

# Alternative Treatments of Tinnitus: Alternative Medicine



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## KEYWORDS

• Tinnitus • Alternative medicine • Treatment

## KEY POINTS

- Trials investigating acupuncture, herbs, vitamins, trace elements, melatonin, hypnosis, and others continue to present contradictory findings on the benefit in tinnitus treatment, yet many exhibit positive results.
- Because of the scarcity of well-designed studies and subsequent inconclusiveness of literature reviews, physicians remain skeptic of alternative treatment options that have been used in Eastern medicine for centuries.
- Based on study results, alternative treatments discussed should undergo trial periods for each tinnitus patient, as a treatment may not work for every patient alike.

## INTRODUCTION

Tinnitus—the perception of sound in the ear or head in the absence of an external stimulus—is a symptom that approximately 10% to 15% of the world population suffer chronically and a burden to a patient's quality of life for which there is currently no universal cure.<sup>1</sup> Although alternative treatment options for tinnitus have not been recommended by the clinical practice guidelines published by the American Academy of Otolaryngology—Head and Neck Surgery,<sup>2</sup> many patients are dissatisfied with the results achieved by conventional medicine and open to a complementary-integrative

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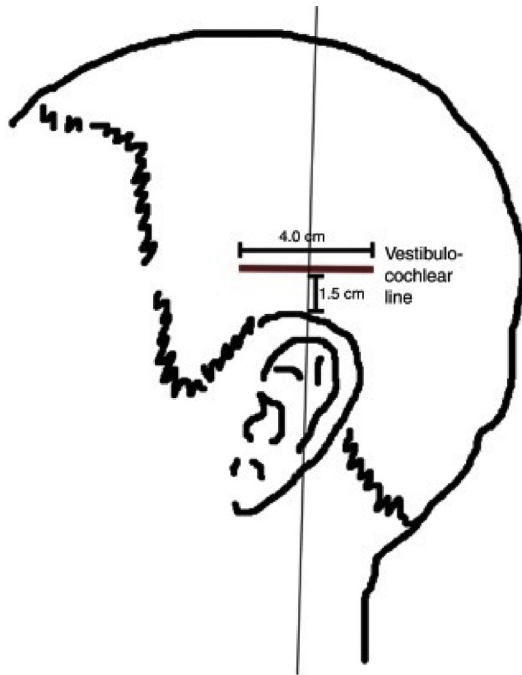
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medical approach. In fact, some treatments such as acupuncture and herbal medicines have been used in Eastern cultures for centuries. Because of the lack of well-designed studies, however, Western physicians' skepticism persists. Yet it is important to acknowledge that no 2 patients are alike and what might benefit one person might not be of help for another. Instead of saying "you will have to live with it," we should listen to our patients and their preferences; we should consider all available options until we find a treatment that may be of benefit for that unique patient. In terms of alternative treatments, the following topics have yielded research, which, although not conclusive, can help provide viable treatment options that are noninvasive and generally speaking well tolerated.

## ACUPUNCTURE

Acupuncture is a deeply seeded component of traditional Chinese medicine and has been used with the goal to rebalance action potentials of neurophysiological systems for centuries.<sup>3,4</sup> As such, acupuncture has been used in the treatment of tinnitus to influence the olivocochlear nucleus.<sup>5</sup> Although multiple studies have evaluated the effectiveness of acupuncture on tinnitus symptoms, the conclusions drawn by systematic reviews remain uncertain. Reviews cite the methodological flaws, sample size, and the bias of Chinese studies toward positive results as main critiques to decrease the studies' validity<sup>3,4</sup>; the differences concerning the number of treatment sessions and placement of acupoints and their effectiveness, unfortunately, were discussed to a lesser degree and deserve greater attention in future reviews. Studies conducting a single treatment session were less likely to report a statistically significant effect<sup>6,7</sup> than studies holding at least 10 acupuncture sessions.<sup>8-10</sup> This was confirmed by Lin and colleagues,<sup>11</sup> who analyzed various factors pertaining to patient demographics, tinnitus characteristics, and treatment and concluded that only the combination of acupoints and number of treatment sessions was statistically related to a better treatment outcome. Based on this review, a minimum of 17 to 24 acupuncture sessions should be the recommendation before determining if acupuncture is a valid treatment option for a particular patient. This being said, in the Center for Integrative Medicine started at Henry Ford Health System by MDS, they would provide 6 treatments over a 6-week time period and if the patient did not experience any improvement they were advised to discontinue. Specific acupoints seem to be an important component in improved tinnitus control. One of these points was shown to be along the vestibulocochlear line as laid out in Chinese scalp acupuncture (**Fig. 1**).<sup>8</sup> The study showed statistically significant improvements using validated tinnitus measures, such as visual analogue scale (VAS) and Tinnitus Handicap Inventory (THI) when compared with baseline and the control group.<sup>8</sup> Although the VAS assesses a patient's tinnitus severity based on pictures, the THI evaluates a patient's quality-of-life handicap through a series of questions regarding the patient's reactions to tinnitus in terms of emotional (eg, anger), functional (eg, difficulties concentrating), and catastrophic (eg, feelings of hopelessness) reactions.<sup>12</sup> No study reported any adverse effects of the treatment modality.

