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Original Research Article

Carnitine deficiency in chronic obstructive lung disease: A study in a tertiary care centre

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ABSTRACT

Background: Chronic Obstructive Lung Disease (COPD) is a condition where there is poor airflow to the lungs and over a period of time this condition worsen, resulting in severe morbidity. L-carnitine (LC) is a soluble qaurtenary amine and is essential for the tissues and lung tone to function normally. This study was therefore find out the association of L-carnitine in patients with chronic Obstructive Pulmonary Disease.
Materials and Methods: 75 patients who came to the Department of Pulmonology of either sex between 40 to 75 years with confirmed COPD were included into patients group and 75 healthy patients were included into the control group. Blood was collected for Fasting blood sugar, AST, ALP, ALT, Urea, Creatinine, Albumin, pre-albumin, iron , magnesium, sodium, phosphorous, calcium, Acylcarnitines, total and free carnitine levels. X-rays were taken and pulmonary function test was done for all the patients.
Results: The mean age of the patients in our study was 62.53 and 61.86 years among the patients and controls respectively. Among the controls the Ph and Fe levels were 3.1 ± 0.9mmol/L and 21.69 ± 3.19 mcg/dL respectively and among the patients the same levels were 2.6 ± 1.9mmol/L and 43.82 ± 8.22mcg/dL respectively. The albumin and the prealbumin in the patients were significantly lower in the patients with 21.81 ± 2.88 and 23.53 ±2.58 mg/dL and in controls they were 32.61 ±3.87 and 26.87 ± 1.93 mg/dL respectively.
Conclusions: There was a considerable carnitine deficiencies in COPD patients when compared to the controls and since carnitine can be found in regular diet, people can be educated to have a proper intake of foods containing carnitine in their regular diet.

1. Introduction

Chronic Obstructive Lung Disease (COPD) is a condition where there is poor airflow to the lungs and over a period of time this condition worsen, resulting in severe morbidity to the patient. It is characterized by shortness of breath, severe cough with sputum production. This condition is common among patients with chronic bronchitis.[1,2]

COPD is the 5^{th} leading cause of mortality worldwide and by 2030, it is estimated to become the 3^{rd} biggest cause of death.[3] In USA, already, it is the 3^{rd} largest cause, with the rest of the world soon following.[4,5] One of the most common risk factor is pulmonary hypertension, which further increases the risk of morbidity and mortality.[6] COPD causes different pulmonary and extrapulmonary manifestations. The pulmonary manifestation is the progressive limitation of the airflow which is not totally reversible. The extrapulmonary manifestations are usually the structural and metabolic changes that occur along with the skeletal muscle dysfunction.[7]

COPD also causes respiratory muscle weakness which is commonly associated with limitation of exercise

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and dyspnea.[8–11] This limited ventilatory capacity can further lead to loss of wasting of skeletal muscle mass, deconditioning, lactic acidosis as well as limited capillarity.[12] Other factors which cause muscle weakness are hypercapnia, deconditioning, inflammation, steroid induced myopathy, hypoxia.[13]

Several studies have established a role of L-carnitine in the improvement of muscle tone among these patients. L-carnitine (LC) is a soluble quaternary amine and is essential for the tissues to function normally, as its main function is to translocate the long chain fatty acids to the mitochondrial matrix from the cytosol so that they can undergo β-oxidation. LC is commonly found in the normal diet such as meat and dairy. It is also a product of biosynthesis in the liver and kidney, which is the most important source. The LC in vegetarians is around 15-30% lesser than the non-vegetarians and take up very little amounts of LC through diet. Their main source comes from biosynthesis, and are in the normal range due to the reabsorption in the kidneys. Total carnitine in healthy individuals is found to be around 25 -50um while that of acetyl carnitine is 3-6 um. Their presence improve the muscle tone, body condition and reduces fatigue related issues.[14–17] There have been studies to show an improvement of muscle tone by reducing proteolysis in skeletal muscle, including improvement of muscle weight and physical performance in rats.[18] However, there are very few studies showing the association of L carnitine and muscle tone in humans. This study was therefore find out the association of L-carnitine in patients with chronic Obstructive Pulmonary Disease.

2. Materials and Methods

This prospective case controlled study was done by the Department of Pulmonary Medicine, Maheswara Medical College and Kamineni Institute of Medical Sciences and Research Center, over a period of 20 months i.e., April 2019 to November 2020 - 75 patients who came to the Department of Pulmonology of either sex between 40 to 75 years with confirmed COPD were included into group A, and 75 healthy patients were included into the control group (Group B). The healthy patients were age and sex matched. All the patients included into the study were non vegetarians so that there is no bias on the LC levels due to vegetarianism. All the women were postmenopausal. Patients with Diabetes mellitus, any hepatic and renal diseases and any acute infections, following vegetarian diet, or any other conditions which could alter the L carnitine levels were excluded from the study.

