Vestibular evoked myogenic potentials in patients with rheumatoid arthritis

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Abstract

Background: Rheumatoid arthritis (RA) is an autoimmune systemic disease. Most common auto-immune diseases are multisystem disorders that may also present with otological manifestations, and autoimmune inner ear disease accompanied by vestibular dysfunction. This study aimed to compare the vestibular function between RA patients and normal subjects using cervical vestibular evoked myogenic potentials (cVEMPs).

Methods: In this cross- sectional study, 25patients with RA (19 female and 6 male: mean (±SD) age, 40.00 (±7.92) years) and 20 healthy subjects (15 female and 5 male: mean (±SD) age, 35.35 (±10.48) years) underwent cVEMPs, using 500 Hz-tone bursts at 95 dB nHL intensity level. Data were analyzed using independent sample t-test through SPSS software v. 16.

Results: The mean peak latency of p13 was significantly higher in RA patients (p<0.001). The mean peak latency of n23 was significantly higher in patients in the left ear (p=0.03). Vestibular evoked myogenic potential (VEMP) responses were present in all (100%) of the participants. There were no significant differences in mean peak to peak amplitude and amplitude ratio between the two groups.

Conclusion: According to the prolonged latency of VEMP responses in RA patients, lesions in the retrolabyrinthine, especially in the vestibulospinal tract are suspected.

Keywords: Rheumatoid arthritis, Vestibular evoked myogenic potentials, Saccule, Sternocleidomas-toid muscle.

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Introduction

Rheumatoid arthritis (RA) is an autoimmune systemic disease in which the body's immune system attacks against normal tissues and produces antibodies to destroy the joints. RA is the most common inflammatory rheumatic disease. It affects 1-2% of the population; women are more affected than men and between 30 to 50 years of age are more likely to develop the disease (1).

In the systemic disease, such as RA, deposition of immune complexes in other organs can cause extra articular manifestations. Patients with RA may develop lung, heart, and eye and skin involvement. Involvement of the inner ear and sensorineural hearing loss (SNHL) has also been seen in about 24 to 60% of patients. Vasculitis, neuropathy, and medications are the suggested causes of SNHL in these patients (1-

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Salvinelli (2004) et al. demonstrated cochlear impairment in patients with RA and found an inverse correlation between the duration of RA and inner ear injury (6). Takatsu (2005) et al. reported that SNHL is more common in RA patients than controls, they also observed a relation between SNHL and erythrocyte sedimentation rate (ESR) in patients with RA (4). Ferrara (1998) et al. reported that electronystagmography (ENG) revealed central vestibular disorders in patients with RA (7). Yilmaz (2007) et al. contrasted the result of ENG test results and accounted the association of RA with vestibular system dysfunction as well as auditory impairment (5). Kakani (1990) et al. evaluated the results of the saccade and the bithermal caloric test on RA patients but did not find abnormalities in the test results (2). King et al. (2002) investigated vestibulo-ocular reflex (VOR), optokinetic reflex (OKR) and postural function in patients with RA and compared with controls, and concluded that RA patients do not present substantial deficits in visual-vestibular function (1).

The studies that assessing the vestibular system in RA patients are limited and the results are controvential. Previous studies used caloric, saccade and optokinetic tests to assess the vestibular system but these tests evaluated just superior vestibular nerve and the function of inferior vestibular nerve remains unknown. Cervical vestibular evoked myogenic potentials (cVEMP) reflect saccular and inferior vestibular nerve (IVN) function (8). VEMP is a brief reduction in strenocleidomastoid (SCM) tone following appropriate acoustic stimuli. High intensity abrupt sounds activate the saccule and a biphasic (positive and negative) response appears, the first wave of the contract, p1 or p13 and the second wave is shown as n1 or n23 (9).

Although medications cannot stop vestibular dysfunction in RA patients, but early diagnosis and early rehabilitation can reverse damage. The aim of this study was to compare VEMP between RA patients and normal people.

Methods

This study is a comparative cross-sectional study. Twenty five patients with RA (19 female and 6 male: mean age, 40.00±7.92 years) and 20 healthy volunteers (15 female and 5 male: mean age, 35.35±10.48 years) enrolled in this study. The RA patients were recruited from the Rheumatology Outpatient's Clinic, Imam Khomeini Hospital, Tehran, and control subjects were studied through the Rehabilitation Faculty of Tehran University of Medical Sciences.

Normal peripheral hearing was the inclusion criteria for the participants. Therefore, all subjects were examined by pure-tone audiometry and tympanometry. Patients with an additional systemic disease such as diabetes mellitus, prior ear surgery, all kinds of conductive hearing loss, and limitation of neck movements were not included in this study.

