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의학석사 학위논문

만성 이명환자의 약물과 이명 재훈련 치료 후
장기 추적관찰 연구

Long-term Treatment and Follow-up Results in Tinnitus
Patients from the point of view of Tinnitus Handicap Inventory

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SUMMARY

Background and Objectives: Tinnitus has been one of the most common, but the challenging complaint of patients with sensorineural hearing loss (SNHL). Tinnitus is commonly treated with medication and cognitive therapy after the introduction of tinnitus retraining therapy (TRT) by Jastreboff in 1990. But little had been published regarding the result of long-term treatment of the symptoms in Korea. The purpose of this study is to evaluate the therapeutic outcome of patients with tinnitus in long-term follow-up

Materials and Methods: A retrospective observational study was conducted on 193 patients visiting clinics from Jan 1, 2010, to Jun 31, 2017, for two years of treatment. Pure tone audiometry (PTA), electrocochlear gram (ECoG), distortion product otoacoustic emissions (DPOAE), auditory brainstem response (ABR), tinnitogram were performed to evaluate the audiologic status of patients and exclude other specific diagnoses of otologic disease. Patients were prescribed with medications like a vasoactive agent, calcium channel blocker, benzodiazepine, prostaglandins depending on the patient's needs and the physician's decision. During the follow-up period, we provided counseling and educated patients for tinnitus rehabilitation. All patients filled out the tinnitus handicap inventory (THI) to evaluate symptomatic change during treatment. Patients were divided into the mild, moderate, severe group (1st quartile, 2nd~3rd quartile, 4th quartile) Significant change was

defined as a 20% change of initial score.

Results: 87 males and 106 females included in this study and mean follow-up was 28.0 ± 4.9 (23 ~ 43 months). Among 193 patients, 99 patients (51.3%) showed significant THI score improvements and 71 patients (36.8%) didn't. Twenty-three patients (11.9%) showed significantly worse THI score.

After two years of treatment, the total score was improved by 7.4 ± 6.8 and F score (3.4 ± 7.6), E score (3.3 ± 5.8). ($p < 0.05$) C score shows improvement (0.7 ± 5.4) but statistically not significant. In the total group, the total score was gradually decreased. This trend was evident after one year ($p < 0.05$). Improvement of THI was always better in severe group than mild and moderate group ($P < 0.05$)

Conclusion: From this study, we proved that the persistent and trustworthy management of tinnitus patients using medication and tinnitus retraining therapy could improve patient's desperate state. Also, patients who showed severe THI score initially showed significantly higher improvements during treatments..

KEY WORDS: Tinnitus, Tinnitus re-training therapy, Long term follow up

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Introduction

In clinical practice, tinnitus has been one of the most common but challenging complaints of the patients with sensorineural hearing loss (SNHL). Tinnitus is defined noise in the ear, and it can be divided into subjective and objective tinnitus. About 5~25 % of patients suffered from tinnitus according to the study population.[1-3] Prevalence of tinnitus in Korea is about 20% of the general population.[2, 3] Among these patients, about 30% of patients had an annoying experience due to tinnitus.[4]

In the neurophysiologic model of tinnitus, tinnitus was augmented by the feedback loop of the limbic and autonomic nervous system. Jastreboff published about the tinnitus retraining therapy in 1990. It aimed to dissociation of this feedback loop. Habituation of appropriate response to tinnitus could achieve this object.[5] Many clinicians applied this approach with some modifications for the treatment of tinnitus.

But little had been published regarding the results of long-term treatment of tinnitus in Korea. The purpose of this study is to evaluate the therapeutic outcome of patients with tinnitus in long-term follow-up.

Materials and Methods

1. Study Design and Patient Selection

From January 2010 to June 2017, patients who visited the outpatient clinic of the otology at the Asan Medical Center complaining about tinnitus were retrospectively reviewed. All enrolled patients completed questionnaires (Tinnitus handicap inventory, THI)[6, 7] for two years to check the improvement of tinnitus.

2. Treatment

History taking, medical and otologic examination and audiometry were performed at initial presentation. Based upon these findings, additional medical, otologic, imaging studies were conducted to evaluate the audiologic status of patients and exclude any specific disease related to tinnitus including tinnitogram, auditory brainstem response (ABR), distortion product otoacoustic emission (DPOAE), electrocochleogram (ECoG), temporal bone computed tomogram (TBCT). All patients completed THI to determine the severity of tinnitus.

