

## ORIGINAL RESEARCH

# Comparison of efficacy of Narrow-Versus Broad-Spectrum Antibiotics in elderly patients with acute exacerbations of chronic obstructive pulmonary disease

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Received: 08 June, 2023

Accepted: 10 July, 2023

### ABSTRACT

**Background:** To compare efficacy of narrow-versus broad spectrum antibiotics in patients aged more than 65 years with AECOPD. **Materials & Methods:** A total of 100 subjects were enrolled. The study focused on subjects aged 65 and above who were hospitalized for acute exacerbation of chronic obstructive pulmonary disease (AECOPD) and received a minimum of 48 hours of antibiotic treatment. The data was collected and result was analysed using SPSS software. **Results:** The study involved a total of 100 patients, with 50 individuals assigned to the narrow-spectrum group and another 50 individuals assigned to the broad-spectrum group. The primary combined outcome was observed in 17 patients (34%) from the narrow-spectrum group and in 22 patients (44%) from the broad-spectrum group, showing no significant difference ( $P = 0.2$ ). **Conclusion:** The primary outcome among hospitalized individuals aged 65 years and older with AECOPD who were treated with either broad-spectrum or narrow-spectrum antibiotics.

**Keywords:** Antibiotics, Exacerbations, Elderly, Chronic obstructive pulmonary disease.

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### INTRODUCTION

Chronic obstructive pulmonary disease (COPD) constitutes one of the principal demands of medical attention in primary care. According to local studies, it is estimated that up to 8%–10% of the population over 40 years of age may be affected by COPD and, in men over 65 years of age, this figure may rise to 20%.<sup>1</sup> Exacerbations are acute episodes of an increase in respiratory symptoms that characterize the course of COPD and result in impaired quality of life, particularly in moderate patients in primary care.<sup>3</sup> Furthermore, they accelerate the decline in lung function, increase health care utilization and constitute the main cause of death of patients with COPD.<sup>4</sup> COPD exacerbations are classified as mild, moderate, or severe. Treatments for exacerbations differ based on their classification. Outpatients experiencing mild exacerbations are managed with short-acting bronchodilators only. Outpatients experiencing

moderate exacerbations are generally treated with short-acting bronchodilators and antibiotics, with or without oral corticosteroids, depending on clinical signs and symptoms. Patients experiencing severe exacerbations are hospitalized with possible intensive care admission.<sup>5</sup> There are many potential causes of COPD exacerbations and many pharmacological options for managing COPD exacerbations. Pharmacological therapies target both the symptoms and the cause of the exacerbation.

COPD is a chronic disease and is mostly managed on an outpatient basis. Part of the natural history of this disease is intermittent acute episodes of increased respiratory symptoms and worse pulmonary function that may be accompanied by fever and other constitutional symptoms, which are characterized as acute exacerbations. These exacerbations are a major driver for office visits, hospitalizations and therefore cost of care in COPD. In advanced disease, they are

also the most frequent cause of death in this disease.<sup>6,7</sup> The frequency of exacerbations varies widely between patients, but is generally correlated with the severity and duration of underlying COPD. A key feature of airway inflammation in COPD is the persistent presence of bacteria in the lower respiratory tract. The most commonly isolated bacteria in the lower respiratory tract of patients with COPD are *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Streptococcus pneumoniae*, with increasing evidence of the importance of *Pseudomonas aeruginosa* infection in severe COPD.<sup>8</sup> These bacteria exhibit high resistance to many antibiotics, and empirical treatment for serious systemic infections often involves a two-drug regimen.<sup>9</sup> The efficacy of combination antibiotic therapy in patients with gram-negative bacillus sepsis has been previously tested, with most studies including a combination of beta-lactam antibiotics and aminoglycosides. Overall, the mortality rate for patients treated with beta-lactam-aminoglycoside combination therapy was not significantly reduced compared with that of patients with gram-negative bacillary sepsis treated with beta-lactam monotherapy.<sup>10,11</sup> Another potentially favorable combination is a beta-lactam plus a fluoroquinolone. However, while these combinations exhibit synergistic strength (i.e., no organisms isolated after the 24-h killing tests) due to the bactericidal activity of the combination, the minimum inhibitory concentrations of organisms recovered were unaltered.<sup>12</sup> With increased antibiotic resistance in gram-negative bacilli, the use of combination antibiotic therapy to treat sepsis caused by these bacilli has resurfaced.<sup>13</sup> Hence, this study was

conducted to compare efficacy of narrow-versus broad spectrum antibiotics in patients aged more than 65 years with AECOPD.

## MATERIALS & METHODS

A total of 100 subjects were enrolled. The study focused on subjects aged 65 and above who were hospitalized for acute exacerbation of chronic obstructive pulmonary disease (AECOPD) and received a minimum of 48 hours of antibiotic treatment. The type of antibiotics that were given to the subjects were compared. The antibiotics were categorized into narrow-spectrum antibiotics, namely azithromycin, and doxycycline. The broad spectrum antibiotics were also included. The main outcome measured was a combination of factors: the need for mechanical ventilation 48 hours after admission, transfer to the intensive care unit within 48 hours of admission, readmission due to chronic obstructive pulmonary disease (COPD) within 30 days, and oxygen levels dropping below 90% either on regular air or requiring more oxygen compared to baseline 48 hours after admission. The data was collected and result was analysed using SPSS software.

## RESULTS

The study involved a total of 100 patients, with 50 individuals assigned to the narrow-spectrum group and another 50 individuals assigned to the broad-spectrum group. The primary combined outcome was observed in 17 patients (34%) from the narrow-spectrum group and in 22 patients (44%) from the broad-spectrum group, showing no significant difference ( $P = 0.2$ ).

