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STUDY OF CHANGES IN VISUAL EVOKED POTENTIAL AMONG SMOKERS AND NON SMOKERS

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ABSTRACT

BACKGROUND & OBJECTIVES: Present study was aimed to assess Visual Evoked Potential (VEP) abnormalities in smokers and to correlate the changes with pack years.

METHODS: Study comprised of 40 smokers and 40 non smokers (30-50 years) with no complaint of visual impairment. Quantum of smoking was calculated by using smoking pack years. VEP was recorded using RMS EMG MKII. Latency and amplitude of P100 wave were analysed. Significant abnormality was defined as variations beyond mean ± 3SD from healthy adults.

RESULTS: Observations revealed significantly prolonged P100 latency and decreased P100 amplitude bilaterally in smokers compared with non-smokers suggestive of axonal loss and demyelination. No significant correlation between P100 amplitude and P100 latency with pack years could be established.

INTERPRETATION & CONCLUSION: Observations suggest that hypoxia in long term smokers is known to effect functional integrity of visual pathway implicating changes in VEP parameters

KEYWORDS : Pack years, Axonal loss, Demyelination

INTRODUCTION:

Tobacco smoke, recognized as the third biggest risk factor for Indians, is enormously harmful to one's health causing both cerebrovascular and cardiovascular complications.Cigarette smoke and hypoxia have both been reported to lead to an enhanced risk of inflammatory and autoimmune diseases[1].

Smoking causes airway obstruction, resulting in alteration of blood gases causing hypoxemia, hypercapnia and respiratory acidosis. Pontomedullary portion of brain is affected resulting in involvement of optic nerve[2]. VEP waveform is generated in striate, peristriate occipital cortex and thalamocortical volleys[3]. It indicates the functional aspects of the optic nerve, optic chiasm and tracts, lateral geniculate bodies and geniculocalcarine projection to visual cortex[4]

The visual evoked potentials are regarded as complementary to clinical examination and neu-ophthalmological investigations. A normal VEP is generally associated with normal visual examination; however an abnormal VEP study may or may not be associated with abnormal clinical findings[5]. The VEP studies provide an objective and sensitive method for documenting the abnormalities in the VEP which are nonspecific and not characteristic of any specific etiology.

The VEP is particularly useful in detecting optic nerve lesion. As the nerve sheath is damaged, the time it takes for electrical signals to be conducted to the eyes is prolonged, resulting in an abnormal VEP. Inflammation of the retinal vascular endothelium can precede demyelination and sometimes visibly manifest as retinal vein sheathing. Myelin loss exceeds axonal loss.[6]

Association of smoking with optic neuropathy has been reported in various studies.[7] **Inflammation of the optic nerve,** associated with swelling and progressive destruction of the sheath covering the nerve, and sometimes the nerve cable results in demyelination. Inflammatory demyelination of the optic nerve is the most common pathologic basis involving optic nerve in smokers. The pathology involves perivascular cuffing, edema in the myelinated nerve sheaths, and myelin breakdown[7]. Retinal ganglion cell sensitivity to mild hypoxemia showed that ganglion cell function is reduced with decreased blood arterial oxygen[8]. Present study was planned to study VEP abnormalities in smokers and to correlate changes with the quantum of smoking .

MATERIALAND METHODS:

The study was conducted in Department of Physiology and was approved by the Institutional ethical committee of Gandhi Medical College (Approval no. 14593-94/MC/7/2014). 40 clinically stable smokers in age range of 40- 60 years having no known endocrinal, metabolic, renal and/or cardiovascular disorder with resting systolic blood pressure < 140/90 mm Hg were chosen for the study. Intraocular pressure of all the cases and controls were within normal limits and visual acuity was 6/6 with or without correction. Smoker was defined by the presence of regular smoking of any type i.e. cigarettes, bidis or hookah, for 1 year or more.[9]Smoking pack years were calculated using Dr N J Masters and Catherine Tutt smoking pack year calculator.[10]

Subjects with any eye pathology or visual impairment and not willing to participate were excluded from the study. For the selection of healthy volunteers to serve as control, non smoker, non tobacco chewer patients in age group 40-60 years with normal blood pressure and fasting blood glucose were subjected to ophthalmic examination. 40 age and sex matched healthy non-smoker attendants were selected. There was no evidence of any neurologic deficit/peripheral neuropathy and visual impairment in these subjects on clinical examination and detailed history. The exclusion criteria of the cases group were also used for the controls. All participants were informed about the study and written consent was obtained.

