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Original article:

Role of Brainstem Evoked Response Audiometry in active Rheumatoid arthritis patients

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Abstract

Introduction: Rheumatoid arthritis (RA) is an autoimmune, chronic systemic inflammatory disease affecting the small joints and also has extraarticular manifestations. Sensorineural hearing loss (SNHL) is common in active disease. There is involvement of hair cells of the inner ear in this active stage of rheumatoid arthritis resulting in sensory hearing loss. It can be diagnosed early by Brainstem Evoked Response Audiometry (BERA) which reveals abnormal wave patterns suggestive of cochlear type of SNHL**.**

Aim: To evaluate the role of BERA in active RA patients

Materials and methods: Thirty RA patients both men and women between 25 and 45 years of age in active stage of RA satisfying 2010 ACR/EULAR, (American College of Rheumatology/ European League against Rheumatism) classification and DAS (Disease Activity Score) and thirty healthy controls with no hearing deficit were included in the study. The increased titre of Anticyclic Citrullinated Protein Antibodies (ACPA) levels was confirmed by ELISA in RA patients and subjected to BERA.

Results: Statistical analysis was done with software SPSS version 21. The study shows a significant increase in absolute latency of wave I with student t test. The latency of wave II-V and interpeak latencies were normal. The above findings reveal the early involvement of cochlear hair cells in active disease indicating peripheral auditory pathology.

Conclusion: Cochlear hair cells are affected in the active stage of RA. Subclinical hearing dysfunction can be identified with BERA and if managed early can preserve the hair cells and decrease the morbidity.

Keywords: Brainstem Evoked Response Audiometry, latency of wave I, Rheumatoid arthritis.

Introduction

Rheumatoid arthritis is an autoimmune, multifactorial, chronic systemic inflammatory disease affecting the small joints and also has extraarticular manifestations. The disease is classified according to ACR – EULAR (American College of Rheumatology/ European League against Rheumatism) classification.[1] It affects 0.5-1% of the population worldwide.[2] The disease activity is assessed according to Disease Activity Score (DAS 28). Duration of the disease for a period of more than six weeks [3] to one year characterised by a DAS 28 score >5.1 indicates active disease. The extra-articular manifestations include various organs like lungs, heart & blood vessels, eyes, ears in 15-25 % of individuals.[4] The increased titre of Anticyclic Citrullinated Protein Antibodies (ACPA's) detected by ELISA & DAS 28 score >5.1 indicate the active stage of the disease. The more specific and sensitive biomarker of the active stage of the disease is the ACPA's detected by ELISA (Rohit Agarwal et al 2009)[5] Demorrulle et al[6] has explained in his study that ACPA's is highly specific for the diagnosis of active disease in RA, its etiology and prediction of future risk and its prevention.

RA affects the auditory system in various ways[7]. Cochlear hair cells are receptors of hearing and play an important role in the amplification of sounds received from the middle ear, sound clarity and Otoacoustic emissions. The hair cells by their synaptic connections with the auditory nerve initiates action potentials that are transmitted to the brain stem. The hair cells cannot regenerate and when damaged results in permanent hearing loss[8].

The hair cells of the inner ear express antigens like 58Kda protein,68 Kda protein etc which initiates abnormal immune response. The hair cells of the inner ear are affected in the inflammatory process of RA. Destruction of cochlear hair cells in active disease occurs due to the deposition of immune complexes[9] and proinflammatory cytokines like Interleukin- 6 (IL-6) resulting in Sensorineural hearing loss of cochlear type. Raut vv et al[10]has explained that SNHL of cochlear type is more common. The hair cells of the inner ear are affected by immune complex deposition resulting in sensorineural hearing loss in the active stage of RA (Magaro M et al1990)[11.] The hair cells affected in active disease are reflected in the receptor potential generated in them and the action potential transmitted in the auditory nerve resulting in abnormalities can be detected by Brainstem Evoked Response Audiometry (BERA). BERA is a disease specific diagnostic test for RA and has a specificity of 95%. in the preclinical and active period of the disease.[12]

