# Alterations in auditory electrophysiological responses associated with temporary suppression of tinnitus induced by low level laser therapy

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# Abstract

Purpose: Tinnitus is the phantom auditory perception of sound in the absence of an external or internal acoustic stimulus. The treatment is difficult due to multiple etiologies and great psychological influence. The purpose of this study was to determine alterations in auditory physiological and electrophysiological responses associated with temporary suppression of tinnitus induced by low level laser therapy (LLLT).

Method: This study was conducted on 20 subjects with subjective tinnitus. VAS (Visual Analog Scale) for loudness, loudness matching of tinnitus (LMT), pitch matching of tinnitus (PMT), Persian-tinnitus questionnaire (P-TQ) and Persian-tinnitus handicap inventory (P-THI) were conducted pre- and post-LLLT for all the subjects. Electrocochleography (ECochG) and Distortion Product Otoacoustic Emissions (DPOAEs) were recorded in 11of subjects. Continuous wave diode lasers, including red (630 nm), infra-red (808 nm) were applied and were both designed by the Canadian Optic and Laser (COL) Center. Twelve sessions of laser therapy were performed, two sessions per week for each subject. Total dose was 120 Joule/ear/session.

Results: Our results provide evidence that treatment with the active LLLT probe could result significant decrease in subjective tests scores consisted of VAS for loudness, PMT, P-TQ, P-THI, but did not result in significant improvement of objective evaluating parameters except of CAP amplitude.

Conclusion: LLLT might be a subjectively effective treatment for short-term improvement of tinnitus. Defining a new protocol for optimizing LLLT parameters may be an option to improve investigating parameters of objective tests.

Keywords: Low level laser, tinnitus, electrocochleography, distortion product optoacoustic emission.

**Introduction**

Tinnitus is the phantom auditory perception of sound in the absence of an external or internal acoustic stimulus1. This symptom is a debilitating condition that is widespread yet difficult to successfully diagnose and treat. The prevalence of chronic tinnitus in general population is estimated between 5-15% and causes to develop serious psychosocial complications in 1% to 3%2. For some subjects, tinnitus is disabling and restricts their work, sleep, and social activities 3, 4, 5. This symptom has forced clinicians to attempt to establish protocols for an accuracy of tinnitus diagnosis and treatment 6.

There are various modalities in the treatment of the chronic tinnitus (pharmacotherapy, physiotherapy, psychotherapy, surgery etc.) targeted at diminishing tinnitus loudness and the quality of subjects’ lives. The disappearance of tinnitus occurs very rarely among the subjects with chronic tinnitus and according to the literature they do not represent a statistically significant group. So searching for new methods of treatment and management and combining to previous methods may help healing the symptom and its annoyance.

The new medical therapeutic method of low-level laser therapy uses low-energy-level lasers or light-emitting diodes to stimulate or inhibit cellular function 7. It has been introduced to be effective in treatment of peripheral and central nervous system injuries and disorders such as wound healing and pain, musculoskeletal injury, Buerger’s disease, nerve repair, sympathetic nervous system dysfunction, hemangioma, immune modulation, bacterial effects, inflammation, and tinnitus. 8, 9, 10, 11

LLL has been used in treating chronic impaired hearing, sudden sensorineural hearing impairment12, Meniere’s disease and some other balance disorders13. It has been reported to decrease tinnitus loudness and hearing level11.

The exact mechanism is unknown. LLLT has been assumed as a thermal stimulation of biochemical processes in the inner ear induced by light 14. It has been reported to improve local microcirculation through blocking sympathetic nerve action potential and increase oxygen supply to hypoxic cells. 10,15 Of studies investigated the effects of LLLT on both hearing loss and tinnitus, some found different levels of improvement in hearing thresholds and tinnitus symptoms 10,16,17,18,19, while others have found no significant effects20,21,22,23 (table 1).

Therapeutic effects of LLLT on tinnitus are controversial and findings are inconsistent. It requires more investigations. Less is known about the therapeutic effects of LLLT on auditory system disorders such as tinnitus using objective evaluating methods pre- and post- therapy. The essential aim of this study was to investigate therapeutic effects of LLL using objective tools of EcochG and DPOAEs pre- and post- LLLT.

