Analysis and interpretation of air-conducted ocular vestibular-evoked myogenic potentials (AC-oVEMP) – our experience in healthy adults

Authors' Contribution:
A – Study Design
B – Data Collection
C – Statistical Analysis
D – Data Interpretation
E – Manuscript Preparation
F – Literature Search
G – Funds Collection

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Article history: Received: 19.11.2019 Accepted: 21.11.2019 Published: 26.11.2019

ABSTRACT:

Background: Ocular vestibular-evoked myogenic potential (oVEMP) is one of recently introduced tests used to assess the function of the equilibrium system. It is still under research and no consensus has been reached yet.

Aim: To analyze AC-oVEMP response parameters in subjects with no history of neurological or vestibular deficits.

Material and Methods: The AC-oVEMPs collected from 50 subjects (100 ears) were analyzed in this prospective study for the response presence in the time domain, the latencies and amplitudes of the waves.

Results: No statistically significant differences were observed between the right and left ear considering both N1 latency, and amplitude. Significant differences were noted when comparing the groups <40 yo vs ≥40 yo (shorter latencies and higher amplitudes were observed in subjects <40).

Conclusions and Significance: This thorough AC-oVEMP analysis in a group of healthy volunteers facilitated the proposal of reference ranges with a simultaneous indication of age-related differences. Shorter oVEMP latencies and higher amplitudes were observed in subjects <40 yo, while in the subjects ≥40 yo the latencies were longer and the amplitudes lower.

KEYWORDS: hearing loss, utricle, vertigo, vestibular evoked miogenic potentials, vestibular nerve

ABBREVIATIONS

AC-oVEMP – ocular vestibular-evoked myogenic potential to air conduction
SCDS – superior canal dehiscence syndrome

INTRODUCTION

Ocular vestibular-evoked myogenic potential (oVEMP) is one of recently introduced tests which are used to assess the function of the equilibrium system. Air-conducted oVEMP (AC-oVEMP) is performed to assess the morphology latency, amplitude of potentials evoked in oculomotor muscles. The stimulation of the utriculus with an acoustic stimulus applied to the ear generates an impulse which, via the superior vestibular nerve, leads to the stimulation of the inferior oblique muscle which is more pronounced in the contralateral side to the stimulated ear [1, 3]. Ocular muscle movement caused by the activation of the vestibular system is called the vestibulo-ocular reflex [1, 2].

VEMP test is a valuable diagnostic tool used in the diagnostics of the diseases that affect the labyrinth, e.g. Meniere's disease, or superior canal dehiscence syndrome (SCDS), vestibular nerve problems (in case of tumors affecting this nerve or demyelinating diseases) and the pathologies of the effector muscles (e.g. in myasthenia) [4–7]. VEMP is one of the most effective diagnostic tools in the case of SCDS [8, 9].

The methodology of oVEMP examination is still under research and no consensus has been reached yet.

AIM

The aim of this study was to analyze AC-oVEMP response parameters in healthy adults with no history of neurological or vestibular deficits.

MATERIAL AND METHODS

Subject description

Fifty subjects, 34 females (65%), and 16 men (35%), mean age 42.8 years ±12.45 with no otological or neurological problems were tested in this prospective study.

The subjects were divided into age groups to define a restricted age span for healthy population. The first group consisted of sub-

Tab. I. N1 wave latencies and amplitudes for acoustically evoked ocular vestibular myogenic potentials (AC-oVEMP), comparison of differences between the right and the left ear (50 subjects). SD – standard deviation.

AC-OVEMP	STIMULATED EAR	MEAN	SD	MEDIAN	MINIMUM	MAXIMUM	MANN-WHITNEY U TEST P-VALUE
N1 – latency (ms)	Left	11.66	1.12	11.40	9.80	15.60	0.38
	Right	11.48	1.35	11.30	8.80	14.60	
N1 – amplitude (µV)	Left	3.21	1.90	2.76	0.71	8.69	0.39
	Right	3.79	2.64	3.08	0.88	13.24	

Tab. II. N1 wave latency values and amplitudes in acoustically evoked ocular vestibular myogenic potentials (AC-oVEMP) for four age groups, for the right and the left ear collectively (50 subjects = 100 ears). SD – standard deviation.