After skin preparation, the active surface electrode was placed over the middle of sternocleidomastoid muscle (SCM), and the reference electrode was placed over the upper sternum. The ground electrode was placed on the forehead (10).

VEMP recordings were performed with an evoked potentials machine (ICS Charter EP, GN Otometrics, US). Subjects were instructed to sitting and turning their head to opposite side of the stimulated ear (11). We used manometer (feedback method) to monitor electromyographic (EMG) level in the two sides (12).

The tone burst (500 Hz), with intensity of 95 dB nHL, rarefaction polarity and repetition rate of 5.1/ sec was delivered monaurally via an ER3A-inserted earphone. A total of 150 responses to stimuli were averaged. Measurements were repeated twice to check test wave reproducibility. Acquisition parameters include: the amplifier gain ✕5000, analysis time 100 ms and filter with a bandwidth of 10-1500 Hz (Fig. 1). We analyzed the amplitude of the first positive-negative peak, p13-n23 ipsilateral to
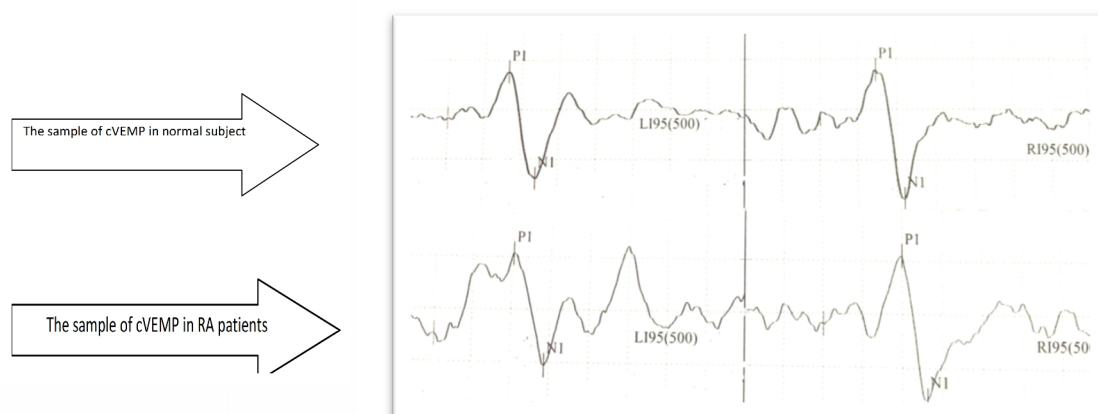
Fig 1. cVEMP responses obtained from a patient diagnosed with RA and a normal subject

the stimulated ear and the latencies of p13 and n23 (13). For the assessment of the amplitude, the percentage of VEMP asymmetry (VA) was calculated as $100[|Ar − Al|/ (Ar + Al)]$, where Ar is the p13-n23 amplitude on the right and Al is the p13-n23 amplitude on the left and $|Ar − Al|$ is the absolute value of $(Ar − Al)$ (14). As the parameters of the latency, we measured the peak latencies of p13 and n23. P13 is the first positive peak of VEMP, and n23 is the first negative peak following p13. Latency is the time from the onset of the stimulus to the peak (13).

The data were analyzed using SPSS version 16. Kolmogrov-Smirnov test was used to check the normality assumption of data and independent sample t-test was used to compare the means. The statistical signifi-

cant level was set at $p<0.05$.

This study was approved by the Ethics Committee of Tehran University of Medical Sciences.

Results

Significant difference was observed between the mean peak latency of P13 between groups ($p<0.001$ in the right ear and $p<0.001$ in the left ear). Also, significant difference was observed between the mean peak latency of n23 in the left ear ($p=0.03$), but in the right ear it was not significant ($p=0.08$). VEMP responses were present in all (100%) of the participants.

There was no significant difference between the mean absolute amplitudes of the two groups ($p=0.52$ in the right ear and $p=0.09$ in the left ear). In addition, there

Table 1. Comparison the mean values of VEMP parameters between control subjects and RA patients

Parameter	Mean	SD	p
Latency of right p13 (ms)	Control group=15.71	0.91	<0.001
	RA patients=17.4	1.50	
Latency of left p13 (ms)	Control group=15.95	1.26	<0.001
	RA patients =17.85	1.88	
Latency of right n23 (ms)	Control group =23.71	1.61	0.080
	RA patients =24.72	2.25	
Latency of left n23 (ms)	control group =23.66	1.89	0.030
	RA patients =25.15	2.45	
Right amplitude (μv)	control group =138.43	64.32	0.520
	RA patients =125.21	74.53	
Left amplitude (μv)	Control group =123.11	64.53	0.090
	RA patients =89.41	62.08	
Amplitude ratio	Control group =15.2	7.4	0.240
	RA patients =20.4	10.3	

RA: rheumatoid arthritis

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was no significant difference between the mean of the interaural amplitude difference ratio between groups (p=0.24). The results are shown in Table 1.