**Methods**

**Subjects:** The studied group included 20 subjects with problem–tinnitus (15 males, 5 females) referred to the ENT and Head & Neck Research Center of Hazrat-e-Rasoul Hospital for evaluation and management of their tinnitus during 2011 and 2012. They were 33 to 84 years old (45.7±9.35). All subjects had intractable permanent chronic unilateral or bilateral moderate to severe tinnitus, which had been present for more than 6 months. They reported subjective tinnitus and there was no evidence of evoked tinnitus. The perceived sense of tinnitus varied among the subjects and included a single high-pitch tone or noise, airplane sound, hissing, whistling or ringing. Tinnitus was located in the left ear in 2 subjects (10%), in the right ear in 3 (15%) and bilaterally in 15 (75%). Subjects were considered homogenous because of the constant and steady-state feature of their tinnitus.

The subjects were included in the study if they fulfilled the following criteria: (1) Normal external and middle ear function and appearance as revealed by otoscopy and tympanometry; (2) behavioral pure tone audiometry threshold levels of ≤ 20 dB HL at octave frequencies of 500 to 4000 Hz (3) not taking specific medications and/or undergoing audiological management at least 3 months prior to the study; (4) right-handedness; (5) no invasive therapeutic interventions on the brain or ears before or after onset of the tinnitus; (6) a primary complaint of chronic tinnitus (i.e., a duration greater than six months); (7) severe tinnitus as indexed by loudness matching of tinnitus more than 4 decibel sensation level (dB SL);score of 45 or more in Persian version of tinnitus questionnaire and score of 43 or more in Persian version of tinnitus handicap inventory (8) the ability to read and speak Persian; and (9) willingness to participate in a research-oriented study.

Exclusion criteria considered: pregnancy, psychiatric disorders (according to psychiatrist verification), any treatment for tinnitus during the previous three months, dementia, seizures or alcohol/drug abuse in the previous six months, head and neck diseases or space occupying lesions, and/or any organic disease that cause tinnitus. Each subject provided informed consent in accordance to the Declaration of Helsinki.

**Procedure:**

Participants lay on a bed in an electromagnetic and sound proof chamber. One pillow was set on the back of neck to reduce muscle contractions. Subjects were asked to remain relaxed and avoid any body movements during recording. VAS for loudness, LMT, PMT, P-TQ and P-THI, DPOAE and ECochG were recorded pre-LLLT. LLLT was presented to subjects 20 minutes for each ear in 12 separate sessions. VAS, LMT, PMT, P-TQ, P-THI, DPOAE and ECochG were recorded again after completion of LLLT sessions (at the end of last LLLT session). Each recording session including preparation and recording lasted about 25 minutes per ear.

Following 12 sessions of LLLT, subjects were categorized into two groups of negative response (NR) and positive response (PR) based on changes in VAS score, LMT and PMT: Increased unchanged or reduced scores less than 2 were considered as NR, 3 scores and more decrements were considered as PR. 13 subjects were RI and 15 subjects were NRI.

The subjective criteria for evaluating tinnitus after LLLT using a psychoacoustic tinnitus assessment included diminishing or worsening of tinnitus loudness by at least 2 dB SL (sensation level) and reduction or increment in the pitch of tinnitus at least by 1000 Hz.

**Visual Analogue Scale:**

VAS is a [psychometric](http://en.wikipedia.org/wiki/Psychometrics) response scale which can be used to measure subjective characteristics or attitudes that cannot be directly measured. VAS was used to measure tinnitus loudness pre- and post- LLLT to monitor changes in tinnitus loudness associated with LLLT. When responding to VAS, participants specified loudness level of their tinnitus by indicating a position along a continuous line between two end-points of 0 to 10.

Changes in tinnitus loudness were classified into three groups: (I) tinnitus became inaudible or reduced (complete or partial residual inhibition); (II) tinnitus was not changed (non-residual inhibition) and (III) tinnitus became worse than before LLLT (rebound effect). In the current study, the subjects with positive response (PR) were group I and subjects with negative response (NR) were considered group II and III.

