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ORIGINAL ARTICLE

Videonystagmography in patients with interstitial lung diseases

Nahlah Gad[1], Maha E. Alsadik[2]

1Nahla Hassan Gad Lecturer of Audiology Department of ENT Zagazig University.
2Maha E. Alsadik Lecturer of Chest Department Zagazig University.

***Corresponding author:**
Nahla Hassan Ahmed
lecturer of Audio-Vestibular Medicine, Department of Otolaryngology head and neck surgery, Faculty of Medicine, Zagazig University, Egypt.

Email:
nahla_audiology@yahoo.com

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ABSTRACT

Background: Interstitial lung diseases (ILD) are a group of diffuse parenchymal lung disorders associated with cough, dyspnea, hypoxemia and restrictive pulmonary function. Vertigo and dizziness are early symptoms of cerebral hypoxia. The aim of this study was to assess the effect of hypoxia and chronic cough in patients with ILD on central and peripheral vestibular functions.
Method: A cross sectional study was conducted in Audio-vestibular unit, ENT Department and Chest Department, Zagazig University Hospitals. Sixty two patients diagnosed to have ILD were included. Full VNG test battery was done.
Results: There was statistical significance decrease in mean of optokinetic speed and smooth pursuit gain at high frequency (0.6) in both Rt & LT sides among cases who had moderate hypoxia compared to cases who had mild hypoxia). No difference was found between mild and moderate cases in other oculomotor tests parameters. Also, there was statistical significance increase in frequency of BPPV among cases who had moderate hypoxia compared to cases who had mild hypoxia.
Conclusions: Degree of hypoxia was correlated with both central and peripheral vestibular functions.
Keywords: ILD, vestibular function, hypoxia, VNG

INTRODUCTION

Interstitial lung diseases are group of diffuse parenchymal lung disorders associated with substantial morbidity and mortality. Interstitial lung disease is a term that broadly describes a diverse collection of more than 200 lung disorders (1). These diseases are classified together because they all affect the tissue and space around the alveoli (air sacs), called the interstitium. Depending on the specific disease, other compartments of the lung, including the alveoli themselves, the airways (trachea, bronchi, and bronchioles), the blood vessels, and the pleura (outside lining of the lung), may also be affected (2). In general, most interstitial lung diseases are characterized by four manifestations: 1) respiratory symptoms such as shortness of breath and cough, 2) specific chest radiographic abnormalities, 3) typical changes on pulmonary function tests consistent with restrictive and/or impaired gas exchange (increased A-aPO2 with rest or exercise or decreased DLCO), and 4) characteristic microscopic patterns of inflammation and fibrosis (2). The vestibular system is one of the most complex systems of the human brain. The vestibular function could be evaluated via Videonystagmography (VNG), that evaluates peripheral and central vestibular functions; it includes a battery of tests that measure eye movements to assess vestibular control of eye movement (It involves the use of infrared goggles to trace eye movements during visual stimulation ,positional &positioning changes).Vertigo and dizziness are also early symptoms of cerebral hypoxia **(3).**We study the effect of hypoxia and chronic cough in patients with ILD on their balance.**Aim of the work:** To study the effect of hypoxia and chronic cough in patients with ILD on central and peripheral vestibular functions.

METHODS

Ethical consideration: Written informed consent was obtained from all participants, the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Study design: Cross sectional study of vestibular functions in ILD was performed in 9 months duration

I) Subjects :Study group: Sixty two patients diagnosed to have ILD of both genders were obtained from outpatient's clinic and chest department . Vestibular functions were assessed at ENT (Audiology unit) departments, Zagazig University Hospitals from November 2018 to July 2019. All participants fulfilled most of the criteria of ILD **(4, 5).** Symptoms: Dry cough, Progressive

dyspnea, Exercise desaturation, Clubbing and Later stages features of right heart failure .The findings of respiratory system examination are fine, bibasilar, and end inspiratory crackles also called "velcro rales".Chest X-ray showing reticular/ nodular opacities. Spirometry showing restrictive abnormality: Reduced forced vital capacity (FVC) with a normal ratio of forced expiratory volume in 1 second (FEV1) to FVC (FEV1 /FVC) suggests a restrictive abnormality. Diffusion capacity of lung for carbon monooxide (DLCO) is reduced. High-resolution computerized tomography (HRCT) is an important diagnostic tool in the evaluation of ILD. Lung biopsy, trans-bronchial (TBLB) or open (OLB) may be required.

