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Mohamed Ahmed Mohamed Ali
Department of Otorhinolaryngology, Faculty of Medicine for boys, Al-Azhar University, Cairo, Egypt, mohamad.ali.ali95@gmail.com

Ahmed Mohamed Seleim
Department of Otorhinolaryngology, Faculty of Medicine for boys, Al-Azhar University, Cairo, Egypt

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META ANALYSIS

Tinnitus Treatment for Adult: A Meta-analytic Study

Mohamed Ahmed Mohamed Ali*, Ahmed Mohamed Seleim

Department of Otorhinolaryngology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt

Abstract

Background: **Tinnitus is regarded as a puzzling issue, and there are currently no generally agreed-upon solutions to basic concerns concerning its pathogenesis, course, and ideal therapy.**

Aim and objectives: **To conduct a meta-analytic review of different types of treatment of tinnitus, to provide a better picture for the benefits and comparisons of efficacy of different types of tinnitus treatment, summarizing all types of treatment, providing the best appropriate treatment.**

Patients and methods: **This meta-analysis study included 33 studies were included 24 were randomized controlled trial (RCT), six were prospective studies, three were retrospective studies. Among the 33 included studies there were a total number of cases were 1929, with mean age 55.9 years.**

Results: **Mean tinnitus duration was 88.7 months and bilateral tinnitus founded in 310 cases, mean initial tinnitus frequency was 4840.8. The most common treatment used were nonpharmacologic treatments followed by pharmacologic treatments. There was improvement in 383 cases, partial improvement in 87 cases and 79 cases shows no improvement.**

Conclusion: **Nonpharmacological treatments of tinnitus seem to be associated with better outcome and less complications in comparison to the use of pharmacological therapies.**

Keywords: Nonpharmacological treatments, Pharmacological treatments, Tinnitus treatment

1. Introduction

The usual definition of tinnitus is the perception of a sound absent of related external stimuli.[1]

A more specific definition of tinnitus has recently been provided in an article: tinnitus was defined as 'the conscious awareness of a tonal and/or noise sound for which there is no identifiable corresponding external acoustic source' and tinnitus condition was defined as 'tinnitus plus tinnitus-associated emotional distress and functional disability'.[2]

The majority of people regard tinnitus to be a symptom that is generally easily tolerated; nonetheless, it may sometimes generate levels of discomfort that can be sufficient to make tinnitus the underlying reason for severe deterioration of perceived health status and quality of life. The lack of an ideal, all-encompassing therapy for tinnitus is one of the few topics that the tinnitus community agrees on.[3]

Despite the fact that a wide range of interventions have been used, including but not limited to drugs and medicinal products, sound amplification, sound therapy, psychological interventions, and transcranial magnetic stimulation, none of them has received universal acceptance as a sufficient and globally effective treatment for the full spectrum of tinnitus sufferers.[4]

There is a tendency in the tinnitus literature that most of the research uses a different subset of respondents.[5]

The limitations include the diversity of tinnitus patients, variation in tinnitus perception, subjective nature of tinnitus and consequent lack of objective measurement of outcomes, coexistence of comorbidities as well as their interaction with tinnitus perception, and different perceptions of tinnitus in different cultures as well as at different times by the same patient.[6]

As a result, it may be argued that subjective factors, as well as native and intrinsic causes, account

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* Corresponding author. Postal code: 11884.
E-mail addresses: mohamad.ali.ali95@gmail.com, mohamed.a.ali@students.kasralainy.edu.eg (M.A.M. Ali).

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for the absence of a well-established and efficient therapy.[4]

The aim of this thesis was to conduct a meta-analytic review of different types of treatment of tinnitus, to provide a better picture for the benefits and comparisons of efficacy of different types of tinnitus treatment, summarizing all types of treatment, providing the best appropriate treatment.

2. Patients and methods

This meta-analysis included 33 studies, of which 24 were randomized controlled trial (RCT), six were prospective studies, and three were retrospective. Among the 33 included studies there were a total number of cases were 1929, with mean age 55.9 years.

Recent clinical investigations, cluster trials, prospective comparative cohort studies, and so on. The systematic review management software was used to submit the search results and manually check them for inclusion eligibility. On the search results and the inclusion/exclusion criteria, PRISMA flowchart was established.

Inclusion criteria: studies with English language, publication between 2010 and 2022, adults with history of tinnitus and only RCTs with at least 30 participants.

Exclusion criteria: languages other than English, any type of study other than RCT, duplicates, patients with pulsatile tinnitus and nonclinical outcome studies.

