

Antimicrobials in acute exacerbations of chronic obstructive pulmonary disease – An analysis of the time to next exacerbation before and after the implementation of standing orders

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OBJECTIVE: To compare the mean time to next exacerbation in patients with acute exacerbations of chronic obstructive pulmonary disease (COPD) before and after the implementation of standing orders.

SETTING: Tertiary care hospital, Halifax, Nova Scotia, Canada.

POPULATION STUDIED: The records of 150 patients were analyzed, 76 were in the preimplementation group, 74 in the postimplementation group.

INTERVENTION: The management and outcomes of patients admitted with an acute exacerbation of COPD before and after the implementation of standing orders were compared.

DESIGN: A retrospective chart review.

MAIN RESULTS: There was no difference in the mean time to next exacerbation between treatment groups (preimplementation group: 310 days, postimplementation group: 289 days, $P=0.53$). Antibiotics were used in 90% of the cases (preimplementation group: 87%, postimplementation group: 93%). The postimplementation group had a 20% increase in the use of first-line agents over the preimplementation group. Overall, first-line agents represented only 37% of the antibiotic courses.

CONCLUSIONS: The implementation of standing orders encouraged the use of first-line agents but did not influence subsequent symptom resolution, length of hospital stay, or the infection-free interval in patients with acute exacerbations of COPD.

Key words: Antibiotics; Chronic obstructive pulmonary disease; Exacerbation

In Canada, chronic obstructive pulmonary disease (COPD) is a major health issue affecting over 750,000 people and the fourth ranked cause of mortality (1,2). Worldwide, it is the second most common chronic noncommunicable disease and the only leading cause of death that is increasing in prevalence (1,3,4). The inpatient mortality associated with COPD exacerbations ranges from 3% to 4% (5). Each year, over 52,000 hospital admissions and 16,000 deaths in Canada are attributed to COPD (1,6). At our institution, Queen Elizabeth II Health

Efficacité des antimicrobiens dans les exacerbations de bronchopneumopathie chronique obstructive : étude du temps écoulé avant l'apparition de l'épisode suivant, avant et après l'application de consignes.

OBJECTIF : Comparer le temps moyen écoulé avant l'apparition de l'épisode suivant de bronchopneumopathie chronique obstructive (BPCO), avant et après l'application de consignes.

LIEU : Hôpital de soins tertiaires, Halifax.

POPULATION À L'ÉTUDE : Ont été examinés les dossiers de cent cinquante patients : 76 avant l'application; 74, après.

INTERVENTION : Nous avons comparé le traitement de patients admis pour une exacerbation de BPCO et les résultats obtenus, avant et après l'application des consignes.

TYPE D'ÉTUDE : Examen rétrospectif de dossiers.

PRINCIPAUX RÉSULTATS : Aucune différence n'a été observée entre les deux groupes quant au temps moyen écoulé avant l'exacerbation suivante (avant l'application : 310 jours; après l'application : 289 jours; $p=0,53$). Des antibiotiques ont été prescrits dans 90 % des cas (avant l'application : 87 %; après l'application : 93 %). Une augmentation de 20 % de l'utilisation des médicaments de première intention a été notée dans le groupe de post-intervention par rapport au groupe de pré-intervention. Dans l'ensemble, ces derniers médicaments ne constituaient que 37 % des cures d'antibiotiques.

CONCLUSION : L'application des consignes a favorisé le recours aux médicaments de première intention mais n'a pas eu d'incidence sur la disparition ultérieure des symptômes, la durée du séjour à l'hôpital ou le temps écoulé sans infection chez les patients atteints d'une exacerbation de BPCO.

Sciences Centre, COPD exacerbations are the third leading cause for admissions to the internal medicine service (preceded by pneumonia and congestive heart failure) (7).

