# CORRELATION OF DISEASE DURATION, SMOKING PACK YEARS AND $FEV_1$% PREDICTED WITH VEP PARAMETERS IN PATIENTS OF COPD.

**Rubiya Shaikh*, Rupali Parlewar****

*Assistant Professor, ** Associate Professor, Department of Physiology, Grant Govt. Medical College & Sir J.J. group of Hospitals, Mumbai- 400 008

**Abstracts**: **Background & Objectives**: The most common risk factor for COPD is tobacco smoking. Inhaled noxious particles cause chronic inflammation in lungs and airways leading to persistent airflow limitation causing hypoxemia. . It not only affects the lungs but also affects the various body systems. Thus COPD is multisystem disorder. Visual evoked potential is useful for subclinical detection of visual impairment. The purpose of study was to correlate duration of COPD, smoking pack years and $FEV_1$% with VEP parameters in COPD patients. **Method**: Spirometry was done to diagnose COPD. Pattern reversal VEP was conducted in 50 COPD patients who were smokers & 50 normal healthy subjects who were non-smokers. VEP parameters (P100 latency & amplitude) were assessed. Unpaired t-test and Pearson's correlation test was used. **Results**: We found significant correlation between VEP parameters with smoking pack years & FEV1% predicted value. While no significant correlation with duration of disease. **Interpretation & Conclusion**: Findings suggest longer disease duration alone could not have significant effect in impairment of visual functioning while more smoking pack years & severe airflow obstruction can cause impaired visual pathway in COPD. It is because of ventilation-perfusion imbalance causing hypoxemia leading to tissue hypoxia which decreases cerebral perfusion.

**Key Words**: COPD, FEV1%, Hypoxemia, Smoking pack years, VEP

**Author for correspondence:** Dr. Rubiya Shaikh, Department of Physiology, Grant Govt. Medical College & Sir J.J. Group of Hospitals , Mumbai – 400008. India. e-mail: rubiya.shaikh@gmail.com

**Introduction:**

COPD is not one single disease but an umbrella term used to describe chronic lung diseases that cause limitations in lung airflow. Several different definitions have existed for COPD [1,2].The recently published and widely accepted definition from the Global Initiative for Chronic Obstructive Lung Disease (GOLD) defines COPD as Chronic obstructive pulmonary disease, a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lungs to noxious particles or gases [3]. The inflammatory response in respiratory tract of COPD patients appears to be amplification of the normal inflammatory response of the respiratory tract to chronic irritants such as cigarette smoke. The inflammatory process is a driving force in the pathophysiology of COPD. Inhaled noxious particles and gases that lead to COPD causes lung inflammation, induces tissue destruction and impairs the defence mechanisms that seem to limit the destruction and thus disrupt the repair mechanisms that may be able to restore tissue structure in the face of some injuries. This inflammatory response does not cease with the removal of the stimulus, but progresses for an unlimited period of time [4,5].

There are various key indicators for considering a diagnosis of COPD like dyspnoea, chronic cough, history of exposure to risk factors and family history of COPD. But Spirometry is required to make a clinical diagnosis of COPD; the presence of a post-bronchodilator $FEV_1/FVC < 0.70$ confirms the presence of persistent airflow limitation and thus of COPD. Worldwide, the most commonly encountered risk factor for COPD is tobacco smoking [6,7,8]. Studies show that approximately 80-90% of patients with COPD have been smoking and approximately 15% of all smokers will develop COPD [9]. Hence correlation of disease duration and smoking pack years with disease process is required.

Visual evoked potential (VEP) is sensitive enough to detect subclinical visual impairment. VEP are electrical potentials recorded from scalp in response to visual stimuli. It is a simple, non-

invasive procedure to detect early impairment of optic nerve and CNS pathway, even in the absence of specific symptoms. VEP provide a qualitative and quantitative measure of the optical pathway, as they indicate the functional aspects of the optic nerve, optic chiasm and tracts, lateral geniculate bodies and geniculocalcarine projection to visual cortex [(10)]. Disturbances anywhere in the visual system can produce abnormal VEP. Hence the present study is carried out to correlate disease duration, smoking pack years and $FEV_1$% predicted value with VEP parameters as all these factors can have relationship with disease process.

**Material and Methods:**

The present study was conducted in the Department of Physiology & Department of Pulmonary medicine in Sir J.J. group of hospitals and Grant Govt Medical College, Mumbai. Before commencement of study, approval was taken from the Institutional Ethical Committee.