**Tinnitus Assessment**

PMT and LMT were evaluated using external tones presented to the contralateral ear by a headphone. This task was accomplished using a Tinnitus Evaluation Device (TinED®) which included 6 channels to reconstruct the most troublesome tinnitus (MTT) with a similar frequency and intensity. TinED® was calibrated according to American Standard Specification for Audiometers, S3.6-2004. . This device is a computer-based sound synthesizer has special software which adapted with standard tinnitus assessments. It has 6 channels to reconstruct the most troublesome tinnitus (MTT) with a similar frequency and intensity. This device provides the possibility to present different tones and noise in terms of frequency and intensity individually or mixed to synthesize tinnitus. Thus the most similar sound to tinnitus is reconstructed.

Pitch and loudness match tests were performed contralateral to tinnitus ear. LMT was obtained at each of the test tones frequencies regardless to pitch of tinnitus. The sound level is increased in 1 dB steps until the subject reports that the external tone is just equal to the loudness of the tinnitus. So the loudness of tinnitus was obtained according to dB SL. The test tone was started just below the subject’s hearing threshold in ascending series of intensity levels to minimize loudness changes of tinnitus. For the tinnitus pitch-match test, we administered a two-alternative forced-choice method. Different pairs of pitch sounds were generated at 15 frequencies (from 125 Hz to 12 kHz) just to loudness match point of tinnitus; we then decreased or increased the pitch. Then subjects were asked to identify which pitch best matched the pitch of their tinnitus. The pitch-match test was typically in multiples of 1 KHz. Finally, we administered an octave confusion test to more accurately determined tinnitus frequency. Finally the loudness obtained at PMT was considered as LMT. The subjects had to have LMT over 4 decibel sensation level (dB SL) to be included in this study.

**Persian Version of Tinnitus Questionnaire**

P-TQ evaluates the dimensions associated with complaints and severity of tinnitus. The subscales consist of emotional, cognitive, emotional and cognitive, auditory perceptual difficulties, intrusiveness, sleep disturbances and score global 24 with Cronbach’s Alpha of 0.95 and the test –retest reliability between 0.91-0.94.

**Persian Version of Tinnitus Handicap Inventory:**

P-THI measures the impact of tinnitus on daily life with Cronbach’s Alpha=0.9325. It describes three functional, emotional and catastrophic effects of tinnitus on participants. The cut-off point in THI score was defined as 38 to discriminate between slight/mild versus moderate or more intensive tinnitus as a severity index.

**Electrocochleography:**

ECochG was recorded using Amplaid MK12 electrophysiological system (Amplaid, Milan). All tinnitus subjects lay on a bed in an acoustically and electrically shielded room. The responses were recorded with a vertical montage of three-disk Ag-AgCl electrodes (non-inverting on the vertex (Cz), ground on the forehead, and inverting electrodes on the mastoid. A scrubbing gel was used to clean and scrub the skin areas under each electrode. Contact impedance for the disk electrodes were less than 2 Kohms except for the inserted ECochG electrode, which was maintained at less than 5 Kohms. ECochG performed to obtain compound action potentials (CAP) using the active surface tympanic membrane electrode (Tymptrode), which was inserted into the lower posterior-inferior region of the external auditory canal at the point closest to the tympanic membrane. A conductive gel was used on the tip of the Tymptrode before inserting it into the ear canal. The Tymptrode was fed into the ear canal until it reached the eardrum. When placed properly, the electrode rested gently on the eardrum, and the gel assisted making contact with the eardrum. The acoustic stimuli were delivered monaurally by a headphone (earphone Telephonics TDH-39 with cushion MX-41/AR) to the tinnitus ear or to the ear with more intense tinnitus in cases of bilateral tinnitus. The stimuli were alternative 0.1 ms clicks presented at a rate of 7.1 per second and a band pass filter of 30-3000 Hz. The responses were recorded with 1000 sweeps. CAP amplitude, latency and threshold were measured and input-output functions for amplitudes and latencies were computed. The threshold level of CAP was determined as the minimum sound pressure level which produces detectable and reproducible waveforms of CAP. In this study, the changes in amplitude and latency of CAP were estimated at 20 dB over its threshold level.