In patients with COPD, acute infectious exacerbations are the most common precipitating factor leading to hospitalization and the most common cause of death (8-10). Up to 80% of acute exacerbations of COPD are due to respiratory infections, with 50% to 70% of these caused by bacteria and only 10% to 30% caused by viruses (11-13). In September 2000, standing

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orders for patients with a COPD exacerbation were implemented at our institution (Figures 1 and 2), with the rationale that prompt institution of optimal care, including controlled oxygenation and maximum bronchodilation, anti-inflammatory, and antibiotic therapy, would improve outcomes. The antibiotic choice included as first-line agents were trimethoprim/sulfamethoxazole (TMP/SMX) and doxycycline hyclate. Second-line agents were azithromycin dihydrate, amoxicillin trihydrate/clavulanate potassium, cefuroxime sodium, and ciprofloxacin. It was our intent to assess the impact of these orders on clinical outcome (time to next exacerbation, clinical symptomatology), antimicrobial outcome (culture eradication), and resource utilization (antimicrobial use) via a quality assurance retrospective chart review.

METHODS

Objectives

Our primary objective was to determine the time to next exacerbation in a population of patients with COPD admitted to the institution before and after the implementation of standing orders. Secondary objectives included comparing the clinical and microbiological outcomes of patients in both treatment groups, analyzing and comparing the use of antibiotics in the treatment groups, and comparing the time to next exacerbation with the type of antibiotic class. Our hypothesis was that the time to next exacerbation differed by at least 21 days in patients with an acute exacerbation of COPD between pre- and postimplementation of standing orders. The 'preimplementation' group consisted of patients admitted between September 1999 and August 2000; the 'postimplementation' group consisted of patients admitted between September 2000 and August 2001. Patients with COPD exacerbations as their major reason for admission were identified from a database maintained by the Division of Respiriology at Queen Elizabeth II Health Sciences Centre. The Research Ethics Board approved the study protocol via an expedited review.

Patients

In order to prevent bias, hospital unit numbers (HUNs) were randomly chosen from the database and, where applicable, assigned to either the pre- or postimplementation group. A total of 832 patients were randomized, 682 of which were excluded for various protocol violations. Patients with Anthonisen Type-III exacerbations were excluded as antibiotic use is not advocated in this population (11). Other exclusion criteria included a diagnosis of asthma or pneumonia, a history of cystic fibrosis or lung carcinoma, or the concomitant use of an antibiotic for another indication.

The Medical Records Department retrieved the charts from the defined randomized list. Over a six-week period (March 2002 to April 2002) a retrospective chart review and data extraction was conducted. Patient data were reviewed for a minimum of nine months to identify the date of the next exacerbation. Subsequent exacerbations were limited to patients who either were admitted to or visited the emergency department of the Queen Elizabeth II Health Sciences Centre. The chart analysis included the collection of baseline characteristics of each patient including age, gender, concomitant disease status, smoking status, pulmonary function tests, antibiotic usage, and steroid usage.

Statistics

Data were compared by Student's *t* test, χ^2 test, Fisher's exact test, and Log-rank test, where appropriate. 95% Confidence Intervals

(95% CIs) were recorded and all P-values were judged to be significant if the result of a two-sided test was less than 0.05. Patients were censored nine months following the acquisition period.

A clinically significant difference between treatment groups was measured as time to next exacerbation. Using a two-tailed alpha of 0.05 and power of 0.8, the required sample to detect a difference between 150 days and 171 days was determined to be 57 patients per group. Accounting for invalid patients, the study required 74 patients per arm, for a total of 148 patients.

RESULTS

Patient demographics

Demographic and clinical characteristics were similar between treatment groups (Table 1). Based on forced expiratory volume in 1 second (FEV₁) data, the majority of patients presented with a severe COPD disease state, while slightly more patients presented with a moderate exacerbation. Patients in the preimplementation group had fewer exacerbations during the preceding year, however, this result was not statistically significant (P=0.69). In keeping with recent epidemiology of the changing face of COPD, this group is predominately female (61%).

Infection free interval

A total of 208 exacerbations (150 initial, 58 subsequent) were recorded. Within the patient group experiencing a subsequent exacerbation, the mean time to next exacerbation was 132±15 days (n=58). Patients in the preimplementation group had an infection-free interval of 134±21 days (n=28), the same was seen for the postimplementation group (130±21 days [n=30], a nonsignificant difference [P=0.89]).