After this study was cleared from the Institutional Ethical Committee, the nature of the study was explained in detail to both the cases and the controls and the informed consent was taken from all of them. Complete demographic details were taken from the patients with the inclusion of smoking status, diet and the intake, medications etc. All the patients were subjected to complete physical examination and blood was collected after 12 hours fasting from the median cubital vein for Fasting blood sugar, AST, ALP, ALT, Urea, Creatinine, Albumin, pre-albumin, iron, magnesium, sodium, phosphorous, calcium. Acylcarnitines were also analyzed as butyl esters. They were analyzed as total and free carnitine levels.

Chest X ray was done for all the patients and pulmonary function tests as per standard protocol as described by American Thoracic Society.[19] The COPD was classified as mild when the FEV1 is > 80%, moderate if FEV1>50% but <80%, severe -FEV1 >30% and <50%, and very severe if FEV1<30% according to spirometry criteria. Spirometery was done using Vmax29 ergospirometer. The patient was seated comfortably in an AC room and the maneuvers were carried out for vital capacity, forced vital capacity, forced expiratory volume per second, and the forced expiratory flow (FEF 25-75%), peak expiratory flow rate (PEFR).

Statistical analysis was done by entering the data in Microsoft excel and using SPSS software. Student t test was done for comparisons in normal distribution and for nonparametric variables, Mann- Whitney test was done. P value of <0.05 was considered to be significant.

3. Results

The mean age of the patients in our study was 62.53 and 61.86 years among the patients and controls respectively. Majority of the patients in both the groups were males. In group A, 51 patients were males and 24 were females and in the Group B, (control group), 46 were males and 29 were females. There was not much of a difference in the body mass index of patients and control. We had chosen nonsmokers among the control, so none of them had a history of smoking, while among the study subjects, 39(52%) were steady smokers, 16(21.3%) had a history of smoking, but were not smokers at the time of the study, 12(16%) were nonsmokers. 8(10.7%) of them were not smokers, but had a close relative or a spouse living in the same house, who was a smoker. The forced expiratory volume (56.39 ± 6.71% of predicted) was significantly lower than that of the controls (83.11 ± 5.19% of predicted)showing impaired airflow (Table 1).

The blood sugar among all the 150 patients under study was in the normal range, 99.38 ± 6.29 mg/Dl among the patient group and 86 ± 8.19 mg/dL among the controls. The triglyceride levels among the patients was 156.84 ± 23.87 mg/dL among the patients and 121.68 ± 16.38 among the controls. There was a significant difference in the albumin, prealbumin, phosphorous and the iron levels. Among the controls the Ph and Fe levels were 3.1 ± 0.9 mmol/L and 21.69 ± 3.19 mcg/dL respectively and among the patients the same levels were 2.6 ± 1.9mmol/L and 43.82 ± 8.22 mcg/dL respectively. The albumin and the prealbumin in the patients were 21.81 ± 2.88 and 23.53 ±2.58 mg/dL

Table 1: Demographic details of patients and controls

Variables	Group A (Cases) n=75	Group B (Controls) n=75
Age (in years) Mean ± SD	62.53	61.86
Gender (M/F) (n)	51/24	46/29
Body Mass Index (kg/m2) Mean ± SD	23.94	25.13
Smoking		
Regular smokers	39 (52%)	0
Passive smokers	8 (10.7%)	0
Prev. smokers	16 (21.3%)	0
Non smokers	12 (16%)	0
Total lung capacity (% of predicted)	87.1 ± 8.2	88.6 ± 6.1
FEV1(% of predicted)	56.39 ± 6.71	83.11 ± 5.19*
FVC (% of predicted)	84.91 ± 9.35	84.17 ± 6.30
FEV1/FVC (% of predicted)	57.91 ± 7.12	87.35 ± 11.36

and in controls they were 32.61 ±3.87 and 26.87 ± 1.93 mg/dL respectively. The ALP levels, Hb and CRP levels were 129.87 ± 28.73 IU/L, 9.61 ± 2.83 g/dL, 3.9 ± 0.9 mg/L among the patients and 87.39 ± 9.33 IU/L, 13.39 ± 2.66 g/dL, 3.0 ± 0.6 mg/L among the controls respectively which was statistically significant, with the p value being <0.00.1 (Table 2).

The free carnitine levels among the patients with COPD was 23.63 ± 8.10 umol/L, which was significant lower than the free carnitine levels of 51.6 ± 9.3 umol/L among the controls (Table 3)

The free carnitine levels were higher in the controls than in the COPD patients. Significantly high free and acetyl L carnitine levels were observed in mild COPD patients in comparison to the other patients. In the case of very severe COPD patients, the free and acyl carnitine levels were very low (Table 4).