**DPOAEs assessment:**

Standard DPOAEs test was performed using ILO92 (OtodynamicLtd) with three different frequency combinations for primary tones (f1 = 818, f2 = 1001 Hz; f1 = 1636, f2 = 2002 Hz and f1 = 3281, f2 = 4004 Hz).They were presented with intensity levels of L1=55 and L2 = 65 dB SPL and ratios of f1/f2 = 1.22. The evoked responses for 2f1 – f2 were assessed pre- and post- LLLT.

**Laser parameters:**

LLLT was conducted for 12 sessions, 2 sessions per week. Diode lasers included PR-100 Red laser designed by COL company, 630 nm, 100 mw, spot size=1 cm2; continuous mode, power density = 0.1 W/cm2; PR-100 Infra-red laser designed by COL company, 808 nm, 100 mw, spot size = 1 cm2; continuous mode, power density = 0.1 W/cm2 to provide the laser stimulation. The two wavelengths were applied sequentially, first infra-red laser, followed by red laser. The time of irradiation of each laser device was manually controlled by a timer. The laser devices were calibrated automatically. Infra-red laser was positioned on three points of mastoid bone behind the ear. The first point was chosen on mastoid bone at the level of auricle just behind the ear; 3 cm above of first point was noted as second point of treatment and the third point was 3 cm below the first point. The subjects had the IR laser applied for approximately 5 minutes per point which made 30 Joule/point; total energy was 90 Joule irradiated on area of mastoid. For the second step, red laser was irradiated directly to the ear canal for 5 minutes which made 30 Joules of energy. Total dose was 120 Joule/ear/session. Laser devices were positioned at contact mode without pressure on tissue and titled at a 90º angle. Preparation and irradiation of laser to each ear lasted about 25 minutes for each session.

**Statistical Analysis:**

All statistical analyses were performed using the Statistical Package for Social Science (SPSS V.16; Chicago, United States). A paired *t*-test was used to compare the studied variables pre- to post- LLLT. Mean differences for the studied variables pre- to post- LLLT were compared between two groups of PR and NR using a student *t*-test. A probability value of less than 0.05 was considered to be significant. The summary data are presented as the means ± SD.

# Results

Paired t-test showed that mean scores of VAS for loudness significantly decreased pre- (*M*=5.7, *SD*=1.5) to post-LLLT (*M*=3.2, *SD*=2.3), *P* < .001. The mean difference for LMT significantly decreased pre- (*M*=5.5, *SD*=1.6) to post-LLLT (*M*=4.05, *SD*=1.8), *P* < .001. The mean scores of P-TQ significantly decreased pre- (*M*=65.7, *SD*=13.7) to post- LLLT (*M*=50.2 , *SD*=17.7), *P* < .001.There was a significant difference in scores of P-THI pre- (*M*=68.6, *SD*=15.2) to post- LLLT (*M*=54.6, *SD*=13.7), *P* < .001.The mean difference for CAP amplitude significantly decreased pre- (*M*=0.25 µV, *SD*= 0.1) to post- LLLT (*M*=0.51 µV, *SD*= 0.1), P<0.001 (Table 2 and 3).

Then, all the patients were divided into two groups based on the alterations of scores in VAS for loudness and LMT pre- and post- LLLT: 1) positive response (PR) and 2) negative response (NR). Analyses were performed using paired t-test to compare data obtained pre- and post-LLLT in each group (Table 4 and 5). In PR group, mean difference of VAS for loudness increased significantly in PR group, pre- (*M*=5.8, *SD*=1.5) to post- (*M*=2.1, *SD*=1.8) LLLT, *P* < .001.Mean difference of LMT decreased significantly pre- (*M*=5.8, *SD*=1.9) to post- (*M*=4.0, *SD*=2.2) LLLT, *P* < .001. P-TQ scores decreased significantly pre- (*M*=67.5, *SD*=13.4) to post- (*M*=46.8, *SD*=18.1) LLLT, *P* < .001. P-THI scores decreased significantly pre- (*M*=70.3, *SD*=16.8) to post- (*M*=51.6, *SD*=14.5) LLLT, *P* < .001. Mean difference for CAP amplitude increased significantly pre- (0.24 µV, *SD*=0.05) to post- (0.5 µV, *SD*=0.1) LLLT, *P* < .05.

