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A one-year prospective study of infectious etiology in patients hospitalized with acute exacerbations of COPD and concomitant pneumonia

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Received 4 December 2007; accepted 18 March 2008

Available online 24 June 2008

KEYWORDS

COPD;
Acute exacerbation;
Pneumonia;
Bacteria;
Viruses

Summary

Aim: This study assessed the infectious etiology of patients hospitalized for acute exacerbations of chronic obstructive pulmonary disease (AECOPD) with concomitant pneumonia.

Methods: Patients admitted to medical wards in an acute hospital were recruited prospectively from May 1, 2004 to April 30, 2005. Sputum culture, blood culture, paired serology, and nasopharyngeal aspirates (NPA) viral culture and polymerase chain reaction (PCR) studies were performed. Spirometry was assessed in stable phase at 2–3 months post-hospital discharge.

Results: Seventy eight subjects were admitted for AECOPD with concomitant pneumonia. The mean (SD) age was 77.1 (7.5) years, with FEV₁ of 41.5 (20.8)% predicted normal. Overall, an infectious etiology could be established in 48.7% of the subjects. Among the 71 subjects with sputum collected, 40.8% had positive bacterial culture. The commonest bacteria identified were *Streptococcus pneumoniae* (8[11.3%]), *Pseudomonas aeruginosa* (7[9.9%]) and *Haemophilus influenzae* (7[9.9%]). Among the 66 subjects with NPA collected, 9.0 and 12.2% had positive viral culture and PCR results, respectively. The commonest viruses identified by NPA PCR were influenza A (4[6.1%] subjects) and rhinovirus (2[3.0%]). Paired serology was positive in 4.4%. Patients on high dose inhaled corticosteroid (ICS) (>1000 mcg beclomethasone-equivalent/day) had a higher rate of positive sputum bacterial culture than those on low-medium dose of ICS (50.0% vs 18.2%, $p = 0.02$).

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Conclusion: An infectious etiology could be established in about half of patients hospitalized with AECOPD and concomitant pneumonia. The majority of identifiable causes were bacterial. Patients on high dose ICS might have impaired airway defense as reflected by the higher rate of positive sputum culture.

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Introduction

Pneumonia is a major cause of morbidity and mortality worldwide. In the US, pneumonia is the 6th most common cause of death and the leading cause of death among all infectious diseases.¹ In Hong Kong, pneumonia and COPD were the 3rd and 5th leading causes of death, with mortality rates of 60 and 28.5 per 100,000 population, respectively.² An observational study in the US reported that patients with community-acquired pneumonia (CAP) with a diagnosis of COPD had a significantly higher 30- and 90-day mortality than non-COPD patients.³ Recently, the use of inhaled corticosteroids (ICS) is associated with an excess risk of pneumonia hospitalization followed by death within 30 days, among elderly patients with COPD.⁴

Most studies on the etiology of CAP did not focus on COPD patients.^{5–7} In addition, some studies of the infectious etiology of pneumonia were conducted in the intensive care unit (ICU) setting, and were again not specific for COPD.^{8,9} On the other hand, many studies of the infectious etiology related to AECOPD have excluded patients with pneumonia as they were not considered as “pure” AECOPD.^{10–13} Our group has previously conducted a retrospective study on the sputum bacteriology of patients with AECOPD with concomitant pneumonia,¹⁴ but the causative role of viruses was not explored. There are currently limited data on the etiological agents in patients with AECOPD and concomitant pneumonia.¹⁵ The aim of this study is to assess prospectively the bacterial and viral etiology of patients hospitalized with AECOPD and concomitant pneumonia. In addition, the associations between the identification of micro-organisms in AECOPD with the use of ICS and clinical outcomes (including mortality and need for non-invasive positive pressure ventilation [NPPV]) were assessed.

