

## ORIGINAL ARTICLE

# Metronidazole As A Component Of Empiric Antibiotic Therapy In Community Acquired Pneumonia

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## ABSTRACT

**Introduction:** Community acquired pneumonia is the most common respiratory disease encountered in clinical practice. The common microbiology in this pneumonia is (i) S.Pneumoniae (40%) anaerobes (25% - 35%), and atypical organisms (2% - 7%).

**Materials and methods:** The present study is a randomized control trial on 106 patients attending Mamata Medical College, diagnosed with community acquired pneumonia on clinical, radiological and laboratory evaluation. These cases having mild pneumonia (CRUB-65 score of 0 to 1) were subjected to empiric antibiotic therapy with cefixime 200mg in BID dosage, azithromycin 250mg in BID dosage and metronidazole 400mg in TID dosage for 7days.

**Results:** A significant improvement was found in 81% of patients at the end of 7<sup>th</sup> day of the empiric therapy. Improvement was noticed in clinical, radiological and laboratory parameters.

**Conclusion:** The importance of adding metronidazole in empiric treatment of community acquired pneumonia cannot be ignored.

**Keywords:** Anaerobic infection, Community acquired pneumonia (CAP), Metronidazole

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## INTRODUCTION

Pneumonia is one of the most common and important cause of human disease in terms of morbidity, mortality and economic cost to the society. The incidence of pneumonia on an average in community is around 10-12 cases per 1000 persons in a year. The incidence of pneumonia varies from 2-15 cases per 1000 persons depending upon age, sex, race and socioeconomic condition. The important mechanism of entry of organisms into the lungs is aspiration of previously colonized bacterial flora of nose and oropharynx through tracheobronchial tree. Development of pneumonia depends upon the bacterial load, virulence of the bacteria and immunological status of the host.<sup>1,2,3</sup>

As there is no gold standard method of diagnosis for pneumonia; patients having symptoms of cough, fever, pleuritic chest pain, sputum along with clinical, radiological signs of consolidation supported by laboratory value of leukocytosis with neutrophilia are diagnosed as a case of pneumonia in everyday practice as etiological (microbiological) diagnosis is frequently not made and antibiotic therapy has to be empirical. Several studies favour microbiological cause of community acquired pneumonia in immunocompetent patients in which streptococcus pneumoniae accounts for 40% of cases.<sup>1,2</sup> Anaerobic bacteria accounts for 20-35% cases, mixed infection around 10% and atypical organisms around 5%.<sup>3</sup> The common empiric antibiotic regimen prescribed to treat community acquired pneumonia is

- A Beta lactam antibiotic plus macrolide
- Amoxicillin clavunate plus macrolide
- Cefixime plus macrolide
- A flouroquinolone alone

Although, anaerobic bacteria constitutes a major

proportion of community acquired pneumonia, routine administration of metronidazole as a component of empiric treatment is not emphasized in most of the studies and not included in the treatment guidelines.

## MATERIALS AND METHODS

In this randomized clinical trial (evidence based) study, 106 patients diagnosed with community acquired pneumonia were selected among the patients attending the outpatient department of pulmonary medicine, Mamata Medical College, Khammam, Telangana state. Within a period of 10 months, (1<sup>st</sup> June 14 to 28<sup>th</sup> Feb 2015) patients having symptoms of cough with sputum of less than one week duration with variable rise of temperature were selected randomly. Patients were subjected for clinical, radiological and laboratory evaluation for community acquired pneumonia. After being diagnosed as community acquired pneumonia, the selected patients were subjected for empiric antibiotic therapy with triple drug combinations of cefixime, azithromycin and metronidazole for 7 days. Cefixime was given in a dose of 250mg BID, azithromycin in a dose of 250mg BID and metronidazole in a dose of 400mg TID; irrespective of the age and sex as considered in the study criteria as follows.

### Inclusion Criteria

- Age group: 15 to 55 years.
- Sex: Both males and females.
- Chief complaints: Cough, sputum, fever, pleuritic chest pain, shortness of breath (along with cough if any one of these symptoms present)
- Duration of symptoms: Less than one week.

### Exclusion Criteria

- Presence of co-morbidities like diabetes mellitus, cardiac diseases, systemic diseases, immunocompromised states/disease, chronic obstructive pulmonary disease, bronchial asthma, pleural effusion.
- With history of past pulmonary tuberculosis and other pulmonary diseases.
- History of hospitalization and antibiot-

ic therapy in the past 12 weeks.

The selected group of patients were initially evaluated clinically, radiologically and on a simple laboratory test of total leukocyte count and differential white cell count. On the basis of supportive criteria of any two out of these three primary evaluatory methods, the patient was diagnosed as a case of community acquired pneumonia and subjected for empiric antibiotic therapy as mentioned earlier. After starting therapy all patients were evaluated at the end of 3<sup>rd</sup> day. Patients showing complete resolution of symptoms were finally followed up at the end of 7<sup>th</sup> day.

Patients not showing complete resolution at the end of 3<sup>rd</sup> day were again followed up at the end of 5<sup>th</sup> and 7<sup>th</sup> day. Radiological evaluation was done for all the patients at the end of 7<sup>th</sup> day. Post evaluation data was collected, arranged and analyzed in the context of medical statistics.

