Prognostic Factors in the Management of Exacerbation of Chronic Obstructive Pulmonary Disease in Kuwait

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Key Words

Chronic obstructive pulmonary disease · Exacerbation · Management · Prognostic factors · Kuwait

Abstract

Objective: To evaluate the clinical presentation and the factors of prognostic importance in the management of exacerbation of chronic obstructive pulmonary disease (COPD). **Subjects and Methods:** One hundred and four patients who were hospitalized because of exacerbation of COPD between 1996 and 2000 were selected for further evaluation. Only patients who fulfilled the American Thoracic Society criteria for diagnosis of COPD were included. The factors examined included age, clinical features, duration of symptoms of exacerbation, severity of underlying disease, comorbid diseases, level of consciousness, previous hospitalization, intubation and assisted ventilation, hypercapnia, degree of acidemia and complications. **Results:** Seventy-four of 104 (71%) hospitalized patients reviewed met the inclusion criteria for COPD. The mean age was 63.68 ± 12.6 years. There was a male:female ratio of 3:1. Fifty-eight patients (78%) had a baseline FEV₁ <50% before hospitalization and 45 (64%) had previous hospitalization. Comorbid disease was found in 50% of the cases, while 78% had acidemia

and 70% hypercapnia. Fourteen (19%) died on admission. Risk factors identified included severity of disease ($p < 0.05$); presence of comorbid disease ($p < 0.01$); acidemia ($p < 0.0001$); hypercapnia ($p < 0.0001$); previous hospitalization ($p < 0.01$), and assisted ventilation ($p < 0.001$). **Conclusion:** This study revealed that the presence of comorbid disease, acidemia, previous hospitalization and assisted ventilation significantly contributed to mortality in patients with exacerbation of COPD.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality worldwide [1]. It is currently the fourth leading cause of death in the world, and further increases in the prevalence and mortality of the disease could be predicted in the coming decades [2]. The major characteristic of COPD is the presence of chronic airflow limitation that progresses slowly over a period of years and is largely irreversible [3]. Several national and international consensus statements have led to international standardization of diagnosis, management and better care [2–4].

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Table 1. Age distribution according to age-groups

Age group	Cases	%
<50	8 (1)	10.81
51–60	18 (2)	24.32
61–70	27 (4)	36.49
>70	21 (7)	28.38
Total	74 (14)	100

Number of deaths in parentheses.

Table 2. Hydrogen ion concentration (pH) on presentation

pH	Cases
>7.4	13
7.25–7.35	26
7.11–7.24	9
7.0–7.10	6
<7.0	4

Exacerbation of COPD is the largest single cause of emergency respiratory admission, accounting for 21%, with a mean hospital stay of 10.3 days in the United Kingdom [5]. Knowledge of prognosis in COPD is mainly derived from studies of carefully selected patient groups. These studies have shown that prognosis is related to age and other lung function indices [6–10]. Hospitalization for acute exacerbation usually occurs in the advanced phase of the disease and is thus associated with a greater risk of mortality in subsequent years [11, 12].

COPD is a rather common disease in Kuwait. The prevalence and frequency of hospitalization of patients have increased in the last two decades, attributable to increased industrial activities and cigarette smoking [13]. This study therefore aims at evaluating some of the factors which may contribute to hospitalization and mortality in these patients. Suggestions towards improving the management of these patients before and during exacerbations are made.

Subjects and Methods

One hundred and four case files of patients hospitalized during exacerbations at Mubarak Al-Kabeer Hospital, Kuwait, a tertiary medical center over a 5-year period (1996–2000) were reviewed. Patients with diagnosis consistent with asthma, bronchiectasis, and left ventricular failure were excluded from the study. Seventy-four patients who fulfilled the American Thoracic Society [3] criteria for diagnosis of COPD were selected for further data analysis. Data retrieved included baseline forced expiratory volume in 1 s (FEV₁) at diagnosis of the disease, duration of the underlying disease, presenting symptoms of exacerbation and history of cigarette smoking, precipitating factors leading to exacerbation, comorbid diseases, history of previous hospitalization, level of consciousness on admission, drug therapy and drug compliance before exacerbation. Physical signs at presentation were recorded. Other data collected included use of home oxygen, arterial blood gases at presentation, chest radiograph and findings, and electrocardiograph records on admission. The types of drugs given during hospitalization were also recorded. Records of management in the intensive care unit, with or without mechanically assisted ventilation, were noted. History of previous intubation and assisted ventilation was also recorded. Complications developed during management, duration of stay in hospital and outcome of the illness were also noted.

