Medication use reported by individuals with tinnitus who are seeking internet-based psychological interventions

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Abstract

Purpose: The study examined medication use by individuals with tinnitus who were seeking help for their tinnitus by means of a psychological intervention.

Method: The study used a cross-sectional survey design and included individuals with tinnitus enrolled in an Internet-based cognitive behavioral therapy (ICBT) trial (n = 439). Study participants provided demographic details, completed various structured questionnaires as well as provided details about the medications used. The self-reported medications were classified using the USP Medicare Model Guidelines v7.0.

Results: Current medication use was reported by 67% (n = 293) of the study participants. Those currently using medication were older, had consulted their primary care physician, had greater tinnitus severity, depression, anxiety, and insomnia when compared with those not reporting any current medication use. The top 10 medication used included: cardiovascular agents (n = 162; 55.3%), antidepressants (n = 80; 27.3%), electrolytes/minerals/metals/vitamins (n = 70; 23.9%), respiratory tract/pulmonary agents (n = 62; 21.2%), anxiolytics (n = 59; 20.1%), hormonal agents/stimulant/replacement/modifying (thyroid) (n = 45; 15.4%), gastrointestinal agents (n = 43; 14.7%), analgesics (n = 33; 11.3%), blood glucose regulators (n = 32; 10.9%), and anticonvulsants (n = 26; 8.87%). Some associations between type of medication used and demographic/ tinnitus-related variables were noted especially for the cardiovascular agents, electrolytes/minerals/metals/vitamins, and anxiolytics.

Conclusions: This exploratory study indicated a large percentage of patients using medication and a range of medications. Further studies are required to assess the effects of such medications on the tinnitus percept and if concurrent medication moderate treatment effects.

Key Words

Tinnitus, Medication use, Supportive care medications, Internet-intervention

Introduction

Tinnitus is the perception of sound in the absence of a corresponding external sound source. It is a prevalent condition, experienced by 10-15% of adults in the general population (McCormack et al., 2016), although approximately 1-2% of the population are severely affected (Bhatt et al., 2016; Davis & Refaie, 2002). Those with tinnitus report various associated difficulties including problems with attention and concentration, increased anxiety and depression, insomnia, and reduced general health-related quality of life (HRQoL) (e.g., Salazar et al., 2020)

Various non-auditory factors including levels of stress, emotional state, mood, life events and general health could mediate the tinnitus perception and its effects on the individual (Andersson & Westin, 2008; Beukes et al., 2020), although the associations between all these factors and tinnitus perception and its consequences remain topics requiring further investigation. While some of these factors can affect tinnitus perceptions in terms of the types and loudness of sounds heard, their influence on the distress associated with tinnitus produce substantial challenges for many patients. Various forms of help-seeking may be demonstrated by patients during these times, including internet searches, trying sound enrichment applications, or the use of prescribed or over-the-counter (self-selected) medication. For example, the use of antidepressants for the treatment of tinnitus is common (e.g., Baldo et al., 2012), and medications are often prescribed or taken to address associated difficulties such as sleep problems (e.g., Lie et al., 2015). Although numerous pharmacological compounds have been tested with the aim to eliminate tinnitus, (Langguth et al., 2019). other investigators have identified ototoxic agents causing and/or exacerbating tinnitus (for review see Ganesan et al., 2018; Rizk et al., 2020).

There remains, however, a limited understanding of the medications used by individuals with tinnitus in general, and the effect of these medications on patients' perception of tinnitus in particular. Patients and research participants often report anecdotal observations regarding how certain medications or supplements have a positive or negative effect on their tinnitus. Further investigations regarding these reports may be useful for several reasons: Firstly, interviewing patients may provide information regarding the potential effects on tinnitus of their general health (Qato et al., 2008, 2016). Secondly, insights may be gained regarding the use of medication for tinnitus-related problems such as insomnia (Cronlein et al., 2011). Thirdly, such questioning will provide patients the opportunity to specify the use of ototoxic medications that may influence their hearing as well as tinnitus perception, as well as to identify positive and/or adverse effects, and potential drug interactions.