Treatment strategy was based on TRT with some modifications. All patients were counseled with one otologist. They were explained about the mechanism and nature of tinnitus and treatment strategy. Patients were prescribed with medication such as vasoactive agents calcium channel blocker, benzodiazepine, prostaglandins, vitamin and trace minerals for

symptomatic relief. Hearing rehabilitation was performed if hearing loss is significant. Sound generator in TRT was replaced by commonly available white noise audio clip in websites. Patients were regularly followed up at 3, 6, 12, 24 months. Audiometry was repeated to rule out specific otologic disease and reassess the audiologic status. Symptomatic improvement was assessed with THI. Patients were re-counseled for habituation.

3. Tinnitus handicap inventory

THI consisted of 25 items, and each item can be classified into three categories. 11 functional (F), nine emotional (E) and five catastrophic (C) items were counted respectively and totally. Patients were divided into five classes along the total score. (Slight, 0-16; mild, 18-36; moderate, 38-56; severe, 58-76; catastrophic, 78-100).) Significant change was defined as a 20% change in the initial score.[6, 7]. Patients were divided into mild, moderate, severe classes along initial total score for subgroup analysis. (1st quartile, 2nd~3rd quartile, 4th quartile) The significant change was defined as a 20% change in the initial score.

4. Statistical Analysis

To examine the effect of the treatment outcomes and serial change of the symptoms, the paired t-test, and one-way ANOVA test was used. All statistical analysis was delivered by using the SPSS software for Windows (version 21.0; SPSS Inc). The significance of the statistical analysis was set at $P < 0.05$.

Results

This study included 193 patients with an average age of 58.5 and consisting of 87 men and 106 women. Tinnitus persisted for an average of more than 33.3 months at the initial presentation. Patients had an average follow-up period of 28.0 ± 4.9 months (23 ~ 43 months). Hearing level of patients changed significantly but very small (1.92 ± 9.9 , $P < 0.05$) (Table 1.) After two years of treatment Total score was improved by 7.4 ± 6.8 , F score (3.4 , ± 7.6) and E score (3.3 ± 5.8). ($p < 0.05$) C score shows improvement (0.7 ± 4.9) but statistically not significant. (Table 2.) Among 193 patients, 99 patients (51.3%) showed significant THI score improvements and 71 patients (36.8%) didn't. Twenty-three patients (11.9%) showed significantly worse THI score.

For subgroup analysis patients into three groups at 1st quartile (18 scores) and 3rd quartile (50 scores). The mild group consisted of 48 patients, moderate group ($n=95$), and severe group ($n=50$). In the total group, the total score was gradually decreased. This trend was evident after 12 months ($p < 0.05$) (Figure 1.) In subgroup analysis, the mild group showed no definite improvement for two years. The moderate and severe group showed significant improvement at 24 months. (Figure 2~4). Improvement of the severe group was always higher than mild and moderate group ($p < 0.05$) (Figure 5.) The severe group showed poor audiometry ($P < 0.05$) Audiometry was not significantly changed during study periods.

Discussion

The present study examined the effect of TRT in 193 patients with long-term follow up. Jastreboff introduced the TRT and described outcomes with the subjective scale of 0 to 10 before, during and after treatment in 1990. With this method, he could estimate the improvement within a few months, but the clear result can be seen in about one year. But the severity of tinnitus was not quantified with standardized questionnaires.[5] In our study, we could similarly get the most improvement after one year

Julie revealed the effect of TRT with an association of audiometry in 2002.[8] She estimated improvement with THI score. In this study, initial audiometry was not associated with severity of tinnitus. After six months of treatment, total THI score was decreased from 52.8 to 25.4. But initial severity of tinnitus was not analyzed for effect of treatment due to small sample size. (n=23)

Henry compared the TRT with tinnitus masking (TM) via standardized questionnaires such as THI in 2006.[9] In this study, Patients were asked their thought about the tinnitus and classified into three groups (Moderate, big and very big problem). After 18 months, patients with moderate tinnitus got the improvement of 18.2 points, big problem with 29.2 points, very big problem with 50.4 points. Patients with severe tinnitus had more improvement after TRT. But initial classification just depended on the patient' s subjective feeling than a quantified scoring system. In our study, we could get poor outcomes, but in more structural stratification of symptoms.