Furthermore, acupuncture has been evaluated for the possibility of affecting cochlear blood flow, which has been implicated as one of the etiologic contributors of tinnitus. Using infrared thermography, Cai and colleagues<sup>7</sup> suggested that a single acupuncture session could stabilize the capillary cochlear blood flow bilaterally, even if acupuncture was only applied on one side. Similarly, assessing cochlear neuronal activity using otoacoustic emissions (OAE) exhibited that acupuncture significantly increased the amplitude of OAE in both the needled and unneedled ears as compared



**Fig. 1.** Vestibulocochlear line according to Chinese scalp acupuncture. Effectiveness of acupuncture therapy as treatment of tinnitus: a randomized controlled trial. (From Doi MY, Tano SS, Schultz AR, Borges R, Marchiori LL. Effectiveness of acupuncture therapy as-treatment for tinnitus: a randomized controlled trial. *Braz J Otorhinolaryngol.* 2016;82(4):458-465. <https://doi.org/10.1016/j.bjorl.2016.04.002>; with permission.)

with the control group, suggesting an effect of acupuncture on cochlear hair cells.<sup>13</sup> Unfortunately, most studies did not identify the form of tinnitus being treated, which may inadvertently affect the rate of success. Nonetheless, acupuncture seems to be a valid treatment option to offer patients suffering for tinnitus, given a sufficient number of treatment sessions.

## HERBS

### *Ginkgo Biloba*

The leaves of the ancient Chinese *Ginkgo biloba* tree have been used as health-enhancing remedies for thousands of years. Today, the herbal supplement is among the 5 most popular medications in the Western world and even licensed to treat cerebrovascular insufficiency in Germany.<sup>14,15</sup> Based on the German Commission E monograph, purified *Ginkgo* preparations, called EGb761, must contain certain percentages of flavonoids, proanthocyanidins, and terpenoids.<sup>15</sup> In the treatment of tinnitus, *Ginkgo biloba* has gained appreciable traction through a substantial number of studies assessing its efficacy and safety. Although many findings contradict each other, systematic reviews generally consider *Ginkgo* as a potential treatment option.<sup>16,17</sup>

Studies failing to detect superiority of *Ginkgo biloba*, as compared with a placebo group, may have used methodologically different protocols from studies concluding statistical significance. Considering that the recommended dosage of *Ginkgo* for

tinnitus, based on German Commission E guidelines, is 240 mg twice daily,<sup>18</sup> it is not surprising that trials using 50 mg three times daily or 120 mg once daily do not conclude the herb's effectiveness over the placebo.<sup>14,19</sup> A review determined that in studies demonstrating significance, the efficacy of Ginkgo over placebo was related to the use of the standardized EGb761. Specifically, studies using EGb761 showed benefit versus studies using a nonstandardized extract.<sup>20</sup> Boetticher concluded standardized Ginkgo EGb761 to be an evidence-based treatment option for tinnitus.<sup>20</sup>

Another treatment option using Ginkgo biloba showing efficacy in the treatment of tinnitus consisted of a Ginkgo infusion pretreatment, followed by 12 weeks of oral Ginkgo.<sup>21</sup> This protocol displayed reduction in hearing loss following the infusion therapy, as well as an additive benefit of oral therapy on tinnitus intensity at the end of the trial.<sup>21</sup> One potential flaw of studies evaluating Ginkgo efficacy seems to be the lack of use of validated assessment measures, such as the VAS and THI,<sup>22</sup> and the only one that did, chose suboptimal dosages.<sup>19</sup> All studies, however, assessed the most important component of treatment success—the patients' perception of their own tinnitus. Based on this evidence, Ginkgo biloba ought to be in the treatment repertoire of a physician's approach to patients with tinnitus.