In NR group, mean difference for LMT decreased significantly pre- (*M*=5, *SD*=0.8) to post- (M=4, *SD*=0.8) LLLT, *P*<0.01. Also, mean amplitudes of CAP increased significantly pre- (*M*=0.27 µV, *SD*=0.1) to post- (*M*=0.52 µV, *SD*=0.1) LLLT, *P* < .01. Mean latencies of CAP decreased significantly pre- (*M*=1.67 ms, *SD*=0.2) to post- (*M*=1.52 ms, *SD*=0.2) LLLT, *P* < .05. No significant differences observed for VAS, PMT, P-TQ and P-THI in NR group.

Student t-test was used to compare the mean differences for all study variables from pre- to post- LLLT between the two groups. No statistically significant difference was found for any of the parameters (Table 6).

**Discussion**

The present study investigated alterations of subjective evaluating parameters of tinnitus, EcochG and DPOAE pre- to post- LLLT on tinnitus subjects. It was considered if LLLT could eliminate tinnitus loudness indexed by DPOAE and ECochG. The statistical analyzes revealed significant differences for subjective evaluations and CAP amplitude.

In contrast to findings of Mirz 22, Nakashima 21 and Teggi 23 we found significant differences for subjective tests consisted of VAS for loudness, LMT, TQ and THI pre- to post- treatment. Consistent with Okhovat 26, Tauber 10, Cuda and Caria 17, Hahn 27 and Salahaldin 19, an improvement in VAS, THI and reduction in loudness were reported pre- to post- LLLT in subjective description of tinnitus.

The efficacy of LLLT for tinnitus suppression according to subjective evaluations has been reported from 0% to 90% in different studies. Previous studies are controversial and difficult to compare because of different study designs, treatment protocols, laser parameters, evaluating tools and theories for tinnitus origin are different.

To our knowledge, none of the previous studies used objective assessments pre- and post- LLLT in tinnitus subjects. Choosing the suitable assessment tools plays an important role in detecting treatment effects. Although subjective evaluating tools are valuable for monitoring treatment effects, but it depends on the subject’s judgments. Tinnitus is a subjective perception and the patient’s estimation of it, is highly individual. It has been found that tinnitus subjects have difficulties in rating their subjective perception on VAS which can introduce errors in results. In fact, we considered subjective evaluations at least as important as objective audiometric assessments.

It has been assumed that low-intensity laser irradiation increases cell proliferation 28, synthesis of ATP and collagen 29, and release of growth factor 30. It also promotes local blood flow in the inner ear and activates repair mechanisms through photochemical and photophysical stimulation of mitochondria in hair cells 31.LLLT been discussed as a therapeutic procedure for cochlear dysfunction 32 in particular for chronic cochlear tinnitus. Since LLLT targeting inner ear was chosen as the therapeutic procedure in this study, DPOAE and ECochG were used to investigate the effects.

Evidence from many studies suggests that most forms of tinnitus result from a loss of inhibition secondary to cochlear damage in central auditory structures. This loss of inhibition disrupts the normal synchronized neural activity constrained by feedforward inhibition to acoustic features of stimulus. In this model of tinnitus, it is supposed that related brain regions are abnormally under-active and to compensate this under-activity, function of neural networks are aberrantly increased when tinnitus is present. 33, 34, 35  We hypothesized that effects of LLLT on inner ear may compensate sensory deprivation in the auditory system. Since DPOAE did not changed after LLLT, it can be inferred that possible cochlear damage was not healed by LLLT or the healing was not so much to be revealed by DPOAE. But, improving CAP amplitude post-LLLT may be an index of reduction in activity of neural networks in presence of tinnitus.

In NR group, despite of no change in subjective tests, mean amplitude of CAP increased and mean latency of CAP decreased significantly pre- to post- LLLT. There was a change in CAP amplitude in both groups and this may be potentially an index for revealing the therapeutic effects of LLLT. Low level laser can cause biological effects on cellular and molecular structures of cochlea and following the improvement of neural function, improvement of CAP may be occurred.