AC-OVEMP RIGHT AND LEFT EAR	AGE GROUP (YEARS OLD)	NUMBER OF SUBJECTS	MEAN	SD	MEDIAN	MINIMUM	MAXIMUM
N1 – latency (ms)	<30	16	10.95	0.69	10.90	10.00	12.40
	30–39	26	11.75	1.06	12.00	9.80	14.00
	40–49	20	11.73	1.07	11.50	10.20	14.40
	≥ 50	38	11.63	1.53	11.40	8.80	15.60
N1 – amplitude (uV)	<30	16	4.33	1.69	3.97	1.75	6.72
	30–39	26	4.50	2.412	3.95	1.58	10.80
	40–49	20	3.24	3.28	1.81	0.77	13.24
	≥50	38	2.61	1.35	2.28	0.71	6.23

jects <30 years of age, the second – between 30 and 39, the third – 40–49, and the last one between 50 and 59.

The exclusion criteria comprised a history of equilibrium system diseases, Meniere's disease, surgery of the ear or eyeball area, facial nerve paresis, radiotherapy within the head and neck, neurological disorders and pathologies of the spine. Prior to VEMP examination pathological changes and inflammations within the inner ear were ruled out in all study participants. Since VEMP response decreases with age [10, 11], the upper age limit was set at 60 in the present study.

Testing protocol, stimulus and signal acquisition characteristics

AC-oVEMPs were acquired using SmartEP, a fully computerized two-channel evoked potential system (Smart-EP, Intelligent Hearing Systems, Miami, FL, USA). The recordings were obtained with each subject lying comfortably on a bed with the upper body elevated at 30 degrees from the horizontal.

In order to obtain AC-oVEMPs, the subjects were instructed to gaze upwards at a target located behind their head approximately 30° from the vertical line to provide deep relaxation of the inferior oblique (IO) muscle. The electrodes were placed on the skin beneath the eyes. The non-inverting (+) electrodes were attached to the skin bilaterally, 0.5 cm beneath the orbital margin in the midline of each eye, the inverting (-) ones were placed bilaterally, approximately 2–3 cm below (Fig. 1.). The ground electrode was positioned on the upper part of the sternum. All electrode impedances were kept ≤ 3 kΩ. The oVEMPs were collected by averaging five sets of 32 sweeps, with a stimulation rate being 3.1/s. Acquisition parameters were as follows: sampling period of 200 ms with 50K amplification of the signal, 6 dB per octave band pass filter, 10 Hz highpass cutoff, and 1000 Hz lowpass cutoff.

Acoustic stimuli consisted of 500 Hz frequency tone bursts, exact Blackman-windowed, and of 5-ms duration. They were presented unilaterally, one ear at a time, for contralateral recordings of oVEMPs. The stimuli were delivered via ER3A insert earphones (Etymotic Research, Inc. Elk Grove Village, IL) at 100 dBnHL intensity.

According to the literature, the averaged number of acquired sweeps should be from 30 to 1500 at a time recorded continuously [12, 13], but prolonged fixation of gaze on one point causes lacrimation and the necessity to blink, which results in the artifacts contaminating the response. Testing that long one ear at a time causes fatigue in the patient [3]. In the present study, the reduction in oculomotor muscle fatigue was attempted by diminishing the number of sweeps to 32 per set and increasing the number of acquired sets to 5 [13]. Subsequently, the recorded responses were averaged (all together), so a higher number of recorded responses averaged in one waveform was obtained reaching 160 sweeps.

AC-oVEMP data analysis

The recorded AC-oVEMP waveforms were analyzed for the response presence in the time domain. The first distinctive negative peak was identified as N1 based on typical visual identification between 8 and 14 ms, followed by a distinctive positive peak P1 (Fig. 2.). The latencies and amplitudes of N1 were measured. The lack of a clear N1 followed by P1 wave was defined as no response.