The study design involved 100 individuals which can be divided in two groups.

Group I –Diagnosed patients of COPD as per GOLD criteria, after applying inclusion and exclusion criteria were accepted for study (n=50)

Group II –Age & sex matched normal healthy adults (n=50).

**The evaluation was done in following stages** -

1) A written informed consent was taken from all participants of this study.
2) A detailed history-taking and thorough clinical examination was done.
3) Spirometric test was performed in both groups and diagnosis of COPD was confirmed in cases.
4) VEP recording was done.

In addition to signs and symptoms, spirometry was done to confirm the diagnosis of COPD (post-bronchodilator $FEV_1$/FVC ratio less than 70%, consistent with airflow limitation that is not fully reversible, GOLD criteria) and the severity of airflow limitation was determined by GOLD gradation criteria. Spirometry test was done in study group with the help of **MEDGRAPHICS Body Plethysmograph** machine.

Among COPD patients, males with age group of 40-60 years those had a duration of COPD for more than 5 years with stable course of disease, having a regular follow up for 1 year with no hospitalization for COPD related illness in preceding 6 months were included in study group. All COPD patients in study were males and had smoking history. They were having moderate to severe airflow limitation. Smoking pack-years were calculated considering (i) total years smoked, (ii) daily consumption, and (iii) mode of smoking (bidi, cigarette). One pack-year involved 20 cigarettes smoked everyday for 1 year. For bidi smokers, pack-years were calculated by applying a weight of 0.5 to cigarette equivalents [(11)]. Controls were Normal healthy male individuals with age group of 40-60 years having no addiction (Non-smokers). Patients as well as controls were having normal vision (6/6).

**Exclusion Criteria:-**

1. Patients of COPD in acute exacerbation.
2. Subjects having any clinical neuropathy.
3. Subjects having visual impairment like cataract, colour vision defect, optic neuritis, glaucoma, optic disc and retinal pathologies.
4. Subjects suffering from another acute/ chronic medical disorder like hypertension, diabetes mellitus, malignancy, leprosy, tuberculosis.
5. Subjects with history of addiction to alcohol, drug abuse.
6. Subjects with history of drug intake known to cause central neuropathy e.g. Reserpine, phenytoin,alphamethyldopa,nitrofurantoin

**Pattern reversal visual evoked potential recording**

Test was carried out with prior appointment to patients. **EMG and EP digital neurophysiological system software**, **Neuro-MEPw** version 3.0, 64.0 was used to conduct evoked potential tests. Standard cup electrodes were used. The electrodes were placed on their respective sites using electrode paste as per 10-20 international system of electrode placement. Subjects having usual glasses were instructed to wear their spectacles at the time of examination. Subject was seated at one meter (100 cm) distance in front of the television screen. Monocular stimulation was performed and

the eye that was not being tested was covered. Subject was instructed to fix gaze and concentrate on a small red rectangle present at the centre of screen with one eye. Checks were made to reverse at rate of 1 Hz and an average of 100 responses was recorded in 400 milliseconds from each eye separately.

Electrode placement:
Active electrode ($O_z$) – mid-occipital i.e.5 cm above inion in midline
Reference electrode ($F_z$) – mid frontal i.e. 12 cm above the nasion in mid-line
Ground electrode ($C_z$) – at vertex.
Machine settings:

1) Filter – Low cut filters (LF) was set at 2 Hz and High cut filters (HF) at 100 Hz.

2) Impedance – The electrode impedance was kept below 5 kΩ.

3) Stimulus - Black and white checker board squares of size 8 × 8 (64'). Reversal pattern type with pattern drawing of chess was used to give stimulus. Small fixed point in red colour was used. Brightness of screen was kept high.

Parameters studied: VEP waveform was recorded and labelled for the peaks N75, P100, N145. Latency of P100, amplitude of P100 was obtained. For judging the reproducibility of the VEP pattern, two trials were recorded, averaged and superimposed.

**Statistical analysis:**

The results were expressed as mean and standard deviation for each variable. Unpaired (independent) t- test was used for intergroup comparisons in the healthy volunteers group and the COPD group. Pearson's correlation coefficient test was applied to correlate between disease duration, smoking pack years and $FEV_1$% predicted with VEP parameters. All statistical analyses were carried out with the help of SPSS version 20.0 software. p value of 0.05 or less has been considered as statistically significant.