Brainstem Evoked Response Audiometry is a non- invasive objective test of hearing. The cochlear potentials recorded in humans was first reported by Sohmer and Feinmesser in 1967. BERA gives information about the function and the site of lesion in auditory pathways. It is the electrophysiological response evoked in response to click stimuli which is recorded within 500milliseconds of the application of the stimulus. The evoked potentials recorded within the first 10 ms after the application of brief stimuli is short latency response (SLR) described as BERA. It comprises of five or more waves with 3 inter peak latencies. The latencies and inter peak latencies provide information regarding the site of lesion in the auditory pathway extending from the cochlea to inferior colliculi.

The hair cells of the inner ear are affected in active RA. So the evoked potentials generated from the hair cells show abnormalities in BERA. The absolute latency of wave 1 is prolonged with normal latencies of wave Il, III & V and the inter peak latencies indicating peripheral cochlear involvement. Sensory hearing loss involving hair cells is characterized by wave I falling outside the normal latency.

Aim & Objectives

The aim of the study is to evaluate the role of BERA in active RA patients. Disease activity is confirmed by increased titres of ACPA, in comparison with age and sex matched controls. It aims to determine the functional integrity of auditory pathway & site of lesion diagnosed with BERA.

The study focusses to identify the early subclinical hair cell damage and measures to be instituted aiming at preserving the functional integrity of hair cells thus preventing the hearing impairment and improving the quality of life in these patients.

Materials and methods

This cross sectional case control study was conducted at the Institute of Physiology and Experimental Medicine, Madras Medical College, Chennai 3, after obtaining ethical approval from the Institutional Ethics Committee, Madras Medical College, Chennai 3.

Inclusion criteria: Thirty men & women patients between 25-45 years of age diagnosed with RA in active stage according ACR/EULAR criteria participated in the study. Thirty age and sex matched apparently healthy people

were selected as controls. Both the cases and controls had normal hearing ability confirmed with Pure Tone Audiometry. The active disease is confirmed by increased titre of ACPA"s by ELISA , DAS 28 score >5.1 and duration of less than 1 year .

Exclusion criteria: Children, Pregnant women, subjects with Diabetes, Hypertension, Tumors, Hearing abnormalities including Presbyacusis were excluded.

Verbal and informed consent was obtained. General examination and ENT examination including Pure Tone Audiometry was done in all the subjects. All the subjects included in the study had no hearing deficit. BERA was done in all the subjects to study the early involvement of cochlear hair cells.

Procedure**:** Recording of BERA is done by the apparatus based on Recommended standards for the clinical practice of evoked potentials which is introduced in Guidelines on evoked potential by American society of Clinical Neurophysiology. The procedure is carried out in a quiet, soundproof and semi darkened room. Active, reference & ground electrodes were placed in their respective places in the vertex and ears. Responses to 2000 clicks presentations were averaged. The result is obtained as a graph plotted with amplitude (in µvolts) on the ordinate and time (in milliseconds from the onset of stimulus) on the abcissa. with 5-7 waves or peaks within 8-10 milliseconds with Roman numerals. Analysis of these waveforms were done with regard to latency, amplitude and morphology that provides information on cochlear and retrocochlear function.

Wave I[13]represents the potentials generated in the hair cells that appears 1.5 ms after the application of stimulus. Wave II is a small peak which appears 2.8 ms and Wave III appears 3.9 ms after the click stimulus. Wave IV appears after 5.1ms and Wave V appears 5.5 msec after the stimulus. Absolute latency is the time interval which is measured in milliseconds from the onset of stimulus to the peak of the wave. The absolute latencies of waves I, III, V and interpeak latencies of I-III, I-V were studied among cases and controls.