Some researchers published outcomes of TRT in Korea. Lee released results of TRT in 2004.[10] He showed decrement of THI score from 46 to 27 during 6months in a huge population (n=1100). Park also conducted a study in 27 patients for 7 months in 2013.[11] Average THI score decreased from 52.9 to 35.9

The difference with other reviews is that we did the initial classification and analysis of result through a standardized scoring system, such as THI with long-term follow up. Patients with more severe patients got more improvement. Mild symptoms didn't improve, but long-term follow up study showed these symptoms did not deteriorate.

And this study had had limitations in retrospective observational studies. Some previous studies with short-term follow up showed the early response of treatment[8, 10, 11] In our study, the patient's got most improvement at about 2 years. But, patients with shorter follow up was excluded. It made bias that early responders were omitted from the study. Han compared treatment effect between good follow up the group and follow up loss group after TRT via telephone survey in 2015. [12] Follow up loss group had significantly lower Post-TRT visual analog scale and THI score. Further studies may be considered to distinguish between early, late, and non-responder after TRT in the early period of treatment.

Conclusion

From this study, we proved that the persistent and trustworthy management of tinnitus patients using medication and tinnitus retraining therapy could improve a patient's desperate state. Patients who showed severe THI score initially showed significantly higher improvements during treatments.

Table 1. Patients characteristics

Patients characteristics	Mean \pm SD
Sex (M: F)	87:106
Age (Mean \pm SD, range)	58.5 \pm 11.4 (20~83)
Onset of tinnitus (months)	33.3 \pm 72.5
Follow up duration (months)	25.4 \pm 16.3
Pure tone average (Initial)	32.7 \pm 19.2
Pure tone average (Last)	34.6 \pm 20.5

Abbreviation: F, female; M, male; SD, standard deviation

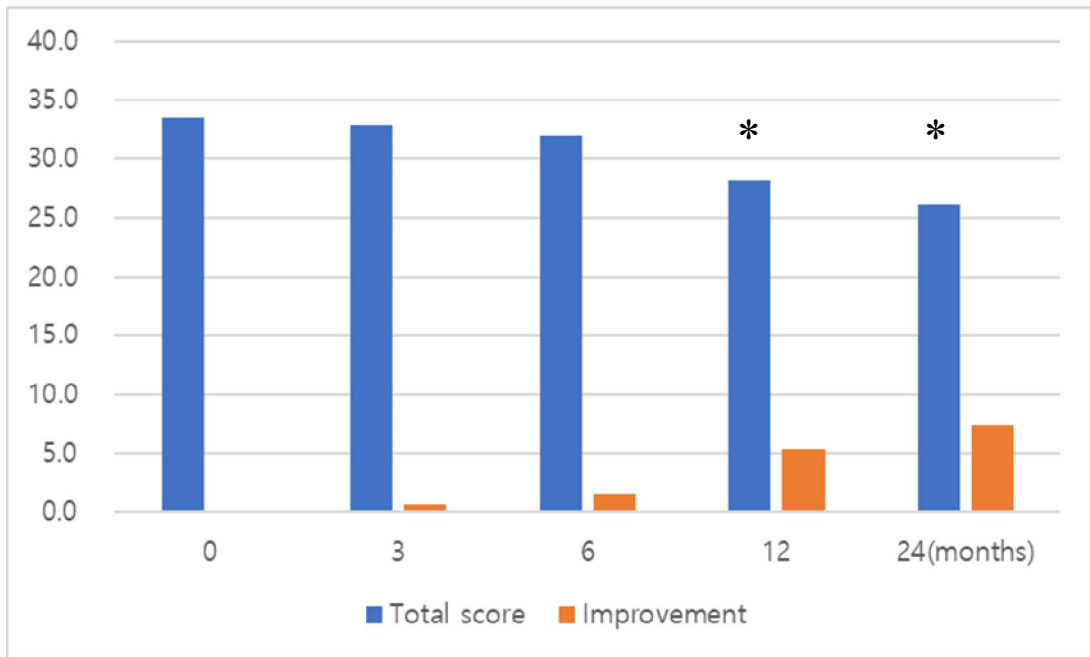
Table 2. Effect of the treatment

THI	Initial	Last	Change	p-value
F score	16.3±11.5	12.9±10.8	3.4±7.6	<0.05
E score	10.7±6.8	7.4±7.2	3.3±5.8	<0.05
C score	6.5±5.2	5.8±5.6	0.7±5.4	0.251
Total score	33.4±21.5	27.3±12.2	7.4±6.8	<0.05