A Kaplan-Meier survival curve was conducted for an analysis of exacerbation events in the overall population (Figure 3). The mean time to next exacerbation was 304±13 days. There was no difference in the overall mean time to next exacerbation (preintervention 310±18 days, postintervention 289±18 days, P=0.53). The estimated probability that a patient will be exacerbation-free for 365 days or more is 63±4%.

Clinical outcomes

Overall symptom resolution, defined as a return to baseline of all Anthonisen symptoms (increased dyspnea, sputum volume, and sputum purulence), was recorded (n=52). A 7% relative increase in symptom resolution was observed in the postimplementation group, this result, however, was not statistically significant (59% versus 63%, P=1.0). The length of stay was longer in the postimplementation group (10.8±0.58 days versus 8.6±1.14 days), but was not statistically significant (P=0.08) (Table 2).

Medication use

Ninety per cent of the patients received a course of antibiotics (87% preintervention, 93% postintervention, P=0.30). Antibiotics were initiated within the first 24 h in 90% of these cases. One hundred seventy-two courses of antibiotics were ordered using 14 different antibiotics. Cefuroxime sodium, doxycycline hyclate, levofloxacin and TMP/SMX represented 77% of the antibiotic utilization. Levofloxacin, cefuroxime sodium and TMP/SMX were used more frequently in the preimplementation group (30%, 22% and 22% respectively) than in the postimplementation group (18%, 12% and 11%, respectively), which trended towards significance (P=0.09). In

<p>Physician Standing Orders Department of Medicine Admission Standing Orders Diagnosis: Exacerbation of COPD</p> <p>Patient: _____ Allergies _____ Smoking Status: _____ Date (YYYY/MM/DD) _____ Time (24h/hh:mm) _____</p> <p>1. The following orders may be used in any patient care area. 2. The following orders will be carried out by a qualified Nurse/Health Care Professional ONLY on the AUTHORITY OF A PHYSICIAN. 3. All orders to be carried out must be checked as appropriate.</p> <p>4. Nutrition <input type="checkbox"/> Diet _____ <input type="checkbox"/> Ht and Wt <input type="checkbox"/> Nutrition consult RMO <input type="checkbox"/> yes <input type="checkbox"/> no</p> <p>5. Mobility <input type="checkbox"/> Activity _____ <input type="checkbox"/> Consult Physiotherapy RMO <input type="checkbox"/> yes <input type="checkbox"/> no</p> <p>6. Vital Signs <input type="checkbox"/> Temp, HR, RR, BP, QID x 48h , then reassess <input type="checkbox"/> Other _____</p> <p>7. Chemstrips <input type="checkbox"/> If known diabetes, do chemstrip (ac & qhs) <input type="checkbox"/> If no known diabetes BID x 48h then reassess <input type="checkbox"/> Contact MD if chemstrip <4 mmol/L or > 15 mmol/L</p> <p>8. Investigations <input type="checkbox"/> Sputum C&S and Gram stain <input type="checkbox"/> Spirometry (admission and within 48h of discharge)</p> <p>9. Oxygen Therapy <input type="checkbox"/> Nasal prongs (uncontrolled FiO₂) @ _____ L/min</p> <p style="text-align: center;">OR</p> <p>If hypercapnic, Venturi Mask (Controlled FiO₂) FiO₂ @ <input type="checkbox"/> 0.24 <input type="checkbox"/> 0.28 <input type="checkbox"/> _____</p> <p>To keep O₂ saturation at: <input type="checkbox"/> 85%-88% or <input type="checkbox"/> 88%-92% <input type="checkbox"/> _____ <input type="checkbox"/> ABG @ _____ (time) <input type="checkbox"/> O₂ saturation in _____h <input type="checkbox"/> O₂ saturation daily</p> <p>----- Date: (YYYY/MM/DD) _____</p> <p>----- License Number _____ QE8020 07/00</p>	<p>10. MEDICATIONS</p> <p>(a) Bronchodilators MDI with spacer <input type="checkbox"/> Ipratropium Bromide 4 puffs q4h x 48h then reassess <input type="checkbox"/> Salbutamol 4 puffs q4h x 48h then reassess <input type="checkbox"/> Salbutamol 4 puffs q2h PRN</p> <p style="text-align: center;">OR</p> <p>Wet Nebulizer <input type="checkbox"/> Ipratropium Bromide 0.5 mg q4h x 48h then reassess <input type="checkbox"/> Salbutamol 5 mg q4h x 48h then reassess <input type="checkbox"/> Salbutamol 5 mg q2h PRN <input type="checkbox"/> Salbutamol 2.5 mg q2h PRN</p> <p>(b) Steroid Therapy <input type="checkbox"/> Prednisone _____ mg po daily</p> <p style="text-align: center;">OR</p> <input type="checkbox"/> Methylprednisolone _____ mg IV q ___h <p>(c) Antimicrobials (Calculate CrCl-see reverse) <i>(If chest x-ray indicates pneumonia, start CAP Pathway and choose antimicrobials from the pathway)</i></p> <p>If 2 of the following, use antimicrobials: Increased dyspnea Increased sputum volume Increased sputum purulence</p> <input type="checkbox"/> TMP-Sulfa DS 1 tab po BID x 10 days <input type="checkbox"/> Doxycycline 200 mg po stat then 100 mg po BID x 10 days (with a full glass of water and sit up x 1h) <i>(For 3 or more exacerbations of COPD in the last year or use of antimicrobials in the last 30 days for a respiratory infection, consider a second line antimicrobial)</i> <input type="checkbox"/> Second line oral antimicrobial agent (see reverse) <p>-----</p> <p>11. <input type="checkbox"/> Consult COPD Case Management Coordinator</p> <p>12. Code Status ("Full code" if there is no order) _____</p> <p>----- Physician's Signature _____</p> <p>----- Physician's Name-Print _____</p>
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Figure 1 Physician standing orders for acute exacerbations of chronic obstructive pulmonary disease (COPD) implemented at the Queen Elizabeth II Health Sciences Centre in September 2000 – front page, emphasizing use of first-line antibiotics. ABG Arterial blood gas; ac Before meals; BID Twice a day; BP Blood pressure; C&S Culture and sensitivity; CAP Community-acquired pneumonia; CrCl Creatinine clearance; FiO₂ Fraction of inspired oxygen; Ht Height; HR Heart rate; IV Intravenous; MDI Metered dose inhaler; PRN As required; RMO Requisition made out; RR Rate of respiration; Wt Weight