Long-term medication usage can be assessed by either examining the medical records and/or using patient self-report methods. While the accuracy of these two methods may vary, research studies often use self-report methods to examine medication use (West et al., 1995). Large clinical studies have generally found agreement between self-reported medication compared with pharmacy records, especially for stable long-term medications (Drieling et al., 2016; Fujita et al., 2015). The value self-report was demonstrated in a recent study using self-reported outcomes to examine the use of medication by treatment-naïve lung cancer patients identifying the need for better screening for pain and depression in this population (Hoang et al., 2020).

Due to the lack of robust studies regarding the effects of medication on tinnitus, the aim of the current exploratory study was to examine the use of medication by individuals with tinnitus who

were enrolled in a psychological intervention study. The specific questions included: (a) Is there a difference in demographic and/or tinnitus related variables in individuals with tinnitus based on the duration and frequency of medication use, (b) What are the most common medications used by individuals with tinnitus? and (c) Is there an association between the type of medication used and demographic and/or tinnitus related variables?

Method

Study Design

This exploratory study used a cross-sectional survey design. Individuals with tinnitus who were enrolled for Internet-based cognitive behavioral therapy (ICBT) trials (Clinical Trials.gov registration numbers NCT04004260, NCT04335812, and NCT04335929) were included (Beukes, Aronson, Andersson, et al., In press; Beueks, Andersson, Fagelson, et al., In press; Beukes et al., 2021c; Manchaiah et al., 2020). Of the 440 people who initiated the registration, one did not complete the questionnaire and was removed; the remaining 439 participants were included. Ethical approval (IRB-FY17-209, IRB-FY20-200-1, and IRB-FY20-200-2) was obtained from the Institutional Review Board at Lamar University, Beaumont, Texas, United States.

Data Collection

The data were collected using a web-based questionnaire which included questions about (a) demographical factors (e.g., age, gender, education, work status), (b) tinnitus-related variables that were assessed using general questions (e.g., duration of tinnitus) as well as standardized questionnaires, and (c) medication use. The standardized questionnaires assessed the tinnitus

126 severity using the Tinnitus Functional Index (TFI; Meikle et al., 2012), anxiety using the
127 Generalized Anxiety Disorder – 7 (GAD7; Spitzer et al., 2006), depression using the Patient
128 Health Questionnaire – 9 (PHQ-9; Kroenke et al., 2011), insomnia using the Insomnia Severity
129 Index (ISI; Bastien et al., 2001), and the HRQoL using the EQ-5D-5L VAS scale (Rabin & de
130 Charro, 2001). Medication use was assessed using an open-ended question worded as: Please list
131 any medications you currently take (select none or list them). Although this study relied on self-
132 reported data, the questioning was shown to be a reliable method in previous studies (Drieling et
133 al., 2016; Fujita et al., 2015). Furthermore, most patients apparently completed the questionnaire
134 online while at home, thus participants had access to their medications to crosscheck when
135 answering such questions.
136
137 If the participants reported any medication, they were categorized as "medication use" group.
138 Those who did not report *any* medication were classified as "non-medication use" group. Also,
139 perceived effect of medication was examined using the question: What effects do these
140 medications have on your tinnitus? Response options included: no effect, improves my tinnitus,
141 or worsens my tinnitus.
142
143 **Medication Classification**
144 The self-reported medications were classified into various categories using the United States
145 Pharmacopeial Convention (USP) Medicare Model Guidelines v7.0, 2017 (United States
146 Pharmacopeial Convention, 2017). This classification has 48 categories and 154 classes. For the
147 purpose of this study, both the prescription and over-the-counter medications were first classified
148 for classes and then grouped in various categories. Individual components were categorized into

separate classes for drug products containing two or more active ingredients. Vitamins and other supplements were categorized in the electrolytes/minerals/metals/vitamins category. A licensed pharmacist (AB) performed the classification of medication and queries were resolved by another licensed pharmacist and Associate Professor of Clinical Pharmacy and Pharmacology (MVT).