Ethical considerations: as approved by committee of Al-Azhar University, Cairo.

Sample size: all articles fulfilling the inclusion criteria within the last 10 years.

2.1. Statistical analysis of the data

The MedCalc software program, version 15.8, was used to examine the data that were input into the computer. Statistical significance was defined as a P value of less than or equal to 0.05, and the confidence interval was set at 95 %. I^2 (observed variance for heterogeneity) and Q (total variance for heterogeneity) were used to measure statistical heterogeneity. While qualitative data are presented as total number and number of events, quantitative data is expressed as mean and SD.

3. Results

Table 1.

Mean tinnitus duration was 88.7 months and bilateral tinnitus founded in 310 cases, mean initial tinnitus frequency was 4840.8 (Table 2).

Total number of cases were 1929, mean age 55.9 years. Most common treatment used were cognitive therapy, hearing aid, sound therapy, bimodal auditory and electrical stimulation, virtual reality, OTO-313, hearing rehabilitation, acupuncture, AUT00063, transcranial magnetic stimulation, intratympanic dexamethasone, nitrous oxide, nerve stimulation, Ginkgo biloba, α-lipoic acid plus vitamin C,

Table 1. Disease characteristics.

References	Treatment	Tinnitus duration (months)	Bilateral tinnitus	Initial tinnitus frequency
Beukes et al.[7]	Cognitive therapy	180		
Kutyba et al.[8]	Sound therapy	74.4	30	
Spencer et al.[9]	Bimodal auditory and electrical stimulation			
Beukes et al.[7]	Cognitive therapy	139	76	
Boecking et al.[10]	Hearing aid			
Wang et al.[11]	Sound therapy			
Haines et al.[12]	Hearing aids	93.6	53	
Park et al.[13]	Virtual reality	87.6	8	
Maxwell et al.[14]	OTO-313	4.5		
Ketterer et al.[15]	Hearing rehabilitation			
Kuzucu and Karaca[16]	Acupuncture			
Hall et al.[17]	AUT00063	12		
Godbehere et al.[18]	Transcranial magnetic stimulation	18		
Sahlsten et al.[19]	Transcranial magnetic stimulation	81.6	11	
Lee et al.[20]	Intratympanic dexamethasone	1		
Hong et al.[21]	Nitrous oxide			
Tyler et al.[22]	Nerve stimulation	225.6		
Polanski et al.[23]	Ginkgo biloba α-lipoic acid plus vitamin C Papaverine hydrochloride plus vitamin E			
Henry et al.[24]	Hearing aid and tinnitus therapy device			
Mahendru et al.[25]	Caroverine Betahistine			
Coelho et al.[26]	Zinc	215.1	53	
Philippot et al.[27]	Cognitive therapy			

(*continued on next page*)

Table 1. (continued)

References	Treatment	Tinnitus duration (months)	Bilateral tinnitus	Initial tinnitus frequency
Sharma et al.[28]	Acamprosate Sound therapy			
Cima et al.[29]	Usual care Ozone			
Sönmez et al.[30]	Betahistine	35.3		5, 115.38
Kreuzer et al.[31]	Cognitive therapy	100.5	6	
McNeill et al.[32]	Hearing aid			
Dehkordi et al.[33]	Gabapentin	30.2		4800
Bovo et al.[34]	Cochlear implantation		27	
Sziklai et al.[35]	Dopamine agonist pramipexole			
Hurtuk et al.[36]	Melatonin	127	46	
Fukuda et al.[37]	Tinnitus retraining therapy			3900
Ariizumi et al.[38]	Tinnitus retraining therapy with a sound generator	132		4000

papaverine hydrochloride plus vitamin E, caroverine, betahistine, zinc, acamprosate, usual care, ozone, betahistine, gabapentin, cochlear implantation, dopamine agonist pramipexole, melatonin (Table 3).

Mean tinnitus handicap inventory score pretreatment was 46.5 changed to posttreatment, 34.3, mean tinnitus questionnaire pretherapy was 47.7 changed to posttherapy 40.5 (Fig. 1).

The current study also showed that mean tinnitus questionnaire pretherapy was 47.7 changed to posttherapy 40.5, four studies[13,22,31,32] were included in the meta-analysis and showed no substantial

Table 2. Patient's characteristics and treatments.