Methods

Subject recruitment

Patients who had been admitted to the Prince of Wales Hospital with AECOPD and concomitant pneumonia between May 1, 2004 and April 30, 2005 were recruited for this study. AECOPD was defined when a patient with background COPD¹⁶ presented with at least two of the following major symptoms (increased dyspnea, increased sputum purulence, increased sputum volume) or one major and one minor symptom (nasal discharge/congestion, wheeze, sore throat, cough) for at least two consecutive days.^{17,18} All chest radiographs (CXR) were assessed by the investigators (respiratory physicians). Pneumonia was defined when there was radiographic evidence of chest

infection (new infiltrates and consolidation on the CXRs). Informed written consent was obtained from each subject and the study was approved by the research ethics committee of the Chinese University of Hong Kong.

Demographic data and management in hospital

Demographic data and length of hospital stay of patients with AECOPD were recorded. Co-morbid conditions were noted and scored by the Charlson index.¹⁹ The scoring of the Charlson index ranged from 0 to 33, with a higher score indicating more in number and severity of the co-existing illnesses. The use of NPPV, invasive mechanical ventilation, and ICU admission were recorded.

Microbiological examination

Expectorated sputum was collected into a sterile container and processed and cultured according to standard procedures as described in our previous study.^{10,20} NPA was obtained by catheter aspiration from the posterior nasal pharyngeal space via the nostril with the patient in the sitting position. NPA viral culture was performed as described in our previous studies.^{10,11} For the viral PCR assessment of the NPA, 5 groups of nested multiplex PCR assays targeting 18 respiratory viruses and three bacteria were applied as described in our previous study.²¹ The viruses and bacteria included influenza A H1N1, H3N2 and H5N1, influenza B, parainfluenza types 1, 2, 3, 4a and 4b, respiratory syncytial viruses (RSV) A and B, rhinovirus, enterovirus, coronaviruses (OC43, 229E, SARS), metapneumovirus, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Legionella pneumophila* and adenovirus.

Paired serum samples for serology were obtained on admission and at 14–28 days later. The presence of antibody specific for influenza A and B, parainfluenza 1, 2, and 3, RSV, adenovirus, *M. pneumoniae*, and *Chlamydia psittaci* was detected by complement fixation test. Seroconversion or ≥ 4 -fold rise in antibody titre was regarded as evidence for current infection. Blood was cultured using the BacT/Alert Microbial Detection System.

Follow up of progress of patients post-discharge

Spirometry pre- and post-bronchodilator was performed at 2–3 months post-discharge (stable COPD) according to the American Thoracic Society Standard²² using the Vitalograph (Buckingham, UK) spirometer. The updated predicted spirometry values for Hong Kong Chinese were adopted.²³ The patients were contacted by phone and their medical records were reviewed 12 months later to check for any deaths or re-admissions.

Statistics

Data were analyzed by the Statistical Package of the Social Science (SPSS) Statistical software for Window, Version 11.5 (SPSS Inc, IL, USA). The associations between the identification of an organism in AECOPD (bacteria in sputum, viruses in the NPA and serology) and the lung function and clinical outcomes of patients (mortality, NPPV use and length of hospital stay) were assessed by Mann–Whitney U test, chi-square test and Fisher-exact test as appropriate. Data were presented as mean (SD) and a *p* value of <0.05 was considered as significant.

Results

Altogether 78 subjects were admitted with the first episode of AECOPD with concomitant pneumonia. The demographic characteristics of the patients are shown in Table 1. Lung function results were available for 64 patients. Twelve patients died before the scheduled appointment for spirometry whereas two refused to return for lung function assessment. Among the 64 subjects with lung function assessment, 5, 13, 23 and 23 patients had mild, moderate, severe, and very severe COPD according to the GOLD classification.¹⁶ Forty-two patients (53.8%) were using ICS before hospitalization. The mean (SD) dose of ICS was 1345 (679) mcg beclomethasone-equivalent per day. There

was no difference in the demographic characteristics (including the mean lung function value) between subjects who were on ICS and those who were not. In addition, by stratifying subjects on ICS into two subgroups of high (>1000 mcg beclomethasone-equivalent per day) and low-medium (\leq 1000 mcg beclomethasone-equivalent per day) dose of ICS, no difference in their demographic data was observed (Supplementary Table 1). The mean (SD) dose of the group on high dose and low-medium dose ICS were 2050.0 (223.6) and 836.4 (283.8) mcg beclomethasone-equivalent per day, respectively.

