Atorvastatin can meritoriously improve the quality of life of chronic obstructed pulmonary disorder patients

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ABSTRACT:

Objective: To demonstrate the impact of Atorvastatin on heath associated quality of life in chronic obstructive pulmonary disease patients.
Methodology: This interventional study carried out in the department of Pharmacology & Therapeutics in alliance with Chest medicine department of JPMC Karachi into 6 months period (December 2011 to May 2012). 85 sufferers with moderate stable COPD, with hsCRP >3mg/lit, had been appraised in this trial. The patients have been allocated to receive Tab. Atorvastatin, for 12 consecutive weeks. The primary efficacy parameters were St. George's Respiratory Questionnaire (SGRQ) and BODE index.
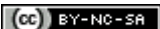**Results:** Out of 85 sufferers most effective 83 (94%) sufferers had been finished the study. The Atorvastatin significantly decreases the all four domains of SGRQ. The mean symptom score was 66.2 ± 1.06 decreases to 54.4 ± 1.31, likewise activity score turned into 51.6 ± 1.35 from 60.4 ± 1.64, impact score changed into 51.6 ± 1.26 from 60.6 ± 0.87 and total score changed into 54.9 ± 0.60 from 61.6 ± 0.73. Atorvastatin had significant impact on improvement of MMRC dyspnea score, spirometric findings and exercise capacity.
Conclusion: This demonstrates that the Atorvastatin effectively enhancing the excellent of existence through having satisfactory impact on the health associated questionnaire of COPD.

Key Words: COPD, SGRQ, QOL, BODE index, Pleiotropic consequences.

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INTRODUCTION

COPD is a continual inflammatory disease characterized by way of expiratory airflow obstacle that isn't completely reversible and affecting about 10% of adults over the age of 40 years[1]. COPD effects other system together with the cardiovascular and the musculoskeletal, making it a multi factor and multisystem ailment[2].

Because of systemic involvement (because of systemic spillover of inflammatory mediators) of COPD nowadays this disease cause major burden of indisposition and mortality globally that executes an ever accumulative economical encumbrance[3]. The main reason of economic burden due to COPD was poor quality of life due to systemic involvement so which needs frequent hospitalization[4].

Two disease associated quality of life questionnaires are broadly used in patients with COPD: the continual respiratory sickness Questionnaire (CRQ) evolved by Guyatt et al in 1987[1] and the St George's respiration Questionnaire (SGRQ) advanced through Jones et al in 1991[5].The SGRQ is a self-administered questionnaire however the CRQ changed into interviewer administered (at an advanced period a self-administered model of the CRQ have become to be had). Both questionnaires were used to evaluate the effects of interventions which include drug treatment options, oxygen remedy, and pulmonary rehabilitation or education programmed[5]. BODE index (body mass index, dyspnea and exercise capacity) is a multidimensional assessment about condition seriousness and prognosis in COPD patients. Bode index is useful convenient index to quantifies the level of pulmonary hindrance (FEV1), particular case that captures those patient's recognition for indications (the MMRC scale). Another two domains of this index which are 6MWT and BMI express systemic results from claiming COPD[6].

The rising recognition that COPD is a complicated disease, characterized not handiest by means of local pulmonary inflammation, nonetheless moreover with the aid of systemic involvement that would have an detrimental impact on numerous systemic tissues, for instance the blood vessels and cardiac tissue, amongst others, emphasizes the need for brand spanking new and more powerful styles of remedy for this incapacitating disorder[7].

Fortuitously, most of the 'well-known' therapeutic preferences used to cure COPD have the capability to persuade systemic associations. Furthermore, numerous novel salutary strategies designed to adjusting the underlying inflammatory events of COPD more mainly are underneath improvement. nevertheless, initial information seem to signify that drugs, including Statins, ACE inhibitors, and PPAR agonists, used to treat a co-morbid conditions have the capacity to benefit COPD patients[7].

Currently pleiotropic consequences of Statin are recognized which are anti-inflammatory and immunomodulatory effects; therefore by those pleiotropic results Atorvastatin might additionally recover the complete consequences (along with cardiovascular mortalities) together with decreases the exacerbation of COPD[8,9].

Supplementary modern therapy options included: Statin, angiotensin changing enzyme inhibitors and peroxisome proliferator activated receptor agonists, which can be beneficial for both pulmonary component of COPD and systemic comorbidities related to COPD. honestly, there is a want for treatment which could gradual the progression of pulmonary sickness, although the method cannot be completely reversed, so there ought to be greater scientific trials of more recent remedy in wish for perfect remedy of COPD[10].