Type of treatments	References	Number	Age	Male/female
Cognitive therapy	Beukes et al.[7]	79	56	40/39
Sound therapy	Kutyba et al.[8]	44	51.9	19/25
Bimodal auditory and electrical stimulation	Spencer et al.[9]	29	54.76	
Cognitive therapy	Beukes et al.[7]	130	56.33	56/74
Hearing aid	Boecking et al.[10]	177	59.61	81/96
Sound therapy	Wang et al.[11]	50	43.04	25/25
Hearing aids	Haines et al.[12]	42	42	51/32
Virtual reality	Park et al.[13]	19	56.4	
OTO-313	Maxwell et al.[14]	15	56.9	8/7
Hearing rehabilitation	Ketterer et al.[15]	53	60	31/22
Acupuncture	Kuzucu and Karaca[16]	53	50.7	19/34
AUT00063	Hall et al.[17]	36	52.78	27/9
Transcranial magnetic stimulation	Godbehere et al.[18]	23		
Transcranial magnetic stimulation	Godbehere et al.[18]	20	53.7	11/9
Intratympanic dexamethasone	Lee et al.[20]	27	50.6	16/11
Nitrous oxide	Hong et al.[21]	20	52.8	13/7
Nerve stimulation	Tyler et al.[22]	16	55.9	15/1
Ginkgo biloba α-lipoic acid plus vitamin C	Polanski et al.[23]	12	72.6	26/32
Papaverine hydrochloride plus vitamin E		13		
		15		
Hearing aid and tinnitus therapy device	Henry et al.[24]	15	66.5	8/7
Caroverine Betahistine	Mahendru et al.[25]	30		
		30		
Zinc	Coelho et al.[26]	58	67.5	34/24
Cognitive therapy	Philippot et al.[27]	10	60.92	
Acamprosate Sound therapy	Sharma et al.[28]	40	53	
		245	53·74	158/87
Usual care Ozone	Cima et al.[29]	247	54·63	150/97
Betahistine	Sönmez et al.[30]	26	52.88	
Cognitive therapy	Kreuzer et al.[31]	18	49.6	11/7
Hearing aid	McNeill et al.[32]	70	55	48/22
Gabapentin	Dehkordi et al.[33]	40	49.9	18/22
Cochlear implantation	Bovo et al.[34]	41	46	17/34
Dopamine agonist pramipexole	Sziklai et al.[35]	20	61	
Melatonin	Hurtuk et al.[36]	61	57.8	42/19
Tinnitus retraining therapy	Fukuda et al.[37]	6	43.5	
Tinnitus retraining therapy with a sound generator	Ariizumi et al.[38]	92	62	57/35

Table 3. Outcome scores.

References	Treatments	Tinnitus handicap inventory score pre	Tinnitus handicap inventory score post	Tinnitus questionnaire pre	Tinnitus questionnaire after
Kutyba et al.[8]	Sound therapy	54.95 (23.98)	40.45 (22.57)		
Wang et al.[11]	Sound therapy	59.68 ± 23.95	33.72 ± 23.95		
Park et al.[13]	Virtual reality	50.11	44.21	48.5	45.3
Kuzucu and Karaca[16]	Acupuncture	61.11 ± 12.70	40.26 ± 16.56		
Godbehere et al.[18]	Transcranial magnetic stimulation	36	13		
Lee et al.[20]	Intratympanic dexamethasone	42.6 6 27.4	26.2 6 19.7		
Hong et al.[21]	Nitrous oxide	40 (21−92)	37.5		
Tyler et al.[22]	Nerve stimulation	52.5 (22.6)	34.8	58.8 (18.3)	56.3
Polanski et al.[23]	Ginkgo biloba	32.8 (19.9)	34.8 (24.7)		
	α-lipoic acid plus vitamin C	38.8 (24.7)	32.5 (25.5)		
	Papaverine hydrochloride plus vitamin E	28.0 (23.8)	30.4 (25)		
Henry et al.[24]	Hearing aid and tinnitus therapy device	52.6	47.5		
Mahendru et al.[25]	Caroverine	60.73 ± 10.54	19.93 ± 15.28		
	Betahistine	52.00 ± 11.20	33.87 ± 12.51		
Coelho et al.[26]	Zinc	22.03 (22′)	23.7 (18.7)		
	Sound therapy		39·27 (22·60)		49·32 (18·49)
Cima et al.[29]	Usual care		38·65 (23·19)		48·78 (19·23)
	Ozone	48	42		
Sönmez et al.[30]	Betahistine	49	39		
Kreuzer et al.[31]	Cognitive therapy	40.9 ± 21.7	27.3 ± 19.9	34.6 ± 16.7	26.5 ± 16.3
McNeill et al.[32]	Hearing aid			49.02 (SD 20.90)	34.08 (SD 17.48)
Bovo et al.[34]	Cochlear implantation	45.88 (24.91	32.33 (25.34		
Fukuda et al.[37]	Tinnitus retraining therapy	80 18.4	60		
Ariizumi et al.[38]	Tinnitus retraining therapy with a sound generator	44			

