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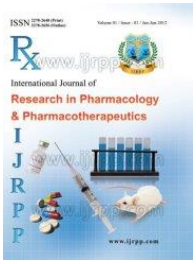

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# An observational study on safety profile of ofloxacin and levofloxacin in treatment of acute exacerbation of chronic bronchitis

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## ABSTRACT

### Background

COPD is predicted to be the third most common cause of death and chronic disability in the world by 2020. The term COPD encompasses several conditions. These include airflow obstruction with little reversibility, chronic bronchitis, emphysema, and small airways disease. Outcomes when hospitalized are poor, with 34% being re-admitted and 14% dying within 3 months.

### Aims and objectives

To monitor, evaluate and compare the adverse effect profile of Ofloxacin and Ciprofloxacin in acute exacerbation of chronic bronchitis.

### Methods

This was a prospective, observational study done in 200 patients of clinically diagnosed acute bronchitis in the department of pulmonology, SMC/GGH, Vijayawada. Newly diagnosed 200patients of acute bronchitis (from January 2017 to June 2017), pulmonology outpatient department, GGH, SMC, VJA of age 18–65 years of either gender who were prescribed either Levofloxacin ($n$ = 100) or ofloxacin (OZP group, $n$ = 100) and who gave written informed consent were enrolled. One group of the patients received Tab. Ofloxacin 400 mg BD and other group received Tab. Levofloxacin 500 mg OD for 7 days. The study duration was 6 months.

### Results

In Ofloxacin group 63 patients reported ADRs out of which 40 are male and 23 are female. In Levofloxacin group, 19 patients reported ADR, of which 10 were men and 09 women (figure 1). Out of 63 ADRs in ofloxacin group 50 patients reported ADRs associated with CNS, 11patients reported ADRs associated with GIT & 02were associated with skin and its appendages. Out of 19 ADRs in levofloxacin group 10 patients reported ADRs associated with CNS, 08 patients reported ADRs associated with GIT & 01were associated with skin and its appendages (figure 2).

**Conclusion**

Even though, fluoroquinolones have excellent efficacy profile there are concerns about their safety. The present study concluded that no serious ADRs noted in both groups. But ofloxacin group of patients have shown increased incidence of ADRs associated with CNS especially Insomnia.

**Keywords:** Levofloxacin, Ofloxacin, ADRS

## INTRODUCTION

COPD is predicted to be the third most common cause of death and chronic disability in the world by 2020 [1]. The term COPD encompasses several conditions. These include airflow obstruction with little reversibility, chronic bronchitis, emphysema, and small airways disease. In the winter months, admission to hospital with acute exacerbations of COPD is the commonest medical emergency. Outcomes when hospitalized are poor, with 34% being re-admitted and 14% dying within 3 months [2]. Acute exacerbations of chronic bronchitis (AECB) affect many of these individuals and account for an estimated 12 million physician visits annually. Exacerbations lead to declines in lung function, cause significant morbidity and mortality, accelerate disease progression, and significantly lower the quality of life, including an increase in the risk of being house bound. Successful management of AECB entails achievement of four goals: rapidly resolving symptoms, preventing relapse, prolonging the time between exacerbations, and interrupting vicious cycle of recurrent infection induced lungdamage Traditionally, ampicillin, tetracycline and doxycycline, broad-spectrum macrolides, second- or third-generation cephalosporin, or trimethoprim and sulfamethoxazole (TMP/SMX) are antimicrobials of choice for treating AECB and CAP .Growing resistance to these agents has raised concerns, however, about their continued effectiveness, particularly against multi–drug-resistant strains of *Streptococcus pneumoniae and beta-lactamase–producing strains of Haemophilus influenzae and Moraxella catarrhalis*. This increasing prevalence of resistance bacteria has resulted in reliance on fluoroquinolones and their widespread use globally[3]. FQ popularity is enhanced by their relatively broadspectrum activity, high bioavailability & Long PAE. Use of fluoroquinolones also has been shown to shorten hospital stay, reduce recurrences, and lower costs. Even though, fluoroquinolones have excellent efficacy profile there are concerns about their safety. Many adverse drug reactions (ADR) have been reported during clinical trials and post-marketing surveillance Throughout India the most commonly used flouroquinolones are Ciprofloxacin, Ofloxacin, and Levofloxacin. In this scenario, the present study was undertaken to asses and compare the adverse effect profile of Levofloxacin and Ofloxacin in acute bronchitis patients.

## OBJECTIVE

To monitor, evaluate and compare the adverse effect profile of Ofloxacin and Ciprofloxacin in acute exacerbation of chronic bronchitis.

