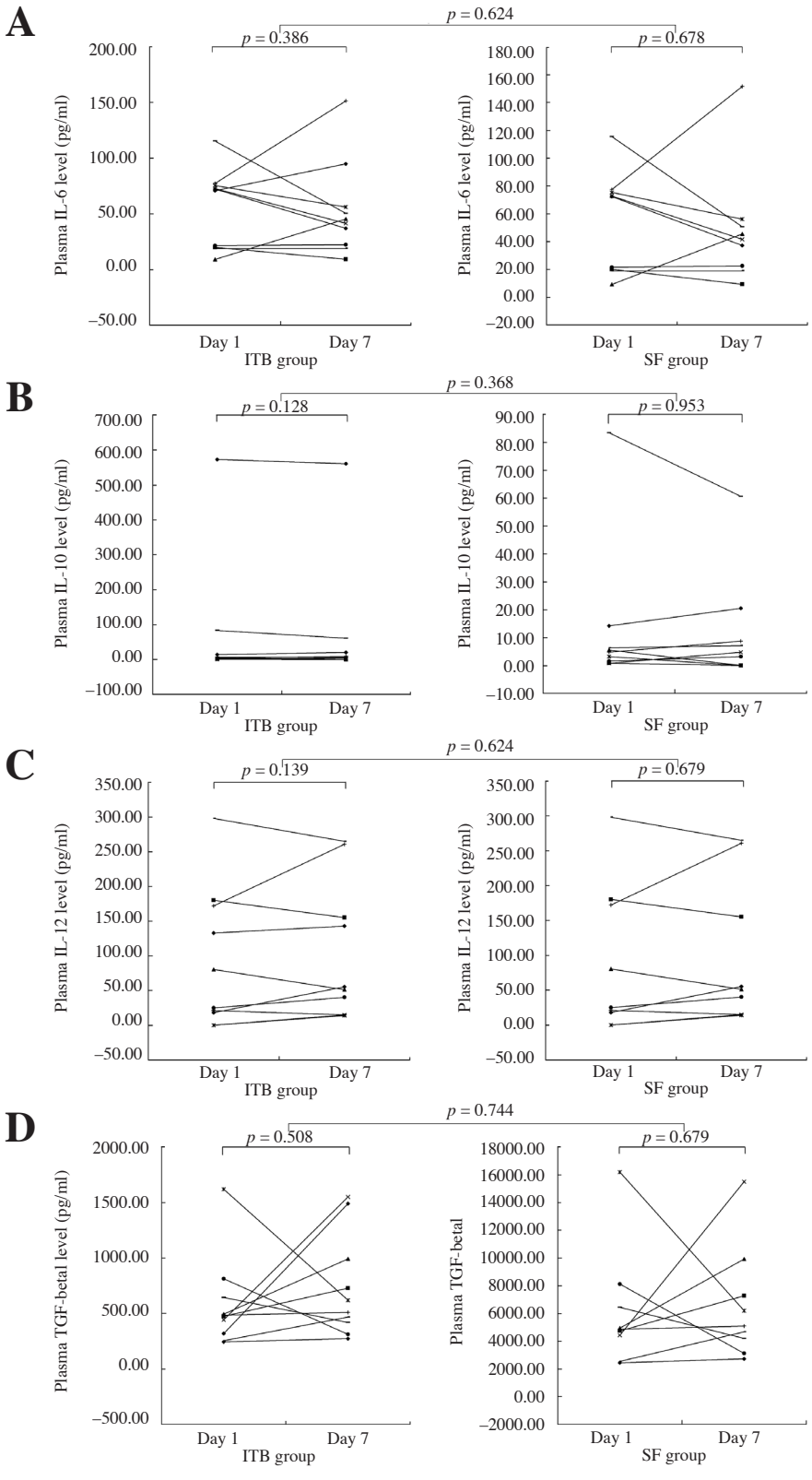

Fig. 2 There were no differences in plasma interleukin (IL)-6 (A), IL-10 (B), IL-12 (C), and transforming growth factor (TGF)-beta1 (D) levels between day 1 and day 7 in the ipratropium/terbutaline/budesonide (ITB) and salmeterol/fluticasone (SF) groups. The changes in plasma IL-6, IL-10, IL-12, and TGF-beta1 levels after 7 days did not differ between the ITB and SF groups.

lated patients.[20,21] In contrast, the performance efficiency of a jet nebulizer is highly variable and depends on many factors (e.g., driving gas flow and fluid volume).[22] At present, the consensus is that a combination of an MDI and a spacer is more efficient than a jet nebulizer for aerosol delivery to the lungs of intubated ventilated patients.[23] In this study, both a jet nebulizer and MDI with a spacer achieved comparable pulmonary parameters, because the drug dose in the nebulizer was much higher than that administered from the MDI with a spacer.

