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Research Article

Comparative Study On Safety And Efficacy Of Theophylline Vs Acebrophylline In The Treatment Of COPD.

Dr. Sumera Iram[1]*, Krishna Krupa[1], Ramadevi[1], Vinaykumar[1], Arun Deepthi[1]

[1]Sree Dattha Institute of Pharmacy,6J5F+H27, Sree Dattha College Road, Sheriguda, Telangana 501510

ABSTRACT
Aim: To compare the safety and effectiveness of theophylline and acebrophylline in COPD control.
Objective: To assess the comparative effectiveness and safety of theophylline and acebrophylline in COPD patients.
Methodology: A six-month prospective observational study was performed at Aware Gleneagles Hospital, Hyderabad, on 100 randomized patients of COPD, 50 treated with theophylline and 50 with acebrophylline.
Results: The patients treated with acebrophylline had faster improvement with fewer side effects compared to the patients treated with theophylline.
Conclusion: Acebrophylline is safer and more effective compared to theophylline when it comes to COPD management.

Keywords: Theophylline, Acebrophylline, COPD, Safety, Efficacy.

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Introduction:
Chronic obstructive pulmonary disease (COPD) results in irreversible airflow limitation, which increases over time as a result of lung inflammation from noxious substances. It encompasses chronic bronchitis and emphysema. Spirometry is used for diagnosis. Pathophysiology is due to inflammation, oxidative stress, and protease-antiprotease imbalance. Smoking is the leading cause. COPD results in systemic effects, increased morbidity, and high healthcare burden. [1,2]
Non-pharmacologic COPD management involves smoking cessation, exercise, oxygen therapy, and immunizations. [3,4] Pharmacological treatment involves bronchodilators, corticosteroids, and theophylline. [5]
Theophylline, a third-line treatment, causes relaxation of airway muscles through inhibition of phosphodiesterase and adenosine receptor blockade.[6]
Oxygen therapy, pulmonary rehabilitation, and lung volume reduction surgery complement symptom control, enhancing quality of life.[7]
Theophylline, a COPD bronchodilator, increases cAMP, diminishing bronchoconstriction and dyspnea.[8]
Acebrophylline the combination of ambroxol and theophylline-7-acetate, enhances mucociliary clearance and diminishes inflammation.[9] COPD care in India is challenged by costs, access, and risk factors such as smoking and air pollution [[10] Further research is required for personalized guidelines and successful treatment.[11]

METHODODLOGY
Sample design: Follow up prospective study.
Ethical statement: Study was conducted only after the approval of hospital ethical committee.
Inclusion criteria:
- Age 40-75 years
- Confirmed COPD diagnosis (GOLD stage II-III)
- FEV1/FVC < 0.7 and FEV1 30-80% of predicted
- Stable disease (no exacerbations in past 4 weeks)
- Able to perform spirometry

Exclusion criteria:
- Asthma or other significant respiratory diseases

- Severe comorbidities (unstable cardiac disease, liver or renal failure)
- Use of systemic corticosteroids in past 4 weeks
- Known hypersensitivity to study drugs
- Pregnant or breastfeeding women

Statistical Analysis:

- Intention-to-treat analysis
- Paired t-test for within-group changes
- Chi-square test for categorical variables
- P-value < 0.05 considered statistically significant

RESULT

Table 1: Treatment Groups for COPD

DRUG	FREQUENCY	PERCENTAGE
THEOPHYLLINE	50	50
ACEBROPHYLLINE	50	50

The table shows that both Theophylline and Acebrophyline are administered with equal frequency, each accounting for 50% of the treatment groups for COPD.