## MATERIAL AND METHODS

The study protocol was approved by the Institutional Ethics Committee and the study was conducted in accordance with the Declaration of Helsinki. Prospective, observational study done in 200 patients of clinically diagnosed acute bronchitis in the department of pulmonology, SMC/GGH, Vijayawada. Newly diagnosed 200patients of acute bronchitis (from January 2017 to June 2017), pulmonology outpatient department, GGH SMC VJA of age 18–65 years of either gender who were prescribed either Levofloxacin ($n$ = 100) or ofloxacin (OZP group, $n$ = 100) and who gave written informed consent were enrolled. One group of the patients received Tab. Ofloxacin 400 mg BD and other group received Tab. Levofloxacin 500 mg OD for 7 days. The study duration was 6 months. Information regarding ADRs were collected by self-reporting by patients, patients were given mobile number of senior residents and postgraduates of departments of pharmacology to report any untoward effects during therapy and they were also given printed forms which consists of expected ADRs from fluoroquinolones and asked them to tick ADRs they have experienced during therapy & submit form at end of one week. The pattern of ADRs reported were analyzed. ADR

causality assessment was done with Naranjo algorithm.

### Inclusion criteria

- Patients of 18 to 65 years of age of either sex were included in the study.
- Clinically diagnosed patients of acute exacerbation of chronic bronchitis treated with Ofloxacin or Ciprofloxacin.

### Exclusion criteria

- Patients with known hypersensitivity to Flouroquinolones.
- Children, pregnant women and nursing mothers.
- Patients suffering from Diabetes, Myasthenia Gravis, Epilepsy, Psychosis and other CNS disorders.
- Patients belonging to athlete population.
- Patients suffering from cardiac failure, renal failure & hepatic failure.

## STATISTICAL METHODS

Data was analyzed using frequency & percentages. Chi-square test is used for comparing attributes and variables of study. *P* <0.05 will be considered as significant. Data was described in form of tables and graphs. Data was entered in Microsoft excel 2007. IBM SPSS software version 21 is used for calculations.

## RESULTS

A total of 200 patients with acute bronchitis were recruited in the study. In Ofloxacin group 63 patients reported ADRs out of which 40 are male and 23 are female. In Levofloxacin group, 19 patients reported ADR, of which 10 were men and 09 women (figure 1).

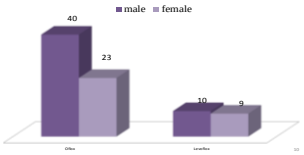


**Figure No.1: Bar diagram showing sex wise distribution of ADR**

Out of 63 ADRs in ofloxacin group 50 patients reported ADRs associated with CNS, 11patients reported ADRs associated with GIT & 02were associated with skin and its appendages. Out of 19 ADRs in levofloxacin group 10 patients reported ADRs associated with CNS, 08 patients reported ADRs associated with GIT & 01were associated with skin and its appendages (figure 2).

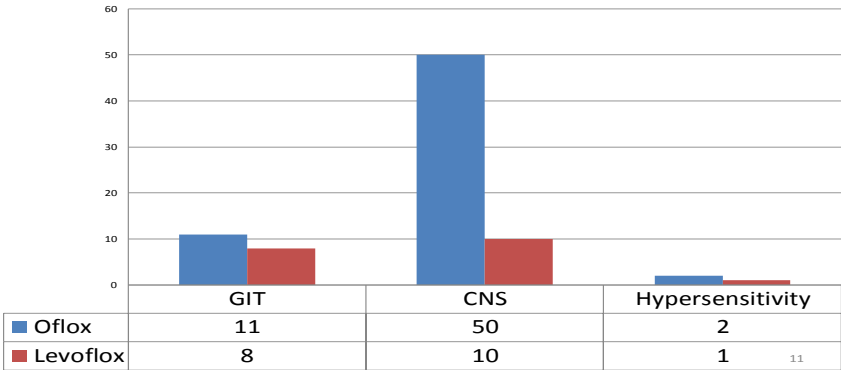


**Figure No. 2: Bar diagram showing system wise distribution of ADR**

Out of 50 CNS ADRs reported in ofloxacin group 40 patients reported insomnia, 07 patients reported headache & 03 patients reported dizziness. Out of 10 CNS ADRs reported in Levofloxacin group 04 patients reported headache, 03 patients reported dizziness, 01 patients reported psychosis and 2 patients reported insomnia (figure 3).