contrast, there was a statistically significant increase ($P<0.01$) in the frequency of doxycycline hyclate use in the postimplementation group (35%) compared to the preimplementation group (5%). Overall, second-line agents were used more frequently than first-line agents (54% versus 37%). There was a 20% increase in the use of first-line agents in the postimplementation group ($P=0.01$) (Figure 4).

Systemic corticosteroids were used in 95% of the patients, with no significant difference between treatment groups with regard to their use ($P=0.75$); however, there was a difference with regard to dosage formulation. Patients in the preimplementation group were more likely to receive intravenous steroids than oral steroids (61% versus 39%, $P=0.03$), while the reverse was true for the postimplementation group.

Microbiological data

Sputum cultures were obtained more often at baseline in the postimplementation group (78% versus 42%, $P<0.01$). Only 15 positive cultures (five preimplementation, 10 postimplementation) were obtained, identifying 21 potential pathogens (seven preimplementation, 14 postimplementation) of which 17 were bacterial and four fungal. *Pseudomonas aeruginosa*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Staphylococcus aureus* accounted for 82% of the bacteria identified (Table 3).

DISCUSSION

Prolongation of the time to the next exacerbation is a secondary outcome of many recent COPD trials. The implementation of our standing orders did not influence the infection-free interval or time to symptom resolution. Although there was a slightly shorter infection-free interval in the postimplementation group, it was not a significant difference over the preimplementation group. This demonstrates that despite the more standardized global, patient-focused approach to treating acute exacerbations of COPD, the overall effects of the therapeutic choices within the standing order are neither beneficial nor detrimental with regard to patient outcomes.