Ethical consideration

This study is a part of a retrospective-prospective project that was approved by the Institutional Ethics Committee Review Board. The patients have given full written and informed consent for the participation in this study. The project conforms to The Code of Ethics of the World Medical Association (Declaration of Helsinki).

Statistical analysis

Detailed statistical analyses included the Mann-Whitney U test, Kruskal-Wallis H test and median test. The level of statistical significance was set at 0.05. Data analysis was conducted with Statistca software (StatSoft Inc., version 12, Tulsa, OK, USA).

RESULTS

AC-oVEMP response latency and amplitude, right vs left side differences

The average latency of N1 wave was 11.66 ms recorded from the left ear. Comparable results were obtained with a stimulus delivered to the right ear; average N1 latency was 11.48 ms (Tab. I.). N1 amplitude was 3.21 μV for the left ear and 3.79 μV for the right ear.

No statistically significant differences were observed between the right and the left ear (Tab. I.) considering N1 latency and amplitude ($P > 0.05$), which facilitated the combination of data obtained from both ears, resulting in a total of 100 tested ears (Tab. II.). Nevertheless, the analyses of latency asymmetry and amplitude Asymmetry Ratio (AR) between the ears were performed separating the results obtained from the right ear and the left ear.

AC-oVEMP and the subjects' age and gender

The study participants were divided into age groups comprising subsequent decades of life. We did not observe any statistically significant differences between groups <30 and 30–49 years old, but there was a difference between groups <30 and 40–49 years old and between <30 and 50–59 years old. A similar relationship was noted between group 30–39 yo and both older groups. Therefore, group <30 yo was combined with 30-39-year-old individuals and group 40–49 yo was combined with 50–59-year-old subjects.

The analyses demonstrated that the mean N1 wave latency value was 11.44 ms in individuals <40 yo, while in the group ≥40 yo it was 11.67 ms (Tab. III.).

The mean value of AC-oVEMP response N1 wave amplitude was 4.43 μV in the group <40 yo, while in the group ≥40 yo it was 2.83 μV (Tab. III., Fig. 3.). The difference was statistically significant.

Careful analysis of AC-oVEMPs presented in this study, concerning N1 latency values and amplitudes, was the basis for the proposed reference ranges for the healthy population in two age groups. The reference range concerning N1 wave latency is proposed between 9.41 and 13.46 ms in the group <40 yo, and between 8.90 and 14.43 ms in the group ≥40 yo. The average value of N1 for <40 yo is 11.44 ms, and the proposed reference maximum (mean +2SD) latency is 13.46 ms; and for ≥40 yo the maximum is proposed to be 14.43 ms. The range of maximum normal amplitude <40 yo is up to 8.76 μV, with the minimum registered being 1.58 μV, and for ≥40 yo the maximum upper limit is proposed to be 7.24 μV with the minimum registered for this age group of 0.71 μV. Amplitude AR was set at <33.25% for patients <40 yo, and <34.45% for patients ≥40 yo.

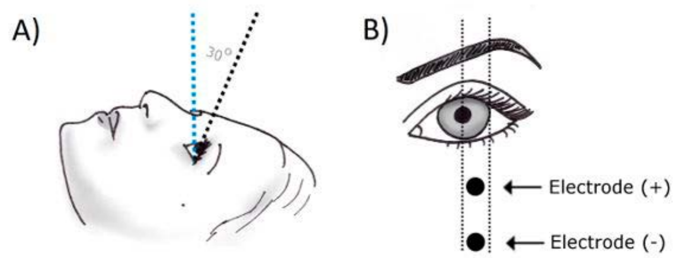

Fig. 1. Eyeball position in subjects during air-conducted ocular vestibular evoked myogenic potential (AC-oVEMP) examination. Panel A. the patient focuses the gaze at the object located behind the head and the viewing angle is 30 degrees from vertical; Panel B. location of electrodes during AC-oVEMP response recording.