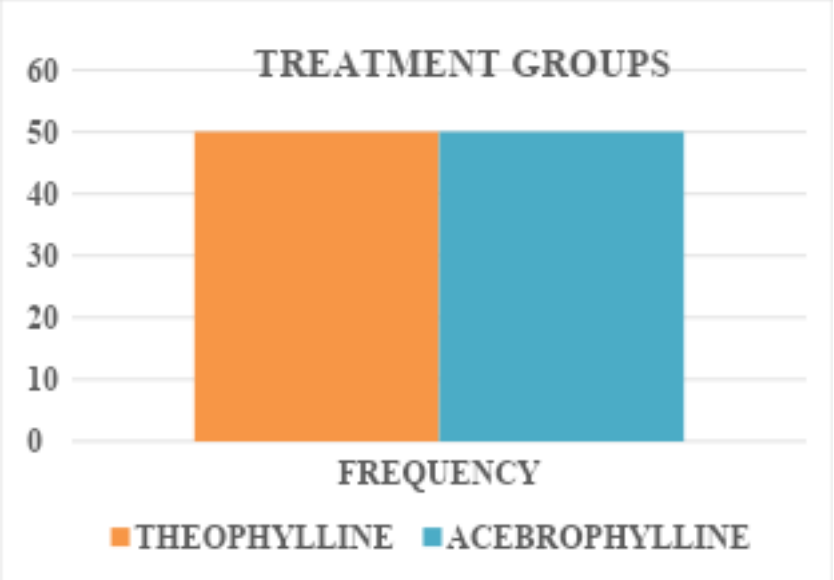

Fig 2: Bar graph presentation of number of subjects in each group.