### **Other Herbs**

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Besides Ginkgo, more recent studies began assessing the efficacy of other herbal supplements, including red ginseng and Gushen Pian. Korean red ginseng, much like Ginkgo, has been used in the Eastern world for more than 2000 years and is known for antioxidative property as well as for showing potential antiapoptotic properties in an experimental model for cisplatinotoxicity.<sup>23,24</sup> Kim and colleagues<sup>23</sup> compared 3000 mg daily of red ginseng with 1500 mg of red ginseng with 80 mg twice daily of Ginkgo, assessing patients after 4 weeks of treatment using THI, VAS, and short-form 36 (SF-36). Ginkgo and low dose of red ginseng (1500 mg) did not demonstrate any improvement in THI, VAS, and SF-36 in this study. Patients given high-dose red ginseng had statistically significant improvement in their THI score compared with the Ginkgo group.

Gushen Pian, on the other hand, is a newly developed Chinese herbal medicine, which is being investigated for the treatment of sensorineural deafness and tinnitus.<sup>25</sup> Gushen Pian is a combination medicine consisting of *Drynaria fortunei*, Danshen, glycyrrhiza, and Calcined Ci Shi, which are said to “ventilate the ear”—or increase its blood circulation—increase overall circulation, balance herbal attributes, and decrease liver overactivity and strengthen bone, respectively.<sup>25</sup> *Drynariafortunei* by itself has also been shown to have protective properties against streptomycin-induced ototoxicity.<sup>26</sup> These herbs and the combination thereof are, according to traditional Chinese medicine, believed to alleviate tinnitus and sensorineural deafness by improving splenonephric perfusion, as it is believed that symptoms such as tinnitus are signals from the body indicating that the kidney's energy needs more support (the kidney is said to regulate the ear).<sup>25,26</sup> In its first trial, Gushen Pian displayed statistically significant therapeutic outcomes over placebo after 4 weeks of treatment in terms of tinnitus, dizziness, aural fullness, insomnia, and pure tone audiometry.<sup>25</sup> Thus, even though there is a long way to go to determine whether herbal medicines such as red ginseng and Gushen Pian could contribute meaningfully to the management of tinnitus, their initial results seem promising.

## **TRACE ELEMENTS**

### **Zinc**

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Zinc can be found throughout the entire human body and participates in the function of more than 300 enzymes as well as several essential growth and maturation

processes.<sup>27–29</sup> Animal studies have shown that the inner ear has the highest zinc content in a guinea pig,<sup>30</sup> which leads to the potential implication of inadequate levels of zinc in functional otologic disorders, such as tinnitus. Although studies have demonstrated a correlation between low zinc levels and tinnitus, the effects of zinc supplementation on tinnitus in general remain an item of debate.<sup>31,32</sup> A Cochrane review examining 3 studies found no improvements in tinnitus after supplementing with 50 to 66 mg zinc for 8 to 16 weeks.<sup>33</sup> Studies now, however, seem to be recognizing that treatments with zinc might have greater impacts on specific patient groups. First, zinc levels seem to decrease as age increases, potentially due to decreased oral intake and intestinal absorption, playing into the positive correlation of tinnitus and age.<sup>34,35</sup> In these older patients specifically, Yetiser and colleagues<sup>28</sup> reported 82% of elder patients indicating a better score following zinc supplementation for 8 weeks. Second, a large population including 2225 participants, among which 460 people suffered from tinnitus, concluded that serum zinc levels were only significantly lower in patients with extreme tinnitus.<sup>36</sup> Similarly, the fact that tinnitus loudness was significantly higher in patients with hypozincemia was determined by 2 additional studies.<sup>30,34</sup> Furthermore, Ochi and colleagues<sup>30</sup> found that particularly patients with tinnitus and normal hearing had significantly lower levels of zinc than healthy controls, as compared with patients with tinnitus and hearing loss who showed no significant difference in zinc levels to healthy controls. This is not to say that tinnitus patients with hearing loss might not benefit from zinc supplementation. On the contrary, 85% of patients participating in a trial on noise-induced hearing loss (NIHL)-associated tinnitus reported a statistically significant improvement in THI—emotional and catastrophic, but not functional—scores following 2 months of 40 mg zinc daily.<sup>37</sup> Although zinc supplementation was well tolerated in these studies, it needs to be noted that at a dose of 200 mg per day acute zinc toxicity may occur. Overall, despite an ongoing debate concerning the efficacy of zinc supplementation, studies are reporting some beneficial implementations of zinc, making a trial of this treatment option with appropriate dosing worthwhile.