Among our subjects, 28 (35.8%), 11 (14.1%), 7 (9.0%), 5 (6.4%), 5 (6.4%), 7 (9.0%) had history of hypertension, cerebrovascular accident, diabetes mellitus, ischaemic heart disease, congestive heart failure and malignancy, respectively. All patients were managed on the general medical wards and none required invasive mechanical ventilation. There were no significant differences in mortality in the same admission, mortality at 12 months, and NPPV usage when comparing subjects on ICS against those who were not, or when comparing subjects who were on low-medium dose of ICS against those on high dose ICS (Supplementary Table 1).

The clinical presentations of the subjects are summarized in Table 2. In 10 episodes, subjects had taken antibiotics within 7 days before hospitalization. All subjects had pneumonic changes on CXRs. Among them, 7 episodes had bilateral CXR changes whereas 13 episodes had pneumonic changes involving more than 1 lobe of the lungs. Three subjects developed pleural effusion. All patients were treated with antibiotic therapy on admission after sputum and blood culture had been collected in the hospital.

The sputum culture results are shown in Table 3. Overall, 40.8% and 3.0% of the episodes had positive sputum bacterial and mycobacterial culture, respectively. Two out of the 8 patients (25.0%) related to *Streptococcus pneumoniae* were resistant to penicillin whereas none of the *Haemophilus influenzae* isolates showed beta-lactamase activity. None had more than one bacterium isolated from the sputum. There was no difference in the rate of positive sputum bacterial culture in the group that had received antibiotic in the previous week when compared to those who did not (3/10[30.0%] vs 26/61[42.6%], *p* = 0.45). Subjects on ICS were not different in terms of the rate of positive sputum bacterial culture from those not on ICS (14/39[35.9%] vs 15/32[46.9%], *p* = 0.35). However, subjects

Table 1 Demographic characteristics of the patients (*n* = 78)

Age (yrs)	77.1 ± 7.5
Sex (male)	66 (84.6)
Body mass index (kg/m ²)	20.71 ± 3.66
Post-bronchodilator FEV ₁ ^a (L)	0.77 ± 0.37
Post-bronchodilator FVC ^a (L)	1.35 ± 0.55
Post-bronchodilator FEV ₁ /FVC ratio ^a	0.58 ± 0.15
Post-bronchodilator FEV ₁ % predicted normal ^a (%)	41.50 ± 20.76
Post-bronchodilator FVC ₁ % predicted normal ^a (%)	51.23 ± 19.69
Pre-morbid status	
Home bound	13 (16.7)
Outgoing but could only walk on level ground	28 (35.9)
Could climb up several flights of stairs	37 (47.4)
Smoking status	
Never-smoker	1 (1.3)
Quitted smoking	61 (78.2)
Current smoker	16 (20.5)
Home oxygen use	20 (25.6)
On inhaled corticosteroid	42 (53.8)
On oral theophylline	29 (37.2)
Received influenza vaccination over the past 12 months	34 (43.6)
Charlson index	1.58 ± 0.88

Data are presented as mean ± SD or *n* (%).

^a Lung function was available in 64 patients.

Table 2 Clinical data of the admissions (*n* = 78 subjects)

Hospital stay in acute hospital (days)	8.7 ± 6.0
Hospital stay in acute + convalescent hospital (days)	16.8 ± 12.7
Fever on admission (temperature > 37.5 °C)	33 (42.3%)
WCC on admission ($\times 10^9$ /L)	14.0 ± 5.7
Use of NPPV	15 (19.2%)
Use of mechanical ventilation	0
Admission to ICU	0

Data are presented as mean ± SD or *n* (%).

WCC = white cell count.

NIPV = non-invasive positive pressure ventilation.

ICU = intensive care unit.

