

Randomized Clinical Trial: Effectiveness of Tinnitus Treatment Using Music de Tinnitus Therapy Compared with Standard Therapy

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ABSTRACT

Background: Tinnitus is the perception of sound heard by a person without an external stimulus. Tinnitus can be divided into two, which tinnitus subjective and objective. About 10%–14.5% of the world's population experience tinnitus. The management of tinnitus is still a challenge for researchers. Until now, there has been no effective management of tinnitus. The last therapy available is to make artificial sounds that imitate the tinnitus sound so that it can mask the actual tinnitus sound. In addition, Song therapy is expected to reduce the stress level of tinnitus patients.

Methods: This research uses a double-blind randomized clinical trial with stratified and matching risk factors from the sample then the sample is randomized to get 104 samples consisting of 52 control groups and 52 experimental groups. Both groups will be assessed objectively with the Tinnitus Handicap Inventory (THI), and Tinnitus Primary Function Questionnaire (TPFQ), and subjectively with the Visual Analog Scale (VAS_T) before and after using the application. Assessment is done using the google form. The control group will be given an application containing a sound generator and the experimental group will be given an application containing de tinnitus Song. Both groups used the app for 2 hours daily for 3 months. Song de tinnitus was obtained from previous studies.

Results: The difference in risk factors in the two groups was 0.01 and the data obtained to be tested is normally distributed with the Kolmogorov Smirnov test (Sig > 0.1). We used a significance level of 95% and a research power of 0.1 with the result that there was a difference between the control group and the experimental group, better on the experimental group test with Chi-Square THI (p ~ 0.005), TPFQ (p ~ 0.004) and VAS_T (p ~ 0.002). THI (Relative risk reduction (RRR) = 59% Absolute risk reduction (ARR) = 25%, number needed to treat (NNT) = 4, TPFQ (RRR = 53.84%, ARR = 26.92%, NNT = 3.71) and VAS_T (RRR = 72.22%, ARR = 25%, NNT = 4).

Conclusion: We got better results using the app with de tinnitus Song (Music de Tinnitus) than using standard therapy.

Keywords: Application, Clinical trial, song, tinnitus.

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1. INTRODUCTION

Tinnitus comes from the Latin “tinnire”, meaning the sound is the perception of sound heard by a person without an external stimulus [1]–[3]. Tinnitus affects 10%–14.5% of the world's population. Tinnitus can occur due to various factors such as congenital, stress, and trauma from the

hearing organ due to noise. Tinnitus is often found in the age group between the ages of 40 to 60 years and impacts a person's emotional level, such as stress, anxiety, to depression [4], [5].

The current tinnitus management strategy uses hearing aids for patients with hearing loss [6]–[8]. However, hearing

aids are considered an ineffective treatment strategy, so the development and incorporation of sound generator amplification therapy with other techniques are carried out using today's technology, such as earphones.

Currently, a therapy that is being developed to treat tinnitus. One of therapy still develop is identifying the amplitude and frequency of the patient's subjective tinnitus sound to get narrow noise, and mixing with a music that can recovery or maintain the patient's emotional, language, motor, cognitive, and social functions [9]. Most tinnitus with severe symptoms has disturbances in emotional function so the use of de-tinnitus songs can improve the patient's emotions [3].

In the first study, a sound generator model was made and tested on several tinnitus sufferers and most of the patients felt comfortable or suitable or in accordance with the sound variations that were made into sound generators. In the second study, a combination of sound generators and tinnitus songs was carried out into de tinnitus Song which had been tested for safety and comfort. The results of the second study of de tinnitus Song are safe and comfortable for sufferers to use. Departing from the two studies above on de tinnitus Song, a simple android application will be made that will be used only for clinical trial purposes which will compare the use of tinnitus applications with other tinnitus treatments or therapies. This application can still be developed even better. With the development of science and technology makes it easier for tinnitus patients to access tinnitus Song therapy through an application on an Android mobile phone to facilitate access to tinnitus sufferers as a therapeutic modality [10].