Results

Statistical analysis was done with software SPSS version 21. The mean age in my study group is 38.47 ± 5.06 in cases & 38.30 ± 4.41. Absolute latency of wave I in BERA shows a significant statistical p value of <0.05 with student t test indicating hair cell dysfunction and peripheral cochlear pathology. Absolute latencies of Waves II, III, V and Inter peak latencies showed an insignificant p value of >0.05 with student t test explaining the absence of central auditory pathology.

TABLE 1: Comparison of mean values of Absolute latencies and Interpeak latency of right ear between active RA patients and controls

S.NO	VARIABLES	CASES	CONTROLS	p VALUE
1	WAVE I	1.84 ± 0.19	1.607 ± 0.07	< 0.001***
2	WAVEII	2.75 ± 0.09	2.78 ± 0.08	0.24
3	WAVEIII	3.77 ± 0.18	3.821 ± 0.15	0.99
4	WAVEV	5.65 ± 0.12	5.65 ± 0.14	0.28
5	IPL I-III	2.37 ± 0.19	2.42 ± 0.20	0.41
6	IPL I-V	4.59 ± 0.41	4.52 ± 0.40	0.54

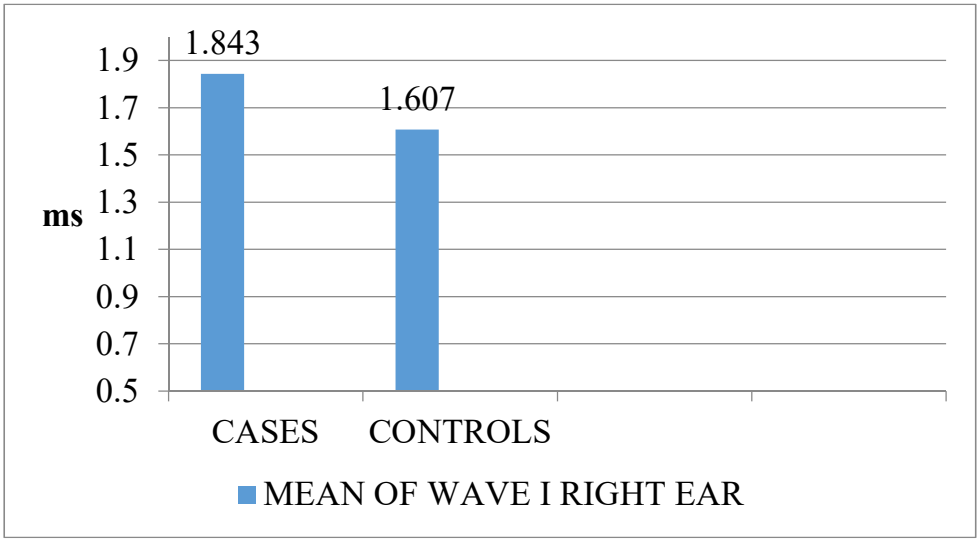
***** very highly significant**

TABLE 2: Comparison of mean values of Absolute latencies and Interpeak latency of left ear between active RA patients and controls