II) Methodology: Videonystagmography (V.N.G): The test battery involved oculomotor evaluation (including saccades, smooth pursuit, OPK and gaze testing), positional, positioning testing and caloric test.Oculomotor testing: the subjects were ordered to sit one meter away from the screen. The stimuli were generated via the VNG software on LCD screen.

Saccades: Administration: For saccadic testing, horizontal stimuli were used randomly with 30º maximum angle. The subjects were kept looking to the moving visual targets with central head. Parameters were accuracy, latency and velocity.

Smooth pursuit: Administration: The target moving back and forth in sinusoidal waveform in the horizontal plane at different frequencies (0.3 & 0.6). The eye movements were recorded for thirty seconds. Parameter was gain of eye velocity

Optokinetic testing: Administration: A series of visual targets moving first to right and then to the left at 20º/sec. The eye movement was recorded for thirty seconds. Parameters were the symmetry and the gain of eye velocity.

Gaze testing: Administration: The subjects was instructed to keep gaze at visual target 20º on right, left, up and down for 10 seconds in each position. Number of nystagmus beats was calculated (more than two beats were considered significant).

Positioning: Dix-hallpikemaneuver:

Administration: While the subject was on table in a sitting position, the subject's head was turned to the right (or the left) at 45º and the subject was taken to the supine position. The patient was left in this position for 30 seconds. If there was no nystagmus the subject was returned to the sitting position. If nystagmus occurred, it was recorded and the subject was returned to the sitting position after fading out of nystagmus.

Positional tests: The subjects were placed in six different positions and evaluated for a minimum 20 seconds (head central, head right, head left, supine, supine head right and supine head left).

Caloric testing: The subjects were placed in a reclining position at an angle of 30º. Before recording, spontaneous nystagmus was observed and calculated if any. Both ears were subjected to bithermal caloric irrigation using cold

III)Equipment: Ulmar video-nystagmography (VNG) version 1.

STATISTICAL ANALYSIS

The collected data were computerized and statistically analyzed using SPSS program (Statistical Package for Social Science) version **25.0**.Qualitative data were represented as frequencies and relative percentages. Chi square test was used to calculate difference between qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation).Independent test was used to calculate difference between quantitative variables. Pearson's correlation coefficient was used to find correlation between different quantitative variables. The significance was fixed at 5% level (P-value) P value of >0.05 indicates non-significant results, P value of <0.05 indicates significant results and P value of <0.01 indicate highly significant results.

RESULTS

The age of the studied group ranged from 38 to 70 years with mean 52.69 years. Regarding sex 54.8% were female, 67.7% of the studied cases had cough, 83.9% had dyspnea and 61.3% were moderate cases (table 1).Oculomotor test parameters were within normative data of our balance unit. The caloric test parameters were normal in all cases (neither unilateral weakness nor directional preponderance DP) (table 2). All cases had no positional and gaze nystagmus. But 19.4% of the cases had positive positioning (table 3).There was statistical significance decrease in mean OPK speed and smooth pursuit gain high in both Rt & LT sides among cases had moderate hypoxia compared to cases had mild hypoxia. No difference was found between mild and moderate cases in other parameters (table 4).There was positive statistical significance correlation between PO2 and OPK speed and smooth pursuit gain at high frequency in both Rt & LT sides also there was positive statistical significance correlation between FVC and OPK speed and smooth pursuit gain at high frequency in both Rt & LT sides .There was positive statistical significance correlation between FVC and velocity in both Rt & LT sides. Finally, there was negative statistical significance correlation between both FVC and PO2 and latency of Saccadic eye movement latency in both Rt& LT sides (table 5). There was statistical significance increase in frequency of positive positioning nystagmus among cases had moderate disease compared to cases had mild (table 6)

Table (1): Demographic data& symptoms among the studied group:

Variable		**(n=62)**	
Age: (years) **Mean ± Sd** **Range**		52.69± 9 38 - 70	
		N	%
Sex	f	34	54.8
	m	28	45.2
Cough	no	20	32.3
	yes	42	67.7
Dyspnea	no	10	16.1
	yes	52	83.9
Severity	Mild	24	38.7
	Moderate	38	61.3
PaO_2: **Mean ± Sd** **Range**		56.92± 8.70 40 - 70	
FVC%: **Mean ± Sd** **Range**		46.5± 7.41 37 - 59	