**Results:**

**Table no.1:** Table showing the patients characteristics (Disease duration, Smoking pack years), Age distribution and Spirometric findings in study group.

| | Cases (Mean ± S.D.) | Controls (Mean ± S.D.) | p value | |
|---|---|---|---|---|
| Age (years) | 52.92 ± 3.93 | 51.48 ± 5.4 | 0.1312 | ns |
| Disease duration (years) | 10.82 ± 2.89 | ——— | ——— | — |
| Smoking pack years | 31.04 ± 6.6 | ——— | ——— | — |
| $FEV_1$% predicted | 47.73 ± 8.13 | 90.71 ± 4.62 | < 0.0001 | s |

p value ≤ 0.05 = Statistically significant
p value > 0.05 = Statistically non-significant
There was no statistical significant difference (p value > 0.05) in age distribution among cases and controls. $FEV_1$ % predicted spirometric value was statistical significantly less in cases compared to controls (p value < 0.05).

**Table no.2:** Table showing the correlation of disease duration with VEP parameters in COPD patients.

| Correlation of Disease duration (yrs) with VEP parameters | | | |
|---|---|---|---|
| | r value | p value | |
| Right VEP parameters | | | |
| P100 Latency (ms) | 0.19 | 0.1867 | ns |
| P100 Amplitude (μv) | -0.18 | 0.195 | ns |

p value ≤ 0.05 = Statistically significant
p value > 0.05 = Statistically non-significant

There was statistically non-significant (p value >0.05), positive correlation between disease duration and P100 latency of right eye while the disease duration was negatively correlated with

P100 amplitude of right eye but had no statistical significance (p value >0.05).

**Scatter diagram no.1:** Showing positive correlation between disease duration and Right eye P100 latency in case group.

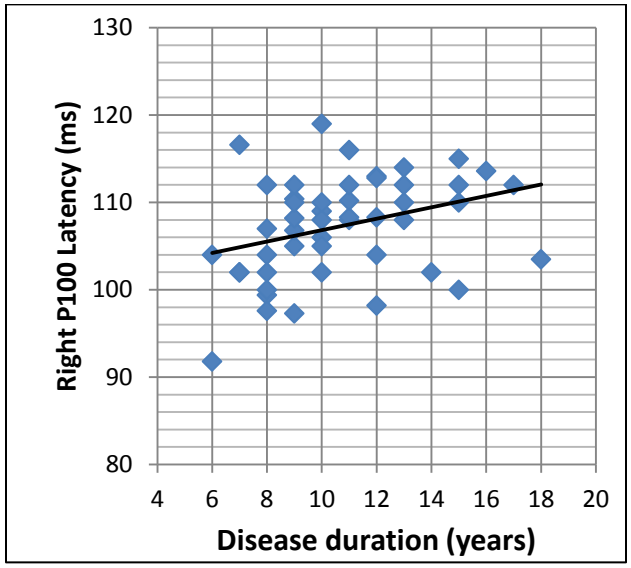


**Table no.3**: Table showing the correlation of smoking pack years with VEP parameters in COPD patients.

| Correlation of smoking pack years with VEP parameters | | | |
|---|---|---|---|
| | r value | p value | |
| Right VEP parameters | | | |
| P100 Latency (ms) | 0.38 | 0.0062 | s |
| P100 Amplitude (µv) | -0.37 | 0.0071 | s |

p value ≤ 0.05 = Statistically significant

p value > 0.05 = Statistically non-significant

It was observed that there was increase in latency of P100 wave of right eye, with increase in smoking pack years indicating a positive correlation with p value <0.05 showing a statistical significance. There was statistical significant (p value <0.05) negative correlation between P100 amplitude of right eye with smoking pack years.

**Scatter diagram no.2:** Showing negative correlation between smoking pack years and P100 amplitude of Right eye in cases.