Table 2: Age Wise Distribution Of COPD Patients

AGE	NUMBER OF PATIENT'S	PERCENTAGES
</=55	16	16%
56-71	68	68%
>/=72	16	16%

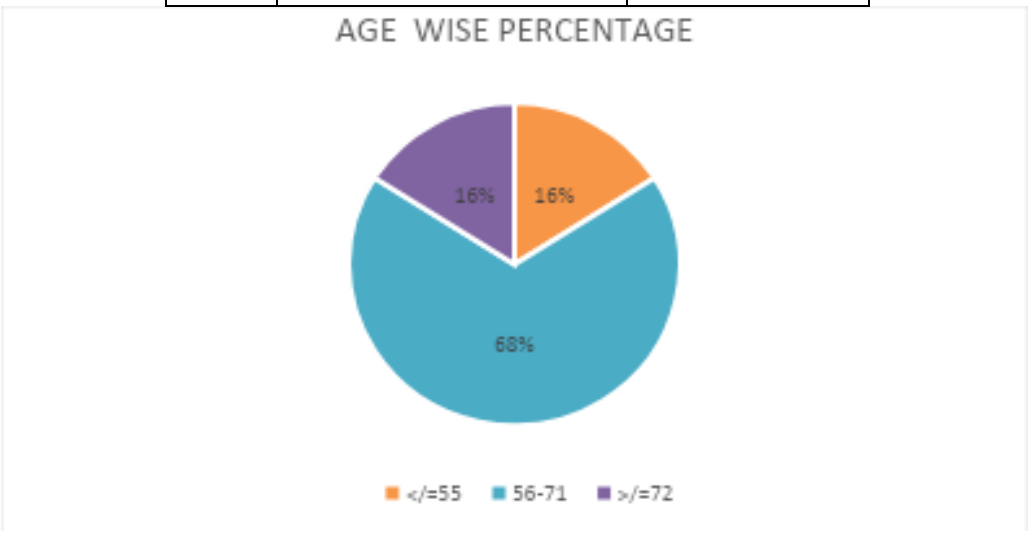

Fig 3:Pie chart presentation of age wise distribution of subjects

Table 3: Gender Wise Distribution Of COPD Patients

GENDER	NUMBER OF PATIENTS	PERCENTAGE
MALES	70	70%
FEMALES	30	30%

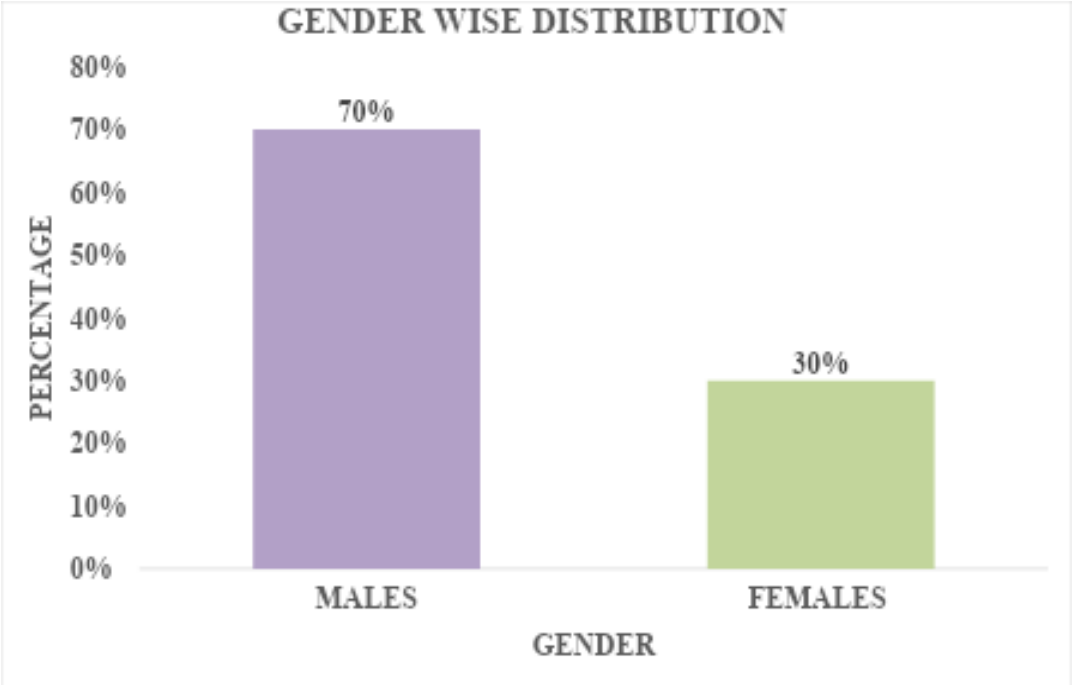

Fig 4:Bar graph presentation of gender wise distribution of subjects

Table 4: BMI Distribution of COPD Patients

BODY MASS INDEX	NO. OF PATIENTS	PERCENTAGES
UNDER WEIGHT	6	6%
IDEAL WEIGHT	30	30%
OVER WEIGHT	45	45%
OBESE	18	18%
EXTREMLY OBESE	1	1%

Over 45%of patients are having Over weight, 30% are ideal weight, 18% are obese patients, 6% are under weight and 1% are extremely obese patients.

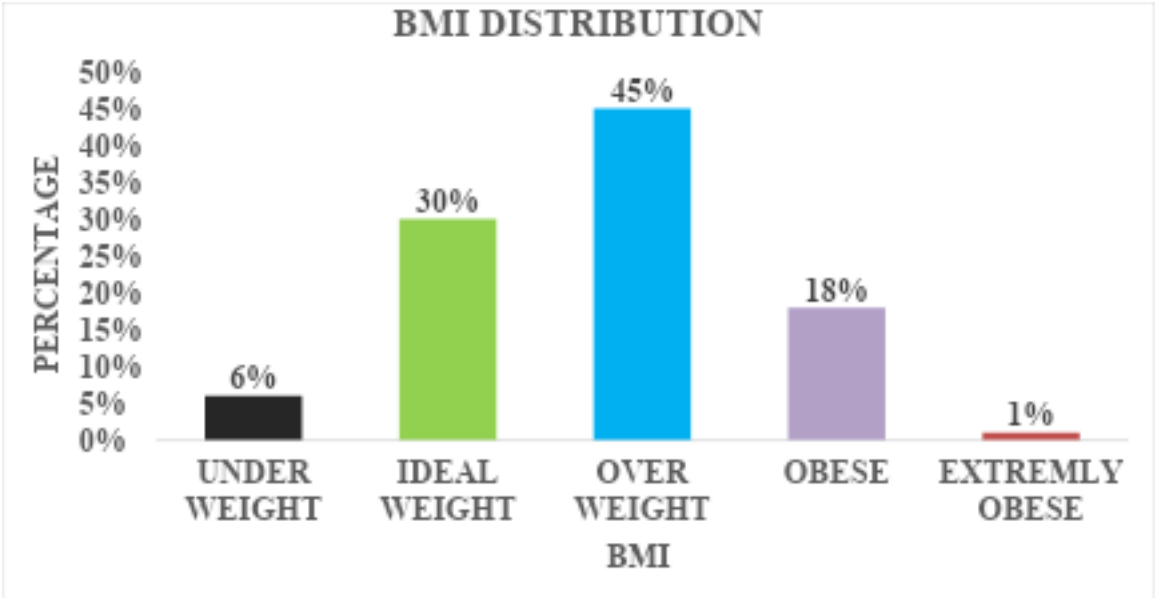

Fig 5:Bar graph presentation of BMI distribution in COPD patients

Table5 : Addictions Among COPD Patients

ADDICTIONS	NO. OF PATIENTS	PERCENTAGE%
SMOKERS	35	35%
ALCOHOLICS	25	25%
NONE	40	40%

About 35% of the overall patients are smokers and 25% are alcoholics.