Technological and scientific developments will also provide better time, place, cost and accessibility efficiency so that all tinnitus patients, both those with severe or mild complaints, can access good therapy. In addition, with the existence of technology, we can obtain patient data needed to develop tinnitus therapy so that it is better and more comprehensive based on the characteristics of each patient.

Based on the background above, the formulation of the problem in this study is as follows, is there a difference between tinnitus therapy using the de tinnitus application and standard therapy using a sound generator application or noise generator? The researchers aimed to find out the difference in patients with tinnitus application therapy with standard therapy, namely noise generator therapy. Besides that, the researcher's goal is to make tinnitus therapy usable anywhere with the development of technological advances. Benefits of research. The results of combining sound imitation and sound variations will become the basic material in making therapies that will be used for the treatment of tinnitus sufferers and will be patented.

2. METHODS

In this study using a double-blind clinical trial. The calculation of the number of samples used a significance level of 95% and a research power of 0.1. From the calculation, the minimum number of samples was 30. In the first study regarding the characteristics of tinnitus patients with normal hearing in Bali, the risk factors for each patient

were calculated. In the fourth study, namely the double-blind clinical trial study, the risk factors were stratified and matched in order to obtain the same risk factors between the control group and the experimental group, then randomized so that the control group and experimental group had a difference of 0.01% which was greater than the experimental group. The inclusion criteria were patients who took part in the first study to the third study, while the exclusion criteria were patients who withdrew.

In this study, several variables are measured. the dependent variable is assessed objectively with the Tinnitus Handicap Inventory (THI) [11], [12], Tinnitus Primary Function Questionnaire (TPFQ) [13], and subjectively with the Visual analog scale (VAS_T) [14] while the independent variable is giving de tinnitus Song with a sound generator or noise generator. Confounding variables such as risk factors have been stratified and matched so that each group has confounding variables that are not much different.

We stratified risk factors for example the degree of deafness, smoking, working noise, diabetic mellitus (DM), body mass index (BMI), depression, and otitis media. Our sample was divided into two groups, a control group and an experimental group. After stratification, we do match based on all the risk factors that the sample has followed by randomization to determine whether the sample is in the control or experimental group.

The first researcher stratified and matched, and then the third researcher called the sample to come to the place where the envelope containing money and the password for the tinnitus application was given. If the password had an odd ending, it became the control group and if the ending was even, it became the experimental group. Envelope collection is carried out for 3 days, the first day will be invited with normal hearing, the second day with moderate hearing loss, and the third day with severe hearing loss. The second researcher will help the sample when he comes to the researcher's place to take the envelope, ask for approval, and install the application. After taking the envelope, if there are questions that are not clear, the third researcher will assist them. The sample will fill out a questionnaire before and after therapy via the Google form. then the fourth researcher will collect data, group the data, and change each sample name to initials. the fifth researcher will perform data processing.

In this study, trials were carried out on samples for 2 hours every day for 3 months, later they would be assessed before and after the action was carried out. The criteria improve if half or more of the criteria before therapy improve both objectively with the Tinnitus Handicap Inventory (THI), Tinnitus Primary Function Questionnaire (TPFQ), and subjectively with the Visual analog scale (VAS_T). From this questionnaire, data analysis will be carried out using SPSS. There are several tests in SPSS 26. A Chi Square test was performed for THI and TPFQ and VAST data. Researchers will assess Relative Risk (RR), Relative risk reduction (RRR), Absolute risk reduction (ARR), and the number needed to treat (NNT).