Table (2): Oculomotor and caloric tests results:

	caloric UW	**DP**	**Opk gain Rt**	**Opk gain Lt**	**Opk speed Rt**	**Opk speed Lt**	**sm gain high Rt**	**sm gain high Lt**
Mean	8.95	8.71	15.60	16.03	0.8742	0.8692	84.74	86.31
Sd	2.877	1.911	1.644	1.659	0.07873	0.07234	6.638	6.391
Rang	3	6	12	13	0.70	0.75	70	68
e	15	13	19	19	1.00	1.00	98	98

	sm gain low Rt	**sm gain low Lt**	**S.accuracy Rt**	**S.accuracy Lt**	**S. velocity Rt**	**S. velocity Lt**	**S. latency Rt**	**S. latency Lt**
Mean	92.85	91.00	86.3871	84.92	316.79	313.81	247.90	248.60
Sd	4.783	5.335	4.3281	5.354	16.904	15.878	13.940	12.394
Range	85	80	77	75	280	290	216	220
	100	99	95.00	97	350	348	270	270

	S. velocity Rt	**S. velocity Lt**	**S. latencyRt**	**S. latency Lt**
Mean	316.79	313.81	247.90	248.60
Std. Deviation	16.904	15.878	13.940	12.394
Minimum	280	290	216	220
Maximum	350	348	270	270

Table (3): Positional, positioning and gaze nystagmus among the studied group:

		N	**%**
Positional	Zero	62	100.0
Positioning	-ve	50	80.6
	+ve	12	19.4
Gaze	Zero	62	100.0

Table (4): Relation between hypoxia severity and different test results among the studied group:

		N	Mean	Sd	Range		t	P
caloric UW	Mild	24	8.88	2.626	5	12	0.17	0.87
	Modertae	38	9.00	3.058	3	15		NS
DP	Mild	24	9.38	1.610	7	12	1.95	0.06
	Modertae	38	8.89	1.985	6	13		NS
Opk gain Rt	Mild	24	15.75	1.422	13	17	0.58	0.56
	Modertae	38	15.50	1.782	12	19		NS
Opk gain lt	Mild	24	16.50	1.842	13	18	1.80	0.08
	Modertae	38	15.74	1.483	14	19		NS
Opk speed Rt	Mild	24	0.90	0.08	0.70	1.00	**3.11**	**0.003**
	Modertae	38	0.84	0.07	0.75	0.95		**
Opk speed lt	Mild	24	0.89	0.07	0.78	1.00	**3.0**	**0.004**
	Modertae	38	0.84	0.06	0.75	0.90		**
sm gai high rt	Mild	24	88.63	6.04	80	98	**4.11**	**<0.001**
	Modertae	38	82.29	5.83	70	90		**
sm gai high lt	Mild	24	89.63	4.24	85	98	**3.54**	**0.001**
	Modertae	38	84.21	6.67	68	95		**
sm gain low rt	Mild	24	92.13	5.27	85	100	0.95	0.34
	Modertae	38	93.32	4.46	85	100		NS
sm gain low lt	Mild	24	91.13	6.16	80	95	1.20	0.23
	Modertae	38	92.82	3.82	88	99		NS
s.accuracy rt	Mild	24	86.75	4.08	77.00	90.00	0.52	0.60
	Modertae	38	86.16	4.52	77.00	95.00		NS
s.accuracylt	Mild	24	84.13	4.00	77	88	1.42	0.16
	Modertae	38	86.05	5.82	75	97		NS
s velocity Rt	Mild	24	313.50	3.15	310	320	1.22	0.23
	Modertae	38	318.87	21.30	280	350		NS
S velocity lt	Mild	24	314.00	4.36	310	320	0.08	0.94
	Modertae	38	313.68	20.10	290	348		NS
S lat rt	Mild	24	243.88	18.53	216	270	1.84	0.07
	Modertae	38	250.45	9.48	235	270		NS
S latlt	Mild	24	245.13	15.50	220	266	1.78	0.08
	Modertae	38	250.79	9.55	235	270		NS

Table (5): Correlation between PaO2 & FVC% and different test results among the studied group:

		Pao2	FVC%
FVC%	r	**0.631****	---
	P	**<0.001**	---
caloric UW	r	0.035	0.202
	P	0.786	0.116
DP	r	0.134	0.20
	P	0.298	0.10
Opk gain Rt	r	**0.321**	**0.247**
	P	**0.009****	**0.040***
Opk gain lt	r	**0.303**	**0.387****
	P	**0.010***	**0.002**
Opk speed Rt	r	-0.195	-0.182*
	P	0.142	0.162
Opk speed lt	r	-0.020	-0.051
	P	0.881	0.716
sm gai high rt	r	**0.335****	**0.333****
	P	**0.008**	**0.008**
sm gai high lt	r	**0.288***	**0.259**