### **Other Elements**

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Although zinc is the most commonly discussed trace element in terms of tinnitus cause and treatment, some investigators are turning their attention to other elements as well. Copper and zinc frequently act together as an enzyme called copper-zinc superoxide dismutase, which might lead to the consideration that in zinc-requiring processes, copper may be implicated as well.<sup>38</sup> Yasar and colleagues<sup>38</sup> measured the serum and hair levels of copper, zinc, and lead of 80 tinnitus patients compared with controls. Only serum copper was statistically significantly lower in the tinnitus group, with no statistically significant differences in the zinc or lead groups compared with controls. This could suggest another trace element that may be implicated in tinnitus. Unfortunately, copper and zinc compete during intestinal absorption, with the sole supplementation of one leading to a potential deficit of the other. Anecdotally, calcium and manganese may also reduce the symptoms of tinnitus after several months of supplementation.<sup>27</sup>

## **ANTIOXIDANT SUPPLEMENTS**

### **B Vitamins**

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B-complex vitamins are necessary for the proper functioning of a healthy central nervous system, such as proper methylation relying on vitamin B12. Deficiencies in B vitamins may, therefore, lead to neuronal dysfunctions, followed by cochlear

dysfunction and finally hearing loss and tinnitus.<sup>27,39</sup> A deficiency of vitamin B12 could furthermore result in an increase of oxygen and nitrogen free radicals due to the B12-dependent activity of methionine synthase.<sup>40</sup> Oxygen-free radicals, in turn, have been connected to age-related and noise-induced hearing loss through the loss of mitochondrial membrane potentials and cochlear hair cells.<sup>41</sup> B vitamins are thus a target of research in the potential treatment of tinnitus.

Shemesh and colleagues<sup>42</sup> first reported a significantly higher prevalence (47%) of vitamin B12 deficiency (<250 pg/mL) in patients with NIHL and tinnitus than in patients with NIHL alone or in controls, with some patients showing tinnitus symptom improvement following replacement therapy. Another study, however, found no significant difference in the prevalence of B12 deficiency (<180 pg/mL) between tinnitus patients and healthy controls, and although 8 patients reported some improvement after treatment, the difference was not significant.<sup>43</sup> In a more recent randomized, double-blind study, patients with chronic tinnitus were injected with 2500 mcg vitamin B12 weekly for 6 weeks. B12 deficiency was considered at less than 250 pg/mL,<sup>39</sup> and the prevalence of deficiency was similar to that found in Shemesh and colleagues' study (42.5%). Following vitamin B12 injections, initial B12-deficient tinnitus patients showed significant improvements in VAS and tinnitus severity index scores.<sup>39</sup> Thus, vitamin B12 may play a therapeutic role in patients with B12 deficiency, given a cutoff level of less than 250 pg/mL.

In addition, a Korean population survey of 1435 participants with tinnitus compared with 6186 without reported a significantly reduced intake and independent association of vitamin B2 with tinnitus.<sup>44</sup> Reduced intake of vitamin B3 was only associated with tinnitus annoyance in patients older than 66 years.<sup>44</sup> This contributes to the possibility that multiple B vitamins could be beneficial in the treatment of tinnitus. As such, a study administering vitamin B complex found a significant increase in OAE in patients with tinnitus.<sup>45</sup>