2.1. Theoretical Framework

The theoretical basis used in this study is in accordance with Fig. 1 such as the first is low frequency (for the brain

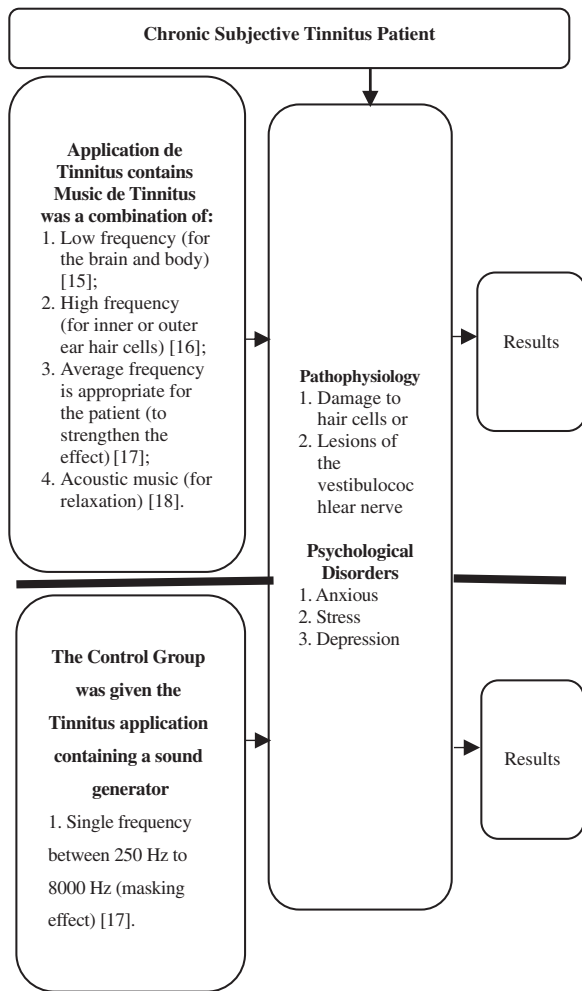


Fig. 1. Theoretical framework.

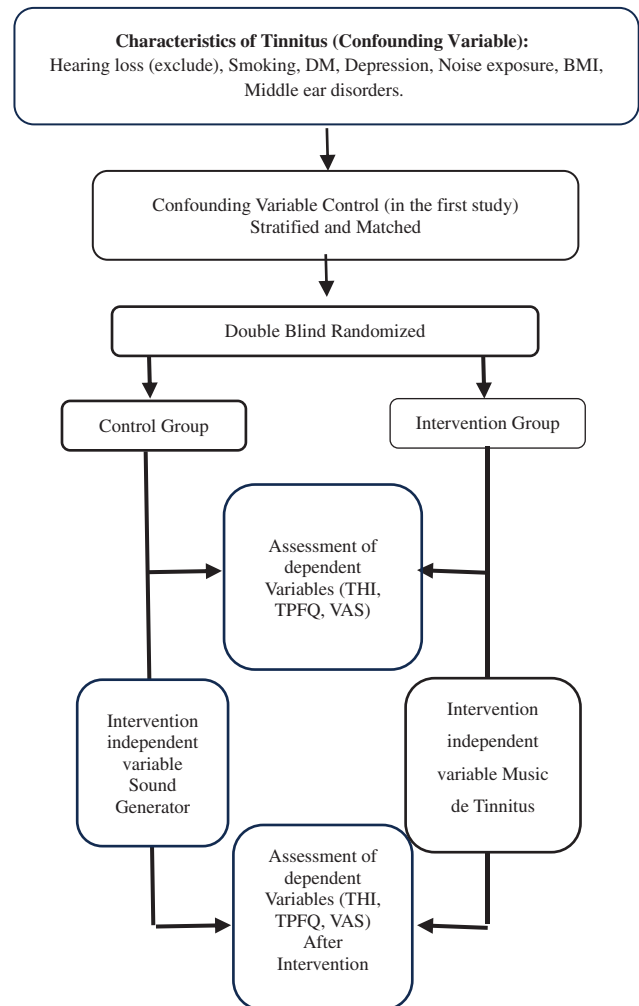


Fig. 2. Conceptual framework.

and body) [15], the second is high frequency (for inner or outer ear hair cells) [16], the third is the average frequency is appropriate for the patient (to strengthen the effect) [17], and The Forth is Acoustic music (for relaxation) [18].