Data Analysis

Data were analyzed using the R software Psych package. Chi square or Fisher's extract test were used to study the association between medication use and demographics/tinnitus related variables. Two sample *t*-test or Mann Whitney *U* test were used to study the difference in demographic or tinnitus related variables based on medication use. In addition, logistic regression was used to study the effect of tinnitus-related variables on medication use, controlling for the participant demographic characteristics.

Results

Effect of Medication Use

Of the 439 participants enrolled in the study, 293 (66.7%) indicated the use of any medication (assigned to the medication group), whereas the remaining 146 (33.3%) were assigned to the non-medication group.

For the overall sample (n = 439), when responding to the question what effects the medications have on tinnitus, 69% (n = 303) reported no effect, 6.8% (n = 30) reported it improved their tinnitus, 4.3% (n = 19) reported that it worsened their tinnitus, and the remaining 19.8% (n = 87) did not answer the

question. For those from the overall sample who reported using medication (n=293), when responding to the question what effects the medications have on tinnitus, 84.3% (n = 247) reported no effect, 9.6% (n = 28) reported that it improved their tinnitus, and 6.1% (n = 18) reported that it worsened their tinnitus. Fisher's Exact test suggested no association ($p = .12$) between perceived effect of medication on tinnitus across the groups.

Association Between Medication Use and Demographic/Tinnitus-Related Variables

Table 1 presents the relationship between demographic variables and medication use. The medication group (mean age of 56.1 years) was significantly older ($p < .001$) when compared to the non-medication group (mean age of 51.1 years). Those who consulted their Primary Care Physicians (PCP) had 1.99 times higher odds of using medications ($p < .001$). None of the other demographic variables showed a significant association with the medication use.

Table 1: Relationship between demographic variables and medication use. All categorical variables were analyzed with either Chi square or Fishers exact tests and corresponding, Unadjusted odds ratio, and significance (*p*-value) are provided. All continuous measurements were summarized with their Mean±SD and analyzed with two sample *t*-test/ Mann Whitney *U* test are provided.

Patient Characteristics	**All subjects [n = 439]**	**Medication group (%) [n = 293]**	**Non medication group (%) [n = 146]**	**Unadjusted Odds Ratio (95% CI)**	***P*-value**
Age (in years)	54.4 ± 13.6	56.1 ± 12.9	51.1 ± 14.3		< .001
Duration of tinnitus (in years)	12.1 ± 13.0	12.6 ± 13.4	11.0 ± 12.3		.13
Gender					
Male	211 (48.06%)	134 (45.73%)	77 (52.74%)	Reference	.17
Female	228 (51.94%)	159 (54.27%)	69 (47.26%)	1.32 (0.89, 1.97)	
Work Type					
Entry level	15 (3.417%)	9 (3.072%)	6 (4.11%)	Reference	
Skilled professional	263 (59.91%)	165 (56.31%)	98 (67.12%)	1.12 (0.39,3.25)	.09
Retired	126 (28.70%)	95 (32.42%)	31 (21.23%)	2.04 (0.67, 6.19)	
Not working	35 (7.97%)	24 (8.19%)	11 (7.53%)	1.46 (0.41, 5.11)	
Schooling					
Less than high	5 (1.14%)	4 (1.37%)	1 (0.69%)	Reference	