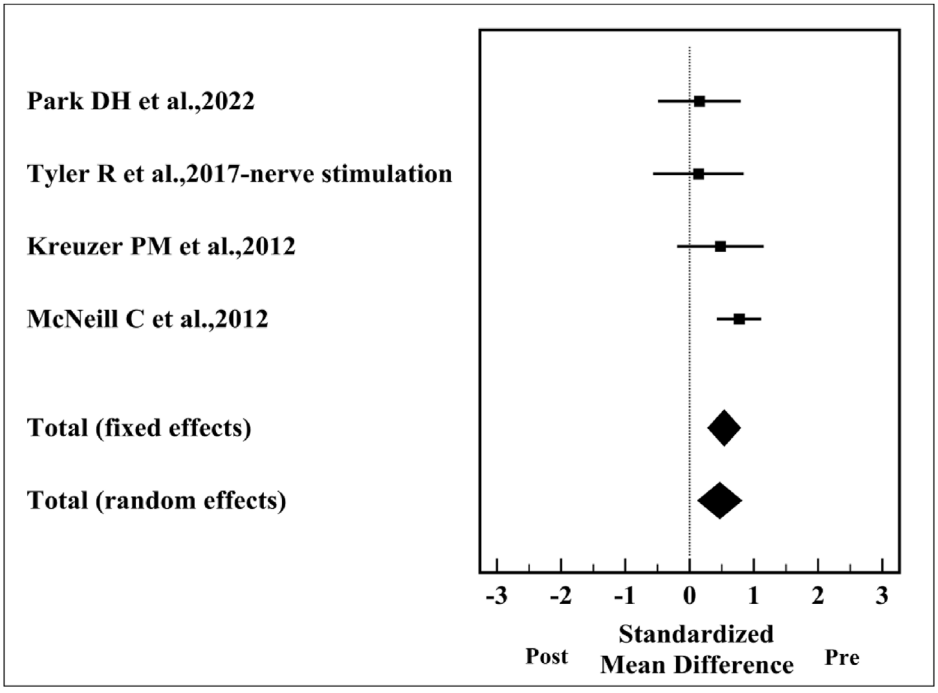

Fig. 1. Forest plot for tinnitus questionnaire.

variations between pretreatment and posttreatment regarding tinnitus questionnaire ($P > 0.05$). The best improvement in tinnitus questionnaire was reported by McNeill et al.[32] who used hearing aid in their treatment (Table 4).

Improvement founded in 383 cases, partial improvement in 87 cases and 79 cases shows no improvement (Table 5).

Twenty studies assessing improvement shows significant heterogenecity between studies with event rate 49.3 %.

Table 4. Tinnitus improvement.

References	Treatment	Tinnitus outcome	Improvement	Partial improvement	No improvement
Beukes et al.[7]	Cognitive therapy		40		
Kutyba et al.[8]	Sound therapy		20	23	1
Spencer et al.[9]	Bimodal auditory and electrical stimulation		6		5
Beukes et al.[7]	Cognitive therapy				
Boecking et al.[10]	Hearing aid				
Wang et al.[11]	Sound therapy				
Haines et al.[12]	Hearing aids		41		1
Park et al.[13]	Virtual reality				
Maxwell et al.[14]	OTO-313				
Ketterer et al.[15]	Hearing rehabilitation		53		
Kuzucu and Karaca[16]	Acupuncture				
Hall et al.[17]	AUT00063				
Godbehere et al.[18]	Transcranial magnetic stimulation				
Godbehere et al.[18]	Transcranial magnetic stimulation		5	15	
Lee et al.[20]	Intratympanic dexamethasone				
Hong et al.[21]	Nitrous oxide		1		19
Tyler et al.[22]	Nerve stimulation		8		
Coelho et al.[26]	Zinc		11		
Philippot et al.[27]	Cognitive therapy				
Sharma et al.[28]	Acamprosate Sound therapy		11	21	5
Cima et al.[29]	Usual care Ozone		6		

(*continued on next page*)