All data was shown by Mean + SD

Abbreviation: C score, catastrophic score; E score, emotional score; F score, functional score; SD, standard deviation; THI, tinnitus handicap inventory

Figure 1. Change of total score for 2 years in total group

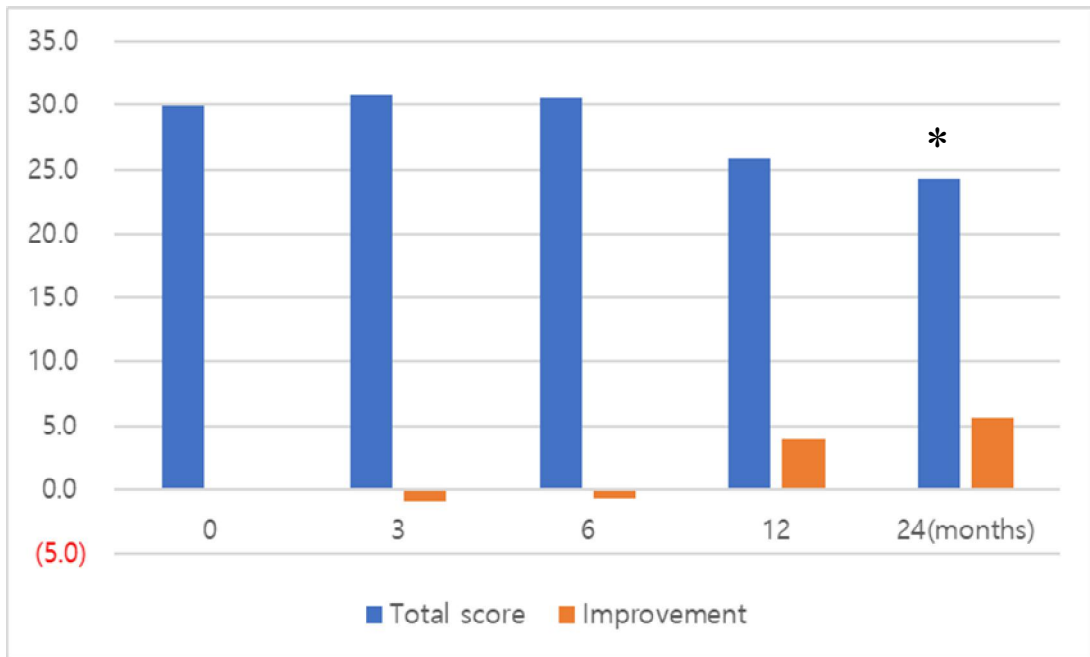


Star(*) indicated significant change from initial score

Figure 2. Change of total score for 2 years in mild group