Table 3 Sputum culture results

Sputum for routine culture (n = 71)		Sputum for mycobacterial culture (n = 66)	
Culture negative	42 (59.2)	Mycobacterium culture negative	64 (97.0)
<i>Streptococcus pneumoniae</i>	8 (11.3)	<i>Mycobacterium tuberculosis</i>	1 (1.5)
<i>Pseudomonas aeruginosa</i>	7 (9.9)	<i>Mycobacterium kansasii</i>	1 (1.5)
<i>Haemophilus influenzae</i>	7 (9.9)		
<i>Klebsiella species</i>	2 (2.8)		
<i>Serratia species</i>	2 (2.8)		
MRSA	1 (1.4)		
<i>Stenotrophomonas maltophilia</i>	1 (1.4)		
<i>Candida albicans</i>	1 (1.4)		

Data are presented as n (%).

There were a total of 71 and 66 episodes of AECOPD with concomitant pneumonia had sputum saved for routine bacterial culture and mycobacterial culture, respectively.

on high dose ICS had a higher rate of positive sputum bacterial culture than those on low-medium dose of ICS (10/20[50.0%] vs 4/22[18.2%], $p = 0.02$).

The results of NPA PCR, NPA viral culture and blood serology are shown in Table 4. The positive rates of NPA PCR, NPA viral culture, and blood serology results were 12.2, 9.0 and 4.4%, respectively. Subjects on ICS had a higher rate of positive viral etiologies (using the combined method of NPA PCR, NPA viral culture and blood serology) than those who were not (10/38[26.3%] vs 2/35[5.8%], $p = 0.02$). There was, however, no difference in the rates of identification of viral etiologies comparing the subjects on low-medium dose ICS against those on high dose ICS (5/22[22.7%] vs 5/20[25.0%], $p = 0.70$). There was also no difference in the rates of positive influenza A or B viruses (using the combined method of NPA PCR, NPA viral culture and blood serology) among those subjects who had received influenza vaccination within 12 months before the admission compared to those without (3/33[9.1%] vs 4/40[10%], $p = 0.90$). All episodes had blood culture performed but none were positive. Among the 3 subjects with pleural effusion, 2 had undergone pleural fluid aspiration. The pleural fluid was exudative in nature with no bacteria identified

Table 4 NPA PCR, viral culture and serology results

PCR (n = 66)	Influenza A (H3)	4 (6.1)
	Rhinovirus	2 (3.0) ^a
	Influenza B	1 (1.5)
	Metapneumovirus	1 (1.5)
	Coronavirus OC43	1 (1.5) ^a
	Negative PCR	58 (87.8)
NPA viral culture (n = 66)	Influenza A	3 (6.2)
	Influenza B	2 (3.0)
	Herpes simplex virus type 1	1 (1.5)
	Negative viral culture	60 (91.0)
Serology (n = 45)	Influenza A	1 (2.2)
	RSV	1 (2.2)
	Negative serology	43 (95.6)

Data are presented as n (%).

^a One case had both rhinovirus and coronavirus OC43 identified in the PCR.

by Gram stain or culture. Overall, the rate of positive identification by sputum culture, NPA PCR, NPA viral culture, and blood serology was 48.7% (38/78). Three subjects (3.8%) had both positive bacterial and viral etiology identified (positive sputum cultures and positive viruses [either from NPA PCR, NPA viral culture or blood serology]).

Among those with bilateral pneumonia (n = 7), 3 had micro-organisms identified (1 *H. influenzae* and 2 influenza A). For those 13 cases with pneumonic changes involving more than 1 lobe (7 of them had bilateral pneumonia also), 4 had bacteria (2 *H. influenzae*, 1 *S. pneumoniae* and 1 *Serratia sp.*) and 3 had viruses identified (2 influenza A and 1 metapneumovirus). None of these subjects had both bacterial and viral etiologies identified at the same time.