Distinctiveness of an oral agent that produces beneficial results (decreased disease development and anti-inflammatory consequences) with a very good tolerability profile might be a treasured addition to the obligated remedy options. The usage of simplified regimens might also enhance patient adherence to remedy and eventually improve fine of life and reduce frequency of exacerbations[10]. Evidence from mutually human plus animal studies showed that Statins partake resilient immunomodulating consequences equally for systemic and pulmonary stream which can also have useful antiinflammatory actions in COPD[11].

Recently multiple pleiotropic consequences such as anti-inflammatory and immunomodulatory effects of Atorvastatin have been diagnosed and which can also have useful twin cardiopulmonary outcomes on COPD sufferers and might purpose high quality effect on excellent of existence on COPD sufferers by means of decreases the continued airway inflammatory methods[12]. Various retrospective studies indicates that the Statin past its cholesterol reducing outcomes can capable of decline the incidences of cardiovascular complications, pneumonia as well as influenza and even in long time use be able to decline the frequencies of lung cancer in COPD sufferers[13]. Contemporary anti-inflammatory tablets which include Steroids be capable of increase the incidences of pneumonia in COPD patients[14].

The main goal was to assess the effectiveness of Atorvastatin in improving the quality of life in COPD patients that may be capable of diminish the frequent systemic related issues in COPD patients.

METHODOLOGY

This interventional study performed in department of Pharmacology, BMSI in alliance with branch of chest medicine department, JPMC, Karachi. The ethical board of this institute authorized the observe protocol.

A total of 85 subjects of Diagnosed COPD that met the inclusion standards had been enrolled. Patients of either sex with moderate COPD as signposted through spirometry assay FEV1 < 80% and FEV1/FVC < 70% and hsCRP levels >3mg/l were enrolled in our study. Patients with unstable COPD, incidences of exacerbations of COPD within 3 months, previously on Statin treatment, or showing preceding static sensitivity or myopathy or myositis, pregnant or lactating mothers, patients with connective tissue problems, sufferers with active or persistent liver disorder, sufferers with evidence of active respiratory tract infections and with documented records of active coronary artery diseases such as recent history of unstable angina and Myocardial infarction were excluded from the study.

The total duration of study extended over 12 week's period. Throughout this period sufferers were allocated to tab. Atorvastatin 20 mg as soon as every day for 12 weeks followed by using 5 follow up visits. At baseline pulmonary function take a look at (FEV1, FVC and FEV1/FVC ratio) had been accomplished. Effect of remedy on health related first-class of life had been assessed by way of BODE index and SGRQ score.

Statistical analysis: SPSS ver 11.5 was used for statistics feeding and analysis. Frequencies and possibilities were designed for qualitative variables whilst imply mean ± SD for quantitative variables. Paired sample student paired t-test used for evaluation of quantitative information from baseline (day-0) to and day-90.

RESULTS

Total 85 COPD patients were nominated for treatment. Two patients withdrew in the course of treatment period.

Patients given tab Atorvastatin for 90 days revealed overall improvement in SGRQ, mean symptom score was 66.2±1.06, whereas activity score was 60.4±1.64, impact score was 60.6±0.87 and total score was 61.6 ± 0.73 at day 0. The mean symptom score was decreases to 63.4±1.12 (4.3%) whereas mean activity score was 59.5±1.57 (1.5%) similarly mean impact score was 59.9±0.84 (1.2%) and the mean total score was 62.3±0.66 (1.2%) at day 30.

At day 60 all the scores of SGRQ further decreases, mean of symptom score was 61.8±1.08 (6.5 %.) ,whereas mean activity score was 57.7±1.46 (4.5%), mean impact score was decreases to 58.6±0.85 (3.3%) and the mean total score was decreases 59.4±0.72 (3.6%).

As compare to day 0 the mean symptom score was decreases 54.4±1.31 (17.9%) at day 90 which was highly significant. The mean activity score was 51.6 ± 1.35 (14.6%) at day 90 which was highly significant. Whereas mean impact score was 51.6±1.26 (14.9%) this was highly significant and mean total score was 54.9±0.60 (10.9 %) which was also highly significant. As depicted in Table 1 and Figure 1.

Patients given tab Atorvastatin for 90 days revealed overall improvement in BODE index, mean FEV1 which was 2.16±0.07, whereas 6MWT was 217±5.7, MMRC score was 2.82±0.13 , BMI was 20.0 ± 0.37 and total points of BODE index was 6.33±0.20 at day 0. The mean FEV1 was 2.25±0.06 (4.2%) whereas mean 6MWT was 221±5.9 (1.9%) similarly mean MMRC score was 2.77±0.10 (1.8%) and the mean total points of BODE index was 6.18±0.15 (2.4%) at day 30.

