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EVALUATION OF EFFICACY AND SAFETY OF GEMIFLOXACIN IN CHRONIC BRONCHITIS PATIENTS

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ABSTRACT: The study aimed to assess the efficacy and safety of Amoxicillin/Clavulanate 625 mg and Amoxicillin/Clavulanate 1 gram in chronic bronchitis patients. Chronic bronchitis, a type of COPD defined by a productive cough that lasts for 3 months or more for at least 2 years, other symptoms include wheezing and breathlessness, upon exertion. It is caused by recurring irritation to the epithelium of bronchi, resulting in chronic inflammation, edema and increased production of mucus by goblet. Clavulanate has high affinity for and binds to certain β -lactamases that generally inactivate amoxicillin by hydrolyzing its β -lactam ring. Combining Clavulanate potassium with amoxicillin extends the antibacterial spectrum of Amoxicillin. The objective is to evaluate the efficacy of monotherapy, adverse drug reaction and perform the comparison of both in Amoxicillin/Clavulanate 625 mg and Amoxicillin/Clavulanate 1 gram. A prospective observational study design was used and the Clinical symptoms, X-ray, PFT (FVC, FEV1, FEF, (FEV1/FVC) and Bacteriologic assessment were assessed to monitor its efficacy and safety. Hence the study concluded that Amoxicillin/Clavulanate 625 mg group was found to be an effective and better alternative to Amoxicillin/Clavulanate with better efficacy and safety.

INTRODUCTION: Bronchitis is an inflammation of the main air passages (bronchi) to the lungs, which results in the production of excess mucous, a reduction in the amount of airflow in and out of the lungs and shortness of breath?

In chronic bronchitis, there is excessive bronchial mucus with a productive cough for three months or more over two consecutive years without any other disease that could account for these symptoms. In the early stages of chronic bronchitis, a cough usually occurs in the morning. As the disease progresses, coughing persists throughout the day.^{1, 2}

In the later stages of chronic bronchitis, the patient cannot clear this thick, tenacious mucus, which then causes damage to the hair-like structures (cilia) that help sweep away fluids and/or particles

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in the lungs. This in turn impairs the lung's defense against air-borne irritants. Compared with acute bronchitis, which may respond quickly to medications, such as antibiotics, chronic bronchitis can be difficult to treat because many patients with chronic bronchitis are susceptible to recurring bacterial infections. This in turn impairs the lung's defense against air-borne irritants. Cigarette smoking is the most common cause of chronic bronchitis. People who have been exposed for a long time to irritants, like chemical fumes, dust and other noxious substances, can also get chronic bronchitis. As chronic bronchitis often coincides with emphysema, it is frequently difficult for a physician to distinguish between the two. Chronic bronchitis also can have an asthmatic component.^{3, 4, 5}

About 5% of the population has chronic bronchitis, and it is two times more common in females than in males. Chronic bronchitis is treated symptomatically. Inflammation and edema of the respiratory epithelium may be reduced with inhaled corticosteroids. Wheezing and shortness of breath can be treated by reducing bronchospasm (reversible narrowing of smaller bronchi due to constriction of the smooth muscle) with bronchodilators such as inhaled β -Adrenergic agonists and inhaled anticholinergics (e.g., ipratropium bromide).^{6,7}

Hypoxemia, too little oxygen in the blood, can be treated with supplemental oxygen. However, oxygen supplementation can result in decreased respiratory drive, leading to increased blood levels of carbon dioxide and subsequent acidosis. The most effective method of preventing chronic bronchitis and other forms of COPD is to avoid smoking cigarettes and other forms of tobacco. On pulmonary tests, bronchitis (bronchitis) may present a decreased FEV1 and FEV1/FVC. However, unlike the other common obstructive disorders, asthma and emphysema, bronchitis rarely causes a high residual volume. This is because the air flow obstruction found in bronchitis is due to increased resistance, which, in general, does not cause the airways to collapse prematurely and trap air in the lungs.⁸

Cigarette smoking is the most important risk factor for the development of chronic bronchitis. Over 90

percent of patients with chronic bronchitis have a smoking history, although only 15 percent of all cigarette smokers are ultimately diagnosed with some form of obstructive airway disease.^{9,10}

Chronic bronchitis is a common but serious respiratory tract ailment associated with significant morbidity and impact on healthcare costs. Bacterial infections are an important cause of chronic bronchitis. Where bacterial infections are suspected, early institution of antimicrobial therapy and supportive measures ensure quicker recovery. The organisms commonly implicated in chronic bronchitis are Haemophilus influenzae, Moraxella catarrhalis and Streptococcus pneumoniae, and the less common ones include non enteric, gram-negative organisms such as Pseudomonas aeruginosa. The commonly used antibiotics were amoxicillin, trimethoprim, doxycycline which were later on superseded by fluoroquinolones, macrolides, second- or third-generation cephalosporins, amoxicillin-clauvulanic acid, due to the emergence of antimicrobial resistance. Mild to moderately severe cases of chronic bronchitis comprise a significant number of patients who attend the outpatient clinics, and institution of oral antibiotic therapy that is effective and tolerable is indicated for those who are of suspected bacterial etiology.¹¹