2.2. Conceptual Framework

The Conceptual framework basis used in this study is in accordance with Fig. 2 such as characteristics of Tinnitus (Confounding Variable) such as hearing loss, smoking, DM, depression, noise exposure, BMI, and middle ear disorders. we carry out stratification and matching so that all risk factors are equally distributed in both groups. The control group received a sound generator, and the intervention group received de-tinnitus music for 2 hours every day for 3 months. Both groups measured THI, TPFQ, and VAS_T before and after intervention.

3. RESULTS

In this study used 116 samples with 12 samples who withdrew. One patient underwent surgery and the tinnitus healing [19]. The sample consisting of 104 was divided into control and experimental groups. Then we stratify and match so that we get a difference in risk factors between the control and experimental groups, which is 0.01% more

in the experimental group. Because we test with Chi-Square, we don't need normal distribution of the Tinnitus Handicap Inventory (THI), Tinnitus Primary Function Questionnaire (TPFQ), and Visual Analog Scale Tinnitus (VAS_T) but we try to compute a normal distribution test.

The normal distribution test that we do uses Kolmogorov Smirnov because the number of samples is above 50 with Sig Kolmogorov Smirnov results 0.1 as shown in Table I.

From the Tables II and III results of the data, the value of p from chi-square for THI ($p \sim 0.005$), TPFQ ($p \sim 0.004$) and VAST ($p \sim 0.002$) shows that the null hypothesis is rejected, which means that there is a difference between the experimental group and the control group. In the calculation of Relative risk reduction (RRR) on the THI assessment (Relative risk reduction (RRR) = 59%, TPFQ = 53.84% and VAST = 72.22%). Relative risk reduction with an average of above 61% shows that treatment with de tinnitus song of more than 61% can reduce therapy failure compared to standard therapy in the control group. In the Absolute risk reduction (ARR) calculation, the ARR value (THI = 25%, TPFQ = 26.92% and VAST = 25%) is in the range of 25.64%, this indicates that the difference in failure between the intervention group and the control group is 25.64% better in the intervention group. In the number needed to treat (NNT) calculation, the average

TABLE I: TESTS OF NORMALITY

	Kolmogorov-smirnov ^a			Shapiro-wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
THI value before therapy	0.063	104	0.200*	0.977	104	0.062
THI value after therapy	0.072	104	0.200*	0.974	104	0.035
TPFQ value before therapy	0.070	104	0.200*	0.971	104	0.021
TPFQ value after therapy	0.073	104	0.200*	0.962	104	0.005
VAS _T value before therapy	0.061	104	0.200*	0.975	104	0.042
VAS _T value after therapy	0.070	104	0.200*	0.965	104	0.008

Note: *. This is a lower bound of the true significance. a. Lilliefors Significance Correction.

TABLE IIA: THI AFTER TREATMENT

Group	Control		THI		Total
			Worsening or no change	Improve	
		Count	22	30	52
		% within group	42.30%	57.70%	100.0%
	Experiment	Count	9	43	52
		% within group	17.30%	82.70%	100.0%
Total		Count	31	73	104
		% within group	29.80%	70.20%	100.0%

TABLE IIC: VAS_T AFTER TREATMENT

Group	Control		VAS _T		Total
			Worsening or no change	Improve	
		Count	18	34	52
		% within group	33.33%	66.67%	100.0%
	Experiment	Count	5	47	52
		% within group	9.61%	90.39%	100.0%
Total		Count	23	81	104
		% within group	22.11%	77.89%	100.0%

TABLE IIB: TPFQ AFTER TREATMENT

Group	Control		TPFQ		Total
			Worsening or no change	Improve	
		Count	26	26	52
		% within group	50 %	50 %	100.0%
	Experiment	Count	12	40	52
		% within group	23.07%	76.93%	100.0%
Total		Count	38	66	104
		% within group	36.53%	63.47%	100.0%

TABLE IIIA: CHI-SQUARE TEST FOR THI

	Value	df	Asymptotic significance (2-sided)	Exact sig. (2-sided)	Exact sig. (1-sided)
Pearson chi-square	7.767 ^a	1	0.005		
Continuity correction ^b	6.618	1	0.010		
Likelihood ratio	7.951	1	0.005		
Fisher's exact test				0.009	0.005
Linear-by-linear association	7.692	1	0.006		
N of valid cases	104				

value (THI = 3.533, TPFQ = 3.29 and VAS = 3.54) is above 3.9. This means that only 3.9 people are required to be treated with de tinnitus song for 3 months to be able to mask one tinnitus patient.