TABLE 1
Patient demographics

Characteristic	Overall n=150 (%)	Pre-implementation n=76 (%)	Post-implementation n=74 (%)	P-value*
Mean age in years ± sd	73 ± 1	72 ± 1	74 ± 1	0.22†
Female	91 (61)	46 (61)	45 (61)	1
Male	59 (39)	30 (39)	29 (39)	–
Smoking status (n = 145)				–
Active	59 (41)	36 (47)	23 (31)	0.95†
Former	78 (54)	33 (43)	45 (61)	0.21†
Never	8 (5)	6 (8)	2 (3)	–
Coronary artery disease	59 (39)	28 (37)	31 (42)	0.59
Congestive heart failure	39 (26)	19 (25)	20 (27)	0.88
Diabetes mellitus	35 (23)	21 (28)	14 (19)	0.29
Anthonisen's Criteria				–
Type I exacerbation	67 (45)	35 (46)	32 (43)	–
Type II exacerbation	83 (55)	41 (54)	42 (57)	–
FEV ₁ on admission (n=80)				0.29
< 35%, severe impairment	57 (38)	28 (37)	29 (39)	–
35-49%, moderate impairment	15 (10)	7 (9)	8 (11)	–
≥ 50%, mild impairment	8 (5)	6 (8)	2 (3)	–
No prior exacerbations‡	76 (51)	41 (54)	35 (47)	0.62
>3 prior exacerbations	9 (6)	3 (4)	6 (8)	–

* χ^2 analysis unless otherwise specified; † student t-test performed; ‡ hospital admission or emergency visit at the Queen Elizabeth II Health Sciences Centre. Anthonisen's Criteria: Type I exacerbation – all three symptoms of increased dyspnea, increased sputum volume and increased sputum purulence; Type II exacerbation – two of the three clinical symptoms. FEV₁, Forced expiratory volume in 1 second

Factors Leading to Admission

#1 Acute deterioration of COPD

#2 Inadequate response of symptoms to outpatient management

#3 Unable to cope with prescribed medical management

#4 Lack of community resources. Consider referral to HCNS

#5 Placement issues. Consider referral to Social Work

#6 Financial issues. Consider referral to Social Work

#7 Conclusion by Emergency Physician or Discharge Planning Nurse patient cannot manage at home with supplementary home care resources not immediately available

#8 Other _____

Antimicrobials

Dosage of TMP-Sulfa:

- If CrCl<30 mL/min **decrease** TMP-Sulfa to 1 DS tab q24h.
- If CrCl<20 mL/min **avoid** the use of TMP-Sulfa and choose Doxycycline or one of the second-line antimicrobials.

CrCl (males) = $\frac{(140 - \text{Age})(\text{IBW in Kg})(60)}{(\text{Scr})(50)}$

CrCl (females) = 0.85 x male

Second-line

If 3 or more exacerbations in the last year or recent use of antimicrobials in the last 30 days, consider one of the following:

- Azithromycin 500 mg po on day one, then 250 mg daily x 4 days.
- Amoxicillin/Clavulanate 875/125 mg po q12h x 10 days.
- Cefuroxime 500 mg po q12h x 10 days.
- Ciprofloxacin 500 mg po q12h x 10 days or ciprofloxacin 750 mg po daily if CrCl<30 mL/min

Figure 2) Physician standing orders for acute exacerbations of chronic obstructive pulmonary disease (COPD) implemented at the Queen Elizabeth II Health Sciences Centre in September 2000 – back page, with second line antibiotic options. CrCl Creatinine clearance; DS Double strength; HCNS Home care Nova Scotia; IBW Ideal body weight; po By mouth; Scr Serum creatinine; TMP Sulfa Trimethoprim/sulfamethoxazole