The identification of the organisms in relation to the lung function of the subjects is shown in Table 5. There was a trend towards a higher rate of positive sputum bacterial culture among the subjects with $FEV_1 < 50\%$ predicted than those with $FEV_1 \geq 50\%$ predicted (19/45[42.2%] vs 2/14[14.3%], $p = 0.04$). However, the rate of positive sputum bacterial culture was not different among patients with $FEV_1 < 30\%$ predicted from those whose FEV_1 was $\geq 30\%$ predicted (8/20[40.0%] vs 13/39[33.3%], $p = 0.61$). Similarly, the rate of positive viral etiology was not statistically different between the COPD subjects with different disease severity based on their lung function.

The hospital length of stay, need for NPPV support, death rates in the same admission and at 12 months, and re-admissions to hospital in 12 months were assessed in relation to the bacteriology and virology results (Table 6). Patients with a positive viral etiology had a higher chance of requiring NPPV support than those without viral identification by either NPA or serology (41.7% vs 11.5%, $p = 0.01$). The age, sex, presence of co-morbid medical illness (such as diabetes mellitus, hypertension, cerebrovascular accident, ischaemic heart disease, congestive heart failure or malignancy) and admissions for pneumonia in the previous 12 months had no association with the presence of bacteria and viruses from the respiratory specimens. In addition, the presence of co-morbidities (as defined above) had no effect on the death rate and the length of hospital stay when compared to the subjects without co-existing medical illness.

Table 5 The identification of the organisms in relation to the lung function

		Mild to moderate COPD	Severe COPD	Very severe COPD
Sputum results (n = 59)	Episodes with lung function performed and sputum saved	14	25	20
	<i>Streptococcus pneumoniae</i>	1 (7.1)	2 (8.0)	4 (20.0)
	<i>Pseudomonas aeruginosa</i>	1 (7.1)	2 (8.0)	0
	<i>Haemophilus influenzae</i>	0	3 (12.0)	2 (10.0)
	<i>Klebsiella species</i>	0	1 (4.0)	1 (5.0)
	<i>Serratia species</i>	0	1 (4.0)	0
	MRSA	0	0	1 (5.0)
	<i>Stenotrophomonas maltophilia</i>	0	1 (4.0)	0
	<i>Candida albicans</i>	0	1 (4.0)	0
	Negative sputum culture	12 (85.7)	14 (56.0)	12 (60.0)
NPA PCR results (n = 53)	Episodes with lung function performed and with NPA saved	16	20	17
	Influenza A (H3)	0	2 (10.0)	2 (11.8)
	Rhinovirus	0	0	2 ^a (11.8)
	Influenza B	0	0	1 (5.9)
	Metapneumovirus	1 (6.3)	0	0
	Coronavirus OC43	0	0	1 ^a (5.9)
	Negative PCR	15 (93.8)	18 (90.0)	12 (70.6)
NPA viral culture (n = 53)	Episodes with lung function performed and with NPA saved	16	20	17
	Influenza A	0	1 (5.0)	2 (11.8)
	Influenza B	1 (6.3)	0	1 (5.9)
	Herpes simplex virus type 1	1 (6.3)	0	0
	Negative viral culture	14 (87.5)	19 (95.0)	14 (82.4)
Serology (n = 41)	Episodes with lung function performed and paired serology saved	10	18	13
	Influenza A	0	1 (5.6)	0
	RSV	1 (10.0)	0	0
	Negative serology	9 (90.0)	17 (94.4)	13 (100)

Data are presented as n (%).

^a One episode with NPA PCR study positive for both coronavirus OC43 and rhinovirus.

When considering individual organisms, the presence of *Pseudomonas aeruginosa* in sputum was associated with older age (84.9 ± 3.7 vs 76.3 ± 7.3 , $p < 0.01$). Apart from that, we could not identify any difference among certain strains of bacteria (including *P. aeruginosa*, *H. influenzae*, *Klebsiella species*) in relation to the subjects' age, body mass index, FEV₁ and long term home oxygen use.