### **Other Antioxidants**

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As the thought of reactive oxygen species contributing to tinnitus continues, Ekinci and Kamaska actually determined that the total oxidant status and mean oxidative stress index were significantly higher in a group of patients with tinnitus compared with controls, supporting the therapeutic use of antioxidants.<sup>46</sup> Besides B vitamins, oral antioxidant therapy consisting of glycerophosphorylcholine, glycerophosphorylethanolamine,  $\beta$ -carotene, and vitamins C and E for 18 weeks showed a significant improvement in VAS and tinnitus loudness in patients with idiopathic tinnitus.<sup>47</sup> A more selective antioxidant therapy for 6 months, consisting of either  $\alpha$ -lipoic acid and vitamin C or papaverine hydrochloride and vitamin E, however, resulted in no appreciable benefit for patients complaining of tinnitus associated with sensorineural hearing loss.<sup>48</sup> Lastly, the antioxidant coenzyme Q10 (CoQ10), which influences mitochondrial electron transport, has also been associated with a potential impact on tinnitus. A study showed that in patients with an initially low serum level of CoQ10, 12 weeks of 300 mg CoQ10 daily significantly improved their Tinnitus Questionnaire (TQ) and SF-36 scores.<sup>49</sup> Thus, although there is paucity of studies on the effect of various antioxidants on tinnitus, some patients may benefit from trial of supplementation with certain antioxidants.

### **CONSIDERATIONS OF TREATMENT COMPOSITION**

Before administering the various herbs and supplements mentioned earlier, however, physicians need to consider differences in preparation of each treatment, so that

patients can experience the greatest benefit possible. As such, some brands of Ginkgo supplements are, despite standardized compositions of 24% Ginkgo flavones and 6% terpenes, not highly purified and, as discussed, will not have the desired effect. Furthermore, minerals are most commonly supplied in their sulfate and carbonate form, which have significantly reduced absorption compared with minerals that are chelated or linked to an amino acid. Thus, zinc sulfate is significantly less absorbed than zinc monomethionate, and calcium carbonate is much less well absorbed compared with calcium glycinate. Similarly, the ubiquinone type of CoQ10 is much less absorbed than its ubiquinol type. Thus, it is important to remember that not all treatment preparations are created equal.

## MELATONIN

Melatonin involved in sleep-wake cycles and produced by the pineal gland has been thought to favorably influence tinnitus through vasodilatory action by decreasing sympathetic tone to preserve labyrinthine perfusion, relaxation of muscular tone, antidepressive effects, and antioxidant effects.<sup>50</sup> In addition, melatonin may have a protective effect on vestibular hair cell loss following aminoglycoside and cisplatin therapy in animal models.<sup>51</sup> Analogous to results concerning zinc and vitamin B12, serum levels of melatonin may be significantly lower among elders suffering from tinnitus compared with those who are not.<sup>52</sup> A double-blind, placebo-controlled crossover study found that after 30 days of 3 mg melatonin daily with a 7-day washout period, the THI did not differ significantly from the placebo posttreatment scores.<sup>53</sup> Tinnitus-associated sleep disturbances, however, decreased significantly by nearly 50%.<sup>53</sup> A similar trial with the same treatment plan but a 30-day washout period, on the other hand, determined a significantly greater improvement in tinnitus matching and self-rated tinnitus scores following melatonin compared with placebo.<sup>54</sup> Thus, the shorter washout period may have influenced the results of the treatment crossover in the study by Rosenberg and colleagues.

Positive effects experienced by melatonin may actually last beyond its treatment duration as after 4 weeks of therapy with 3 mg melatonin daily the significant decrease in THI and Pittsburgh Sleep Quality Index was still present at 4 weeks posttreatment cessation.<sup>55</sup> Melatonin may even outperform guideline-recommended antidepressants,<sup>35</sup> as demonstrated by Abtahi and colleagues. Following 3 months of 3 mg melatonin daily compared with 50 mg sertraline daily, THI scores declined significantly for both groups; THI scores for melatonin, however, decreased significantly more than for sertraline.<sup>56</sup> Whether melatonin works for everyone, however, is questionable. Based on the results by Hurtuk and colleagues,<sup>54</sup> melatonin may be most efficacious in patients who are male, patients with severe bilateral tinnitus, patients with previous noise exposure, patients without a history of depression, and patients who have not tried any previous tinnitus treatment. Despite this plethora of positive results, systematic reviews cannot confirm the clinical efficiency of melatonin due to methodological weaknesses and investigators' potential exaggeration of treatment effect but recognize melatonin's potential usefulness in tinnitus and associated sleep disturbances depending on the patient.<sup>57,58</sup> No adverse effects of melatonin at a dose of 3 mg per day have been reported to date with the exception of an increase in vivid dreams or nightmares.