VEP recording was done using RMS EMG EP MAK II. All the cases and controls were explained the test to ensure proper cooperation and were asked to avoid hair oil or spray after hair wash. The usual spectacles if any were used during the test. Recording, ground and reference electrodes were placed at Oz (as per 10-20 international system of EEG electrode placement), vertex (Cz), Fpz or 12 cm above nasion respectively. Electrode impedance was kept below 5 Ω.

VEP test was performed in a specially equipped electro diagnostic procedure room (darkened, sound attenuated room). Initially, the subjects were made to sit comfortably approximately 100 cm away from the pattern-shift screen. Subjects were placed in front of a video monitor displaying black and white checkerboard pattern. The checks of alternate black /white to white/black at a rate of approximately twice per second. Every time the pattern alternates, the subject's visual system generates an electrical response that was detected and recorded by surface electrodes, which were placed on the scalp overlying the occipital and parietal regions with reference electrodes on the midline of frontal region (Fz). The subjects were asked to focus his gaze onto the centre of the screen. Each eye was tested separately (monocular testing).[11]

Channel 1: Oz- Fpz
Channel 2: Oz-A1 A2
Ground: Cz

Recording conditions
Band pass: 1-300 Hz
Analysis time: 250 ms

Number of epochs: 200 Stimulation
Black and white checkerboard or vertical grafting
Contrast- 50-80%
Full field size >8%
Size of pattern 14 × 16 min
Rate of stimuli 2 Hz
Mean luminance of the central field 50 cd /m2
Background luminance 20-40 cd /m2

P100 latency and amplitude was recorded in the study population.

Statistical Analysis:
All values were expressed as Mean ± Standard deviation. Student t test was used to compare groups. Bivariate correlations between variables were evaluated by Pearson's correlation. Statistical analysis was done using SPSS-16.0 (Statistical package for Social science)

Result:Table No 1 Relevant Baseline Characteristics Of Study Population

S.No	VARIABLES	CONTROLS (N = 40)	CASES (N=40)
1.	AGE (years)	46.05 ± 7.88	49.12 ± 10.86
2	BMI (Kg/m2)	23.58 ± 2.48	24.14 ± 4.24
3	PULSE (bpm)	71.55 ±3.68	83.21 ± 11.34
4	R RATE (PM)	14.27 ± 2.03	18.31 ± 3.79
5	SBP (mmHg)	111.2 ± 4.87	128.53 ± 9.03
6	DBP (mmHg)	72.75 ± 2.93	83.31 ± 6.27
7	Pack years	-	38.04 ± 24.61

- The mean age of control group and cases were 46.05 ± 7.88 years and 49.12 ± 10.86 respectively (age range 40-60 years).
- The body mass index was in normal, overweight or obese range12.
- Quantum of smoking was assessed by pack years. Controls taken in the study were non smokers.
- The mean values of cardio- respiratory parameters measured were on higher side as compared to controls.

Table no 2 : Latency and amplitude of P100 wave measurements in study population

	Right eye Latency (ms)	Left eye latency (ms)	Right eye amplitude (mV)	Left eye amplitude (mV)
CONTROLS (n=60)	98.07 ±5.02	98.57±5.02	6.2±2.08	5.64±2
SMOKERS (n=60)	110.11±6.87	110.29±6.81	3.18±1.9	3.05±1.7
t	**10.38**	**10.73**	**8.3**	**7.64**
p	**0.0001**	**0.0001**	**0.0001**	**0.0001**

- The mean latency of P100 wave of the right as well as left eye was found to be statistically prolonged as compared to the corresponding eye in healthy control group ($p<0.0001$).
- The mean amplitudes of P100 wave in both the eyes of smokers were significantly decreased ($p<0.0001$) as compared to the corresponding eye of the healthy volunteer

Table 3 : Correlation of pack years with VEP variables

VEP variables		PACK YEARS
P100 LATENCY RIGHT	r	0.18
	p	NS
P100 LATENCY LEFT	r	0.18
	p	NS
P100 AMPLITUDE RIGHT	r	-0.07
	p	NS
P100 AMPLITUDE LEFT	r	-0.10
	p	NS

**No significant correlation of VEP parameters with quantum of smoking could be established.

Table 4 : Distribution of optic neuropathy in smokers

TYPE OF NEUROPATHY	RIGHT EYE	LEFT EYE
AXONOPATHY	15	11
DEMYELINATION	00	02
MIXED LESION	22	23

** Out of 40 stable smokers, 37 patients were observed to have significant VEP abnormalities. Predominantly mixed optic neuropathy was identified in both the eyes.