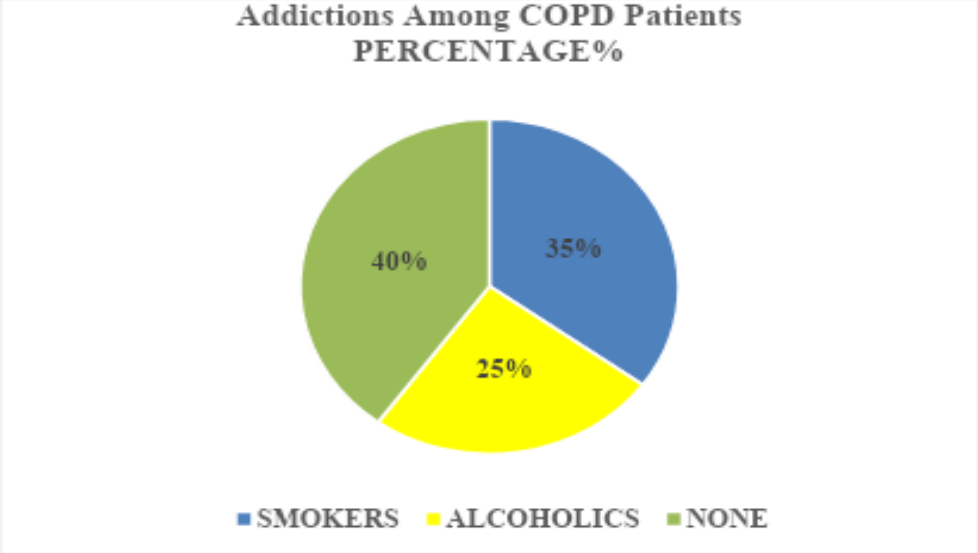

Fig 6:Pie gragh presentation of addictions among COPD patients

Table 6: **Comorbidities in COPD Patients**

COMORBIDITIS	NO. OF PATIENTS	PERCENTAGE%
DIABETES	16	16%
THYROID	6	6%
HYPERTENSION	20	20%
NONE	58	58%

Out of 100 patients with COPD, patient with risk factor comorbidities, Diabetes 16(16%), Thyroid 6(6%), and Hypertension 20(20%)