## HYPNOSIS AND BIOFEEDBACK

Hypnosis and biofeedback, similarly to cognitive-behavioral therapy (CBT), aim at giving patients the power to control their conscious mind to bring about change. In the



treatment of tinnitus, CBT is the only therapy recommended by the American Academy guideline, with hypnosis and biofeedback being commonly overlooked. During hypnosis and self-hypnosis, patients are guided to a state of deep relaxation while focusing their minds to allow increased control over their thoughts and behaviors.<sup>59</sup> Studies examining the effects of hypnosis on patients with tinnitus have been scarce since the late 1900s but generally report some benefit. Ericksonian hypnosis (EH) is the most commonly used technique, which begins with an exploration of the impact of tinnitus of the patient's life, followed by sessions focusing of relaxation and metal imagery.<sup>59,60</sup> The largest of such studies included 393 participants undergoing a 28-day course of inpatient therapy, evaluation by TQ and SF-36, and a 12-month follow-up.<sup>61</sup> Results were compared with controls on a waiting list. TQ scores decreased in nearly 90% of patients with subacute and chronic tinnitus, with the mean score decreasing significantly.<sup>61</sup> Other trials, using an outpatient approach, achieved comparable results after only 3 to 10 sessions of EH with statistically significant improvements in THI.<sup>59,60</sup> Although Maudoux and colleagues<sup>60</sup> invested additional sessions to teach patients self-hypnosis, only 3 sessions were necessary to attain improvements still present at 6-month follow-up.<sup>59</sup> Distinguishing between particular types of tinnitus, Mason and Rogerson found that although hypnosis has positive impacts in patients without hearing loss, patients with hearing loss did not benefit from therapy.<sup>62</sup> Although in all studies symptoms of tinnitus continued, the quality of life of patients improved dramatically. Thus, suggesting hypnosis as a noninvasive therapy, while potentially including instructions on self-hypnosis, may be a worthwhile treatment modality that could continue long beyond the actual treatment sessions. Because of the paucity and lack of comparability of data, however, no definitive statements can be made by current systematic reviews.<sup>63</sup>

Biofeedback includes learning to control autonomous physiologic processes through receiving immediate feedback while experiencing the physiologic change.<sup>64</sup> Few studies investigating the usefulness of biofeedback in tinnitus treatment concluded that combining CBT with biofeedback displayed stable and highly effective improvements of psychophysiological interrelationships through psychological coping and physiologic control mechanisms; whether psychological and physiologic responses are depended on one another is unclear.<sup>65,66</sup> Alternatively, biofeedback-relaxation techniques seem to improve coping mechanisms, relief stress and muscle tension, and potentially reduce tinnitus intensity through increased peripheral vascular circulation.<sup>67-69</sup> Going along with these results, Haller and colleagues<sup>64</sup> demonstrated that biofeedback could help patients reduce activation of auditory brain areas through real-time functional MRI neurofeedback. Thus, the addition of biofeedback to other treatment modalities may aid improving patients' quality of life, but its value as a stand-alone therapy has not been substantiated.

## **ELECTRICAL STIMULATION**

### ***Nerve Stimulation***

Transcutaneous electrical nerve stimulation is a noninvasive therapy used for tinnitus treatment during which patch electrodes are attached to the auricular area for low-intensity vagus nerve stimulation (VNS). It is hypothesized that this therapy decreases neuronal firing frequencies and sympathetic tone to potentially increase auditory circulation.<sup>70,71</sup> Studies investigating this treatment modality have thus far reported a more than 60% subjective improvement with statistically significant decreases in VAS and THI scores after 8 to 10 treatment sessions<sup>70,72</sup> and the ability to restore an autonomic nervous system imbalance in tinnitus patients with sympathetic predominance.<sup>71</sup>



Measuring brain activities, VNS has also been shown to suppress the auditory and limbic areas implicated in tinnitus etiology, which could potentially hamper tinnitus awareness.<sup>73</sup> None of the studies reported adverse events related to VNS, with one study stating that few patients have been using this technique every day for 3 years.<sup>71,72</sup>

### ***Transcranial Magnetic Stimulation***

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Similar to VNS, transcranial magnetic stimulation (TMS) is a noninvasive treatment method with the capability of altering the excitability of brain cortices. During TMS for tinnitus, an electromagnet is positioned at the dorsolateral and temporoparietal cortices and stimulates at less than 1 Hz frequency to induce inhibition.<sup>74</sup> A previous review of TMS on chronic tinnitus concluded that most studies described little greater than 50% improvement rates but voiced criticism for small sample sizes and incomparable outcome measures.<sup>75</sup> More recent studies found that although TMS alone did not have significant effects on tinnitus perceptions,<sup>74,76</sup> TMS combined with low-level cochlear laser therapy or audio relaxation techniques did.<sup>76</sup> After 10 treatment sessions administered every other day over 3 weeks, both combination therapies reported significant decreases in THI, with the relaxation/TMS effect still present at 10 weeks post-treatment.<sup>76,77</sup> Nevertheless, electrical stimulation techniques for tinnitus treatment remain underresearched, which limits its use in everyday practice.