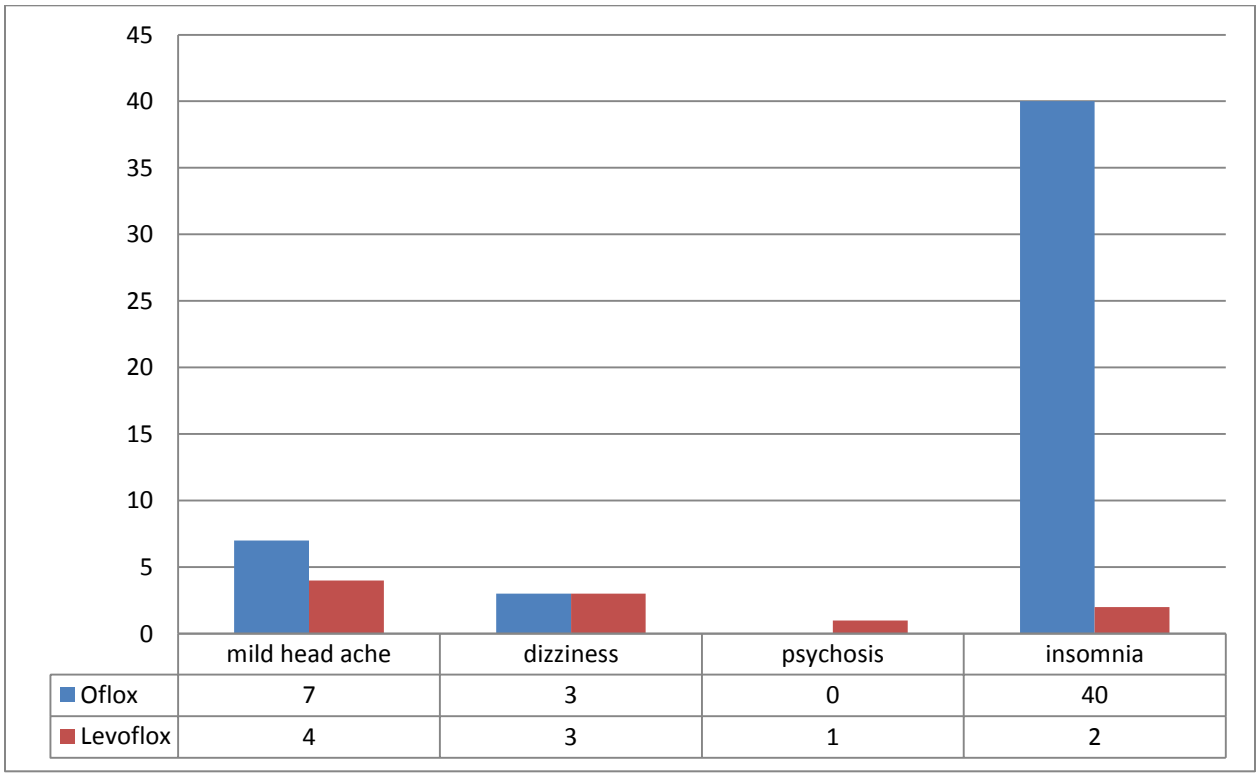


**Figure No.3: Bar diagram showing CNS ADRs of Ofloxacin and Levofloxacin**

Chi square test showed this difference in CNS ADRs is statistically significant ($p<0.001$). Insomnia was significantly higher in Ofloxacin group ($p<0.001$)