At day 60 all the parameter further improved mean of FEV1 was 2.35±0.86 (8.8 %.) which was significant, whereas mean 6MWT was 231±6.4 (6.5%) which was significant, mean MMRC score was 2.69±0.08 (5%) and the mean Total points was 6.00±0.15 (5.3%).

As compare to day 0 the mean FEV1 was increases 2.48±0.06 (14.9%) at day 90 which was highly significant. The mean 6MWT was increases to 243 ± 5.6 (12%) at day 90, which was highly significant. Whereas mean MMRC dyspnea score was 2.48±0.07 (13.1%) which was also significant and mean total points of BODE index was 5.87±0.19(6.2 %). As shown in table 2.

Table 1: EFFECTS OF ATORVASTATIN ON SGRQ IN COPD PATIENTS

Variables	Mean± SEM Baseline (n=85)	Mean ± SEM 1st follow up (n=85)	Mean ± SEM 2nd follow up (n=85)	Mean±SEM 3rd follow up (n=85)	p-value
Symptoms score	66.2 ± 1.06	63.4 ± 1.12 (4.3%)	61.8 ±1.08 (6.5%)	54.4 ± 1.31** (17.9%)	0.001**
Activity score	60.4 ± 1.64	59.5 ± 1.57 (1.5%)	57.7 ± 1.46 (4.5%)	51.6 ± 1.35** (14.6%)	0.001**
Impact score	60.6 ± 0.87	59.9 ± 0.84 (1.2%)	58.6 ± 0.85 (3.3%)	51.6 ± 1.26** (14.9%)	0.001**
Total score	61.6 ± 0.73	62.3 ± 0.66 (1.2%)	59.4 ± 0.72 (3.6%)	54.9 ± 0.60** (10.9%)	0.001**

N=85; Follow up available=83; SGRQ= St. George's Respiratory Questionnaire; %=Percentage change
**= $p < 0.01$, highly significant as compared to day 0

Table 2: EFFECTS OF ATORVASTATIN THERAPY ALONE ON THE BODE INDEX

Variables	Atorvastatin (group A)				P-value
	Mean± SEM Baseline	Mean± SEM 1st follow up (%change)	Mean± SEM 2nd follow up (%change)	Mean± SEM 3rd follow up (%change)	
FEV1	2.16 ± 0.07	2.25 ± 0.06 (4.2%)	2.35 ± 0.06 * (8.8%)	2.48 ± 0.06 * (14.9%)	0.003*
6 minutes' walk test (6MWD) test	217 ± 5.7	221 ± 5.9 (1.9%)	231 ± 6.4 (6.5%)	243 ± 5.6 (12%)	0.010*
MMRC Dyspnea score	2.82 ± 0.13	2.77± 0.10 (1.8%)	2.69 ± 0.08 (5%)	2.48 ± 0.07 * (13.1%)	0.028*
BMI (Body Mass Index)	20.0 ± 0.37	20.3 ± 0.19 (1.5%)	20.4 ± 0.18 (2%)	20.6 ± 0.17 (3%)	0.365
Total points	6.33 ±0.20	6.18±0.15 (2.4%)	6.00±0.15 (5.3%)	5.87±0.19 (6.2%)	0.262

*= $p < 0.05$, Statistically significant from Day-0; **= $p < 0.01$, Highly significant from Day-0;
Percentage changes in parenthesis