Statistical Analysis

A univariate analysis of each variable was performed. Confidence intervals (CIs) for odds ratio (OR) of significant variables were calculated for the risk factors. Values of $p < 0.05$ were considered statistically significant.

Results

Table 1 shows age distribution; mean age was 63.68 ± 12.6 years and the male:female ratio was 3:1. The mean duration of symptoms before admission was 3 days. Fifty-eight of the 104 (78%) patients had a moderate to severe underlying disease. The FEV₁ on diagnosis for the moderate (45%) and severe cases (40%) was 35–40% and <35% of the predicted value, respectively. History of cigarette smoking was present in 54 (73%) patients. Only 20 patients did not smoke cigarettes.

The predominant precipitating factor for exacerbation was respiratory tract infection in 81% of the cases. Comorbid diseases occurred in 50% of the patients, the most common being ischemic heart disease; the rest were diabetes mellitus, obesity and sleep apnea syndrome, chronic renal failure, chronic liver disease and cerebrovascular disease. Acidemia was observed at presentation in 77% of cases. Nine patients had a pH of 7.0 and below. Hypercapnia occurred in 70% of the cases, the highest partial pressure of carbon dioxide recorded being 17.2 kPa (table 2).

Table 3. Factors contributing to death in patients with exacerbation of COPD

Variables	Alive (n = 60)	Dead (n = 14)	OR (95% CI)	p value
Age				
>65 years		8	1.21	0.78
<65 years		6	(0.37–3.93)	
Sex				
Male	46	10	1.31	0.77
Female	14	4	(0.23–2.60)	
Severity of underlying disease				
FEV ₁ <50% predicted	33	13	0.09	<0.05
FEV ₁ >50% predicted	27	1	(0.01–0.77)	
Duration of symptoms before hospitalization				
>3 days	35	9	0.78	0.77
<3 days	25	5	(0.23–2.60)	
Comorbid disease				
Present	22	12	0.10	<0.01
Absent	38	2	(0.02–0.47)	
pH				
<7.30	15	13	0.03	<0.0001
>7.30	45	1	(0.003–0.21)	
pCO ₂				
>6.0 kPa	15	12	0.06	<0.0001
<6.0 kPa	45	2	(0.01–0.28)	
Level of consciousness				
Drowsy	10	8	0.15	<0.01
Alert	50	6	(0.04–0.53)	
Previous hospitalization				
Yes	5	10	0.09	<0.01
No	45	4	(0.02–0.34)	
Intubation/assisted ventilation				
Yes	10	10	0.09	<0.01
No	50	4	(0.02–0.34)	
Complications				
Yes	9	9	0.10	<0.0001
No	51	5	(0.03–0.36)	
Domiciliary O ₂ (LTOT)				
Yes	10	3	0.73	0.70
No	50	11	(0.17–3.12)	
Oral corticosteroids				
Yes	19	3	1.70	0.53
No	41	11	(0.42–6.81)	

Twenty (26%) of the patients were admitted to the intensive care unit and were intubated and mechanically ventilated. Fourteen patients had fatal outcome and of these, 9 had assisted ventilation. Seventy-one percent of the patients had at least one previous hospitalization, 10 of the 14 who died belonged to this category.

Complications were recorded in 18 (24%) patients, the commonest being congestive heart failure. The duration of hospitalization varied, the majority remained in hospital for 7–14 days. Factors that were observed to affect mortality are shown in table 3. These included severity of underlying disease as judged by FEV₁ ($p < 0.05$), acidemia ($p < 0.0001$), comorbid diseases ($p < 0.01$), PaCO₂ ($p < 0.0001$), previous hospitalization ($p < 0.01$), intubation and assisted ventilation ($p < 0.001$).

Discussion

The outcome of patients hospitalized with exacerbation of COPD is dependent on a number of factors including severity of the underlying disease, presence of comorbidity and frequency of hospitalization [11, 14–18]. In this study, age was not observed to be prognostically related to mortality as reported in a recent North American study [18]. However, the Canadian guidelines for COPD [15] recommended that age above 65 is a prognostic factor for COPD mortality. It is worth noting that 60% of patients who died in our study during hospitalization were above the age of 65.