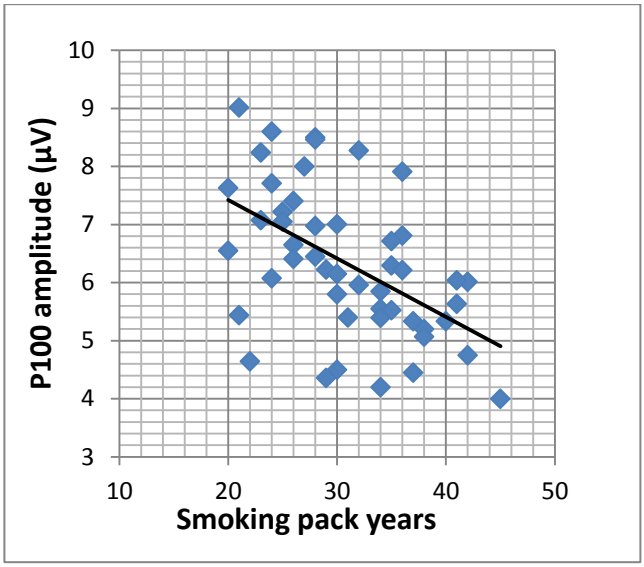


**Table no.4**: Table showing the correlation of post-bronchodilator $FEV_1$% predicted value with VEP parameters in COPD patients.

| Correlation of $FEV_1$ % predicted with VEP parameters | | | |
|---|---|---|---|
| | r value | p value | |
| Right VEP parameters | | | |
| P100 Latency (ms) | -0.4 | 0.0037 | s |
| P100 Amplitude (µv) | 0.35 | 0.0126 | s |

p value ≤ 0.05 = Statistically significant

p value > 0.05 = Statistically non-significant

Table shows that there was statistical significant (p value <0.05) negative correlation between post-bronchodilator $FEV_1$% predicted value and right eye P100 latency, indicating prolongation of latencies of VEP with reduction in FEV1% predicted

value. While P100 amplitude of right eye was positively correlated with a statistical significance showing reduction in amplitude of VEP along with reduction in $FEV_1$% predicted value.

**Discussion:**

The average smoking pack years of COPD patients in the present study is 31.04 ± 6.6 and the FEV1% predicted is 47.73 ± 8.13 in COPD patients as compared to 90.71 ± 4.62 in controls. Correlation of patients characteristics with VEP parameters was given in table no. 2,3,4. Present study found that there was non-significant correlation between disease duration and VEP parameters which suggests that longer disease duration alone could not have significant effect in impairment of visual functioning in COPD patients. While there was significant correlation of VEP parameters with smoking pack years and severity of airflow obstruction.

Similar findings are present in some studies Hafez et al [(12)] (2009). **Hafez et al** found positive correlation of BAEP & VEP with disease duration, smoking pack years & $PaCO_2$. Their study showed negative correlation with spirometric indices [(12)].

**Prem Parkash Gupta et al** found statistically significant inverse correlations between P100 latency (right eye) and FEV1/FVC %. The rest of the correlations between characteristics of COPD patients (including age, duration of illness, smoking pack-years) with VEP parameters were not statistically significant [(11)].

**Ozge and co-workers** suggested that the optic nerve is commonly involved in patients with severe COPD, possibly as a part of polyneuropathy. They concluded that VEP abnormalities were related to acidosis, hypercarbia, and airway obstruction, but independent of disease duration, smoking, and age [(13)].

When genetically susceptible individuals expose to these risk factors (tobacco smoking) for a long duration and at high doses, chronic inflammation occurs and clinical, physiological and pathological changes of chronic bronchitis and/or emphysema develop. As the disease advances hypoxemia develops as a result of ventilation/perfusion imbalance [(14).] Some studies showed that tobacco results in optic neuropathy and affects the evoked potential [(15,16)].

In present study, the COPD patients were smokers and had moderate to severe airflow obstruction (stage 2,3). The subclinical VEP impairment in patients of COPD was due to the severity of airflow obstruction which causes chronic hypoxemia. The content of tobacco smoke causes chronic inflammation in lungs & airways leading to airway obstruction causing hypoxemia. The progressive chronic hypoxemia leads to development of tissue hypoxia and decreases the cerebral perfusion; also it slows the nerve conduction in visual pathways which causes prolongation of latency. Thus factors related to COPD like severity of airflow obstruction & smoking pack years affect functioning of visual pathway and causes VEP impairment.

**Conclusion:** There was non-significant positive correlation between disease duration and VEP parameters while there was significant positive correlation of VEP parameters with smoking pack years and significant negative correlation with FEV1% predicted. Thus, more quantum of smoking & decreased FEV1% predicted can have impact on visual functioning causing prolongation of latency and decrease in amplitude of VEP.

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