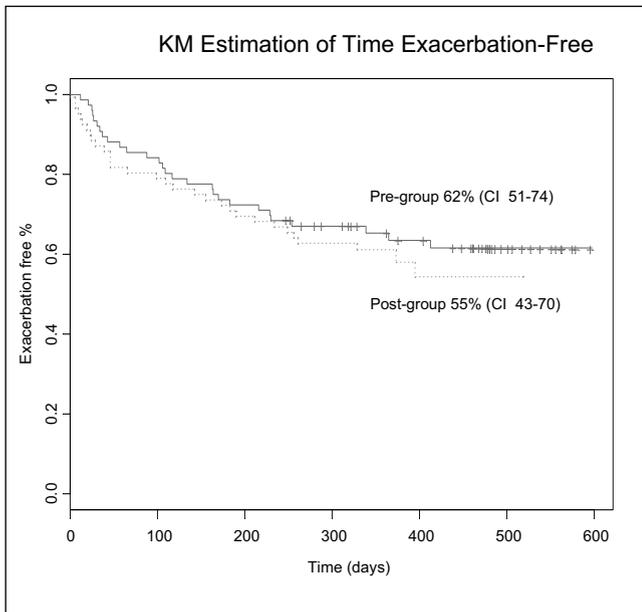


Figure 3) Kaplan Meier (KM) analysis of the time to next exacerbation. The top line (solid) represents the estimate of infection-free interval of the preimplementation group. The bottom line (dashed) represents that of the postimplementation group

TABLE 2
Clinical results

Variable (mean ± SD)	Overall	Pre-implementation	Post-implementation	P value
Length of stay	9.7 ± 0.6	8.6 ± 1.1	10.8 ± 0.6	0.08
Days between exacerbation*	132.2 ± 14.9	134.3 ± 21.0	130.3 ± 21.4	0.89
Days to next exacerbation†	303.6 ± 12.6	309.7 ± 17.5	288.9 ± 17.8	0.53‡

*subgroup of patients with a subsequent exacerbation (n=58); †estimate of the overall study population; ‡Log-Rank test

Treating exacerbations of COPD with antibiotics has been an area of controversy over the past 40 years. Since the 1960s, there have been several placebo-controlled trials analyzing the efficacy of antibiotics in COPD exacerbations. Seven trials analyzing similar antibiotics as those commonly prescribed at this institution have demonstrated an overall benefit for the patient (11,14-19). Albeit small, this benefit was reinforced by two meta-analyses of 11 randomized, placebo-controlled trials by Saint et al in 1995 (20) and McCrory (21). These analyses, however, had difficulty accounting for heterogeneity between trials as there has been a lack of consensus regarding the description of a COPD exacerbation as well as the use of concomitant medications. Variable rating systems and ever-changing outcome measures between trials further challenge the notion of antibiotic use. Although not conclusively demonstrated, it is clear that patients who present with evidence of a bacterial infection with moderate to severe exacerbations (Anthonisen Type-I or Type-II) benefit from antibiotics. The use of antibiotics is reinforced by various sets of national consensus guidelines (3,4,6,21-26). Canadian anti-infective guidelines have also encouraged risk stratification, suggesting certain individuals in whom it would be more appropriate to commence therapy with a second-line antibiotic (25).

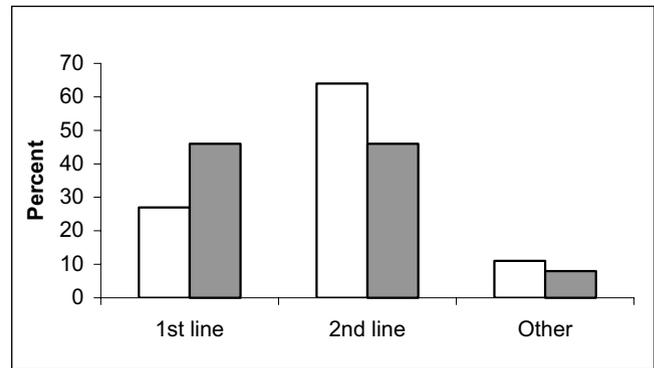


Figure 4) Per cent of antibiotics used during the study, grouped according to antibiotic class. The white bar represents the preimplementation group while the dark bar represents the postimplementation group. First-line antibiotics included trimethoprim/sulfamethoxazole and doxycycline hyclate. Second-line antibiotics included azithromycin dihydrate, amoxicillin trihydrate/clavulanate potassium, cefuroxime sodium and ciprofloxacin