Gemifloxacin, a newer generation fluoroquinolone, has pharmacokinetic and pharmacodynamic properties similar to other members of the class but has demonstrated better in vitro activity against S. pneumonia with lower minimal inhibitory concentration (MIC) values than the other respiratory fluoroquinolones. Antimicrobial activity against gram-negative respiratory pathogens (H. influenzae, M. catarrhalis) and atypical pathogens, such as Chlamydia pneumoniae, Legionella pneumophila, and Mycoplasma pneumoniae, are however comparable. Hence this study examined the efficacy and safety of monotherapy of Gemifloxacin in chronic bronchitis patients.^{12, 14, 15}

METHODOLOGY:

This was a prospective observational study in patients with chronic bronchitis performed in Department of Pulmonary Medicine SRM Medical College and Research Centre Kattankulathur,

Kancheepuram District Tamil Nadu. Patients were included in the study after obtaining written informed consent form and were selected based on the inclusion and exclusion criteria. Both Inpatients and out patients were included in the study. Men and women who were between 25-65 years of age were included in the study. Patients with chronic bronchitis having the symptoms of increased purulent sputum, increased cough and dyspnea also included in the study. Pregnant and Lactating Women, Pediatric patient, Asthma patient, Pneumonia patient, Lungs cancer patient, Renal and hepatic impaired patients and patients with Known hypersensitivity to Gemifloxacin were excluded in the study. The administration of Gemifloxacin 320 mg is done for the duration of 5 days (OD) in patients.

Patient demographic details like name, age, sex, date of admission, height and details like past medical history, past medication history, present medication and baseline value for parameters like X-ray, Pulmonary Function Test- Forced Vital Capacity (FVC), Forced Expiratory Volume (FEV₁), Force Expiratory Flow (FEF) and ratio of the (FEV₁/FVC) and sputum sample were collected. During review (After 7 days), the same parameters were measured once again. Based on the patient details and above parameters was analyzed, used to assess the efficacy and safety from the following clinical and bacteriological assessments:

Clinical Assessment and outcome measures

The clinical status of patients was assessed at regular intervals throughout the study. Assessments were performed at least once during treatment within 72 Hours; Clinical response was determined 5 to 10 days after the completion of study treatment and was classified as improvement, cure or failure. Cure was defined as resolution of all signs and symptoms of chronic bronchitis that had been present at study entry without need for further antibiotics.

Improvement was defined as the improvement is seen in symptoms what it's not resolved completely. Failure was defined as no improvement seen in signs or symptoms of chronic bronchitis or worsening of signs or symptoms after the therapy.

Bacteriologic Assessment and outcome measures

Specimens for bacteriologic assessment were obtained from spontaneously expectorated sputum, which was collected once within the 48 hours before the first dose of study medication and post treatment phases. The bacteriologic response of post treatment pathogens was determined after the completion of treatment and was classified as eradication, presumed eradication, persistence. Eradication was defined as the absence of the original pathogen on a post treatment sputum culture. Presumed eradication was defined as a clinical response of cure (improvement or a return to baseline of all signs and symptoms related to the acute infection and no new signs or symptoms of infection. Persistence was defined as identification of the original pathogen on a purulent post treatment sputum culture.

Safety Assessment and outcome measures

Patients who received at least one dose of study medication were included in the safety analysis. All adverse events were recorded and assessed for its severity.

RESULTS AND DISCUSSION:

A total of 63 patients were enrolled for the study, and treated with Gemifloxacin 320 mg based on inclusion and exclusion criteria. During the study period, 3 patients were excluded from study, due to lack of exact information. The data of remaining 60 patients were analyzed.

Age wise distribution of patients, 4 (6.67%) patients were in the age group of 25-35 years, 6 (10%) patients were in the age group of 36-45 years, 20 (33.33%) patients were in the age group of 46-55 years and 30 (50%) patients were in the age group of 56-65 years.

Out of 60 (100%) patients included in the study, 40 (66.7%) were males and 20 (33.3%) were females. Most of the patients participated in the study were males.

Out of 60 (100%) patients included in the study 34 (56.7%) patient had family history of respiratory disease and 26 (43.3%) did not have family history of any respiratory disease.