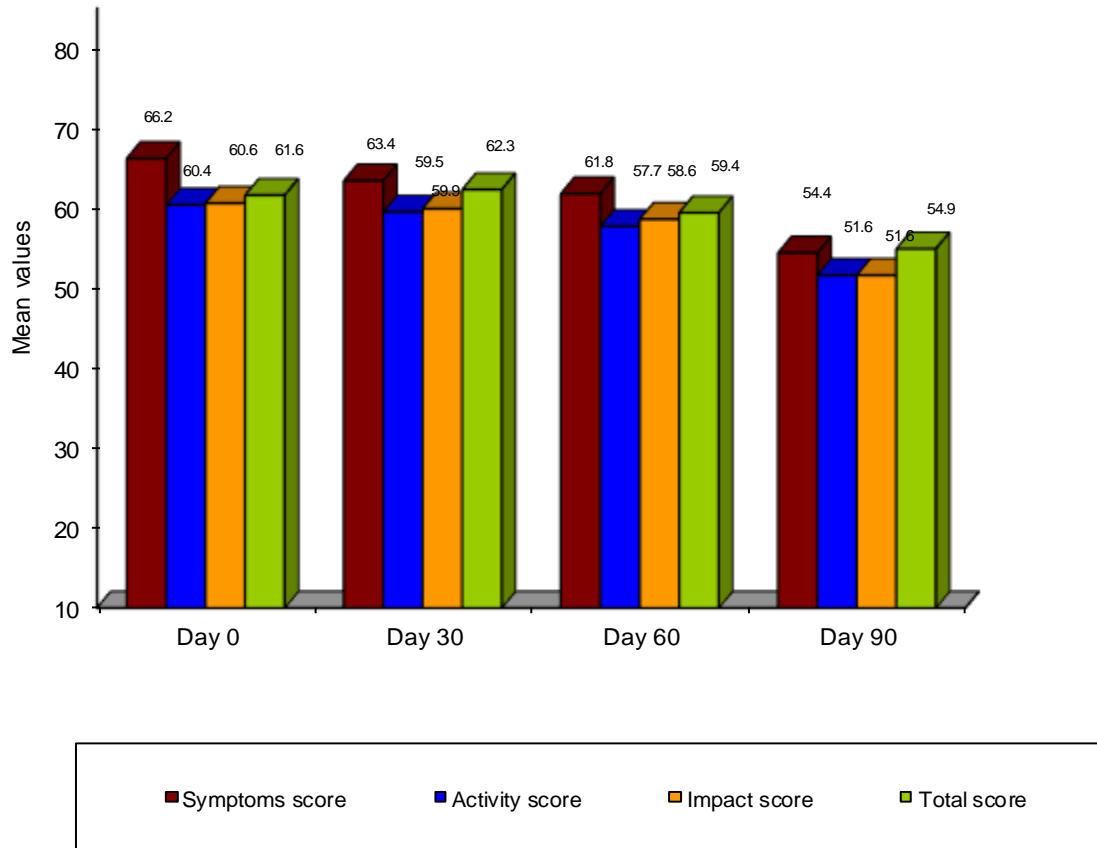**FIGURE 1: EFFECTS OF ATORVASTATIN ON SGRQ IN COPD PATIENTS**
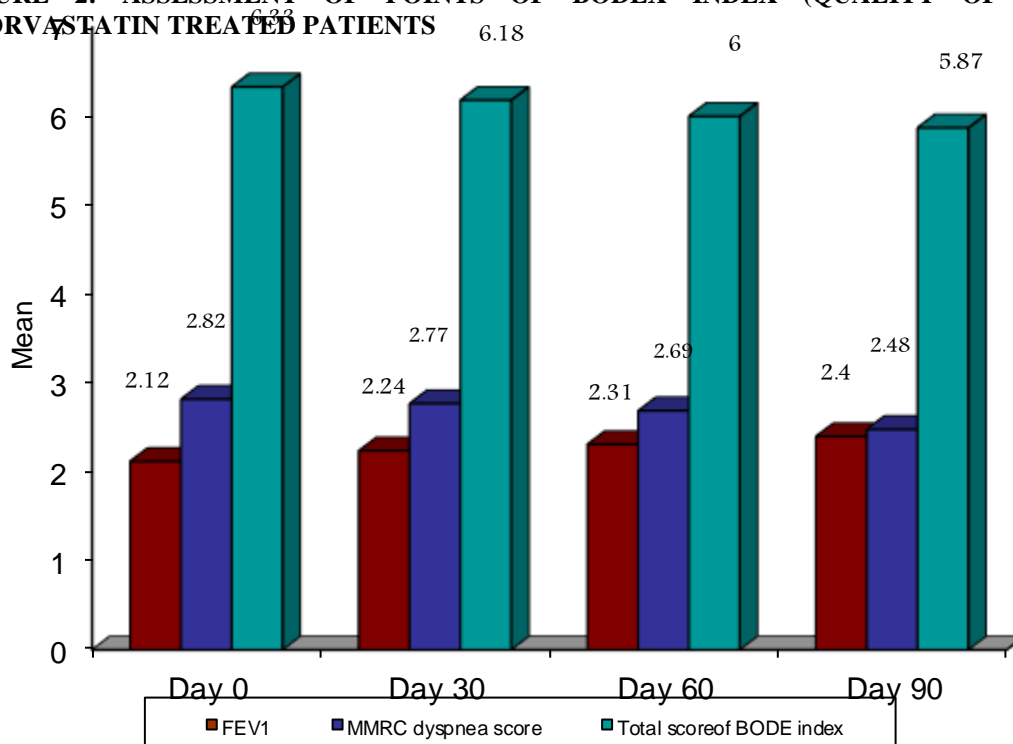