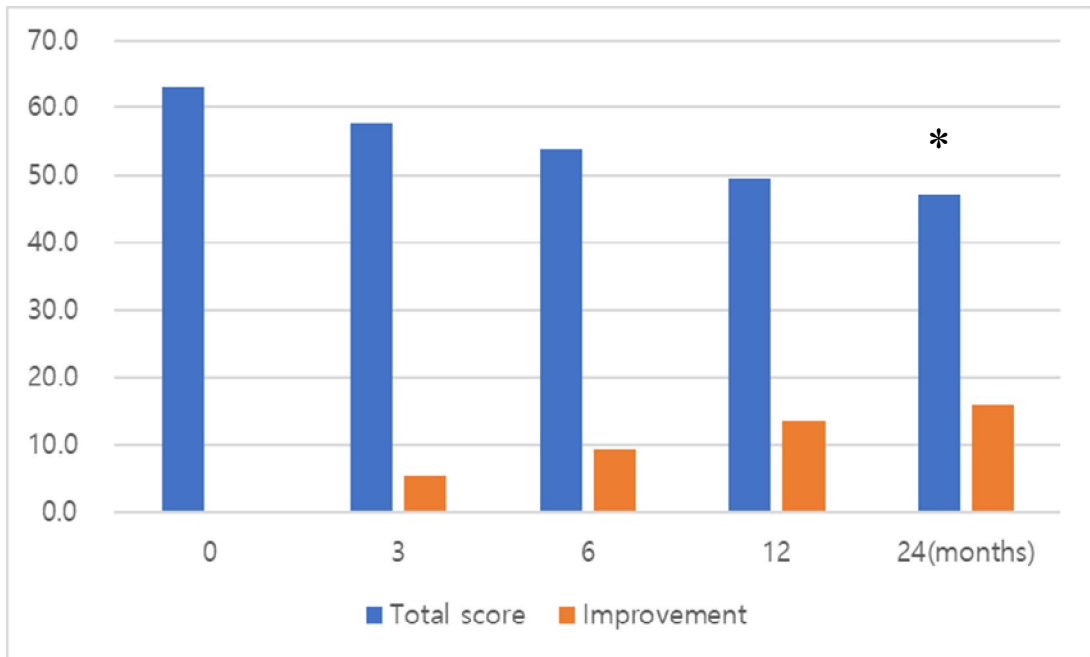


Figure 3. Change of total score for 2 years in moderate group



Star(*) indicated significant change from initial score

Figure 4. Change of total score for 2 years in severe group



Star(*) indicated significant change from initial score

Figure 5. Improvement along the group for 2 years

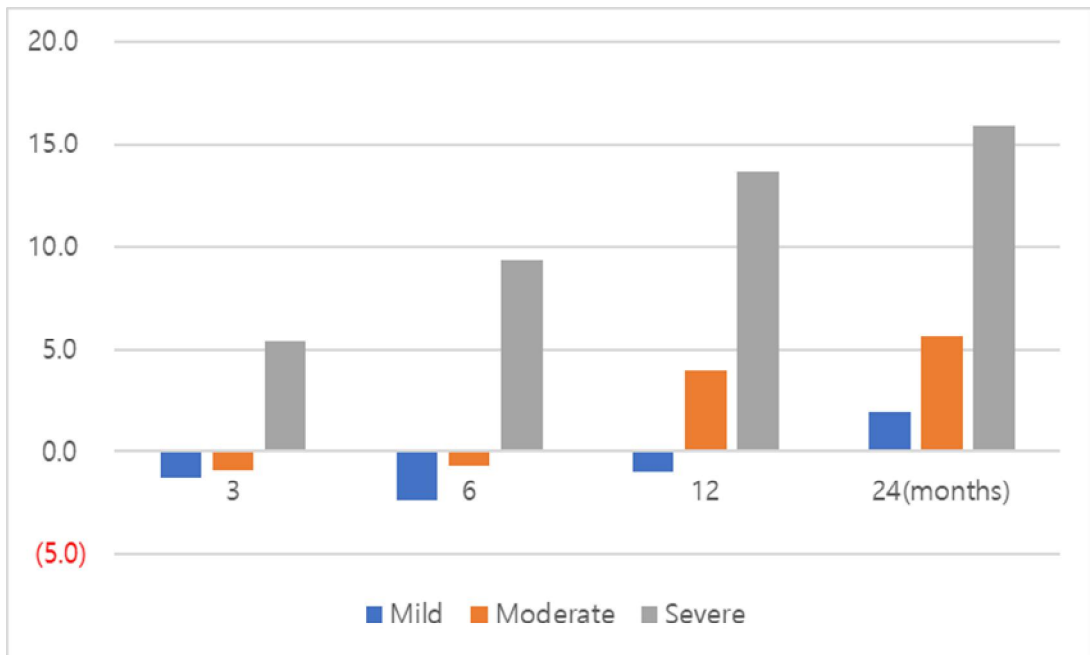
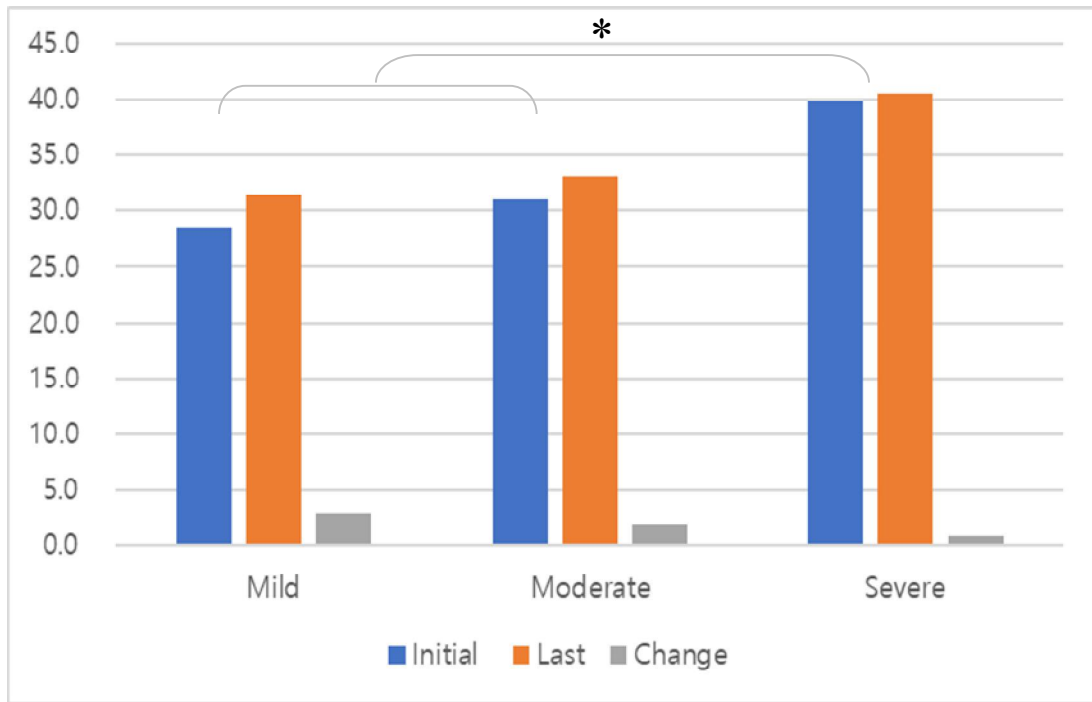