 The reason of this change is unclear precisely. Maybe the subjective criteria used for grouping the subjects were not effective and appropriate enough. More researches are needed to verify this observed CAP amplitude increment in NR and PR group.

It seems interesting that some subjects with bilateral equal tinnitus demonstrated the same amount of improvement in VAS scale in both ears although irradiation was sent only to one ear. The reason is unknown but maybe one ear has been more affected in comparison to other side and brain produced tinnitus signals from the other side (similar to phantom pain of limbs) or equal perception of tinnitus in the ears has been reported mistakenly because of the masking effects. Recently, different studies have been published that some central mechanisms may be involved in tinnitus. 32, 33, 34, 35

Physiological and electrophysiological tests of DPOAEs and ECochG are sensitive to defects of cochlea and distal portion of cranial 8th nerve. Unfortunately we could apply objective tests only for 11 subjects and not all of them. No statistically significant differences were found for any of the objective parameters except for CAP amplitude.

**Conclusion**

The effects of LLLT on tinnitus are under investigation yet. Based on our findings, it seems that our laser protocol might not be objectively qualified and defining a new protocol for optimizing LLLT parameters may be an option. It is suggested that the study be repeated with including tinnitus subjects with cochlear damage showed by OAEs. Also using input-output function of DPOAE may be a better choice than DPOAE thresholds to investigate the effects of LLLT on cochlea. Conducting a randomized clinical trial using animal models with larger groups of subjects in a longer time period may better reveal the effects. Considering the results of subjective tests, LLLT was effective in producing a reasonable improvement in subjects’ complaints of long-standing tinnitus despite previous treatment of the condition.

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**Table1.** **Overall review of studies published on effects of low level laser irradiation on tinnitus suppression which gained positive results. (N=number of patients, imp=improvement, S=sessions, W=week).**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Study (year) | Methodof LLLT |  Protocol | EvaluationMethod |  Results |
| Mahmoudianet al., 2014 N=20  | Red &IR270j/ear | 12 S.Twice/W. | VAS , ECochG,DPOAEs | Significant decrease of subjective testsCAP imp. |
| Ales Hahn et al.2012 N=420 | IR120j/ear | 10 S.3times/W | VAS | 56.7% imp. |
| Salahaldinet al.,2010N=65 | Red6j/ear | Once dailyFor 3months | VAS | 56.9% imp. |
| Okhovat2007N=61 | Red6j/ear | 20 S.Once daily | VAS | T reduction 49.1%T disappeared 18% |
| Quittner2004N=32 | IR240-480J/ear | 5 S.Every other day | VAS | 90.6% some degreeOf imp. |
| Touber2003N=35  | Red&IR4 J/cm2 | Not stated | VAS | Loudness reduction in 13 patients |
| Prochazka2002N=35 | IR175J/ear |  8-10 S. Twice/ w. |  VAS | 43% >50% imp. |
| Shiomi1997N=38  | IR14.4J/ear |  10 S. once a week |  VAS | 26% duration imp.58% loudness imp.55%annoyance imp. |
| Wilden1996N=139 | Red&IR132J/ear |  15 S. Daily |  VAS | 77.4% imp. |
| Witt1989N=500 | Red&IR |  Not stated |  VAS | Imp.>60% |

**Table2. Results of paired t-test showing changes of subjective tests pre- to post- LLLT (N = 20)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Pre LLLT(mean±SD) | Post LLLT(mean±SD) | P value(pair t test) |
| VAS for loudness | 5.7 ± 1.5 | 3.2 ± 2.3 | 0.0001 |
| LMT | 5.5 ±1.6 | 4 ± 1.8 | 0.0001 |
| P-TQ | 65.7 ± 13.7 | 50.2 ± 17.7 | 0.0001 |
| P-THI | 68.6 ± 15.2 | 54.6 ± 13.7 | 0.0001 |