High school	46 (10.48%)	28 (9.56%)	18 (12.33%)	0.29 (0.07, 3.57)	.74
Some college	129 (29.39%)	85 (29.01%)	44 (30.14%)	0.578 (0.66, 0.51)	
University	259 (58.99%)	176 (60.07%)	83 (56.85%)	0.64 (1.0, 0.57)	
Ethnicity					
Hispanic	90 (20.50%)	55 (18.77%)	35 (23.97%)	Reference	.20
Non-Hispanic	349 (79.49%)	238 (81.23%)	111 (76.03%)	1.365 (0.84, 2.21)	
Race					
American Indian	4 (0.91%)	3 (1.02%)	1 (0.69%)	Reference	.06
Asian	9 (2.05%)	3 (1.02%)	6 (4.11%)	0.11 (0.02, 2.33)	
Native Hawaiian	1 (0.228%)	1 (0.341%)	0 (0.000%)	0.25 (0.03, 53.51)	
Black	9 (2.05%)	8 (2.73%)	1(0.69%)	1.0 (0.18, 32.14)	
White	389 (88.61%)	264 (90.10%)	125 (85.62%)	0.524 (0.13, 6.19)	
More than one	27 (6.15%)	14 (4.78%)	27 (8.90%)	0.250 (0.06, 3.58)	
Consulted Primary Care Physician (PCP)					
No	221 (50.34%)	131 (44.71%)	90 (60.64%)	Reference	< .001

Yes	218 (49.66%)	162 (55.29%)	56 (38.36%)	1.99 (1.33, 2.98)	

Table 2 presents the relationship between tinnitus-related variables and medication use groups examined using the Mann Whitney U test. The medication group had significantly higher tinnitus severity, anxiety, depression, and insomnia, compared with those who did not use medications. There was no difference between the groups for the general HRQoL. Furthermore, logistic regression was used to examine the relationship between tinnitus-related variables and medication use controlling for participants' demographic variables (i.e., age, gender, race, and ethnicity). As per the likelihood ratio test, tinnitus severity ($p = 0.92$), anxiety ($p = 0.71$), and depression ($p = 0.12$) and insomnia (0.38) were not significantly associated with medication use.

Table 2: Tinnitus severity, anxiety, depression, insomnia and general health-related quality of life between medication and non-medication groups. Mean, Standard deviation and significance (*p*-value) based on Mann Whitney U test are provided.

Patient Characteristics	Mean ± SD			*p*-value
	All subjects [n = 439]	Medication [n = 293]	Non-medication [n = 146]	
Tinnitus severity (TFI)	52.5 ± 21.7	54.5 ± 21.9	48.4 ± 20.8	.0078
Anxiety (GAD7)	7.24 ± 5.68	7.71 ± 5.79	6.26 ± 5.35	.012
Depression (PHQ9)	7.38 ± 5.95	8.06 ± 6.20	5.97 ± 5.14	.001
Insomnia (ISI)	11.3 ± 6.74	12.0 ± 6.74	9.82 ± 6.54	.0015
General health-related quality of life (EQ-5D-5L VAS)	74.2 ± 15.9	74.0 ± 15.7	74.6 ± 16.3	.5930

Commonly Used Medications by Individuals with Tinnitus

Medication use was reported for 27 of the 48 UPS categories in the Medicare Model Guidelines v7.0, although frequency of use was less than 5% in 14 of these categories (see Figure 1). The top 10 medications were used by at least 9% of those from the medication group, including: cardiovascular agents (n = 162; 55.3%), antidepressants (n = 80; 27.3%), electrolytes/minerals/metals/vitamins (n=70; 23.9%), respiratory tract/ pulmonary agents (n=62;