TABLE 3
Microbiological results

Positive culture organism identified	Overall n=21 (%)	Pre-implementation n=7 (%)	Post-implementation n=14 (%)
<i>Pseudomonas aeruginosa</i>	4 (19)	—	4 (29)
<i>Haemophilus influenzae</i>	3 (14)	—	3 (21)
<i>Streptococcus pneumoniae</i>	4 (19)	—	4 (29)
<i>Staphylococcus aureus</i>	2 (10)	2 (29)	—
Other*	8 (38)	5 (71)	3 (21)

*includes methicillin-resistant *Staphylococcus aureus*, *Serratia marcescens*, *Stenotrophomonas maltophilia*, Group B-hemolytic streptococcus species, and *Candida albicans*

The use of antibiotics in acute exacerbations of COPD has become a standard of practice; what is not clear is which antibiotics should be used and when. This uncertainty continues because studies have not clearly demonstrated the benefit of newer antibiotics over older antibiotics (27). The present study was not powered to evaluate such a question but it does perpetuate the question at hand: does the specific antibiotic or antibiotic class affect patient outcome?

Despite the general agreement that antibiotics should be a part of the management of patients with acute exacerbations of COPD, 10% of patients in this study did not receive an antibiotic. This rate was not significantly different in the postimplementation group (13% versus 7%, P=0.19).

There were several discrepancies in antibiotic use between treatment groups, an obvious reflection of the impact of the standing orders. First-line agents were used more frequently in the postimplementation group, a direct result of the 87% increase in doxycycline hyclate use. The use of levofloxacin, the drug of choice before the implementation of the standing orders, decreased by 36%. The continued use of this antibiotic may be due, in part, to the growth of knowledge in regard to the 'respiratory quinolones' over the past several years.

Interestingly, in the subgroup of patients with a subsequent exacerbation, levofloxacin (a second-line fluoroquinolone antibiotic) was the antibiotic most frequently used in the preimplementation group, with a relative difference of 40%. One would expect that if this antibiotic, or class of antibiotic, was superior to others, as demonstrated by Wilson et al (28), fewer patients in the preimplementation group would have subsequently had another exacerbation within the follow-up period. Another interesting finding from this subgroup was that patients with a subsequent exacerbation were more likely to have received a second-line agent during their initial exacerbation, regardless of treatment group. This finding is contradictory to a retrospective analysis (29) that demonstrated that antibiotic selection is not an independent risk factor for clinical failure.

The standing orders have had a dramatic impact on antibiotic use, apparent in the postimplementation subgroup. Within this group of 74 patients, physicians were more likely to prescribe doxycycline hyclate if the orders were implemented. If not implemented, 500 mg of levofloxacin once daily was the antibiotic of choice. It is apparent that the standing orders for acute exacerbations of COPD streamline the use of antibiotics. However, the effects of this antibiotic rationalization on patient outcome is unclear.

Organisms identified from sputum cultures were in keeping with expectations, however, the variance in the distribution of organisms among treatment groups is puzzling. In the

postimplementation group, *Pseudomonas aeruginosa* was present in almost 30% of the cultures, whereas it was not present in the preimplementation group. Caution should be used in extrapolating these findings because only 15 samples were positive and we were not able to distinguish between colonizer and pathogen. Furthermore, current practice does not advocate obtaining a repeat culture, especially if the patient is clinically improving.

As with any study, there are limitations. Because it was a retrospective study we were unable to accurately account for antibiotic use before admission to hospital. This is important because it could influence the initial antibiotic used upon admission, and therefore, would provide additional insight into the general health of the patient and any possible resistant organisms he or she may be harboring. Patients' subsequent exacerbations were only accounted for if they returned to our institution, therefore transient patients or patients who sought medical attention elsewhere were not captured. The largest limitation of the study is that it only analyzes a subsection of a comprehensive treatment protocol affecting clinical outcomes in patients with exacerbations of COPD.

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