Discussion

The latency of p13 was significantly higher in RA patients than control group. Also, n23 latency was higher in patients than the control group, but it was statistically significant just in left ear. The SD of n23 was greater than that of p13, resulting in a wider normal range of n23 than p13. Therefore, p13 is a better parameter to evaluate the latency of VEMP (15). To our knowledge, this is the first report of evaluating the vestibular system in RA patients with VEMP test, but in systemic lupus erythematosus which is an autoimmune systemic disorder, latency of VEMP is significantly higher than controls (16). In 2001 Murfushi et al. investigated VEMP in patients with multiple sclerosis (MS) and concluded demyelinating lesions can cause slow conduction along the vestibulospinal pathway and lead to eliminate VEMP response or prolonged latency. In addition, large acoustic neuroma showed latency prolongation, if compress the brainstem. Vestibular nerve and brainstem can be involved in acoustic neuroma, and MS is a representative disease of the central nervous system but Meniere disease is representative of labyrinthine lesions. It is unlikely that prolonged VEMP latencies are a sign of inner ear lesions, because in Meniere disease latency is not affected. VEMP latency prolongation is an abnormality characteristic of central vestibulopathy. In midbrain and upper pontine lesions, VEMP is not affected because these are above the level of vestibular nuclei. However, in medullary and mid to lower lesions VEMP abnormalities were present (15). There are an evidence of the involvement of peripheral and central nervous system in inflammatory connective tissue diseases such as rheumatoid arthritis, lupus erythematosus and Behcet syndrome (17). Probable mechanisms for central nervous involvement are: vascular lesions (vasculitis and thrombosis); production of autoantibodies to neuronal antigens, ribosomes, and phospholipids'; and the inflammation induced by local cytokine production, and maybe an inflammatory demyelinating process of the spinal cord which occurs in this disease. Demyelinating lesions, (lipoid sclerosis) can cause clinical characteristics and imaging findings that are very similar to MS (17, 18). Central vestibular involvement in RA has been reported in previous studies (5, 7). Ferrara et al. (1998) reported that ENG revealed central vestibular disorders in RA patients (7). Yilmaz et al. (2007) compared the results of smooth pursuit, saccade, positional, and caloric tests between RA patients and control group and reported that both central and peripheral system can be involved in RA (5).

In the present study, the incidence of VEMP in RA patients and control group was 100%. Murfoshi et al. (2001) reported that absent VEMP could occur in MS, Meniere and Vestibular Schwannoma (15). Although VEMP is present in RA patients, but there is abnormality in latency, thus, maybe the severity of the lesion was not enough to be able of eliminating responses.

There was no statistically difference between groups in absolute amplitude and interaural amplitude difference ratio. Murofushi et al. (2001) reported that the patients with Meniere disease showed decreased amplitudes or absent responses (15). VEMP amplitude depends on sound intensity and constriction of SCM muscle. The range of amplitude is from 25 μv to 250 μv. Due to the large variation range, absolute amplitude is not considered as an important factor in the differential diagnosis. Therefore, to investigate the unilateral vestibular dysfunctions, comparing the interaural amplitude difference ratio is more reasonable. Abnormal asymmetry in the amplitude of the VEMP is the indicator of unilateral vestibular dysfunction (19, 20). In the present study for this parameter, no

significant difference was seen between groups. These findings support the possibility of the symmetrical function of the vestibular system in both sides in the patient group.

Autoimmune inner ear disease (AIED) is a progressive bilateral SNHL that is accompanied by vestibular symptom (21). Various connective tissue diseases are such as Wegener's granulomatosis, polyarthritis nodosa, RA, systemic lupus erythematosus (SLE) and Cogan's syndrome with involvement of the inner ear, auditory and vestibular dysfunction (22). Immune mechanisms proposed for these symptoms include attacks of humoral antibodies to inner ear antigens, ototoxicity, and cell antigen-induced immune complex disease of the inner ear in small vessels (23).

One of the main important limitations of our study, was using just one otolitic test. Moreover, the large distance between sampling and performing test led to lose a lot of patients.

Conclusion

The significant finding in the present study is prolongation of latency. Prolonged latency is abnormal characteristic finding in central vestibulopathy and representive of vestibulospinal tact lesions. Vestibular rehabilitation and treatment is more beneficial if diagnosed early. Therefore, the authors suggested monitoring vestibular function in these patients. Future studies with more samples are recommended.

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