EJPMR, 2026, 13(4), 158-160 **Research Article** **Impact Factor: 8.158**

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

ISSN (O): 2394-3211
ISSN (P): 3051-2573
Coden USA: EJPMAG

ADVERSE DRUG REACTION PROFILE OF THEOPHYLLINE IN COPD PATIENTS WITH AND WITHOUT TYPE 2 DIABETES MELLITUS

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DOI: https://doi.org/10.5281/zenodo.19309032

How to cite this Article: Dr. Ramesh Kumar Prajapati[1]*, Dr. Raj Kumar Rathore[2], Dr. Rishi Raj Sharma[3]. (2026). Adverse Drug Reaction Profile of Theophylline in Copd Patients with and Without Type 2 Diabetes Mellitus. European Journal of Pharmaceutical and Medical Research, 13(4), 158–160.

Article Received on 28/02/2026 **Article Revised on 19/03/2026** **Article Published on 01/04/2026**

ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a major global health problem characterized by persistent airflow limitation and chronic airway inflammation. Theophylline is widely used as a bronchodilator in COPD management, however its narrow therapeutic index makes it prone to adverse drug reactions (ADRs). Diabetes mellitus is a common comorbidity among COPD patients and may influence drug metabolism and pharmacokinetics. **Objective**: To evaluate and compare the adverse drug reaction profile of theophylline in COPD patients with and without Type 2 Diabetes Mellitus. **Methods**: A cross-sectional observational study was conducted including 74 COPD patients. Patients were divided into two groups: COPD without diabetes (Group A) and COPD with Type 2 diabetes mellitus (Group B). All patients received a fixed dose combination of Etofylline 77 mg and Theophylline 23 mg administered three times daily. ADRs were monitored and causality was assessed using WHO-UMC criteria. **Results**: Nausea was the most commonly reported ADR followed by seizures and arrhythmias. The incidence of ADRs did not differ significantly between COPD patients with and without diabetes. WHO-UMC causality assessment showed that most reactions were classified as possible or probable. **Conclusion**: The study demonstrates that theophylline therapy is associated with predictable ADR patterns and careful monitoring is essential due to its narrow therapeutic index.

KEYWORDS: COPD, Theophylline, Adverse Drug Reactions, Diabetes Mellitus, WHO-UMC.

INTRODUCTION

COPD is one of the leading causes of morbidity and mortality worldwide.[1] The disease is characterized by chronic airflow limitation, airway inflammation and progressive deterioration of lung function. Pharmacological therapy plays a critical role in reducing symptoms, preventing exacerbations and improving quality of life in COPD patients.[1] Among the various bronchodilators available, methylxanthines such as theophylline continue to be used particularly in developing countries due to their affordability and availability.[2]

Theophylline exerts bronchodilatory effects mainly through inhibition of phosphodiesterase enzymes, resulting in increased intracellular cyclic AMP levels.[3,4] In addition, the drug has anti-inflammatory and immunomodulatory properties. Despite these benefits, the therapeutic use of theophylline is limited by its narrow therapeutic index and variable pharmacokinetics among individuals.[5]

Adverse drug reactions associated with theophylline are relatively common and may involve the gastrointestinal, cardiovascular and central nervous systems.[6] Nausea, vomiting, tachycardia, arrhythmias and seizures are among the frequently reported reactions.[7] These adverse effects are often related to elevated plasma or serum concentrations of the drug.

Diabetes mellitus is a common comorbidity among patients with COPD. Metabolic disorders such as diabetes may influence hepatic enzyme activity, renal drug clearance and protein binding of medications.[8]

Such alterations can modify drug pharmacokinetics and may potentially increase the risk of adverse drug reactions.

Considering the widespread use of theophylline and the high prevalence of diabetes among COPD patients, it becomes important to evaluate the adverse drug reaction profile of theophylline therapy in these populations. Monitoring ADRs and assessing their causality using standardized systems such as the WHO-UMC scale helps improve drug safety and rational pharmacotherapy.

OBJECTIVE

To evaluate and compare the adverse drug reaction profile of theophylline in COPD patients with and without Type 2 Diabetes Mellitus.

MATERIALS AND METHODS

A cross-sectional observational study was conducted in COPD patients receiving theophylline-based therapy. A total of 74 patients were included and divided into two equal groups consisting of COPD patients without diabetes and COPD patients with Type 2 Diabetes Mellitus. Patients were treated with a fixed dose combination tablet containing Etofylline 77 mg and Theophylline 23 mg administered three times daily.