**Table 1: Antibiotics prescribed**

Antibiotics	Number of subjects
Narrow spectrum	50
Azithromycin	44 (88)
Doxycycline	4 (8)
Broad spectrum	50
Fluroquinolone	20(40)
Third generation cephalosporin with azithromycin	19(38)

**Table 2: Primary and secondary outcomes**

Outcomes	Narrow	Broad	P-value
Composite outcome	17 (34)	22 (44)	0.2
Mechanical ventilation 48 hours after admission	1 (2)	2(4)	0.3
O <sub>2</sub> saturation 48 hours after admission	0	1(2)	1
O <sub>2</sub> requirements increased increased after 48 hours after admission	13(26)	18(36)	0.2
Adverse drug reaction to study medications	1 (2)	0	1

## DISCUSSION

Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death in the United States and the 6th leading cause worldwide. It is estimated that by 2020, it would become the 3rd leading cause of death in the US and worldwide. Affecting 24 million people in the US, up to half of them undiagnosed, it

accounts for 13.76 million office visits, 1.5 million emergency room visits and 726,000 hospitalizations annually, at an estimated direct cost of \$18 billion.<sup>14</sup> Hence, this study was done to compare efficacy of narrow-versus broad spectrum antibiotics in patients aged more than 65 years with AECOPD.

In the present study, the study involved a total of 100 patients, with 50 individuals assigned to the narrow-spectrum group and another 50 individuals assigned to the broad-spectrum group. A study by Joyner KR et al, patients were compared based on the spectrum of their antibiotic therapy. Narrow-spectrum antibiotics included: azithromycin, doxycycline, sulfamethoxazole/trimethoprim, or aminopenicillin. The primary outcome was a composite of mechanical ventilation 48 hours after admission, transfer to the intensive care unit 48 hours after admission, 30-day chronic obstructive pulmonary disease (COPD) readmission, and oxygen saturation less than 90% on room air or increased oxygen requirements from baseline 48 hours after admission. Two hundred fifty-three patients were included in this analysis; 127 patients were included in the narrow-spectrum group, and 126 patients were included in the broad-spectrum group. Patient demographics and comorbid conditions were similarly distributed in each group. The incidence of the primary composite outcome occurred in 50 (39.3%) and 60 (47.6%) of patients in the narrow- and broad-spectrum groups, respectively ( $P = .19$ ). No difference was found in the primary outcome in inpatients aged  $\geq 65$  years with AECOPD who received empiric broad-spectrum or narrow-spectrum antibiotics.<sup>15</sup>

In the present study, the primary combined outcome was observed in 17 patients (34%) from the narrow-spectrum group and in 22 patients (44%) from the broad-spectrum group, showing no significant difference ( $P = 0.2$ ). Another study by LlorC et al, a total of 137 patients were enrolled in the study (68 assigned to amoxicillin and 69 to amoxicillin/clavulanate). The mean forced expiratory flow in one second was 61.6% and the mean age was 71.4 years. At EOT, 92.8% of patients in the amoxicillin/clavulanate and 90.9% in the amoxicillin group were considered clinically cured, a statistically non-significant difference. Adverse effects were observed in 11 subjects, 3 in the amoxicillin group and 8 in the amoxicillin/clavulanate group, 2 of whom required a change in treatment. Amoxicillin was at least as effective clinically and as safe as amoxicillin/clavulanate in the treatment of acute exacerbations of COPD in mild to moderate patients in primary care.<sup>16</sup> These findings indicate that respiratory infections are strongly associated with most cases of COPD exacerbations. Despite this, the use of antibiotics in the treatment of COPD exacerbations remains controversial. When warranted, the use of antibiotics results in positive patient outcomes, regardless of which antibiotic was utilized. In a systematic review that included 10 trials and a total of 917 patients, the effects of antibiotic therapy in treating moderate-to-severe COPD exacerbations were evaluated. The results demonstrated a 77% reduction in mortality rates, a 44% reduction in sputum purulence, and a 53% reduction in treatment failure in patients included in stratification.<sup>17</sup> In the

landmark MOSAIC trial, patients were randomized to either moxifloxacin (a fluoroquinolone) or standard therapy with amoxicillin, cefuroxime, or clarithromycin. The study found a significant improvement in the symptoms of those who completed therapy with moxifloxacin compared to those who received standard therapy. Additionally, there was a superior bacteriologic response of 91.5% in the moxifloxacin treatment arm compared to 81% in the standard therapy arm. The trial also demonstrated the long-term benefits of therapy with moxifloxacin. At five months follow-up, the time until the next exacerbation was prolonged in those that were treated with moxifloxacin compared to those that received the standard therapy (131 days until the next exacerbation in the moxifloxacin group compared to 104 days in the standard therapy group).<sup>18</sup> Acquisition of strains of bacterial pathogens that are new to the host from the environment appears to be the primary event that puts the patient with COPD at risk for an exacerbation.<sup>19</sup> Variations among strains of a species in the surface antigenic structure, as is seen with NTHI, *S pneumoniae* and *M catarrhalis* allow these newly acquired strains to escape the pre-existing host immune response that had developed following prior exposure to other strains of the same species of bacteria. These strains can therefore proliferate in the lower airways and induce acute inflammation in the airways. The virulence of the strain and as yet unidentified host factors may determine if the acute inflammatory response to the pathogen reaches the threshold to cause symptoms that present as an exacerbation.<sup>20</sup>

## CONCLUSION

The study did not identify any distinction in the primary outcome among hospitalized individuals aged 65 years and older with AECOPD who were treated with either broad-spectrum or narrow-spectrum antibiotics.

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