### **CANNABINOIDS**

Since the approval of cannabinoids for the treatment of medical conditions, cannabinoids drugs have been readily used for chronic pain and epilepsy. The notion of cannabinoids having antiepileptic properties by decreasing neuronal hyperactivity could in theory imply that cannabinoids might have a similar effect on the CB1 receptors located in auditory brain areas, such as the cochlear nucleus, and therefore benefit the treatment of tinnitus.<sup>78</sup> Thus far, however, there have only been animal studies displaying an antiepileptiform effect. Similarly, there have been no studies on humans investigating the potential of cannabinoid drugs for tinnitus symptoms. Although neuronal inhibitory effects have been documented, they seem to be outweighed by simultaneously stronger excitatory effects, leading to net excitation of the auditory system and subsequent worsening of tinnitus.<sup>79</sup> Two studies examining the effects of selective as well as nonselective cannabinoid receptor agonists on salicylate-induced tinnitus in guinea pigs and rats, respectively, found that neither drug attenuated tinnitus perception based on tinnitus-related animal behavior but may actually intensify the symptom.<sup>80,81</sup> One of the problems in studying cannabinoids, however, is that *Cannabis* contains more than 400 chemicals, including 66 Cannabis-unique ones, with each different plant within the *Cannabaceae* family containing varying concentrations of said chemicals.<sup>78</sup> This alone leaves the question of whether some plants might have better efficacy than others. Based on anecdotal evidence, the potential for cannabinoids to improve tinnitus is quite variable and depends on the patient. Although some patients of the senior investigators as well as on Cannabis blogs online report relief of tinnitus or psychologically associated symptoms and sleep quality improvements, others describe a spiking in intensity.<sup>82,83</sup> Thus, cannabinoids may not be at a stage of recommended treatment of tinnitus, but should a patient take initiative in trying Cannabis with a successful outcome, it may be right for that person.

### **SUMMARY**

Based on the evidence provided, complementary/integrative medicine poses viable options in the management of tinnitus. Although some physicians may be hesitant

to use these treatment modalities, complementary/integrative medicine should not be looked upon as a last resort but as a complementary approach that might be less invasive and work for patients for whom conventional medicine does not. Especially, if patients are receptive to acupuncture, supplements, and herbal medicines, these options should be considered sooner rather than later during the course of treatment. Patients will communicate what works best for them and what does not, if they perceive their physician to be genuinely listening, emphasizing, and giving them hope. Sometimes, patients might even figure what works for them on their own, as in the case of cannabinoid usage.

In addition to patient preferences and trial and error, alternative treatment can be integrated in a more systematic approach to symptom improvement. Based on the presented research, patients' initial serum levels should be examined for the aforementioned possible deficiencies to further deduct if supplementation with B vitamin, zinc, and copper may be more or less helpful.

Considering many studies have come to contradictory results as to whether a treatment shows statistically significant improvements or not, it is obvious that not every treatment discussed will benefit every patient and that more double-blinded, placebo-controlled trials are needed. As described by the studies, some treatments may be more beneficial to certain patient populations, and just because one option might work for patient A does not mean it will work for patient B. Just as conventional medicine for the treatment of tinnitus, not every alternative treatment will work for everyone. Thus, these *Complementary Integrative Medicine* options should be in the repertoire of every physician taking care of patients with tinnitus, because the absence of trying is worse than failure in the face of giving everything.

## DISCLOSURE

M.D.Seidman: Body Language Vitamins—Founder of nutritional supplement company; (7) patents—Intellectual property; Acclarent—Consultant; Auris Medical AM 101 & 111—Clinical trials for tinnitus-noncompensated (Research); Envoy Medical—Assisting in postmarket studies-noncompensated (Research); NIH—Simulation Work/July 2012–June 2019 (Research); MicroTransponder, Inc—Vagal Nerve Stimulator Clinical Trial for tinnitus-non-compensated (Research).

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