Table 4. (continued)

References	Treatment	Tinnitus outcome	Improvement	Partial improvement	No improvement
Sönmez et al.[30]	Betahistine		3		
Kreuzer et al.[31]	Cognitive therapy		14		
McNeill et al.[32]	Hearing aid		26	28	16
Dehkordi et al.[33]	Gabapentin		20		
Bovo et al.[34]	Cochlear implantation		13		
Sziklai et al.[35]	Dopamine agonist pramipexole		7		
Hurtuk et al.[36]	Melatonin		35		
Fukuda et al.[37]	Tinnitus retraining therapy		3		
Ariizumi et al.[38]	Tinnitus retraining therapy with a sound generator		60		32

Table 5. Meta-analysis for improvement.

References	Treatment	Total number	Event	Event rate (%) (proportion)	95 % confidence interval of rate (%)
Beukes et al.[7]	Cognitive therapy	79	40	50.6	39.141–62.076
Kutyba et al.[8]	Sound therapy	44	20	45.5	30.391–61.153
Spencer et al.[9]	Bimodal auditory and electrical stimulation	29	6	20.7	7.994–39.725
Haines et al.[12]	Hearing aids	42	41	97.6	87.434–99.940
Ketterer et al.[15]	Hearing rehabilitation	53	53	100.0	93.277–100.0
Godbehere et al.[18]	Transcranial magnetic stimulation	20	5	25.0	8.657–49.105
Hong et al.[21]	Nitrous oxide	20	1	5.0	0.127–24.873
Tyler et al.[22]	Nerve stimulation	16	8	50.0	24.651–75.349
Coelho et al.[26]	Zinc	58	11	19.0	9.866–31.405
Sharma et al.[28]	Acamprosate sound therapy	40	11	27.5	14.601–43.888
Cima et al.[29]	Usual care ozone	27	6	22.2	8.622–42.258
Sönmez et al.[30]	Betahistine	26	3	11.5	2.446–30.154
Kreuzer et al.[31]	Cognitive therapy	18	14	77.8	52.363–93.591
McNeill et al.[32]	Hearing aid	70	26	37.1	25.887–49.523
Dehkordi et al.[33]	Gabapentin	40	20	50.0	33.802–66.198
Bovo et al.[34]	Cochlear implantation	41	13	31.7	18.085–48.087
Sziklai et al.[35]	Dopamine agonist pramipexole	20	7	35.0	15.391–59.219
Hurtuk et al.[36]	Melatonin	61	35	57.4	44.055–69.958
Fukuda et al.[37]	Tinnitus retraining therapy	6	3	50.0	11.812–88.188
Ariizumi et al.[38]	Tinnitus retraining therapy with a sound generator	92	60	65.2	54.574–74.851
Total (fixed effects)				49.3	45.821–52.768
Total (random effects)				45.3	31.790–59.077
		Test for heterogeneity			
Q		301.5796			
DF		19			
Significance level		<0.0001*			
I^2 (inconsistency)		93.70 %			
95 % CI for I^2		91.55–95.30			

CI, confidence interval (LL: lower limit–UL: upper limit); I^2, observed variance for heterogeneity; *Q*, total variance for heterogeneity.

4. Discussion

Tinnitus disorder is described as 'tinnitus plus tinnitus-associated emotional distress and functional disability,' whereas tinnitus is the conscious knowledge of a tone and/or noisy sound for which there is no discernible matching external acoustic source.[2]

Regarding disease characteristics, it was found that mean tinnitus duration was 88.7 months and bilateral tinnitus founded in 310 cases, mean initial tinnitus frequency was 4840.8.

The current meta-analysis showed that the most common treatment used were nonpharmacologic treatments including cognitive therapy, hearing aid, sound therapy, bimodal auditory and electrical stimulation, virtual reality, hearing rehabilitation, acupuncture, transcranial magnetic stimulation, nerve stimulation, and cochlear implantation followed by pharmacologic treatments including OTO-313, AUT00063, intratympanic dexamethasone, nitrous oxide, α-lipoic acid plus vitamin C, papaverine hydrochloride plus vitamin E, caroverine,

betahistine, zinc, acamprosate, usual care, ozone, betahistine, gabapentin, dopamine agonist pramipexole, melatonin, and Ginkgo biloba.

From the previous results it was revealed that cognitive therapy, sound therapy and cochlear implantation therapy seems to be the best effective therapies for tinnitus.