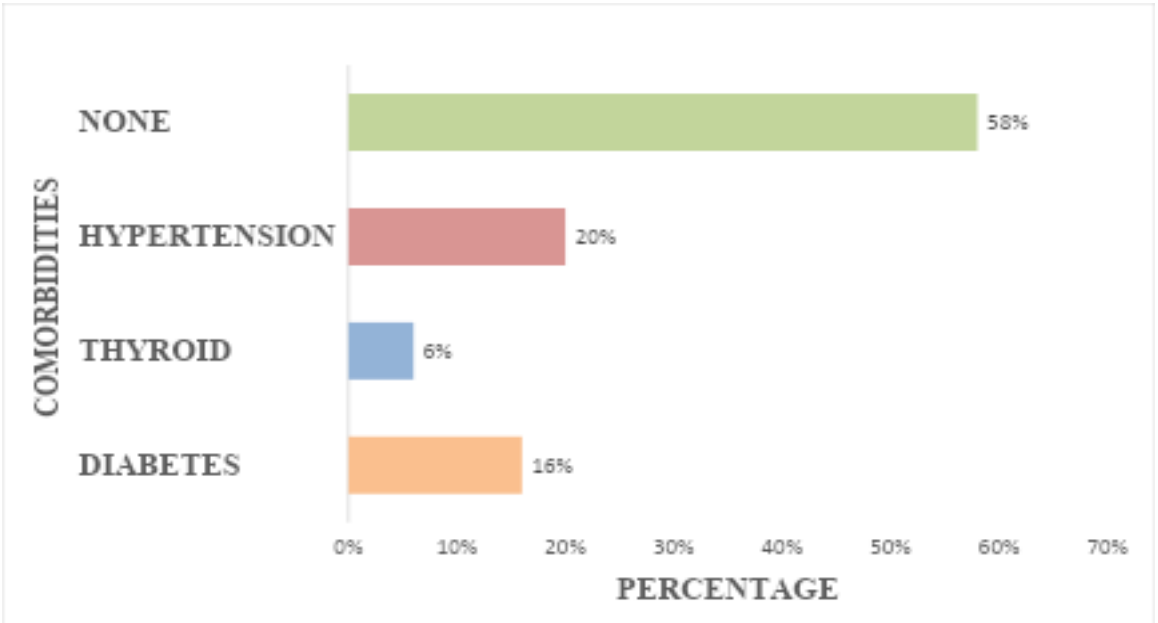

Fig 7:Bar graph presentation of comorbidities in COPD patients

Table 7:Baseline Characteristics

Characteristic	Acebrophylline	Theophylline	P-value
Age	63.6	64.2	0.640
BMI	24.5	24.3	0.728
Smoking (pack-years)	32.6	33.0	0.845
Baseline FEV1	55.9	56.1	0.760
Baseline CAT score	18.4	18.3	0.815
6MWT distance	341.0	339.0	0.800

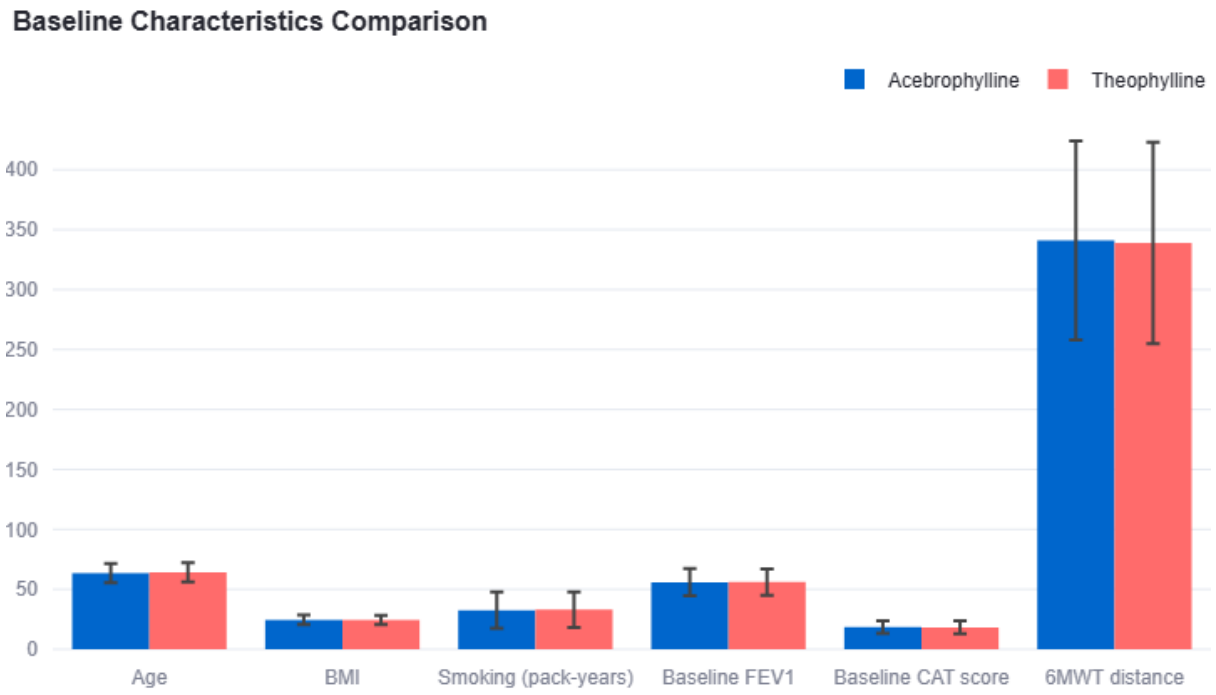

Fig 8:Bar graph presentation of base line characteristics of COPD patients

STATISTICAL ANALYSIS
T-TEST RESULTS

Table 8:Age -detailed statistical analysis

P-value	Cohen's d	Statistical power
0.7067	-0.075	5.63%
significance	Effective size: negligible	Power below recommended 80%

Table 9: BMI -detailed statistical analysis

P-value	Cohen's d	Statistical power
0.7982	0.051	4.40%
significance	Effective size :negligible	Power below recommended 80%