4. DISCUSSION

This study used a double-blind clinical trial method using a sample size of 104, a significant level of 95%, and a research power of 0.1. In the first study, stratification and matching were carried out so that the experimental group and the control group differed by 0.01% in risk factors. In the fourth study, we randomized the samples into the control group and the experimental group, the risk factors were not much different. In the study, 12 samples withdrew.

In the results, the THI, TPFQ, and VAS data were normally distributed, and then the Chi-Square test was carried out with the results that there were differences between the control group and the experimental group. Calculation of the value of p from chi-square for THI ($p \sim 0.005$), TPFQ ($p \sim 0.004$) and VAS ($p \sim 0.002$). The results showed that therapy with de tinnitus song had a better masking effect than therapy with a sound generator. can be seen from the value of RRR, ARR and NNT.

In the third study [3], we tested the safety of using de tinnitus songs with several musical instruments, both acoustic and electric, as well as Balinese musical instruments, namely the gamelan and we also tested the safety of sound android program until the sound goes out to headset. In future studies, control patients who do not

TABLE IIIB: CHI-SQUARE TEST FOR TPFQ

	Value	df	Asymptotic significance (2-sided)	Exact sig. (2-sided)	Exact sig. (1- sided)
Pearson chi-square	8.128 ^a	1	0.004		
Continuity correction ^b	7.008	1	0.008		
Likelihood ratio	8.274	1	0.004		
Fisher's exact test				0.008	0.004
Linear-by- linear association	8.049	1	0.005		
N of valid cases	104				

TABLE IIIC: CHI-SQUARE TEST FOR VAS_T

	Value	df	Asymptotic significance (2-sided)	Exact sig. (2-sided)	Exact sig. (1- sided)
Pearson chi-square	9.434 ^a	1	0.002		
Continuity correction ^b	8.039	1	0.005		
Likelihood ratio	9.895	1	0.002		
Fisher's exact test				0.004	0.002
Linear-by- linear association	9.344	1	0.002		
N of valid cases	104				

improve with the sound generator will be given de-tinnitus song therapy so that researchers can see the effectiveness of each musical instrument which is best at different tinnitus frequencies, so that tinnitus sufferers can mask tinnitus sounds.

Technological developments have made it possible for tinnitus therapy to use Android and iPhone applications to listen to the de-tinnitus song for 2 hours so that tinnitus treatment can be more easily obtained, and easier to use. We have created a screening program for tinnitus sufferers, but we haven't done a trial to compare it with the gold standard. If all research has been achieved, it is hoped that it will be easy to carry out screening and therapy through tinnitus applications.

5. CONCLUSION

Tinnitus is the perception of sound that a person hears without any external stimulus. Tinnitus is caused by hearing loss in the inner hair cells leading to loss of normal auditory nerve function.

This study used a double-blind clinical trial to test the treatment of tinnitus using a sound generator in the control group with a de-tinnitus song in the experimental group and got better results in the experimental group than in the

control group. For the assessment use the THI questionnaire, TPFQ, and VAST before and after therapy. Therapy is given 2 hours every day and for 3 months.

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AUTHOR CONTRIBUTIONS

All of the authors equally contribute to the study from the conceptual framework, data gathering, and data analysis until reporting the study results through publication.

ETHICS CONSIDERATION

This study obtained an Ethics Approval issued by the Research Ethics Committee of the Faculty of Medicine, Udayana University, on May 31, 2022, before the study was conducted.

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CONFLICT OF INTEREST

Authors declare that they do not have any conflict of interest.

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