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Original Research Article

ASSESSMENT OF LOWER LIMB REACTION TIME IN SUBJECTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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ABSTRACT

Background: COPD is characterised by irreversible airflow obstruction, which brings about hypoxemia, hypoxia and cerebral hypo-perfusion leading to cognitive impairments and peripheral muscle dysfunctions which get worse with the severity of the disease.

Purpose: Cognitive reaction time that forms the pre-motor event of the reaction time loop has been seen to be slower in COPD as compared to healthy controls. But the motor event of the loop has not been assessed in this population. The present study aimed at assessing the lower limb reaction time in COPD subjects.

Materials and Methods: 30 male COPD subjects (GOLD criteria) were included in the study. The study was a single blinded experimental observation design. Lower limb reaction time was calculated using a simple reaction time software accurate up to 0.1 millisecond.

Analysis: Mean, standard deviation of the demographic data (age, height and weight) and the reaction time was calculated using Microsoft Excel. One-way ANOVA was used to test for statistical significance between the means of the three groups(mild, moderate and severe) COPD.

Results: The difference of means between the three groups was statistically significant (p=0.001). Although the correlation between severity and lower limb reaction time was not statistically significant, there was an association between the two parameters.

Conclusion: This study shows an association between lower limb reaction time and severity. Lower limb reaction time has been found to follow a trend as the severity of the disease increases.

Implication: There arises a need for incorporating balance training and for improving lower limb reaction time as a part of pulmonary rehabilitation in COPD subjects.

KEY WORDS: COPD, Reaction time, Cognitive deficits.

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a progressive inflammatory disease characterized by chronic obstruction to airflow which is often irreversible or not fully reversible [1]. The overall prevalence of COPD globally has been reported as 9-10% of the population.

COPD is now considered as a multi-system disease. There is an imbalance seen between oxidants and anti-oxidants in the body, giving rise to oxidative stress in the body [2]. On-going inflammation and higher oxidative stress give rise to most of the systemic manifestations in these patients [3]. Symptoms like weight loss, muscle wasting and tissue depletion are also seen as markers of chronic inflammation [4]. There is also alteration of hormones like insulin, growth hormone, testosterone and glucocorticoids [5]. Owing to the above reasons, people with COPD suffer from peripheral muscle dysfunctions like muscle wasting and weakness.

Peripheral muscle wasting and weakness: Oxidative capacity is the ability of the muscle to utilise oxygen effectively and thus preventing further damage. When the oxidative capacity falls, the oxidative stress on the muscle increases [4]. Presence of hypoxemia, higher levels of pro-inflammatory mediators, reduced activity of mitochondrial enzymes and an impaired oxidant-antioxidant balance in these patients contributes to increased oxidative stress, which in turn forms the main cause of peripheral muscle dysfunction in these patients [4-7].

Premature lactic acidosis leads to reduced mitochondrial activity [8,9]. The prevalence of peripheral muscle dysfunction in this population is seen to be 30% [10]. There is preferential loss of muscle seen in COPD especially in the lower extremities as suggested by the finding that the reduction in mid-thigh cross-sectional area is higher than the total loss of body weight [11,12]. Another factor contributing to this is an imbalance between anabolism and catabolism [4]. There is loss of anabolism due to increase in levels of insulin and insulin like growth factor (IGF) seen in these patients, leading to further breakdown of muscle fibres [13]. Owing to less oxygen reaching the muscles due to reduced availability of oxygen, there is a shift in the fibre type. There is preservation of a proportion of type I fibres in mild to moderate COPD, but from moderate to severe COPD the proportion of type I fibres is reduced with a reciprocal increase in type IIb fibres resulting in less energy efficient muscles [3,14,15]. Hence, the endurance and the oxidative capacity of the muscle is reduced. Owing to protein degradation in peripheral muscles, there is breakdown of myosin heavy chains, leading to less formation of actin-myosin cross-bridging. All these factors along with apoptosis and muscle protein degradation leads to muscle wasting.

The preferential muscle wasting of the lower extremities affects the strength of the muscles. In a study conducted by Debigare et al in 2003 indicated that there was no change in the contractile properties of the muscle or the neural recruitment, and it confirmed loss of muscle mass as the main reason for muscle weakness.

Cerebral hypo perfusion: Another consequence of chronic airflow obstruction is cerebral hypo-perfusion. Cerebral hypo-perfusion has been attributed as the main cause for cognitive impairments in patients with COPD. Studies have shown that these patients have delayed psychomotor speed, reduced attention time etc. Klein et al in 2010 conducted a study to test various components of attention and cognitive reaction time in patients with COPD. The results of the study reported a delay in cognitive and overall reaction time in the COPD group as compared to the healthy controls.