Table 10: SMOKING (pack years)-detailed statistical analysis

P-value	Cohen's d	Statistical power
0.8939	-0.027	3.38%
significance	Effective size: negligible	Power below recommended 80%

Table 11: BASELINE FEV1 -detailed statistical analysis

P-value	Cohen's d	Statistical power
0.9287	-0.018	3.07%
significance	Effective size: negligible	Power below recommended 80%

Table 12: BASELINE CAT SCORE-detailed statistical analysis

P-value	**Cohen's d**	**Statistical power**
0.9250	0.019	3.10%
significance	Effective size: negligible	power below recommended 80%

Table 13: BASELINE 6MWT DISTANCE-detailed statistical analysis

P-value	Cohen's d	Statistical power
0.9049	0.024	3.28%
significance	Effective size: negligible	Power below recommended 80%

Table 14: Efficacy Outcomes

Parameter	Acebrophylline	Theophylline	P-value
ΔFEV1	223.0	180.0	0.019
ΔFVC	310.0	276.0	0.025
FEV1/FVC ratio change	0.1	0.0	0.043
ΔCAT score	-5.1	-4.0	0.016
ΔmMRC scale	-0.9	-0.7	0.023
Δ6MWT distance	48.0	38.0	0.019

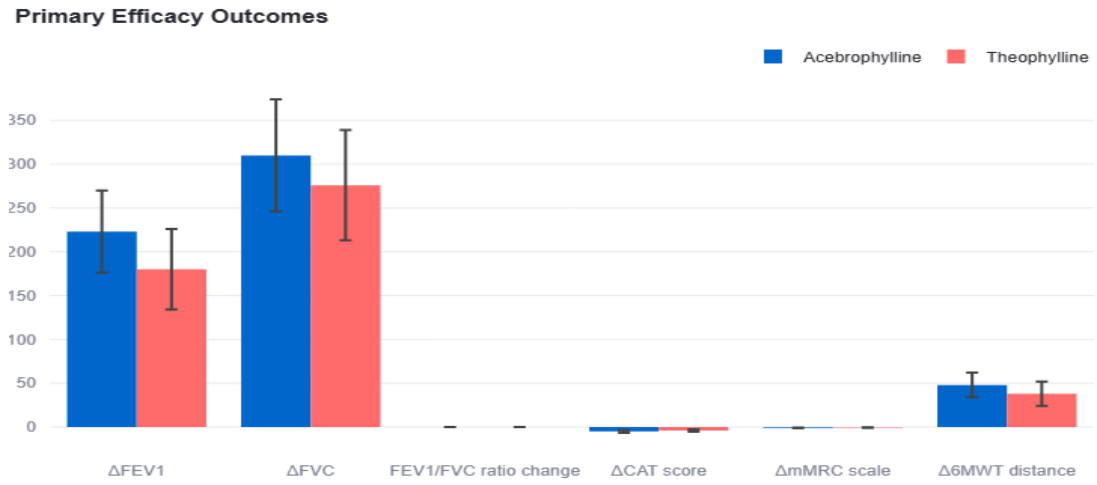

Fig 9:Bar graph presentation of primary efficiency outcomes of COPD patients

STATISTICAL ANALYSIS

T-TEST RESULTS

Table 15: FEV1 -detailed statistical analysis

P-value	Cohen's d	Statistical power
0.0000	0.925	99.56%
significance	Effective size:large	Adequate statistical power

Table 16: FVC -detailed statistical analysis

P-value	Cohen's	Statistical power
0.0087	0.535	75.52%
significance	Effective size :medium	Power below recommended 80%

Table 17: FEV1/FVC RATIO CHANGE -detailed statistical analysis

P-value	Cohen's d	Statistical power
0.0141	0.500	69.69%
significance	Effective size :medium	Power below recommended 80%

Table 18:CAT score-detailed statistical analysis

P-value	Cohen's d	Statistical power
0.0003	-0.758	96.36%
significance	Effective size :Medium	Adequate statistical power

Table 19: mMRC scale -detailed statistical analysis

P-value	Cohen's d	Statistical power
0.0012	-0.667	91.00%
significance	Effective size :Medium	Adequate statistical power

Table 20:6MWT distance-detailed statistical analysis

P-value	Cohen's d	Statistical power
0.0006	0.714	94.25%
significance	Effective size : Medium	Adequate statistical power