215 21.2%), anxiolytics (n = 59; 20.1%), hormonal agents, stimulant/ replacement/ modifying
216 (thyroid) (n = 45; 15.4%), gastrointestinal agents (n = 43; 14.7%), analgesics (n = 33; 11.3%),
217 blood glucose regulators (n = 32; 10.9%) and anticonvulsants (n = 26; 8.87%).
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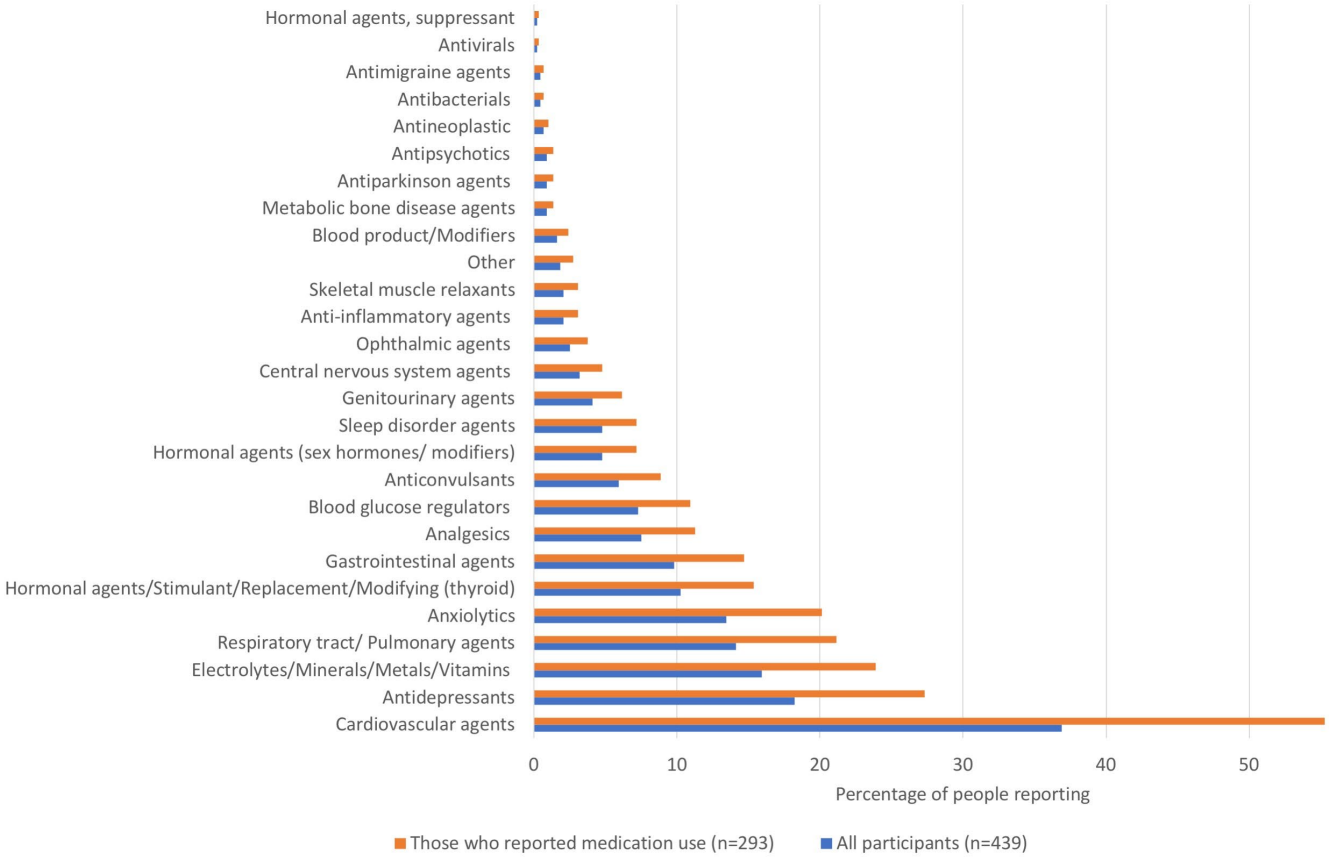

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220 **Figure 1: Percentage of participants reporting various medications arranged in ascending**
221 **order of the usage**
222

223 **Association Between Type of Medication and Demographic/Tinnitus-Related Variables**
224 Table 3 presents the relationship between type of medication used and demographic as well as
225 tinnitus-related variables for the top 5 most frequently used medications. The variables, work
226 type ($p < .001$), ethnicity ($p = .006$) and perceived medication effect ($p = .003$) showed a

significant relationship with the use of cardiovascular medication. The unadjusted odds ratio for the use of cardiovascular medication was 2.56 times higher for retirees compared with those whose work was regarded entry level. Non-Hispanic medication users had 2.31 times higher odds of using cardiovascular medications compared to the Hispanics. Those who used cardiovascular agents were significantly older ($p < .001$), had longer duration of tinnitus ($p = 0.045$), lower anxiety ($p = .001$), and lower depression ($p = .013$) than those who did not report using these medications.