For those cases with bilateral pneumonia, their length of hospital stay (8.7 ± 5.0 vs 8.7 ± 6.2 days, $p = 0.95$), NPPV use (28.6[2/7]% vs 18.3% (13/71)%, $p = 0.62$) and death rate in the same admission (28.6[2/7]% vs 9.9[7/71]%, $p = 0.18$) were not different from those with unilateral pneumonia. Similarly, among those cases with pneumonia involving more than 1 lobe, their length of hospital stay (8.8 ± 4.5 vs 8.7 ± 6.3 days, $p = 0.93$), NPPV use (30.8[4/13]% vs 16.9 ± [11/65]%, $p = 0.26$) and death rate in the same admission (15.3[2/13]% vs 10.8[7/65]%, $p = 0.64$) were not different from those with pneumonia that affected just 1 lobe. For the 3 cases with both bacterial and viral etiologies (one with MRSA + influenza B, one with *H. influenzae* + influenza A, one with *S. pneumoniae* + rhinovirus + coronavirus), one

patient had required NPPV support during hospitalization but they all survived over the next 12 months.

Discussion

To the best of our knowledge, this is the first prospective study that has included examination of sputum bacteriology and viral multiplex nested-PCR assessment of respiratory specimens from patients admitted to the medical wards with AECOPD and concomitant pneumonia. An infectious etiology could be established in 48.7% of the episodes of admissions. The rates of positive sputum bacterial culture and NPA viral PCR were 40.8% and 12.2%, respectively. The commonest bacteria identified were *S. pneumoniae*, *P. aeruginosa* and *H. influenzae* whereas the common viruses involved were influenza A and rhinovirus. Interestingly, patients on higher dose of ICS (>1000 mcg beclomethasone-equivalent per day) had a higher rate of positive sputum bacterial culture than those on lower dose of ICS.

The largest study published to date that specifically assessed pneumonia in COPD patients was conducted in

Table 6 Relationship between clinical outcomes of the patients and the sputum, NPA and serology results (the first admission of the patients was assessed)

	Sputum culture (N = 71 patients)		Viral PCR or viral culture or serology (N = 73 patients)	
	+ve (n = 29)	-ve (n = 42)	+ve (n = 12)	-ve (n = 61)
Length of stay in acute hospital (days)	8.52 ± 6.38	9.05 ± 6.16 <i>p</i> = 0.73	7.67 ± 3.92	8.95 ± 6.48 <i>p</i> = 0.51
Length of stay in both acute and convalescent hospital (days)	16.31 ± 9.07	17.36 ± 14.09 <i>p</i> = 0.73	18.25 ± 14.74	16.38 ± 12.70 <i>p</i> = 0.65
Required NPPV support	5 (17.2%)	8 (19.0%) <i>p</i> = 0.85	5 (41.7%)	7 (11.5%) <i>p</i> = 0.01*
Death in the same admission	3 (10.3%)	4 (9.5%) <i>p</i> = 0.93	1 (8.3%)	10 (16.4%) <i>p</i> = 0.51
Death in the next 12 months	8 (27.6%)	13 (31.0%) <i>p</i> = 0.76	4 (33.3%)	20 (32.8%) <i>p</i> = 0.97
Readmission in the next 12 months	15 (51.7%)	26 (61.9%) <i>p</i> = 0.39	8 (66.7%)	32 (52.5%) <i>p</i> = 0.37

**p* Value <0.05.

NPPV = non-invasive positive pressure ventilation.

Spain involving 124 subjects.¹⁵ With extensive bacteriological tests, the investigators identified infectious etiology in 64% of the cases but their study did not include any viral assessments.¹⁵ In our study, *S. pneumoniae* and *P. aeruginosa* were the commonest bacteria identified, in contrast to the findings by Torres et al. that the commonest organisms were *S. pneumoniae* (43%) and *C. pneumoniae* (12%). Atypical organisms (such as *M. pneumoniae*, *C. pneumoniae* and *L. pneumophila*) were not detected by both serology and NPA viral PCR in our study. A recent study that specifically looked for atypical pathogens in patients with AECOPD without pneumonia has failed to identify these organisms by sputum PCR assessment.²⁴

Another study that involved 23 patients admitted with "pneumonic" AECOPD found that the infectious etiologies (both bacterial and viral) were identified in 78% of the patients using paired blood serology testing and the rate was markedly higher than our findings.²⁵ Our study subjects had similar lung function (mean FEV₁% predicted of about 40%) to the study by Torres et al., and the difference in results could not be explained on the basis of lung function.¹⁵ Previous studies on CAP not specific to COPD patients observed a geographic difference in the bacterial etiologies. For example, a study from Malaysia noted a higher prevalence of Gram-negative bacilli when compared to the western countries.⁷ It is uncertain whether geographic or other factors could explain the differences in microbiology pattern in the various studies.