**Table 3.Results of paired t-test showing changes of objective tests pre-to post LLLT (N=11)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Pre LLLT(mean±SD) | Post LLLT(mean±SD) | P value(Pair t test) |
| CAP threshold | 46.9 ± 3.3 | 46.8 ± 2.8 | 0.75 |
| CAP amplitude | 0.25 ± 0.1 | 0.51 ± 0.1 | 0.0001 |
| CAP latency | 1.6 ± 0.2 | 1.5 ± 0.2 | 0.2 |
| SP/AP ratio | 29.2 ± 5.8 | 29.4 ± 4.8 | 0.92 |
| DPOAEs(1001Hz) |  1.85±7.2 | 1.54±5.32 | 0.81 |
| DPOAEs(2002Hz) | 6.29±5.53 | 3.40±8.85 | 0.21 |
| DPOAEs(4004Hz) | -2.37±5.08 | -5.35±4.38 | 0.10 |

**Table4. Results of independent t-test comparing variables of the study pre-to post LLLT in PR and NR groups.**

|  |  |  |
| --- | --- | --- |
|  PR group (N=13) |  |  NR group(N=7) |
|  | Before(mean±SD) | After(mean±SD) | P value |  | Before(mean±SD) | After(mean±SD) | P value |
| VAS | 5.8±1.5 | 2.1±1.8 | 0.0001 |  | 5.4±1.8 | 5.2±1.7 | 0.35 |
| LMT | 5.8±1.9 | 4.0±2.2 | 0.0001 |  | 5±0.8 | 4±0.8 | 0.004 |
| PMT | 5541±2054 | 5821±2109 | 0.23 |  | 6000±1632 | 6300±1778 | 0.33 |
| P-TQ | 67.5±13.4 | 46.8±18.17 | 0.0001 |  | 62.2±14.5 | 56.4±16.1 | 0.33 |
| P-THI | 70.3±16.8 | 51.6±14.5 | 0.0001 |  | 65.6±12.4 | 60.2±10.5 | 0.13 |

**Table5. ECochG / DPOAEs characteristic mean differences and monitored *P* value according to PR and NR groups.**

|  |  |  |
| --- | --- | --- |
|  |  |  PR group (N=5) NR group (N=6) Before After  *P* value Before After *P* value(mean±SD (mean±SD) (mean±SD) (mean±SD) |
| CAP threshold | 46.4±2.1 | 46.8±2.1 | 0.1 |  | 47.3±4.1 | 46.8±3.5 | 0.2 |
| CAP amplitude | 0.24±0.05 | 0.5±0.1 | 0.02 |  | 0.27±0.1 | 0.52±0.1 | 0.005 |
| CAP latency | 1.64±0.2 | 1.59±0.1 | 0.7 |  | 1.67±0.2 | 1.52±0.2 | 0.03 |
| SP/AP ratio | 32.6±5.5 | 29.2±3.7 | 0.1 |  | 26.5±4.8 | 29.6±6.0 | 0.2 |
| DPOAEs(1001) | 3.9±5.2 | 3.1±3.2 | 0.7 |  | -1.9±8.3 | -1.1±4.3 | 0.7 |
| DPOAEs(2002) | 7.4±4.7 | 2.2±10 | 0.2 |  | 1.3±6 | 0.4±7.5 | 0.8 |
| DPOAEs(4004) | 0.7±4.4 | -3.2±9.3 | 0.1 |  | -0.6±3.8 | -4.6±5.4 | 0.2 |

**Table6. Results of independent t-test comparing mean differences from before to after LLLT between PR and NR groups.**

|  |  |  |  |
| --- | --- | --- | --- |
| ECochG characteristic | PR group(mean±SD)  | NR group(mean±SD)  | P valuet-test |
| CAP threshold | 0.40 ± 0.54 | -0.50 ± 1.04 | 0.10 |
| CAP amplitude | 0.26 ± 0.17 | 0.26 ± 0.00 | 0.97 |
| CAP latency | -0.07± 0.33 | -0.15 ± 0.12 | 0.61 |
| SP/AP ratio | -3.40 ± 3.84 | 3.17±6.17 | 0.06 |
| DPOAE 1001 | 3.26 ± 2.92 | 0.91 ± 5.15 | 0.19 |
| DPOAE 2002 | -4.82 ±8.48 | -0.9 ± 8.34 | 0.23 |
| DPOAE 4004 | -3.96 ± 5.73 | -3.96 ± 7.20 | 0.49 |