DISCUSSION:
In the present study we detected VEP abnormality in 92.5 % in right eye and 90% in left eye of smokers.

Out of 40 smokers, 37 smokers were having significant VEP abnormalities. None of these subjects had any concomitant visual impairment and any evidence of central neuropathy clinically. VEP was considered abnormal when either P100 wave latency was prolonged suggesting nerve demyelination and decrease in P100 amplitude suggesting axonal degeneration[13]. P100 wave latency and amplitude were interpreted as abnormal when the differences exceed 3 standard deviation above and below the mean of age matched control respectively.[14]

In our study the mean latency of P100 wave was significantly prolonged and amplitude of P100 wave was significantly reduced in both the eyes in cases as compared to healthy controls.

An attempt was made to correlate VEP parameters with quantum of smoking in all the smokers. No correlation of pack years with P100 latency and amplitude could be established.

Hafez M et al (2009)[15] studied impairment of visual and brainstem auditory evoked potentials in smokers and reported prolonged right and left P100 latency. They established positive correlation with smoking index and $PaCO_2$.

Gupta et al(2010)[16] reported prolonged P100 latency and decreased amplitude in both the eyes in COPD smokers and suggested that chronicity of illness and heavy smoking might be the possible cause of VEP abnormalities. Reduced sample size could be the possible reason for this.

Hypoxemia, hypercapnia and acidosis results in impairment of nerve conduction in brain stem causing VEP abnormalities. This reflects that low PaO2, high PaCO2 and acidosis exerts deleterious effect on highly specialized neurons[15].Demyelinating dysfunction of the cerebral cortex is believed to be the probable cause of increased P100 latency as reported in various research studies[17].An investigative study on the impact of smoking on visual evoked response of healthy volunteers was done by Kothari R et al and they observed predominant P100 latency delays in 60% of cases, of which 55.56% had markedly prolonged latencies.[18]

Inthe oresent study in right eye axonal degeneration was electro physiologically diagnosed in 15 cases and evidence of both demyelination and axonal degeneration in 22 cases. Electrophysiological study of left eye showed evidence of axonal degeneration in 11 patients and mixed degeneration was seen in 23 patients. This prolongation of latency could be attributed to the impairment of neurovascular coupling caused by cigarette smoking which is primarily due to structural changes of the vessels as postulated by Boms et al.[19] (2010). This term defines a complex neurovascular control mechanism, during which neuronal activity evokes regional vasodilation and thus localized changes in blood flow in the brain. A study by Pandey k et al[20] (2018) reported no significant changes in P100 latency and amplitude in smokers as compared to non smokers.
Wimpissinger et al (2004) studied the effect of smoking on eye and emphasized the role of decreased blood flow in ocular and retinal blood vessels.[7]

Abnormal VEP parameters in maximum smokers explains deleterious effect of smoking on retinal sensitivity thus causing central neuropathy.

Various studies on smokers causing peripheral neuropathy affecting nerves of upper and lower limb explain neuropathic changes in smokers[16].

Involvement of both central and peripheral neuropathy among smokers explains the nerve ischaemic changes in early stage without clinical symtoms.

Cigarette smoking is associated with increased oxidative stress, lipid peroxidation, fibrinogen levels, and platelet aggregation. It is also

associated with reduced plasma high-density lipoprotein and antioxidant levels[21] and can cause non-oxidative chemical damage to the retina. Cigarette smoking also causes inflammation by activating complement C3 and other inflammatory mediators and reducing serum levels of complement factor H[22] which diminish choroidal blood flow through atherosclerosis and vasoconstriction resulting in VEP changes[23]

All these biochemical changes in the eyes results in nerve ischaemia causing axonal degeneration , more commonly selective loss of large fast conducting fibres resulting in reduced amplitude. Farther accumulation of microfilaments and increased apoptotic and inflammatory mediators causes disruption of Schwann cells and changes in axoplasmic transport causing demyelination and thus P100 latency prolongation.

CONCLUSION:

Our study concluded that smoking causing axonal loss and loss of myelin which results in axonal degeneration and demyelination and thus optic neuropathy. Thus decrease in arterial blood oxygen and hypercapnia causes nerve ischaemia resulting in optic neuropathy causing VEP changes.

Study limitation: Blood gas analysis of cases and controls was not done in our study.

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