Recently, the use of ICS has been implicated to increase the risk of CAP among patients with COPD.^{4,26} However, the mechanism underlying this observation is unclear. The increase in pneumonia did not appear to represent an increase in the number of deaths.²⁶ We observed that subjects on high dose ICS had a higher rate of positive sputum bacterial culture than patients on low-medium dose of ICS. Our observation concurred with that by Ernst et al.⁴ that the adjusted risk ratio of hospitalization for pneumonia was the greatest with the highest dose of ICS

use (>1000 mcg fluticasone equivalent dose per day). ICS can decrease the inflammation in the airway.²⁷ Whether this decrease in inflammation, with possibly concomitant decrease in defense against micro-organisms, could explain the observation of a higher rate of positive sputum culture in our patients with AECOPD and concomitant pneumonia on high dose ICS, and the higher rate of pneumonia in COPD patients on ICS,^{4,26} certainly requires further study.

Viruses are important causative agents for CAP. Among the CAP patients (not specific for COPD patients) admitted to hospital in Chile, respiratory viruses were found in 32% of the patients using viral immunofluorescence assay of nasal swabs, serology and urinary antigen.²⁸ The commonest virus identified in their study was parainfluenza viruses (in 17 samples), followed by influenza A (8 samples) in contrast to our finding that influenza A virus was the commonest virus. We have chosen viral PCR technique as the main method of virus identification as we have demonstrated previously that PCR technique had a 2.7 times higher diagnostic yield than conventional viral culture.¹¹ It appears that bacteria are far more common than viruses as the etiological agents in patients with AECOPD and concomitant pneumonia whereas the overlap between viral and bacteria etiologies was also low (3.8%) in our study.

Our study is limited by the fact that this was a single center study with a relatively small sample size. In addition, lung function data were not available in 12 patients who had died before their scheduled lung function appointments. Furthermore, NPA PCR was performed in this study instead of sputum PCR. Sputum PCR assessment probably would assess the lower respiratory tract infection better than using NPA specimens. Previous studies using both sputum and nasal lavage PCR have shown that the diagnostic yield for AECOPD patients (without pneumonia) were higher in induced sputum than in nasal lavage.¹³ Comparison of the infectious etiology of pneumonia in subjects with and without COPD was not available as we had not collected the clinical data and respiratory specimens from

subjects with pneumonia but without COPD in this current study. An early study of CAP in 90 subjects (13% with chronic bronchitis) in Hong Kong in 1988 found that 41% had identifiable etiologies but there was no comparison between subjects with and without COPD.²⁹ Their etiologies appeared different from ours, with *S. pneumoniae* and *Mycobacterium tuberculosis* (each 12.2%) as the commonest organisms.

In summary, an infectious etiology could be established in about half of patients hospitalized with AECOPD and concomitant pneumonia, and the majority of identifiable causes were bacterial. We have observed that the use of higher dose ICS was associated with a higher rate of positive sputum bacterial culture in patients with AECOPD and concomitant pneumonia. Further studies are needed to investigate why COPD patients on ICS appear more prone to pneumonia as reported by recent studies.^{4,26}

Conflict of interest

All the authors have no conflicts to disclose.

Acknowledgement

We would like to thank Miss Mabel Tong for performing the spirometry tests and Mr. Kenneth Lai for assisting with the statistical analysis.

Supplementary data

Supplementary data associated with this article can be found in the online version, at [doi:10.1016/j.rmed.2008.03.019](https://doi.org/10.1016/j.rmed.2008.03.019).

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