

# Study on Effect of Atorvastatin on High Sensitivity C-reactive Protein, Pulmonary Function and Quality of Life in Chronic Obstructive Pulmonary Disease

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## ABSTRACT

**Introduction:** Statins have been demonstrated to have anti-inflammatory and immunomodulatory properties which are capable of attenuating inflammatory response in sepsis. Their lipid-lowering capabilities have been well known specifically in patients at risk of atherosclerotic cardiovascular events.

**Methodology:** The population of this study in 60 cases. Which were divided in two groups. In group I cases received treatment for COPD & in group II Who received treatment for COPD along with 20 mg/day atorvastatin. The duration of study was over a period of one year. This study was conducted in the Department of Pulmonary medicine, Department of Biochemistry & Department of Pharmacology, PMCH, Patna.

**Results:** In group I we found the ratio of male: female was 22:8, while in group II male: female was 23:7. In this study we observed that stage of severity of COPD in both groups; which were seen moderate 27 & 25 in group I & group II respectively.

**Conclusion:** The study concludes that a significant decrease

in serum hs-CRP levels in COPD patient with the use of 20 mg/day atorvastatin for 12 weeks.

**Keywords:** CRP, Pulmonary Function Test, COPD.

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## INTRODUCTION

Worldwide, chronic obstructive pulmonary disease (COPD) is a common disease. It is described by repeated episodes of dyspnea that necessitate frequent hospitalization. Stay in hospital increases the cost of care. Though COPD affects a large magnitude of population, still there is a lack of effectual therapies for the treatment or limitation of disease process. It has been revealed by the studies of pathogenesis of COPD that it involves inflammatory processes.<sup>1</sup>

Recently, statins have become known as a potential disease-modifying agent in COPD.<sup>2</sup> Statins are 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors that are commonly used for their lipid-lowering effects. They also possess many pleiotropic effects, anti-inflammatory effect is one of them, which may impart positive effect in COPD.<sup>3</sup> This hypothesis is supported by animal studies. These studies are showing that statins inhibit the progression of emphysema in mice models.<sup>4</sup>

Several retrospective studies suggest that statins may have an important role in decreasing morbidity and mortality in COPD patients.<sup>5</sup> Though, there is a lack of information on the effects of specific statins in most of the reviewed observational studies.

Many studies revealed that high-sensitivity C-reactive protein (hs-CRP) levels are a predictor of COPD morbidity and mortality<sup>6</sup>, and statins have been shown to decrease serum levels of CRP.<sup>7</sup> Lipophilic statins like simvastatin and atorvastatin have additional anti-inflammatory potential.<sup>8</sup> As most of the data of effect of statin on COPD are based on observational studies, interventional studies were required to evaluate the therapeutic effect of specific statins in COPD.

Statins have been demonstrated to have anti-inflammatory and immunomodulatory properties which are capable of attenuating inflammatory response in sepsis.<sup>9-11</sup> Their lipid-lowering capabilities have been well known specifically in patients at risk of atherosclerotic cardiovascular events. In the prevention and mitigation of sepsis, pleiotropic properties of statins have also been intensely investigated. It has been found in a meta-analysis of 26 observational studies that on infection and sepsis, statins were related with a significant decrease in mortality.<sup>12</sup> Though, in contrast to these observational studies, the meta-analysis of randomized controlled trials (RCTs) on this issue did not report any survival benefit.<sup>12,13</sup>

**MATERIALS & METHODS**

**Study Population:** The population of this study in 60 cases. Which were divided in two groups. In group I cases received treatment for COPD & in group II Who received treatment for COPD along with 20 mg/day atorvastatin.

**Study Duration:** The duration of study was over a period of one year.

**Study Area:** This study was conducted in the Department of Pulmonary medicine, Department of Biochemistry & Department of Pharmacology, PMCH, Patna.

**Data Collection:** It was an open-label interventional study conducted on chronic stable COPD patients. Approval for the study was obtained from the hospital's Institutional Research Committee and Institutional Ethical Committee. Patients suffering with COPD in stable condition for ≥3 months, aged between 40 and 80 years, and having abnormal lipid profile (low-density lipoprotein [LDL] - 130–160 mg/dl) were included in the study. The exclusion criteria were a history of bronchial asthma, prior exposure to statins, acute exacerbation of COPD for ≥3 months, any active infection, renal disease, hepatic dysfunction, and pregnant and nursing females. After taking written informed consent, sixty patients were randomized into two groups – Group I receiving only the medications for COPD and Group II receiving 20 mg atorvastatin along with other medications for COPD. At baseline, the patients were evaluated with physical examination, pulmonary function test, blood test, and health-related quality of life questionnaire.

**Data Analysis:** Analyzed by using Microsoft excel & Statistics.

**RESULTS**

In this study, we included 60 cases. All cases were divided in two groups. In group I we included those cases who received treatment for COPD & in group II who received treatment for COPD along with 20 mg/day atorvastatin. In group I we found the ratio of male: female was 22:8, while in group II male: female was 23:7. In this study we observed that stage of severity of COPD in both groups; which were seen moderate 27 & 25 in group I & group II respectively. While severe stage were seen 3 & 5 in group I & group II respectively. Different Baseline characteristics were observed in this study which showed in table 4 & 5.