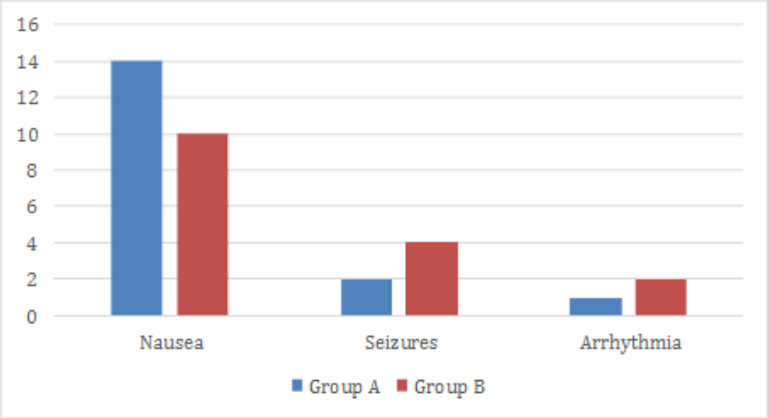
Patients were monitored for the development of adverse drug reactions during therapy. Clinical evaluation and laboratory investigations were performed as required. Serum theophylline concentrations were analyzed at different time intervals.

Statistical Analysis: Continuous variables were expressed as mean ± standard deviation (SD) and compared using the student's unpaired t-test. Categorical variables such as ADR incidence were analyzed using the Chi-square test. A p value <0.05 was considered statistically significant. All suspected ADRs were documented and evaluated using the WHO-UMC causality assessment system.

RESULTS

Adverse Drug Reaction	COPD without DM(Group A)	COPD with DM(Group B)
Nausea	14	10
Seizures	2	4
Arrhythmias	1	2

Distribution of adverse drug reactions among COPD patients with and without diabetes mellitus.



Statistics	Value
Chi-square	2.21499E-08
Degree of freedom	3
p-value	1
significance	Notsignificant(p>0.05)

WHO-UMC Causality Assessment

Category	Number of Cases
Certain	0
Probable	9
Possible	17
Unlikely	7

Serum Theophylline Concentration

Serum Theophylline Concentration Comparison.

Parameter	COPD without DM	COPD with DM	p-value
1 hr Serum Level (µg/ml)	10.64 ± 0.51	10.10 ± 0.45	0.392
2 hr Serum Level (µg/ml)	11.03 ± 0.44	11.61 ± 0.52	0.430
Cmax	12.42 ± 0.38	12.69 ± 0.42	0.638

P-values indicated no significant differences between the groups (P > 0.05).

DISCUSSION

The present study evaluated the adverse drug reaction profile of theophylline in COPD patients with and

without diabetes mellitus. Theophylline remains an important bronchodilator in many clinical settings but its use is limited by a relatively high incidence of adverse drug reactions.[9]

In the present study nausea was the most frequently observed ADR. Gastrointestinal symptoms are commonly reported with methylxanthine therapy and are often related to stimulation of gastric acid secretion and central nervous system effects. Seizures and arrhythmias were observed in a smaller number of patients but represent clinically significant reactions that require careful monitoring.

The WHO-UMC causality assessment in this study classified the majority of ADRs as possible or probable.[10] This indicates a reasonable temporal relationship between drug administration and occurrence of adverse reactions.

Comparison of serum theophylline concentrations between the two groups did not show statistically significant differences. This suggests that the presence of diabetes mellitus did not substantially alter the pharmacokinetic behavior of the drug in the study population. Theophylline has a narrow therapeutic index, and even small variations in serum drug concentration may result in toxicity. Therefore, monitoring serum theophylline levels is important for optimizing therapy and preventing adverse drug reactions.

The findings of the present study highlight the importance of therapeutic drug monitoring and careful ADR surveillance during theophylline therapy.

CONCLUSION

The study concludes that adverse drug reactions associated with theophylline therapy are relatively common but predictable. Nausea was the most frequently reported reaction followed by seizures and arrhythmias. Serum theophylline concentrations observed in the study were within the therapeutic range and did not differ significantly between COPD patients with and without diabetes mellitus. The incidence of ADRs was comparable between COPD patients with and without diabetes mellitus. Regular monitoring and causality assessment using WHO-UMC criteria are essential to ensure safe use of theophylline.

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