FIGURE 2: ASSESSMENT OF POINTS OF BODEX INDEX (QUALITY OF LIFE) IN ATORVASTATIN TREATED PATIENTS

DISCUSSION

COPD is a public fitness trouble globally and the prevalence of this disease remains growing[15,16] The WHO estimate that COPD is presently the 12th most commonplace reason of morbidity and the sixth foremost reason of demise inside the world. With the aid of 2020, it's far anticipated to turn out to be the 5th maximum not unusual cause of disability and the third most frequent reason of demise just in the back of coronary and cerebrovascular sickness[17].

COPD is one of the most crucial reasons of death in most countries. The worldwide burden of sickness has projected that COPD, which ranked 6th because the motive of dying in 1990, will become the third leading motive of death worldwide through 2020. This improved mortality is pushed by way of the expanding epidemic of smoking and the changing demographics in maximum nations with greater of the population living longer[18]. COPD is the quickest growing motive of death inside the developed world and a growing problem inside the growing international[19]. COPD is continual inflammatory disorder with ongoing development can cause big deleterious consequences on first-rate of existence of sufferers with frequent health center visits and because of heightened lung inflammation and spillover of the inflammatory mediators into the systemic move can cause systemic consequence e.g., peripheral muscle weak spot, cognitive impairment, melancholy, stroke, acute coronary syndrome and atherosclerosis[20].

In COPD, the most broadly used to assess HRQoL is the Saint George's breathing Questionnaire (SGRQ).This questionnaire was established for use in Brazil in 2000. The SGRQ encompassing 50 items and seventy six weighted responses divided into 3 constituents: symptoms, interest, and impacts[21]. The signs and symptoms aspect carries objects concerned with the level of symptomatology, which include occurrence of cough, sputum production, wheeze, breathlessness, and the length and frequency of breathlessness or wheeze. The hobby element is worried with bodily activities that both motive or are constrained by way of breathlessness. The affects component covers such elements as employment, being in control of fitness, panic, stigmatization, the need for medicine and its aspect outcomes, expectations for fitness and disturbance of each day lifestyles[22]. Ratings starting from zero to a hundred are calculated for each thing, as well as a complete rating which summarizes the responses to all gadgets. A zero score indicates no impairment of first-class of lifestyles. The questionnaire takes nearly 10 min to complete and so far has been revealed to be reproducible, valid and responsive in both COPD and asthmatic populations[22]. Atorvastatin had vast anti-inflammatory and immunomodulatory actions, as they suppress the innate immune response in vitro by using hindering Neutrophil migration, oxidative strain, NF-kB-activation, proinflammatory mediator release, expression of matrix metalloproteinases[23]. Keddissi et al. confirmed that use of Statin became associated with an attenuated decline in lung function as well as a decrease frequency of respiratory related emergency visits and/or hospitalization in sufferers with obstructive lung disease means that Statin might also have a direct condition ornamental effect on COPD[24].

Neutrophil migration into the subendothelial matrix is a critical event inside the progression of a number of inflammatory diseases. Maher et al demonstrate that pravastatin, simvastatin, and Atorvastatin extensively lessen neutrophil transendothelial migration closer to the chemoattractant component MLP via an inhibition of RhoA activity[25].

In gift have a look at Atorvastatin causes extensive development of health related great of lifestyles, which changed into evaluated by using the consequences of Atorvastatin at the domains of the SGRQ. Our end result are in favors with the have a look at performed by the Bartiziakas et al. (2011) as they carried out prospective studies on 245 admitted sufferers for exacerbations of COPD (ECOPD) for 365 days, they discovered that the usage of Statins in sufferers hospitalized for ECOPD was related to a decrease danger for next ECOPD and improved health related exceptional of lifestyles (SGRQ). Those data help a possible useful role of Statins in COPD[26]. Another trial conducted by Giri et al. (2003) revealed that statin can significantly improve the exercise capacity as evaluated via 6MWT in patients with Peripheral arterial diseases (PAD) [27]. They demonstrated that endothelial functional might play a pivotal role in improvement in exercise capacity. As in COPD mostly patients suffer from PAD, thus Statin usage can improve endothelial dysfunction and had favorable impact on exercise capacity in COPD.

Conclusion

Atorvastatin have the generous beneficial effects on the quality of life of COPD patients via lowering the continuing cascade of respiratory inflammation which was implicated via its pleiotropic anti-inflammatory and immunomodulatory outcomes.

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