**Table 1: Distribution of cases according to Groups**

Groups	n
Group I Who received treatment for COPD	30
Group II Who received treatment for COPD along with 20 mg/day atorvastatin	30
<b>Total</b>	<b>60</b>

**Table 2: Distribution of cases according to Gender**

Gender	Group I	Group II
Male	22	23
Female	8	7
<b>Total</b>	<b>30</b>	<b>30</b>

**Table 3: Distribution of cases according to severity stage**

COPD severity stage	Group I	Group II
Moderate	27	25
Severe	3	5
<b>Total</b>	<b>30</b>	<b>30</b>

**Table 4: Distribution of cases according to Baseline characteristics**

FEV1 after bronchodilator use (percentage of predicted value)	Group I	Group II
FEV1/FVC	43.9±11.1	44.2±13.5
Hb (g/dl)	10.43±0.52	10.37±0.73
SGRQ-total score (mean±SD)	46±16.7	47±16.5
BDI score	6.3±1.5	6.1±1.8
LDL cholesterol	135.7±2.19	134.3±3.19
hs-CRP (mg/L)	4.82±0.77	4.34±0.97

**Table 5: Distribution of cases according to Pre-study medications for COPD**

Pre-study medications for COPD	Group I	Group II
Inhaled glucocorticoids and long-acting beta2-agonist	7	7
Long-acting muscarinic antagonist and long-acting beta2-agonist	4	3
Inhaled glucocorticoids, long-acting muscarinic antagonist, and long-acting beta2-agonist	15	15
Theophylline	4	5

**DISCUSSION**

The present study was conducted to evaluate the effect of 20 mg atorvastatin on FEV1, hs-CRP, and quality of life in COPD patients. The findings of the study showed that 20 mg of daily atorvastatin had no effect on the lung function and disease-specific quality of life in patients with moderate-to-severe COPD. However, there was a statistically significant decrease in the hs-CRP levels with the use of atorvastatin. There was no difference found in the adverse drug reaction in both the groups. These results clearly indicate that daily use of 20 mg atorvastatin for 3 months has no role in the improvement of pulmonary function but has a significant improvement of hs-CRP levels. The present study preferred to use atorvastatin as it is easily accessible and affordable in India. Additionally, being a lipophilic agent, it is assumed to have greater anti-inflammatory potential. It has a dose-dependent anti-inflammatory effect ranging from 10 to 80 mg dose<sup>14</sup>, hence a dose of 20 mg atorvastatin was chosen to minimize dose-related adverse effects.<sup>15</sup> In this study, no effect has been found on the pulmonary function with the use of 20 mg atorvastatin. Similar results were found in some randomized controlled studies.<sup>16,17</sup> The reason behind this could be that the shorter duration of follow-up in these studies as compared to the longitudinal trials where the patients were followed up till 8–9 years.<sup>18-21</sup> Other factor which could be responsible for no effect can be a relatively lower dose of 20 mg used in the present study. Apart from this, only moderate-to-severe COPD patients were included in our study. Therefore, the feasibility of the beneficial effect of statins in a patient with less severe impairment could not be evaluated.

Our study has found that there was a significant reduction in the levels of hs-CRP with 3 months of 20 mg/day atorvastatin therapy. These findings were consistent with some other studies which have exhibited a decrease in hs-CRP levels in COPD patients.<sup>22,23</sup>

In contrast to our study findings some other studies have reported a statistically nonsignificant change in hs-CRP levels after the use of 40 mg/day simvastatin for 3 months in patients with COPD.<sup>24-26</sup> This could be due to the small sample size and short treatment period in these studies. In this study, SGRQ scores had similar progress in both Group I not receiving atorvastatin and Group II receiving atorvastatin (decrease of 7 points vs. 5 points;  $P > 0.05$ ). In contrast a study reported a significant improvement in SGRQ (St. George's Respiratory Questionnaire) with mean SGRQ decreased by 12 points after treatment with 40 mg/day atorvastatin for 12 weeks ( $P = 0.012$ ) as compared with placebo. The reason behind these findings of this study was a small sample of patient ( $n = 18$ ) as compared to the present study sample. Similarly, another study has also found improved asthma quality of life with short-term treatment with atorvastatin in mild asthmatic smokers.<sup>27</sup> Since ambiguous results are observed for the effect of atorvastatin on SGRQ scores in COPD patients, further research on larger groups and the effects of long-term intervention on clinical outcomes are required.

## CONCLUSION

A significant decrease in serum hs-CRP levels in COPD patient with the use of 20 mg/day atorvastatin for 12 weeks. Though, our study did not show any significant effect on other clinical outcomes such as pulmonary functions or quality of life. The major limitation of this study was that it was an open-labeled study, had small sample size, and was of short duration.

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