Reaction time is the interval between the application of a stimulus and starting of a response. Its physiology is dependent on the nature and type of activity or stimulus given. There are various types of reaction times. Simple reaction time has one stimulus and one response, whereas Choice reaction times have multiple stimuli and multiple responses to it. The type of stimulus offered can be visual, auditory or other type of sensory stimuli. The reaction time loop can be divided into pre-motor and motor event. The pre motor event comprises of the time starting from the application of the stimulus until the processing time of the brain. The end point of this part of the loop is taken when the first change in action potential is seen in the effector organ. The motor event begins at the first change in the action potential until the appearance of the first response.

Cognitive reaction time, which forms the pre motor part of the loop, has already been studied in COPD population, and is found to be delayed when compared with healthy controls. But limb reaction time which forms the motor event of the loop has not been studied in this population. COPD is characterised by airflow obstruction which can be quantitatively measured. The Global initiative for Obstructive Lung Disease (GOLD) uses the ratio between FeV1 and FVC values to categorise COPD as mild, moderate and severe. Higher level of airflow obstruction yields lower FeV1 values which is suggestive of higher level of impairment. The systemic manifestations in COPD have seen to become worse as the severity increases [12]. Other studies have reported a reduction in mid-thigh cross-sectional area by approximately 30% in moderate to severe COPDs [11,16]. Altered muscle physiology and delay in reaction time leads to impaired balance in these patients making them more prone to falls [17]. Worsening of the systemic symptoms with increase in severity only contributes more to this. There is enough reason to believe that altered muscle physiology along with cerebral hypo-perfusion may contribute to alteration in lower limb reaction time, which in turn may affect overall reaction time in this population. Assessing the lower limb reaction time in the COPD population will help us know if reaction time too has a similar behaviour as other systemic manifestations with respect to severity of the disease. Establishing the presence of any change in the reaction time across the stages of COPD would help us include training for improvement of reaction time as part of the long-term rehabilitation program, which also forms the need for this study.

The Aims and Objectives of the study were 1) To assess lower limb reaction time across the three stages of severity of COPD- Mild, Moderate and Severe and 2) To measure significant delay in lower limb reaction time as severity of the disease progresses.

MATERIALS AND METHODS

The Type of study was Interventional and Single blinded observational experimental Study design. The sample size was 30 COPD subjects distributed across mild, moderate and severe categories.Convenience sampling technique was used.

Sources of data collection: 1) List of COPD patients admitted in hospital throughout the year 2014 obtained from medical records department of the hospital. 2) COPD patients coming for follow up in chest medicine and medicine out patient department. 3) In-patients in the wards admitted under medicine or surgery who are known cases of COPD and not in acute exacerbation.

Inclusion criteria: Males, between the ages of 35-80 years, diagnosed with COPD by a physician and FEV1 and FVC values in spirometry suggestive of obstructive disease according to GOLD criteria updated in the year 2014.

Exclusion criteria: Subjects of COPD in acute exacerbation, Known/diagnosed case of COPD with spirometry values suggestive of restrictive or combined aetiology, Any primary neuromuscular disease, Uncontrolled diabetes or hypertension, Peripheral neuropathies, Peripheral vascular diseases, Weakness of the dominant side, upper or lower limbs or both, Sensory deficits on the dominant side, Amputation due to vascular diseases, Cardio pulmonary surgeries and conditions, Language or cognitive deficits that limit understanding of the informed consent or any part of the procedure.

Materials: Laptop with simple reaction time software with mouse designed to be operated by the lower limb, Sound treated room, PFT machine, Chairand Table of appropriate height to set up the laptop **(figure 1)**, Notebook and pens.

Fig. 1: Materials and position of the subject during reaction time test.

Procedure: An ethical clearance was obtained from the Ethical Committee of the institution. Patients who met the inclusion criteria were asked to come to the physiotherapy department. An informed consent was given to them that included a patient information sheet which had all the details regarding the study. A choice of withdrawing from the study at any point in time was also presented to the subject. After obtaining subject's signature on the informed consent, they were again explained about the procedure in detail by the researcher.

Demographic data including height and weight was recorded. A brief neurological assessment was done. Drug history was taken in detail including use of supplemental oxygen and its dosage, if any. An assessor trained in performing and interpreting spirometry test took the patients for test in a different room. 3 trials were given before final reading was taken. The results stayed with the assessor until end of data collection. The researcher was blinded to the result of the spirometry test. Subjects were then taken to a sound treated room for the reaction time measurement.

The device consisted of a laptop uploaded with a software designed for measurement of reaction time. The software measured reaction time accurate up to 0.1 millisecond. A computer mouse with large left key button was fixed in a padded box such that only the left key was outside and the rest of the mouse was covered. The size of the padded box was made according to the biggest foot size in males in India. This device was connected to the laptop similar to a USB drive.