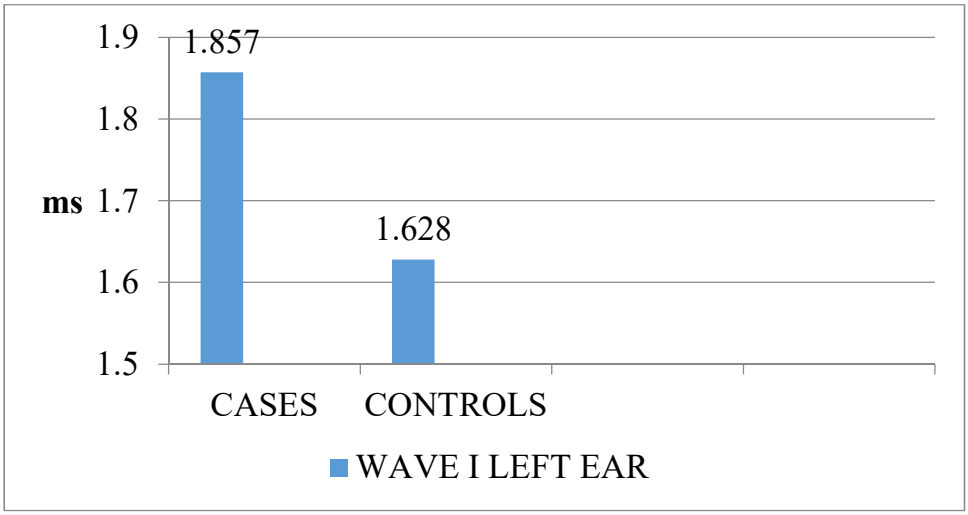
S.NO	VARIABLES	CASES	CONTROLS	p VALUE
1	WAVE I	1.857 ± 0.2	1.628 ± 0.08	< 0.001***
2	WAVEII	2.804 ± 0.04	2.805 ± 0.06	0.9
3	WAVEIII	3.70 ± 0.22	3.72 ± 0.22	0.7
4	WAVEV	5.57 ± 0.20	5.60 ± 0.21	0.5
5	IPL I-III	2.48 ± 0.30	2.53 ± 0.39	0.5
6	IPL I-V	4.39 ± 0.48	4.38 ± 0.54	0.9

***** very highly significant**

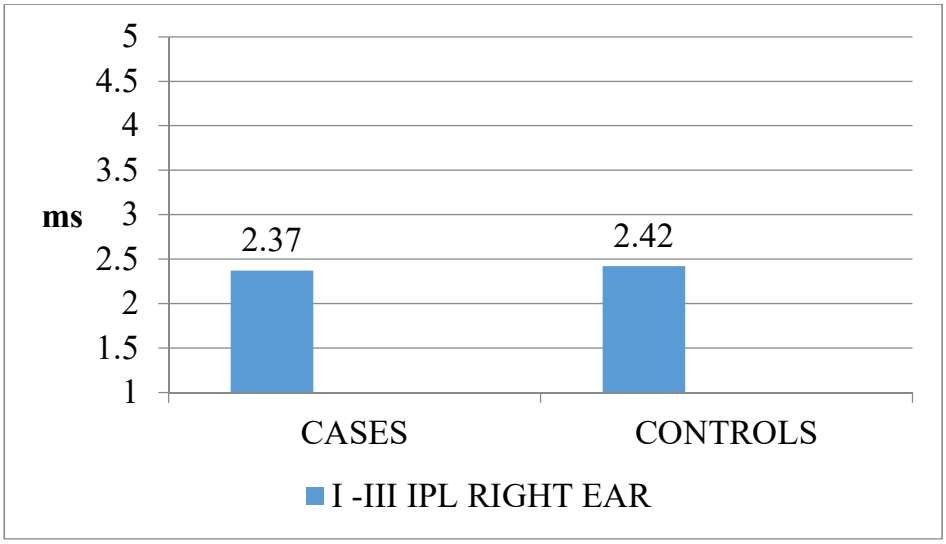
GRAPH I: Comparison of mean values of absolute latencies of wave I between active RA patients and controls in the right ear