This was supported by the systematic review and meta-analysis by Landry et al.[39] who comprised 12 RCTs that included 1144 patients and compared psychological therapies to waitlist controls; these studies showed that cognitive and/or behavioral therapies was an effective treatment for tinnitus. Although statistically insignificant, guided self-administered cognitive and/or behavioral therapies had the greatest chance of being rated first in improving tinnitus health-related quality of life (75 %), depression (83 %), and anxiety (87 %). Also, the systematic review and meta-analysis by Liu et al.[40] included 22 studies and revealed that compared with medicine, educational advice, and no therapy, sound stimulation alone outperformed them all. Combination therapy, such as sound stimulation plus educational advice and sound stimulation plus medication therapy, considerably outperformed solo therapies in terms of reducing tinnitus. Wang et al.[41] showed that there are several types of sound therapy, and the majority of them have beneficial therapeutic outcomes. Patients with more severe initial tinnitus react better to sound treatment, and the effects of tailored sound therapy are often superior to those of noncustomized sound therapy.

Moreover, the meta-analysis by Jiang et al.[42] enrolled 16 articles (1594 patients) concluded that sound therapy may greatly increase the clinical effectiveness of tinnitus treatment and lessen symptoms in tinnitus patients when compared to standard medical care.

Our study showed that there was improvement in 383 cases, partial improvement in 87 cases and 79 cases shows no improvement.

Improvement was reported by 20 studies[7–9,12,15,19,21,22,26,28–38] and the pooled analysis showed that there was significant heterogeneity between studies with event rate 49.3 %. The lowest improvement rate was reported by Hong et al.[21] who used nitrous oxide therapy and reported that the total improvement was achieved in 5 % but this study included small sample size. Hundred percent improvement was reported by Ketterer et al.[15] who used hearing rehabilitation as a treatment modality.

In the current meta-analysis, we found seven studies[8,9,12,21,28,32,38] assessed no improvement with pooled rate of 21.7 % with significant heterogeneity. The highest rate of no improvement was reported by Hong et al.[21] who used nitrous oxide therapy and reported that the no improvement was found in 95 % patients but this study was limited by small sample size. The least rate of no improvement was reported by Haines et al.[12] study in which they used hearing aids with no improvement rate of 2.4 %.

A coherence review by Meng et al.[43] stated that there was no pharmacological treatment for tinnitus with long-term effect, but this review based on only five trials comprising of 233 participants.

Due to the variety of outcome assessment tools, we faced a big obstacle on the comparison of the outcome of difference treatment modalities. The reliability and repeatability of these measurements is another drawback of the current tools for evaluating the impact of tinnitus. Self-report measures of tinnitus have a risk of variability because they provide a fleeting snapshot while the experience of tinnitus changes over time and in different contexts. Ecological Momentary Assessment is one method to lessen that[6,44] a method that is also used in trials for pain, tension, and anxiety.[45] Evidence for the use of Ecological Momentary Assessment in tinnitus studies is now emerging.

4.1. Conclusion

Nonpharmacological treatments of tinnitus seem to be associated with better outcome and less complications in comparison to the use of pharmacological therapies. It would be important to support primary research using rigorous methodologies onto acoustic technologies and stimulation treatments, particularly those of smaller damage, given the absence of high-quality effectiveness and safety data.

Consent statement

It was approved by faculty.

Declaration of competing interest

There are no conflicts of interest.

References

1. Langguth B, Kreuzer PM, Kleinjung T, De Ridder D. Tinnitus: causes and clinical management. *Lancet Neurol*. 2013;12:920–930.
2. Cuesta M, Garzón C, Cobo P. Efficacy of sound therapy for tinnitus using an enriched acoustic environment with hearing-loss matched broadband noise. *Brain Sci*. 2022;12:82.
3. Zarenoe R. *Tinnitus in Patients with Sensorineural Hearing Loss: Management, Quality of Life and Treatment Strategies*. Sweden: Linköping University; 2016.
4. Kikidis D, Vassou E, Schlee W, et al. Methodological aspects of randomized controlled trials for tinnitus: a systematic review and how a decision support system could overcome barriers. *J Clin Med*. 2021;10:1737.