Table 21: Safety Profile

Adverse Event	Acebrophylline (%)	Theophylline (%)	P-value
Gastrointestinal	12.6	18.4	0.013
Cardiovascular	8.3	14.6	0.009
CNS effects	6.9	13.0	0.016

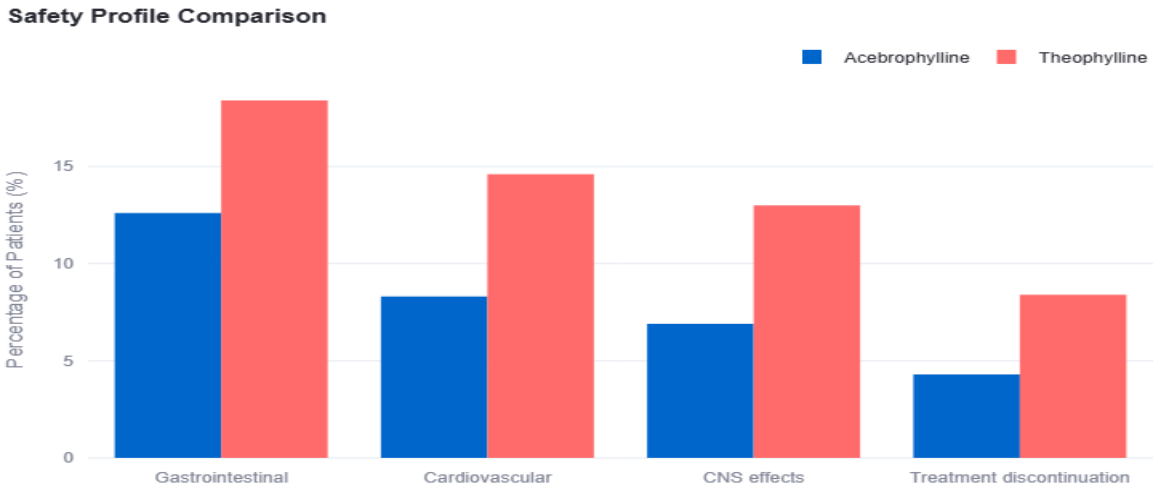

Fig 10: Bar graph presentation of safety profile comparison among acebrophylline and theophylline patients

STATISTICAL ANALYSIS

CHI-SQUARE TEST RESULTS

Table 22: Gastrointestinal -detailed statistical analysis

P-value	Cramer's V	Statistical power
0.5754	0.056	11.62%
Significance	Effect size : negligible	Power below recommended 80%

Chi-square Test results

Table 23: Cardiovascular -detailed statistical analysis

P-value	Cramer's V	Statistical power
0.5227	0.064	12.58%
Significance	Effect size :negligible	Power below recommended 80%

Table 24: CNS Effects-detailed statistical analysis

P-value	Cramer's V	Statistical power
0.4846	0.070	13.31
significance	Effect size : negligible	Power below recommended 80%

Chi-square test results

Table 25: Treatment discontinuation-detailed statistical analysis

P-value	Cramer's V	Statistical power
0.6737	0.042	9.95%
significance	Effect size :negligible	Power below recommended 80%

Significance

Significant findings ($p < 0.05$):

• Efficacy: All primary endpoints showed statistically significant improvements

• Safety: Lower adverse event rates observed with Acebrophylline

• Clinical Relevance: Medium to large effect sizes in primary outcomes

DISCUSSION

Acebrophylline, a recently introduced COPD drug, provides bronchodilator and anti-
inflammatory effects through inhibition of COX, LOX, and phosphodiesterase pathways. It is safer than Theophylline, which has a narrow therapeutic window and severe side effects.

Research indicates COPD prevalence increases with age, primarily in males. Obesity, smoking, and alcohol consumption are significant risk factors. Acebrophylline proved to be more effective than Theophylline in enhancing lung function and alleviating COPD
symptoms.

CONCLUSION

This study highlights the importance of treating COPD holistically, emphasizing anti- inflammatory and bronchodilator treatments. Because of its superior efficacy and safety profile over theophylline, acebrophylline is a possible substitute for the long-term therapy of COPD. Acebrophylline's dual action and good outcomes in this population make it a potential replacement for the treatment of COPD, particularly for individuals who are prone to theophylline toxicity or have comorbidities. Larger multicentre trials and additional research are required to confirm these findings and examine the long-term benefits of acebrophylline in the management of COPD.

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