Figure 6. Hearing change for 2 years



Hearing level was not significantly changed during study periods.

Star(*) indicated hearing difference between groups.

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국문 요약

목적: 이명은 감각신경성 난청 환자에서 가장 흔하지만 치료하기 어려운 흔한 증상 중 하나다. 이명의 치료로 소리발생기, 청각재활, 약물 치료 및 인지 치료 등이 주로 사용되고 있으며 Jastreboff 의 이명재훈련 치료 역시 각광받고 있는 치료 중 하나다. 하지만 한국에서 이명재훈련 치료에 대한 장기간의 효과관찰은 아직 이루어지지 않고 있다. 이 연구의 목적은 장기간 이명재훈련 치료를 받은 환자들의 치료결과를 비교하는 것이다.

방법: 2010 년 1 월부터 2017 년 6 월 사이, 이명을 주소로 서울아산병원에 내원하여 2 년간 치료를 받은 환자 193 명을 대상으로 후향적 관찰연구를 시행하였다. 순음어음청력검사, 전기와우도, 변조이음향검사, 청성뇌간반응, 이명도검사 등이 환자의 이과학적 상태 및 감별진단을 위하여 시행되었다. 환자는 약물 치료 및 이명재훈련 치료를 위한 상담을 받았으며 청력 저하가 심한 경우 청각재활을 시행하였다. 치료의 효과를 평가하기 위해 이명장애지수 (Tinnitus handicap inventory)를 작성하였으며 이에 따라 환자군을 경증, 중등증, 중증의 3 군으로 나누어 하위집단 분석을 시행하였다. 처음 이명장애지수로부터 20% 이상의 변화가 있는 경우 유의한 이명장애지수의 변화로 정의하였다.

결과: 87 명의 남성, 106 명의 여성이 연구에 포함되었으며 평균 연구기간은 28.0 ± 4.9 (23~43) 개월이었다. 99(51.3%)명의 환자가 유의한 장애지수의 호전을 보였으며 71(36.8%)는 유의한 변화를 보이지 않았고 23(11.9%)의 환자는 유의한 악화를 보였다.

2 년의 치료 후 총점수 (7.4 ± 6.8 , $p < 0.05$), 기능지수 (Functional score, 3.4 ± 7.6 , $p < 0.05$), 감정지수 (Emotional score, 3.3 ± 5.8 , $p < 0.05$)의 호전을 보였으나 재앙지수 (Catastrophic score, 0.7 ± 6.5)는 유의한 호전을 보이지 않았다. 전체군에서 총점수는 지속적으로 감소하는 경향을 보였으며 1년 이후 유의한 변화가 관찰되었다 ($p < 0.05$). 중증군에서의 호전 정도는 경증, 중등증군의 환자보다 항상 높았다 ($p < 0.05$)

결론: 장기간의 약물 및 이명재훈련을 통해 환자의 이명이 호전되는 것을 볼 수 있었다. 이명의 중증도가 심한 환자에서 치료의 효과가 더 높은 것을 관찰할 수 있었다.

중심단어: 이명, 장기추적관찰연구, 이명 재훈련 치료