In this study, comparison of the total cost of care between the SF and ITB groups was difficult. However, the daily drug costs in the SF group were 66.1 New Taiwan dollars (NT$), lower than the ITB group at 239.7 NT$. A prospective, randomized, double-blinded, placebo-controlled trial found that total costs for acute asthma adult patients in the emergency department were lower in an MDI group than a nebulizer group.[24] Thus, an MDI with a spacer may be a more economical alternative to nebulizer delivery.

This study was carried out for 2 years because of the strict inclusion and exclusion criteria. There are few pure intubated COPD patients without pneumonia. Intubated COPD patients with pneumonia were not enrolled because pneumonia influences respiratory parameters and plasma cytokine levels, compared with inhaled bronchodilator and corticosteroid. There were 4 limitations to this study. First, the respiratory parameters were not determined before delivery of the inhaled medication. The respiratory parameters were checked after 3 hrs of ICS and inhaled bronchodilators because the effect of salmeterol reaches peak level after 3 hrs of inhalation.[25] Second, the respiratory parameters and cytokine levels were not determined during COPD acute exacerbation, mainly because of ethical concerns. The concept of administering ICS to COPD patients with an acute exacerbation is not widely accepted by pulmonary physicians. Patients could not be allowed not to use systemic steroids during a COPD acute exacerbation for this clinical study. Third, FEV1 and FVC data were unavailable because they can cannot be measured in intubated patients. Fourth, the sample size in the two groups was small. Bias might have occurred in the statistical analysis.

In conclusion, patients with inhaled SF treatment had a lower RSI than those with ITB treatment. In stable intubated COPD patients on ventilator support, the effects on respiratory parameters and systemic biomarkers with inhaled salmeterol and fluticasone via an MDI with a spacer were similar to those of inhaled nebulized ipratropium, terbutaline and budesonide in this preliminary study. Based on our results, salmeterol and fluticasone given by an MDI with a spacer might be the choice of inhalation treatment when an intubated ventilator patient needs ICS treatment and inhaled bronchodilators.

Acknowledgements

The authors thank members of the department of respiratory therapy for providing clinical assistance. The authors would also like to thank Chang Gung Memorial Hospital, Keelung, Taiwan, R.O.C., for financially supporting this research under contract number CMRPG250231.

REFERENCES

1. Burge S, Wedzicha JA. COPD exacerbations: definitions and classifications. Eur Respir J Suppl 2003;41:46s-53s.
2. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. Updated 2008. USA: National Institutes of Health, 2008.
3. Seemungal TA, Donaldson GC, Bhowmik A, Jeffries DJ, Wedzicha JA. Time course and recovery of exacerbations in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2000;161:1608-13.
4. Mahler DA, Wire P, Horstman D, Chang CN, Yates J, Fischer T, Shah T. Effectiveness of fluticasone propionate and salmeterol combination delivered via the Diskus device in the treatment of chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2002;166:1084-91.
5. Calverley P, Pauwels R, Vestbo J, Jones P, Pride N, Gulsvik A, Anderson J, Maden C. Combined salmeterol and fluticasone in the treatment of chronic obstructive pulmonary disease: a randomised controlled trial. Lancet 2003;361:449-56.
6. Szafranski W, Cukier A, Ramirez A, Menga G, Sansores R, Nahabedian S, Peterson S, Olsson H. Efficacy and safety of budesonide/formoterol in the management of chronic obstructive pulmonary disease. Eur Respir J 2003;21:74-81.
7. MacIntyre NR. Evidence-based ventilator weaning and discontinuation. Respir Care 2004;49:830-6.
8. MacIntyre N. Discontinuing mechanical ventilatory support. Chest 2007;132:1049-56.
9. Dellinger RP, Carlet JM, Masur H, Gerlach H, Calandra T, Cohen J, Gea-Banacloche J, Keh D, Marshall JC,