The software used was specifically designed for measurement of simple reaction time. The stimulus used was visual type. The subjects were asked to place their dominant leg, which was right in all the cases, over the padded box with their great toe resting on the button (left mouse key). Subjects were instructed to perform flexion and extension of the toes only and not to move their ankle or foot. The test began with the subject pressing down on the button and keeping it that way, until the colour on the screen changed from Green to Red **(figure 2)**.

Fig. 2: Showing the dominant foot on the device for measurement.

Instructions were given to the subject's was- release the button as soon as you see the colour red. The response expected was extension of the toes. 5-10 trials were given until the subject perfectly understood what he was expected to do. Before taking final readings the room was sealed and all lights were switched off to minimise any other kind of sensory stimulus. Subject was asked to start the test and continue doing it until asked to stop. 10 readings were taken.

Data Analysis: The data collected were entered in Microsoft Excel sheet and data analysis was done using One-way ANOVA. Descriptive statistics comparing the baseline characteristics of the three groups (age, height, weight, FEV1/FVC values) were analysed. Mean of individual reaction times was assessed to obtain group mean. One-way ANOVA was used to determine whether the difference between the means of reaction time of the groups was statistically significant.

RESULTS

34 subjects were recruited for the study, 7 in mild group, 13 in moderate and 10 in severe group. There were 4 drop outs.

Table 1: Represents demographic data of the subjects. It shows the mean and standard deviation of age, height and weight in the mild, moderate and severe group of COPD.

	MILD		MODERATE		SEVERE	
	Mean	SD	Mean	SD	Mean	SD
Age	57.43	8.58	69.3	8.49	68.8	6.66
Height	167.07	4.36	164.23	5.01	171.85	6.11
Weight	63.14	7.59	63.54	8.78	73.3	14.59

Table 2: Shows the lower limb reaction time across the stages of COPD. It states the mean and standard deviation of lower limb reaction time across mild, moderate and severe COPD.

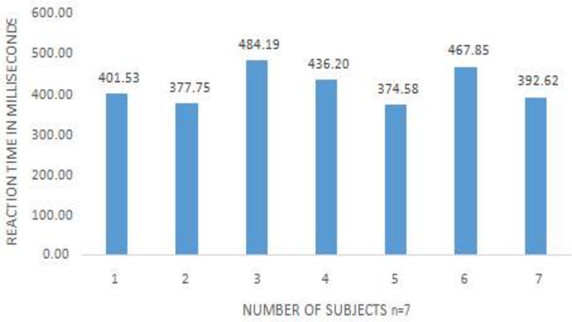
	MILD	MODERATE	SEVERE
MEAN	419.25	489.07	679.97
STANDARD DEVIATION	43.98	108.35	128.23

Table 3: Denotes the comparison in reaction time between three groups:

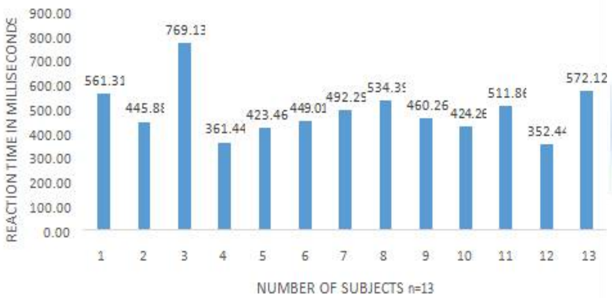
Source of Variation	SS	df	MS	F	P-value	Fcrit
Between Groups	183061.1	2	91530.55	8.223828	0.001625	3.354131
Within Groups	300507.8	27	11129.92			

Difference in mean reaction time between the three groups that is mild, moderate and severe was calculated using One-way ANOVA and was found to be significant at p=0.001.

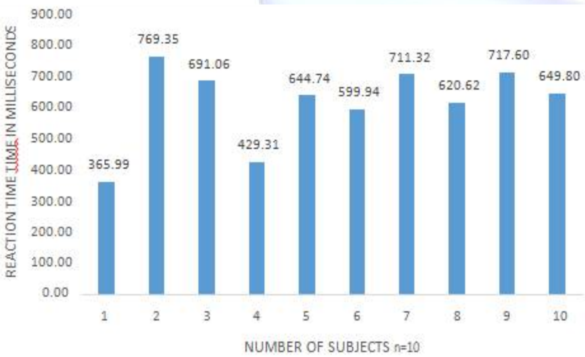
Graph 1: Represents the mean of individual reaction time of subjects in mild group.