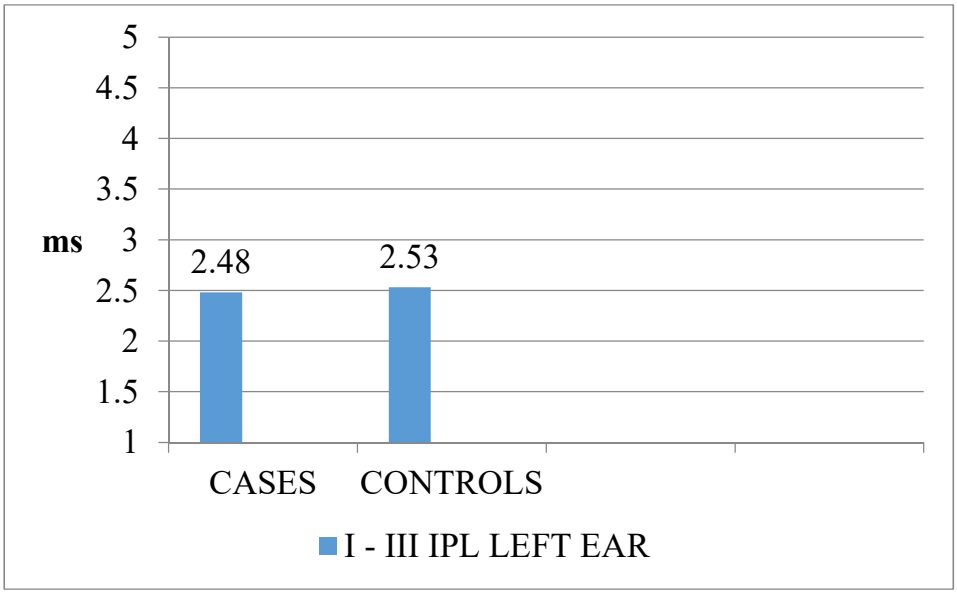
GRAPH 2 : Comparison of mean values of absolute latencies of wave I between active RA patients and controls in the left ear



GRAPH 3 : Comparison of mean values of I-III IPL between active RA patients and controls in the right ear



GRAPH 4: Comparison of mean values of I-III IPL between active RA patients and controls in the left ear



Discussion

Disease activity of Rheumatoid arthritis patients in the study was assessed according to DAS score >5.1, increased titre of ACPA and duration of < than 1 year which goes in parallel to studies by Dr. Shyam et al.[14]which reveals that active RA cases of less than one year duration were selected with DAS-28>5.1 and increased titres of ACPA are associated with high disease activity ($p< 0.001$). Mielants H et al in his study has explained that extra-articular manifestations are common in active RA with DAS score >5.1 with evidence of increased mortality[15]

The study clearly reveals that the hair cells are affected in active disease resulting in sensory type of hearing deficit which can be diagnosed early with BERA. BERA showed prolonged latency of wave 1 with normal latencies of wave II to V and normal interpeak latencies indicating peripheral cochlear pathology in my study.

This goes in line with studies by Liberman et al 2002, takeno et al 1994, kujawa and, Buchwald & Huang 1975 which explains that Wave 1 in BERA represents the summated activity generated in the hair cells and propagated to the auditory nerve through the synapse existing between them. So abnormalities in wave1 of BERA indicates hair cell dysfunction & synaptic transmission. Abnormal wave I with normal waves II –V indicates significant peripheral hearing impairment[16] . Amy et al observed prolonged latency of wave l with normal waves ll , lll ,V & IPL in BERA in cochlear sensory lesions. Elberling, 1981 observed a prolonged wave I in cochlear lesions. Hall, 1992 in his study showed that Wave ll, lll & V latencies are prolonged in retro cochlear hearing losses. Prolonged latencies of wave I is noticed in BERA that affects the cochlea[17]
Dikci o et al[18] attributed prolonged latency of wave 1 to active RA .Salvinelli et al[19]described increased Wave I latency (p=0.03). Rebecca uribe et al[20] stated in his study that there is damage to outer and inner hair cells that is reflected in the auditory nerve which results in increased latency of wave I in active RA with p <0.001 which is similar to my study.

Conclusion

The study reveals the early subclinical involvement of cochlear hair cells in the active stage of Rheumatoid arthritis . Increased titres of ACPA can be claimed as a biomarker of active disease. Brainstem evoked response audiometry is an important tool to diagnose subclinical hair cell dysfunction. Early diagnosis with BERA and early intervention with measures like antioxidants, intratympanic steroids, vasodilators etc may preserve the hair cells thus preventing hearing disability promising a better quality of life in the society for these patient.

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For any images presented appropriate consent has been obtained from the subjects: NA
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