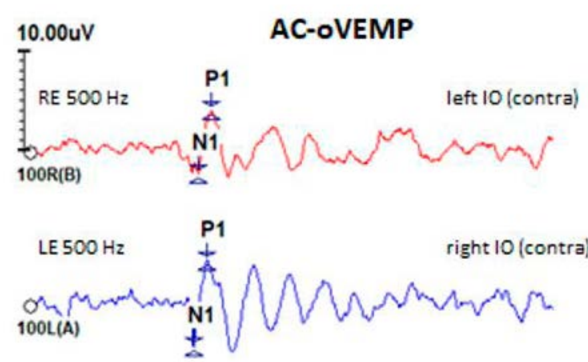

Fig. 2. A set of recordings obtained from one subject - an example case. Air-conducted ocular vestibular evoked myogenic potentials (AC-oVEMP) averaged waveforms from the stimulated left (blue) and right ear (red) are shown. The first row shows responses recorded from the left inferior oblique (IO) contra to the right ear; the second row from the right IO muscles (contra to the left ear). Acoustic stimulus (500 Hz) was delivered to each ear via an insert earphone. In each recording the waves N1 and P1 are marked.

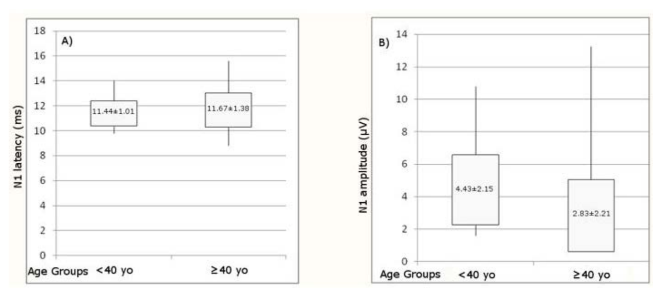

Fig. 3. Comparison of air-conducted ocular vestibular evoked myogenic potentials (AC-oVEMP): A) N1 latency for age groups <40 yo and ≥40 yo; B) amplitude for age groups <40 yo and ≥40 yo.

Regarding gender of the subjects N1 wave latency was slightly longer in males than in females. However, it was not a significant difference ($P = 0.43$). A significantly higher N1 amplitude was found in males (3.96 μV) than in females (3.29 μV), $P = 0.014$ (Tab. IV.).

DISCUSSION

oVEMP is used to assess the functions of the utriculus and ascending vestibular pathways via the vestibulo-ocular reflex [2, 3, 7, 9, 14].

Tab. III. N1 wave latency values and amplitudes in acoustically evoked ocular vestibular myogenic potentials (AC-oVEMP) in two age groups: <40 yo and ≥40 yo. SD – standard deviation.

AC-OVEMP RIGHT AND LEFT EAR	AGE GROUP (YEARS OLD)	NUMBER OF SUBJECTS	MEAN	SD	MEDIAN	MINIMUM	MAXIMUM	MANN-WHITNEY U TEST P-VALUE
N1 – latency (ms)	<40	42	11.44	1.01	11.40	9.80	14.00	0.6240
	≥40	58	11.67	1.38	11.40	8.80	15.60	
N1 – amplitude (μV)	<40	42	4.43	2.15	3.95	1.58	10.80	0.0001
	≥40	58	2.83	2.21	2.06	0.71	13.24	
Amplitude Asymmetry Ratio (%)	<40	21	14.39	9.43	12.35	0.59	37.70	0.6371
	≥40	29	15.66	9.40	14.46	0.79	38.75	

Tab. IV. N1 wave latency and amplitude in acoustically evoked ocular vestibular myogenic potentials (AC-oVEMP) with reference to the gender of the subjects. SD – standard deviation.