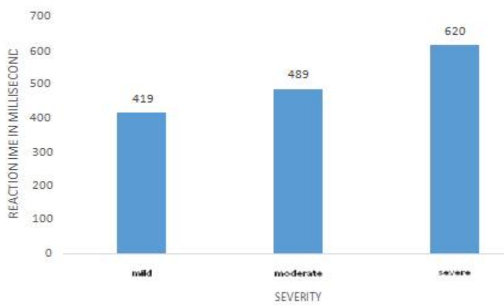
Graph 2: Denotes the mean of individual reaction time of subjects in moderate group.



Graph 3: Represents the individual reaction time of subjects in severe group.



Graph 4: Explains the trend of lower limb reaction time with severity. It was seen that as the disease stage progressed from mild to moderate to severe, the lower limb reaction time kept on increasing.



DISCUSSION

This current study primarily measured the lower limb reaction time in subjects with COPD across the three stages of the disease. The aim was also to see if there existed any trend in lower limb reaction time as the severity of the disease progressed from mild to severe.

The lower limb reaction time was assessed by calculating means of 10 trials of each subject. An average of all the individual means was taken to calculate the mean of the group. Mean of reaction time in mild group was found to be 419 milliseconds, moderate group had a mean of 489 milliseconds and severe group had a mean of 680 milliseconds. There was a wide range of variability seen between the means of individual reaction times. The range was between 374-484 milliseconds in mild group, 352-572 milliseconds in moderate group and 365-769 milliseconds in severe group. A probable reason behind this occurrence could be the learning effect which happened owing to the fact that each subject was given trials before beginning of the test. There was variable amount of airflow obstruction within the group itself which could also contribute to this. Measurement of defining parameters like level of hypoxia in each subject and parameters of peripheral muscle dysfunction was not done. Knowledge about these parameters may definitively provide an answer to the question of variability seen in each group.

A trend was observed in the lower limb reaction time as the disease progressed from mild to moderate, as indicated by the difference between the means of the three groups-70 milliseconds between mild and moderate, and 190 milliseconds between moderate and severe. According to previous studies cognitive deficits have been reported in subjects with COPD as compared to age matched healthy controls. These studies have also shown a significant relationship between the level of cognitive impairments and severity of the disease. The fact that reaction times were most delayed in the severe group only confirms this fact. Although the correlation between severity and reaction time was not statistically significant, an association between severity and reaction time can be seen definitively. Cognitive reaction time specifically has not been assessed with respect to severity, but taking into consideration the fact that a relationship exists between cognitive deficits and severity, it may be applied to the trend observed in this study.

The software used was for Simple reaction time which is not designed to measure accuracy as there is only one stimulus and one response. The subjects in the severe group needed more number of practise trials as compared to the other groups, where the subjects could perform the test accurately within first five practise trials itself. Previous studies have reported poor accuracy in the severe and very severe COPD population when compared to healthy controls [18]. These studies have shown a significant correlation between partial pressure of oxygen in the blood and deterioration in the neuropsychological tests. There have been studies done on the effect of long term oxygen therapy on COPD. The result obtained was that there was a positive effect of oxygen therapy on cognitive performance. It was also noted that subjects who had more knowledge about their condition and were better educated performed better as compared to other subjects in the same group. Although the level of education was not formally taken as a part of methodology, it seemed to have a positive effect on their individual reaction times. The distribution of the subjects across the three stages was not uniform owing to blinding of the researcher to the spirometry results. Such an occurrence could be minimised by increasing the total sample size and by equal distribution of subjects in each group. Many previous studies have taken blood oxygen and carbon di oxide levels prior to neuropsychological testing, owing to the fact that hypoxia forms one of the main reasons in cognitive delays and deficits. This parameter could not be done in the present study due to ethical issues. Although future studies should include level of oxygenation as part of the methodology in order to support the findings.

Further studies should be done where present state of hypoxia and lower limb muscle dysfunction parameters should be taken into consideration to effectively identify and quantify lower limb reaction time in COPD population so that training for improvement of reaction time can be included as part of long term rehabilitation for the COPD population.

CONCLUSION

The purpose of the current study was to assess lower limb reaction time in patients with COPD across the three stages of severity. After assessing the lower reaction time in 30 subjects with COPDs it was found that there was significant difference in the lower limb reaction time between mild, moderate and severe COPDs. From the means of the reaction time in each group, significant difference between the means was found between each group. Therefore, it can be concluded that lower limb reaction time increases with increase in severity.

Clinical Implications: Training for improvement of Reaction time as a part of long term rehabilitation program.

ABBREVIATIONS

COPD - Chronic Obstructive Pulmonary Disease

PFT - Pulmonary Function Test

FEV1 - Forced expiratory volume in first second

FVC - Forced vital capacity

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Conflicts of interest: None

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