Parker MM, Ramsay G, Zimmerman JL, Vincent JL, Levy MM. Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. Crit Care Med 2004;32:858-73.
10. Nava S, Compagnoni ML. Controlled short-term trial of fluticasone propionate in ventilator-dependent patients with COPD. Chest 2000;118:990-9.
11. Pinto-Plata VM, Livnat G, Girish M, Cabral H, Masdin P, Linacre P, Dew R, Kenney L, Celli BR. Systemic cytokines, clinical and physiological changes in patients hospitalized for exacerbation of COPD. Chest 2007;131: 37-43.
12. Perera WR, Hurst JR, Wilkinson TM, Sapsford RJ, Mullerova H, Donaldson GC, Wedzicha JA. Inflammatory changes, recovery and recurrence at COPD exacerbation. Eur Respir J 2007;29:527-34.
13. Mak JC, Chan-Yeung MM, Ho SP, Chan KS, Choo K, Yee KS, Chau CH, Cheung AH, Ip MS. Elevated plasma TGF-beta1 levels in patients with chronic obstructive pulmonary disease. Respir Med 2009;103:1083-9.
14. Zhu X, Gadgil AS, Givelber R, George MP, Stoner MW, Sciurba FC, Duncan SR. Peripheral T cell functions correlate with the severity of chronic obstructive pulmonary disease. J Immunol 2009;182:3270-7.
15. Sin DD, Man SF, Marciniuk DD, Ford G, FitzGerald M, Wong E, York E, Mainra RR, Ramesh W, Melenka LS, Wilde E, Cowie RL, Williams D, Gan WQ, Rousseau R. The effects of fluticasone with or without salmeterol on systemic biomarkers of inflammation in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2008;177:1207-14.
16. Huang CJ, Lin HC. Association between adrenal insufficiency and ventilator weaning. Am J Respir Crit Care Med 2006;173:276-80.
17. van Houwelingen HC. The future of biostatistics: expecting the unexpected. Stat Med 1997;16:2773-84.
18. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005;171:388-416.
19. Geller DE. Comparing clinical features of the nebulizer, metered-dose inhaler, and dry powder inhaler. Respir Care 2005;50:1313-21.
20. Marik P, Hogan J, Krikorian J. A comparison of bronchodilator therapy delivered by nebulization and metered-dose inhaler in mechanically ventilated patients. Chest 1999;115:1653-7.
21. Arnon S, Grigg J, Nikander K, Silverman M. Delivery of micronized budesonide suspension by metered dose inhaler and jet nebulizer into a neonatal ventilator circuit. Pediatr Pulmonol 1992;13:172-5.
22. Rau JL. Design principles of liquid nebulization devices currently in use. Respir Care 2002;47:1257-75.
23. Dhand R. Special problems in aerosol delivery: artificial airways. Respir Care 2000;45:636-45.
24. Dhuper S, Chandra A, Ahmed A, Bista S, Moghekar A, Verma R, Chong C, Shim C, Cohen H, Choksi S. Efficacy and cost comparisons of bronchodilatator administration between metered dose inhalers with disposable spacers and nebulizers for acute asthma treatment. J Emerg Med 2011;40:247-55.
25. Malliotakis P, Linardakis M, Gavriilidis G, Georgopoulos D. Duration of salmeterol-induced bronchodilation in mechanically ventilated chronic obstructive pulmonary disease patients: a prospective clinical study. Crit Care 2008;12:R140.

分別用 Salmeterol/Fluticasone 與 Ipratropium/Terbutaline/Budesonide 治療使用呼吸器的慢性阻塞性肺病病患，比較呼吸道參數與血漿細胞激素之差別

吳黃平[1,2] 劉育志[1,2] 林溪泉[2] 簡明儀[2] 廖芳淳[2] 張淑娟[2] 謝文斌[1,2]

背 景： 使用吸入性 salmeterol/fluticasone 治療使用呼吸器的慢性阻塞性肺病病患，是否比用傳統的吸入性 ipratropium/terbutaline/budesonide，對氣管擴張與抗發炎的效果好，目前仍未知道。

方 法： 19 名穩定的呼吸衰竭慢性阻塞性肺病病患被隨機分成兩組。SF 組使用吸入性 salmeterol/fluticasone，藉由定量噴霧器合併間隔器傳送藥物。ITB 組使用 ipratropium/terbutaline/budesonide，藉霧化藥物來讓病患使用。

結 果： 從第一天到第七天，SF 組的快淺指標比 ITB 組低，SF 組與 ITB 組在病患每分鐘換氣量、本身吐氣末期正壓、呼吸道阻力上，並沒有差異。無論在 SF 組或 ITB 組，血漿間介素-6、間介素-10、間介素-12、轉化生長因子 β1 濃度，在第一天與第七天之間並沒有差異。

結 論： 使用 salmeterol/fluticasone 的患者有較低的快淺指標。salmeterol/fluticasone 與 ipratropium/terbutaline/budesonide 對穩定呼吸衰竭慢性阻塞性肺病病患的氣管擴張與抗發炎的效果是相似的。

(長庚醫誌 2012;35:373-81)

關鍵詞： 慢性阻塞性肺病，呼吸衰竭，呼吸器，salmeterol/fluticasone

長庚醫療財團法人基隆長庚紀念醫院 [1]胸腔重症暨睡眠科，[2]呼吸治療科；長庚大學 醫學院
受文日期：民國99年9月10日；接受刊載：民國101年3月14日
通訊作者：謝文斌醫師，長庚醫療財團法人基隆長庚紀念醫院 胸腔重症暨睡眠科。基隆市204安樂區麥金路222號。
Tel: (02)24313131轉3173; Fax: (02)24335342; E-mail: binshieh@cgmh.org.tw