4. Discussion

The membranes of mitochondria is impermeable to fatty acids. In order to enter, fatty acids must be conjugated with carnitine to form acylcarnitine.[20,21] Thus, there is an essential role of L- carnitine levels in the oxidation of fatty acids. One of the features of Diabetes mellitus is carnitine deficiency.[22,23]

39(52%) of the patients were regular smokers and 21% of them were ex-smokers. There was a significant difference in the triglyceride, Iron and Phosphorous levels between the patients and the controls. The ALP and CRP levels were considerably higher in the present study in comparison to the controls. Similar levels of CRP were found in another study by Pinto et al., where there was an elevation of CRP levels in smokers with COPD.[24] Pentosa et al., observed carnitine deficiency in patients with elevated CRP levels. It indicated by them that the higher carnitine levels improved the cellular defense mechanism of the patients against inflammation and oxidative stress, probably the modulation of the specific signal transduction cascade which was activated nu the increased production of the cytokines.[25]

The forced expiratory volume (56.39 ± 6.71% of predicted) was significantly lower than that of the controls (83.11 ± 5.19% of predicted) showing impaired airflow. Similar results were observed in a study by Elsammak et al.,.[26]

In the present study, the total carnitine levels and acylcarnitine levels were estimated for COPD patients as well as in controls who were matched for age and sex. We have observed a considerable reduction in the levels of both these substances in among the COPD patients in comparison to the controls. In a study by Biltagi et al., where a similar study was done in asthmatic children, low free an total carnitine levels were observed which was in concurrence with our study as was another study by Asilsoy et al., who found that the carnitine levels were considerably decreased in children with moderate asthma.[27,28] Although we have not performed the effects of L-carnitine supplementation therapy, in a study by Biltagi et al., it was found that on supplementation, there was a considerable improvement in the pulmonary function tests and C-ACT in children.[27]

As the severity of COPD increased, the levels of total carnitine and acylcarnitine were significantly reduced. This resulted in increased weakness of the respiratory and peripheral muscles in the COPD patients. Reduced carnitine levels were also found to affect the fatty acid's oxidative metabolism thereby resulting in the increased muscle weakness and myopathy.

The lower levels of the carnitine levels were probably due to the lower nutritional intake as is seen with lower levels of hemoglobin, albumin in COPD patients as compared to the controls. Burnstein et al., and Devakonda et al., in their respective studies have described the nutritional status of a person can be identified using prealbumin as a biomarker.[29,30]

5. Conclusions

This study has shown a lowered carnitine levels in COPD patients when compared to the controls, which could be attributed to the lowered nutritional status of the patient,

Table 2: Biochemical parameters

Parameter Mean ± SD	Group A (Cases)	Group B (Controls)	Significant/ Non-significant
Random Blood sugar (mg/dL)	99.38 ± 6.29	86 ± 8.19	NS
Triglycerides (mg/dL)	156.84 ± 23.87	121.68 ± 16.38	S
Total Cholesterol (mg/dL)	172.75 ± 15.87	166.45 ± 9.45	NS
BUN (mg/dL)	4.71 ± 0.64	4.22 ± 0.99	NS
Creatinine (mg/dL)	0.86 ± 0.22	1.05 ± 0.43	NS
Prealbumin (mg/dL)	23.53 ±2.58	32.61 ±3.87	S
Albumin (mg/dL)	21.81 ± 2.88	26.87 ± 1.93	S
Sodium (mEq/L)	138.92 ±32.72	135.18 ± 29.86	Ns
Potassium (mmol/L)	3.9 ± 0.8	3.7 ± 1.1	NS
Phosphorous (mmol/L)	2.1 ± 1.9	3.1 ± 0.9	S
Iron (mcg/dL)	21.82 ± 8.22	43.69 ± 3.19	S
Calcium	9.33 ± 1.37	8.91 ± 1.62	NS
25 OH Vitamin D (ng/ml)	11.92 ± 1.7	14.7 ± 1.53	NS
ALP (IU/L)	129.87 ± 28.73	87.39 ± 9.33	S
Hemoglobin (g/dL)	9.61 ± 2.83	13.39 ± 2.66	S
CRP (mg/L)	3.9 ± 0.9	3.0 ± 0.6	S

Note: S: significant with p<0.001; NS: not significant-p>0.001

Table 3: Free carnitine levels in controls and patients

Group	Free carnitine levels (umol/L)
Group A (Patients)	23.63 ± 8.10
Group B (Controls)	51.6 ± 9.3

Table 4: Free and acyl carnitine levels in COPD patients

	Free Carnitine (umol/L)	Acetyl L- Carnitine (umol/L)
Mild COPD	27.5 ± 2.7	8.2 ± 2.1
Moderate COPD	21.41 ± 3.1	7.49 ± 1.3
Severe COPD	8.84 ± 1.63	2.19± 0.45
Very severe COPD	4.93 ± 0.36	4.15 ± 0.98

thereby further reducing the respiratory and peripheral muscular strength as well as the forced expiratory volume. Since carnitine can be found in diet, people can be educated to have a proper intake of foods containing carnitine in their regular diet.

6. Acknowledgment

None.

7. Conflict of Interest

The authors declare that there are no conflicts of interest in this paper.

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None.

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