	GENDER	MEAN	SD	MEDIAN	MINIMUM	MAXIMUM	MANN-WHITNEY U TEST P-VALUE
N1 – latency (ms)	Mężczyźni	11.70	1.09	11.40	10.20	14.60	0.4300
	Kobiety	11.51	1.30	11.40	8.80	15.60	
N1 – amplitude (μV)	Mężczyźni	3.96	1.95	3.67	1.81	10.80	0.0140
	Kobiety	3.29	2.45	2.36	0.71	13.24	

The stimulation of the utricular macula triggers the reflex in oculomotor muscles. Presumably, the potential evoked from the inferior oblique muscle is not influenced by other cranial nerves (such as the cochlear and facial nerve) [3] and the oVEMP potential originates from the vestibulo-ocular reflex via the superior branch of the vestibular nerve. oVEMP responses are absent in patients who suffer from disorders of the superior branch of the vestibular nerve (e.g. in neuronitis vestibularis) [2], and are normal in patients with dysfunctions of the inferior branch of the vestibular nerve [2, 15].

oVEMP may be performed both in children [10] and in adults, but the diagnostic value decreases with age. Tseng et al. [10] obtained oVEMP in 100% of study participants aged 20–59 and only in 40% of the population older than 70 years [10, 11]. N1 latency extended with age, while the amplitude decreased [2, 4, 10, 14, 16]. According to the literature, the amplitude decreases by an average of 2.9 μV per decade [4, 16], while the latency increases by 0.12 ms [14]. Similar results were obtained in the present study, with the latency increasing with age. The reduction in oVEMP amplitude is explained by the reduction in the number of neurons of the vestibular nerve with age and decreasing number of epithelial hair cells in the vestibule. According to Rosenhall [17] the number decreases by 6% per decade. Numerous authors confirmed a higher risk of otolith organ dysfunction with age [4, 18]. Nguen et al. [19] reported a decrease in oVEMP amplitude in subjects over 50 years old without any significant change in wave latency.

Piker et al. [11] noted that oVEMP amplitude was higher in older subjects with stimulus frequency of 750 Hz (68% of participants) and 1000 Hz (38%), while in the majority of younger individuals the highest amplitude was obtained with stimulus frequency of 500 Hz and 750 Hz. Piker et al. [11] divided a group of subjects into 3 age subgroups (18–39 yo, 40–59 yo, and over 60 yo). No statistically significant intergroup differences were noted for young adults (18–39 yo) and middle-age adults (40–59 yo). However, they noted a marked reduction in amplitude value in older adults (≥60 years). In the present study, statistical analyses revealed differences and similarities between age groups. Initially, each age group covered a decade. However, no significant differences were found either between two younger groups (<30 vs 30–39 yo), or between two older groups (40–49 yo vs ≥50 yo). Significant differences were noted when comparing the groups <40 yo vs ≥40 yo. In the present study, analyzed N1 latency values and amplitudes were the basis for the proposed reference ranges for the healthy population in two age groups presented in Tab. III.

The present study revealed significant differences regarding amplitude values between males and females. Some authors [4, 14] did not report any significant differences between oVEMP latency and amplitude in males and females, and others, like Brantberg et al. [12], and Rosengren et al. [4] reported higher oVEMP N1 latencies in men. In the presented study, the results showed a significantly higher N1 amplitude in males. Some authors stated [14] that N1 latency value depended on the size of the head and the muscle mass. However, no study is available to confirm such a hypothetical correlation. No such measurements were conducted in the present study either. Therefore, a prospective study would be interesting to assess the correlation between head circumference, muscle fatigability, fat level, weight, BMI and oVEMP latency and amplitude.

CONCLUSIONS

This thorough AC-oVEMP analysis in a group of healthy volunteers facilitated the proposal of reference ranges with a simultaneous indication of age-related differences. Shorter oVEMP latencies and higher amplitudes were observed in subjects <40 years old, while in the subjects ≥40 the latencies were longer and the amplitudes lower. A higher amplitude of oVEMP responses was observed in males. No other differences were found between males and females regarding AC-oVEMP response.

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Word count: 2780 Tables: 4 Figures: 3 References: 19

DOI: 10.5604/01.3001.0013.5924 Table of content: https://otolaryngologypl.com/issue/13074

Competing interests: The authors declare that they have no competing interests.

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Cite this article as: Zwierzynska K., Lachowska M., Tataj E., Niemczyk K.: Analysis and interpretation of air-conducted ocular vestibular-evoked myogenic potentials (AC-oVEMP) – our experience in healthy adults; Otolaryngol Pol 2020; 74 (3): 6-11