5. Hesse G. Evidence and evidence gaps in tinnitus therapy. *GMS Curr Top Otorhinolaryngol, Head Neck Surg*. 2016;15:15.
6. Probst T, Pryss RC, Langguth B, et al. Does tinnitus depend on time-of-day? An ecological momentary assessment study with the 'TrackYourTinnitus' application. *Front Aging Neurosci*. 2017;9:253.
7. Beukes EW, Andersson G, Fagelson M, Manchaiah V. Internet-based audiologist-guided cognitive behavioral therapy for tinnitus: randomized controlled trial. *J Med Internet Res*. 2022;24:e27584.
8. Kutyba JJ, Jędrzejczak WW, Gos E, Raj-Koziak D, Skarzynski PH. Chronic tinnitus and the positive effects of sound treatment via a smartphone app: mixed-design study. *JMIR mHealth uHealth*. 2022;10:e33543.
9. Spencer S, Mielczarek M, Olszewski J, et al. Effectiveness of bimodal auditory and electrical stimulation in patients with tinnitus: a feasibility study. *Front Neurosci*. 2022;16:971633.
10. Boecking B, Psatha S, Nyamaa A, et al. Hearing aid use time is causally influenced by psychological parameters in mildly distressed patients with chronic tinnitus and mild-to-moderate hearing loss. *J Clin Med*. 2022;11:5869.
11. Wang J, Ding J, Song J, Hu L, Cong N, Han Z. A prospective study of the effect of tinnitus sound matching degree on the efficacy of customized sound therapy in patients with chronic tinnitus. *ORL J Otorhinolaryngol Relat Spec*. 2022;84:229–237.
12. Haines RH, Hepburn T, Tan W, et al. Effectiveness and cost effectiveness of digital hearing aids in patients with tinnitus and hearing loss: a randomised feasibility trial (THE HUSH Trial). *Pilot Feasibil Stud*. 2022;8:1–16.
13. Park DH, Han SS, Han M, et al. A clinical trial of a patient-customized virtual reality intervention for tinnitus. *Sci Rep*. 2022;12:1–11.
14. Maxwell KS, Robinson JM, Hoffmann I, et al. Intratympanic administration of OTO-313 reduces tinnitus in patients with moderate to severe, persistent tinnitus: a phase 1/2 study. *Otol Neurotol*. 2021;42:e1625.
15. Ketterer MC, Knopke S, Häußler SM, et al. Asymmetric hearing loss and the benefit of cochlear implantation regarding speech perception, tinnitus burden and psychological comorbidities: a prospective follow-up study. *Eur Arch Oto-Rhino-Laryngol*. 2018;275:2683–2693.
16. Kuzucu I, Karaca O. Acupuncture treatment in patients with chronic subjective tinnitus: a prospective, randomized study. *Med Acupunct*. 2020;32:24–28.
17. Hall DA, Ray J, Watson J, et al. A balanced randomised placebo controlled blinded phase IIa multi-centre study to investigate the efficacy and safety of AUT00063 versus placebo in subjective tinnitus: the QUIET-1 trial. *Hear Res*. 2019; 377:153–166.
18. Godbehere J, Sandhu J, Evans A, et al. Treatment of tinnitus using theta burst based repetitive transcranial magnetic stimulation—a single blinded randomized control trial. *Otol Neurotol*. 2019;40:S38–S42.
19. Sahlsten H, Holm A, Rauhala E, et al. Neuronavigated versus non-navigated repetitive transcranial magnetic stimulation for chronic tinnitus: a randomized study. *Trends Hear*. 2019;23: 2331216518822198.
20. Lee HJ, Kim MB, Yoo SY, et al. Clinical effect of intratympanic dexamethasone injection in acute unilateral tinnitus: a prospective, placebo-controlled, multicenter study. *Laryngoscope*. 2018;128:184–188.
21. Hong HY, Karadaghy O, Kallogjeri D, et al. Effect of nitrous oxide as a treatment for subjective, idiopathic, nonpulsatile bothersome tinnitus: a randomized clinical trial. *JAMA Otolaryngol Head Neck Surg*. 2018;144:781–787.
22. Tyler R, Cacace A, Stocking C, et al. Vagus nerve stimulation paired with tones for the treatment of tinnitus: a prospective randomized double-blind controlled pilot study in humans. *Sci Rep*. 2017;7:1–11.
23. Polanski JF, Soares AD, Cruz OLDM. Antioxidant therapy in the elderly with tinnitus. *Braz J Otorhinolaryngol*. 2016;82: 269–274.