## RESULTS

Effect of empiric antibiotic therapy with cefixime +Azithromycin+ Metronidazole in those patients were noted as follows:

Fever subsided in 76 patients at the end of 3<sup>rd</sup> day, in another 4 patients at the end of 5<sup>th</sup> day and in another 6 patients at the end of 7<sup>th</sup> day. Total in 86 patients fever subsided on 7<sup>th</sup> day out of 106 patients. However fever persisted in 20 patients after 7<sup>th</sup> day.

Cough subsided in frequency as well as in sputum production in 66 patients at the end of 3<sup>rd</sup> day. In another 18 patients at the end of 5<sup>th</sup> day and in another 2 patients at the end of 7<sup>th</sup> day. Total in 86 patients cough settled on 7<sup>th</sup> day. However cough persisted in 20 patients after 7<sup>th</sup> day.

Leukocytosis comes to normal in 70 patients at the end of 3<sup>rd</sup> day. In another 12 patients at end of 5<sup>th</sup> day, and in another 4 patients at end of 7<sup>th</sup> day. Total in 86 patients leukocytosis restored to normal. However it persisted in 20 patients at the end of 7<sup>th</sup> day. Out of 74 patients showing radiological opacities, 50 patients showed resolution at the end of 7<sup>th</sup> day.

In 18 patients radiological improvement was not appreciated and in 6 patients radiological opacities were worsened. Overall 86 patients

were improved fully at the end of 7<sup>th</sup> day. 14 patients were advised for hospitalization at the end of 3<sup>rd</sup> day, 4 patients at the end of 5<sup>th</sup> day and 2 patients at the end of 7<sup>th</sup> day due to persistent fever and cough. So total 20 patients needed hospitalization.

As per trimode evaluation methods of these patients it has been observed that

**Symptom wise:**

- Fever, cough with sputum were present in all 106 patients
- Mild shortness of breath was present in

26 patients

- Pleuritic chest pain was present patients

**Clinical Examination/Lab study/Radiology wise:**

- Clinical signs of consolidation was present in all these patients.
- Leukocytosis (mild to moderate) was present in all these patients.
- Radiological signs of consolidation was present in 74 patients. (Table 1)

S.NO	Evaluation Parameters	3 <sup>rd</sup> day end Improved	5 <sup>th</sup> day end Improved	7 <sup>th</sup> day end Improved	Not Improved	Total
1	Fever	76	(4)	(6)	20	106
2	Cough	66	(8)	(2)	20	106
3	Leukocytosis	70	(12)	(4)	20	106
4	Radiological shadow	Not repeated	Not repeated	Repeated 50 (Out of 74 Patients)	24	74

**Table-1:** Shows the outcome of community acquired pneumonia in the study group evaluated through clinical examination, lab findings and radiological features.

**DISCUSSION**

The use of metronidazole in combination with penicillin in treating aspiration pneumonia is based on several studies from 1970s that reported predominantly anaerobic flora from percutaneous, transtracheal and thoracocentesis samples.<sup>4,5,6</sup> However no trials have compared empiric antimicrobial regimens for aspiration pneumonia with and without metronidazole. No definite data is available to describe the value of add on therapy of metronidazole for aspiration pneumonia. Still consensus exists that it should not be used as monotherapy in the treatment of community acquired pneumonia.<sup>7</sup>

Despite references to metronidazole in review of aspiration pneumonia treatment, adequate clinical data is lacking to describe its safety and efficacy when added to empiric regimen for community acquired pneumonia.

Fever and cough were the main symptoms found invariably in all the patients, shortness of breath (24%), and pleuritic chest pain (0.5%) are the least symptoms. Radiological abnormality was

present in (70%) cases and leukocytosis with neutrophilia were present in (100%) cases. On addition of metronidazole with empiric therapy, post 3<sup>rd</sup> day relief was found in majority of cases like in fever (71%) cough (62%), leukocytosis (66%). Radiological improvement was assessed at the end of 7<sup>th</sup> day and improvement noticed in 67%. Improvement in the evaluation parameters after 5<sup>th</sup> & 7<sup>th</sup> day constitutes another 5% to 12%. 20 patients (18%) did not improve during the course of therapy and were advised hospitalization for further evaluation and treatment.

Aspiration is the commonest mechanism for the disease process of CAP. Anaerobes are isolated in a major portion of CAP in various studies.<sup>8,9</sup> Most of the patients (80%) need ambulatory treatment with empiric regimens. Though a definite indication of metronidazole is well established in treating anaerobic infection in several studies, but this drug is still not included in empiric treatment of CAP in most of the guidelines. Several studies showed clinical improvements in 53% to 67% patients after 7<sup>th</sup> to 14<sup>th</sup> days of post empiric treatment, containing regimens without metronid-

azole.<sup>8-10</sup>

Benefit of metronidazole includes its low cost, availability as intravenous and oral formulations, generally mild adverse effect profile and extremely low levels of resistance while no trials have specifically evaluated metronidazole in combination with other antibiotics for treatment of CAP. However Sanford guide to antimicrobial therapy, recommends metronidazole in combination with either amoxicillin-clavulanate or ceftriaxone as an alternative regimen for treating CAP.

## CONCLUSION

Our study showed favorable criteria to add metronidazole in empiric antibiotic treatment for CAP, as evidenced by a significant decrease in overall symptoms, control and resolution of CAP. So, it should be included in various guidelines for treating community acquired pneumonia.

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