		Pao2	FVC%
	P	**0.023**	**0.047***
sm gain low rt	r	-0.167	-0.176
	P	0.195	0.190
sm gain low lt	r	-0.004	-0.168
	P	0.991	0.197
s.accuracy rt	r	0.183	0.032
	P	0.154	0.804
s.accuracylt	r	-0.099	-0.002
	P	0.445	0.986
s velocity Rt	r	-0.039	**0.355****
	P	0.761	**0.005**
S velocity lt	r	0.058	**0.475****
	P	0.653	**<0.00`**
S lat rt	r	**-0.456****	**-0.477****
	P	**<0.001**	**<0.001**
S latlt	r	**-0.281**	**-0.271***
	P	**0.021***	**0.033**

Table (6): Relation between hypoxia severity and positioning among the studied group:

			Hypoxia Severity		X^2	P
			Mild	Moderate		
positioning	negative	Count	24	26	**9.40**	**0.002****
		% within Severity	100.0%	68.4%		
	positive	Count	0	12		
		% within Severity	0.0%	31.6%		

DISCUSSION

Interstitial lung disease (ILD) comprises a wide range of acute and chronic pulmonary disorders that affect both the airways and lung parenchyma with variable amounts of inflammation and fibrosis. Cough is a common symptom in patients with pulmonary fibrosis. A study by Sinha et al (6) reported that 50% of patients had a chronic cough and this was associated with poor health-related quality of life. Hypoxia is also a major complication of ILD and associated with central and peripheral nervous system affection. In vestibular pathway, axons of the first-order vestibular afferents which have their cell bodies in Scarpa's ganglion travel in the vestibular portion of the cochleovestibular nerve to enter the brain stem at the junction between the pons and medulla. Most of those afferents project to at least one of the four close vestibular nuclei within the rostral medulla and caudal pons. A few of the vestibular afferents go on to the cerebellum through the inferior cerebellar peduncle. Hypoxia is a state with different degrees, the brain can respond naturally to mild hypoxia with acute and chronic adaptive mechanisms. These mechanisms involve systemic, central metabolic and vascular processes that are mediated by hypoxia-inducible factor (HIF)-1. HIF-1-mediated cerebral angiogenesis is completed within 3 weeks of exposure onset and is reversible over the same time frame if normoxia is restored (7). Shigeo Yoshida et al. (1988) studied the effect of hypoxia on vestibular system of rats by electrophysiological testing and found that the lateral vestibular nucleus neurons are much more sensitive to hypoxia than the spinal trigeminal nucleus neurons. The failure of transmission within the monosynaptic neurons of the lateral vestibular nucleus is usually recommended to result to the inhibition of excitability of the postsynaptic membrane.In our study, all cases showed mild to moderate degrees of hypoxia (excluding cases with severe hypoxia to avoid confusion and lack of concentration). VNG is a tool that assesses vestibular function both centrally and peripherally. Saccadic parameters velocity, latency and accuracy were normal (Table 2) with no significant correlation with degree of hypoxia (table 4). However, smooth pursuit gain at high frequency and OPK speed were significantly reduced with increasing degree of hypoxia.This compromise of the central vestibular system is demonstrated by the oculomotor test alterations. Smooth pursuit eye movements are also mediated by neurons in the paramedian pontine reticular formation (PPRF), but are under motor control

centers other than those controlling saccadic eye movements. Motion sensitive neurons in extra striate areas of the dorsal visual stream, middle temporal and medial superior temporal areas are essential for the initiation and accurate guidance of smooth pursuit. These neuronal signals are transmitted either directly to the dorsolateral pontine nucleus or indirectly via the frontal pursuit region within the frontal eye fields before reaching the cerebellum, which provide the final processing of the motor command executed by both the vestibular nucleus and the PPRF (9) The sensitivity of the visual and oculomotor systems to hypoxia is well established in many studies. Oculomotor functions that are sensitive to hypoxia include extraocular muscle functioning, accommodation, convergence and coordination (10,11). Functional oculomotor deficits under hypoxia include deficits in saccadic (12,13) and SPEM (14). But in our study absent correlation between saccadic parameters and degree of hypoxia could be explained by absence of severe hypoxia cases. Tissue hypoxia and subsequent cochleovestibular degeneration are known theories in BPPV (15). This was in agreement with our study in which cases with BPPV were correlated with increasing degree of hypoxia (table 6).

CONCLUSION

The chronic hypoxic state leads to development of a reduction in vestibular function.

Long term oxygen therapy is a must in ILD patients with significant hypoxia to improve vestibular function and overall quality of life.

Conflict of interest: no conflict of interest.

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