Out of 60 (100%) patients included in the study, 40 (66.7%) were chronic smoker, 4 (6.7%) were occasional smoker, 8 (13.3%) were domestic smoker and 8 (13.3%) were non smoker. Most of

the patients participated in the study had the chronic smoking habits.

In Pulmonary Function Test, the base and review levels of FEV₁ were 43.10±5.215 and 77.70±4.452, FVC were 51.53±6.532 and

80.20±6.435, FEV₁/FVC were 49.77±10.006 and 79.47±6.516 and for FEF were 22.77±2.315 and 35.87± 2.956 respectively Hence all the base and review levels of three groups show the significant p value. (P value = 0.0001 S). (Table 1)

TABLE 1: BACTERIOLOGICAL ASSESSMENT IN DIFFERENT GROUPS

Bacteriologic assessment	Gemifloxacin 320 mg	
	No. of patients (n=30)	Percentage (%)
Eradication	46	76.7
Presumed Eradication	8	13.3
persistence	6	10.0

Spontaneously expectorated sputum was collected for bacteriologic assessments before 48 hours of treatment and after the completion of the treatment.

Out of 60 patients, 46 (66.7%) were in the state of eradication, 8 (13.3%) were in the state presumed eradication, 6 (10%) were in the condition of persistence (Table 2)

TABLE 2: CLINICAL ASSESSMENTS AND OUTCOMES

Stage	Gemifloxacin 320 mg	
	No. of patients (n=30)	Percentage (%)
Cured	34	56.7
Improved	20	33.3
Failure	6	10.0

In Clinical assessments and outcomes measurement total 60 patients who treated with Gemifloxacin 320 mg, 34 (56.7%) were cured completely, 20

(33.3) patients condition were improved and 6 (10%) patients condition were not improved. For the assessment of adverse drug reactions,

categorized in to different category like diarrhea, nausea and vomiting, stomach pain and headache. Amongst all the patients, 6 (10%) experienced diarrhea, 2 (3.3%) patient had vomiting, 52 (86.7%) of patients not shown any adverse drug reaction. (Figure 1)

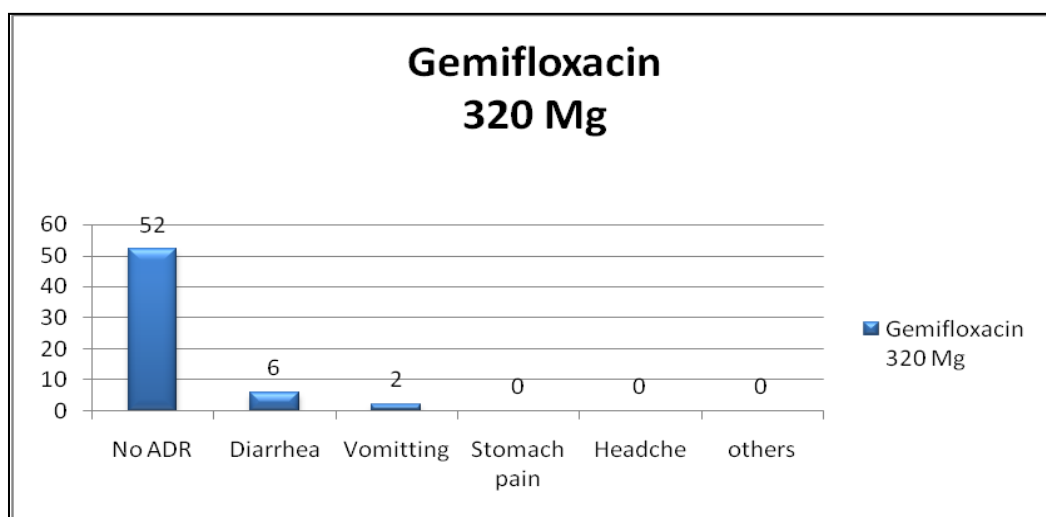


FIGURE: 1 GRAPHICAL REPRESENTATIONS OF ADVERSE DRUG REACTION

CONCLUSION: The overall clinical cure and bacteriologic eradication rates were seen significantly higher after the treatment, Gemifloxacin 320 mg shows the better clinical

success rate. Antimicrobial treatment has been found to provide beneficial clinical effects for patients with chronic bronchitis leading to earlier symptoms resolution and lower relapse rate. Although the number of studies to date is limited, the available evidence suggests that chronic bronchitis may be adequately treated with short-course therapy of Gemifloxacin 320 mg.

It was observed that safety profile of the Gemifloxacin 320 mg group was better and safe for the treatment of chronic bronchitis. Hence the study suggested that, the clinical and bacteriological success rate was found to be better in Gemifloxacin 320 mg with the lower incidence of adverse drug reaction. Hence Gemifloxacin 320 mg is a better alternative for the treatment of chronic bronchitis.

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