In this study, the severity of the underlying disease, as judged by the value of FEV₁, was associated with poor prognosis consistent with previous reports [14, 16–18]. Thirteen of the patients with fatal outcome had FEV₁ of less than 50% predicted value. Dewan et al. [18] in a recent study showed that patients with FEV₁ <35% predicted value had a poor prognosis. Comorbidity was found to be a significant prognostic factor in this study ($p < 0.001$) similar to other studies [14, 19], but Dewan et al. [18] reported that comorbidity, just as age, did not affect the treatment outcome. Hospitalization for acute exacerbation of COPD usually occurs in the advanced phase of disease and is thus associated with a greater risk of mortality in subsequent years [10–12, 18].

In this study, our observation that frequent hospitalization was associated with fatal outcome ($p < 0.05$) is in agreement with previous reports [10, 12, 18, 20], which showed that repeated hospitalization accompanied by intubation and assisted ventilation was a poor prognostic factor for mortality. Noninvasive positive pressure venti-

lation was not used to ventilate any of the patients who were intubated. This facility was not available at our center during the period of the study. However, it has become available now for treating COPD patients with mild to moderate exacerbation, thus reducing the need for intubation, and improving patients' quality of life.

Smoking is the most common etiological factor, associated with the disease in 75% of the patients in agreement with other studies [21, 22]. Occupational exposure and/or atmospheric pollution have not yet been seriously associated as etiological factors in this environment, but they may feature prominently in decades to come, as many more industries emerge in Kuwait. These factors have, however, been well established in other studies [23]. One patient, below the age of 40, in this study had α -antitrypsin deficiency associated with CDPD. This association has been well established by Larson and Barman [24].

Hypercapnia and acidemia were the other factors of significant prognostic significance in this study similar to previous studies [25–27]. Plank et al. [25] observed that 20–47% of patients have CO₂ retention at presentation and 20% may be acidotic on admission.

Corticosteroids have been shown to improve FEV₁ and shorten the median hospital stay [27–29]. It is conceivable that the limited use of systemic steroids in this study (26%) may be a contributory factor in patients with poor outcome. However, all the patients in this study were on maintenance therapy of inhaled corticosteroids (beclomethasone dipropionate) in doses ranging from 450 to 800 μ g daily. Some studies have demonstrated improvement in FEV₁ after administration of inhaled corticosteroids to stable COPD patients [30, 31].

The findings from this study revealed that despite the severity of the underlying illness, many of the patients did not use domiciliary oxygen before admission. This was observed to be a significant factor. Garcia-Aymerich et al. [32] have shown that underprescription of long-term oxygen therapy (LTOT) was independently associated with a higher risk of admission for a COPD exacerbation, whereas the use of LTOT was associated with a lower risk of admission. A reduced mortality has been reported in earlier studies [33, 34] when oxygen supplementation was used for at least 15 h per day, but another study [35] concluded that home oxygen therapy had not shown convincing evidence that it alters exacerbation rate.

It was observed from the records that most of the patients failed to attend the outpatients follow-up clinics regularly, making it difficult to monitor their clinical status. Many of these patients reported at the emergency room only when in severe exacerbations. In fact, 60% of

patients who succumbed were admitted in a drowsy or comatose condition. The lack of a home and social support system, which is critical to the long-term management of these patients, was probably responsible for their inability to attend an outpatient clinic for follow-up and frequent hospitalization.

Based on the findings of this study we recommend pulmonary rehabilitation after hospitalization, and use of domiciliary oxygen for patients with severe underlying disease. These measures will benefit the patients, thereby reducing the frequency of exacerbations, and consequently improve the quality of life. Home, psychological, and social support should be developed in order to improve patients' compliance with drug therapy. Finally, recent evidence now suggests that mucolytics and antioxidants may have some benefits in reducing exacerbation rate [36, 37]. There is also new evidence that introduction of the newer long-acting inhaled anticholinergics in stable state reduces dyspnea and frequency of disease exacerbations, in addition to improving the quality of life [38, 39]. Furthermore, early recognition of patients at particular risk may reduce considerably the morbidity and mortality from complications associated with COPD exacerbations.

Conclusion

In conclusion, this study has highlighted some of the factors which lead to poor outcome in the management of patients hospitalized for exacerbation of COPD. The occurrence and/or frequency of some of these factors can be reduced or eliminated by the concerted efforts of patients, their relations and the attending physicians. It is necessary to introduce and implement appropriate measures, which will assist to reduce significantly the burden of COPD in this environment.

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