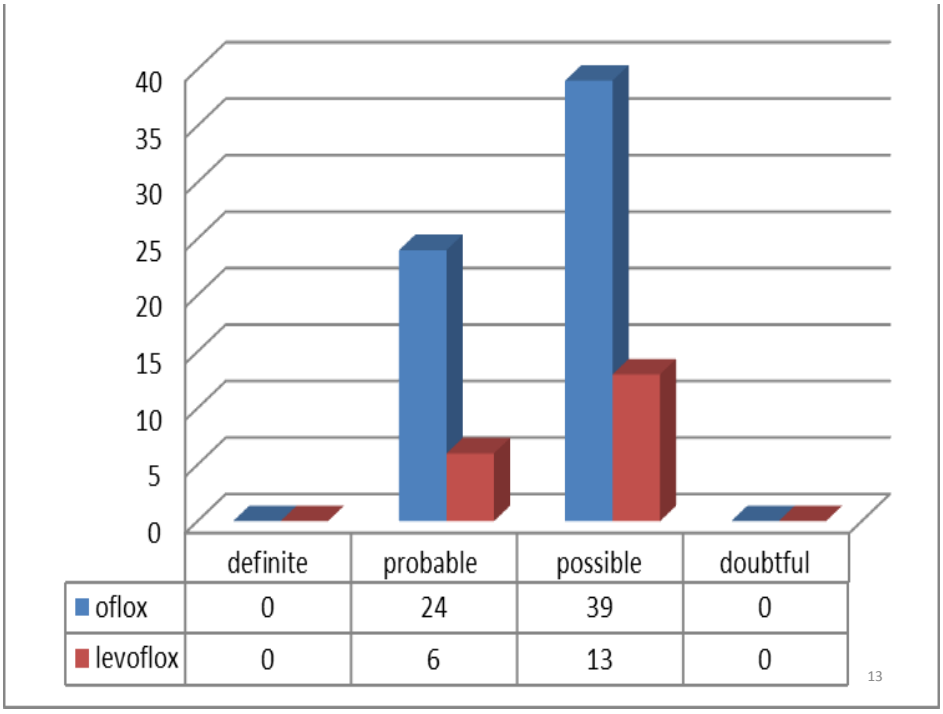


**Figure No.4: Bar diagram showing causality assessment of Ofloxacin and Levofloxacin.**

## DISCUSSION

In general, flour quinolones are well tolerated, with most side effects being mild to moderate. Common side effects include gastrointestinal effects such as nausea, vomiting and diarrhea, CNS side effects such as headache, dizziness & insomnia. On occasion, serious side effects occur. Gatifloxacin may cause disturbances in glucose metabolism and therefore it should be used with caution. This finding is not solely in those with diabetes, but particular care should be taken with this group of patients. Another potential side-effect of the class is photosensitivity. The incidence of this has been observed most in those taking sparfloxacin and lomefloxacin. Fluoroquinolones are associated with prolongation of the QTc interval and associated torsade de pointes.

In our study ADRs related to neurological disorders especially insomnia, gastrointestinal disorders, and skin and appendages disorders were reported more than any other system-organ class. This trend is similar to previous ADRs reported to fluoroquinolones [4]. However, few earlier studies had reported more gastrointestinal than neurological ADRs [5]. Our findings are also contrasting to the early postmarketing surveillance of ofloxacin evaluated 2 years later, which showed a preponderance of ADR reporting to skin and appendages, followed by neurological and gastrointestinal disorders.

In few studies CNS symptoms following administration of quinolones occur at an overall incidence of 1%–2%. Of these, the more commonly reported symptoms have included dizziness, headache, and somnolence[6]. Other, less commonly reported, CNS events have included agitation, delirium, confusion, acute organic psychosis, and abnormal vision.

In Our Study Out of 50 CNS ADRs reported in ofloxacin group 40 patients reported insomnia, 7 patients reported headache & 3 patients reported dizziness. Out of 10 CNS ADRs reported in Levofloxacin group 2 patients reported insomnia, 4 patients reported headache, 3 patients reported dizziness & 1 case of psychosis was reported

There is statistically significant difference in CNS ADRs ($p<0.001$). Insomnia was significantly higher in Ofloxacin group ($p<0.001$). Spontaneous adverse event reports indicate that the incidence of CNS-related adverse events was higher in association with quinolone use (12.2%) than with the use of other systemic antimicrobials (This may, otherwise, suggest an increased trend for neurological ADRs which would require an intense pharmacovigilance. The increased reports of neurological ADRs to fluoroquinolones and the associated serious effects

were the main reasons for recent change in labeling of this class of drugs and revision of the boxed warning by the FDA (USFDA, 2016). This also contributes to the restricted use of fluoroquinolones in Europe.

The mechanism of toxicity of flouroquinolones have been attributed to their interaction with different receptor complexes, such as blockade of GABA A receptor complex within central nervous system, leading top excitotoxic type effects and oxidative stress.

In 2016, FDA recommended that "serious side effects associated with flouroquinolones generally outweigh the benefits for the patients with acute sinusitis, acute bronchitis and uncomplicated UTI" The FDA further recommended that fluoroquinolone should be reserved for use in patients who have no alternative treatment options for acute bacterial sinusitis (ABS), acute bacterial exacerbation of chronic bronchitis (ABECB), and uncomplicated urinary tract infections (UTIs)

## CONCLUSION

Growing resistance to ampicillin, tetracycline and doxycycline, broad-spectrum macrolides, second- or third-generation cephalosporin, or trimethoprim and sulfamethoxazole (TMP/SMX) lead to wide spread use of flouroquinolones in treating AECB. Even though, fluoroquinolones have excellent efficacy profile there are concerns about their safety. The present study concluded that no serious ADRs noted in both groups. But ofloxacin group of patients have shown increased incidence of ADRs associated with CNS especially Insomnia. However, further large scale, multi-centric studies are needed to confirm these results.

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