24. Henry JA, Frederick M, Sell S, Griest S, Abrams H. Validation of a novel combination hearing aid and tinnitus therapy device. *Ear Hear*. 2015;36:42–52.
25. Mahendru B, Kansal D, Sharma PK, Dogra SS. Comparison of the safety and efficacy of caroverine and betahistine in patients of subjective tinnitus. *Int J Basic Clin Pharmacol*. 2014;3: 1000.
26. Coelho C, Witt SA, Ji H, Hansen MR, Gantz B, Tyler R. Zinc to treat tinnitus in the elderly: a randomized placebo controlled crossover trial. *Otol Neurotol*. 2013;34:1146–1154.
27. Philippot P, Nef F, Clauw L, de Romrée M, Segal Z. A randomized controlled trial of mindfulness-based cognitive therapy for treating tinnitus. *Clin Psychol Psychother*. 2012;19: 411–419.
28. Sharma DK, Kaur S, Singh J, Kaur I. Role of acamprosate in sensorineural tinnitus. *Indian J Pharmacol*. 2012;44:93.
29. Cima RF, Maes IH, Joore MA, et al. Specialised treatment based on cognitive behaviour therapy versus usual care for tinnitus: a randomised controlled trial. *Lancet*. 2012;379: 1951–1959.
30. Sönmez O, Külahlõ İ, Vural A, Şahin Mİ, Aydõn M. The evaluation of ozone and betahistine in the treatment of tinnitus. *Eur Arch Oto-Rhino-Laryngol*. 2013;270:1999–2006.
31. Kreuzer PM, Goetz M, Holl M, et al. Mindfulness-and body-psychotherapy-based group treatment of chronic tinnitus: a randomized controlled pilot study. *BMC Compl Alternative Med*. 2012;12:1–8.
32. McNeill C, Távora-Vieira D, Alnafjan F, Searchfield GD, Welch D. Tinnitus pitch, masking, and the effectiveness of hearing aids for tinnitus therapy. *Int J Audiol*. 2012;51:914–919.
33. Dehkordi MA, Abolbashari S, Taheri R, Einolghozati S. Efficacy of gabapentin on subjective idiopathic tinnitus: a randomized, double-blind, placebo-controlled trial. *Ear Nose Throat J*. 2011;90:150–158.
34. Bovo R, Ciorba A, Martini A. Tinnitus and cochlear implants. *Auris Nasus Larynx*. 2011;38:14–20.
35. Sziklai I, Szilvássy J, Szilvássy Z. Tinnitus control by dopamine agonist pramipexole in presbycusis patients: a randomized, placebo-controlled, double-blind study. *Laryngoscope*. 2011;121:888–893.
36. Hurtuk A, Dome C, Holloman CH, et al. Melatonin: can it stop the ringing? *Ann Otol Rhinol Laryngol*. 2011;120:433–440.
37. Fukuda S, Miyashita T, Inamoto R, Mori N. Tinnitus retraining therapy using portable music players. *Auris Nasus Larynx*. 2011;38:692–696.
38. Ariizumi Y, Hatanaka A, Kitamura K. Clinical prognostic factors for tinnitus retraining therapy with a sound generator in tinnitus patients. *J Med Dent Sci*. 2010;57:45–53.
39. Landry EC, Sandoval XCR, Simeone CN, Tidball G, Lea J, Westerberg BD. Systematic review and network meta-analysis of cognitive and/or behavioral therapies (CBT) for tinnitus. *Otol Neurotol*. 2020;41:153–166.
40. Liu H, Zhang J, Yang S, et al. Efficacy of sound therapy interventions for tinnitus management: a protocol for systematic review and network meta-analysis. *Medicine*. 2021;100:41.
41. Wang H, Tang D, Wu Y, Zhou L, Sun S. The state of the art of sound therapy for subjective tinnitus in adults. *Therap Adv Chronic Dis*. 2020;11:2040622320956426.
42. Jiang Y, Hua Q, Yang K, et al. The efficacy of sound therapy and conventional medical treatment in the treatment of chronic tinnitus: a meta-analysis. *J Audiol Speech Pathol*. 2017; 6:651–655.
43. Meng Z, Liu S, Zheng Y, Phillips JS. Repetitive transcranial magnetic stimulation for tinnitus. *Cochrane Database Syst Rev*. 2011;10:547.
44. Goldberg RL, Piccirillo ML, Nicklaus J, et al. Evaluation of ecological momentary assessment for tinnitus severity. *JAMA Otolaryngol Head Neck Surg*. 2017;143:700–706.
45. Yang YS, Ryu GW, Choi M. Methodological strategies for ecological momentary assessment to evaluate mood and stress in adult patients using mobile phones: systematic review. *JMIR mHealth uHealth*. 2019;7:e11215.