Participants who used antidepressants had significantly higher self-reported anxiety ($p= .019$) and depression ($p < .001$) scores from the GAD7 and PHQ-9 questionnaires, respectively. The variables gender ($p = 0.013$), education ($p = 0.0047$), ethnicity ($p = 0.04$), and perceived effect of medication on tinnitus ($p = .017$) has a significant association with the use of electrolytes/minerals/metals/vitamins. Females had a 2.03 times higher odds for using the electrolytes/minerals/metals/vitamins, whereas individuals with college education (OR 0.09) and non-Hispanic (OR 0.5) were at lower odds of electrolytes/minerals/metals/vitamins use.

The variables gender ($p = .016$) and ethnicity ($p = .04$) have significant association with the respiratory tract/ pulmonary agents medication use, with females (OR 2.05) and non-Hispanic (OR 2.5) having a higher odds of using this medication. The variable perceived medication benefit ($p < .001$) had a significant association with anxiolytics, with those reporting medication use improves their tinnitus were at a 5.1 times higher odds of using this class of medication. Those reporting the use of anxiolytics also had higher tinnitus severity ($p < .001$), anxiety ($p< .001$), depression ($p = .002$), and insomnia ($p = .003$).

Table 3: Relation between type of medication used and demographic as well as tinnitus-related variables. Significance (* = $p < 0.05$; ** = $p < 0.01$) based on the Chi square test, Fishers exact test, or either two sample *t*-test/ Mann Whitney *U* test are provided.

Demographic and tinnitus-related factors	Medication categories				
	Cardiovascular agents	Antidepressants	Electrolyte	Respiratory tract/ Pulmonary agents	Anxiolytics
Age	**				
Duration of tinnitus	*				*
Gender			*	*	
Work type	**				
Education			**		
Ethnicity	**		*	*	
Race					
Consulted PCP					
Hearing loss					
Perceived effect of medication on tinnitus	**		*		**

Tinnitus severity (TFI)					**
Anxiety (GAD7)	**	*			**
Depression (PHQ-9)	*	**			**
Insomnia (ISI)					**
General health-related quality of life (EQ-5D-5L VAS)					**

255

256

257 ## Discussion

258 The current study examined medication use by individuals with tinnitus who were participants in
259 a treatment trial. As tinnitus is often associated with comorbidities such as anxiety, depression,
260 and insomnia, the use of medication is not uncommon amongst individuals with tinnitus.
261 However, the usage and effects of such medications on tinnitus remain areas of speculation and
262 investigation. The objective of the current study was to examine the types, numbers, and effects
263 of medications used by individuals with tinnitus who are seeking psychological intervention. The
264 key findings are discussed below.

265

Two thirds (67%) of the current study participants reported using some kind of medication. When comparing those that used and did not use medication, participants reporting medication use were significantly older than those who denied use. These results are comparable with the findings from the general US population, as 46% of participants, and 85% of those of 60 years and over, indicated they used drugs when questioned regarding drug use during the past 30 days (Martin et al., 2019). The average age of participants in the current study was 54 years, suggesting that while the medication use in tinnitus population in the US is comparable to general population, the percentage of patients reporting use could vary depending on the age group studied.

Those using medication had not shown significantly higher scores on indices related to tinnitus severity, depression, anxiety, and insomnia when compared to those who did not report any current medication use after adjusting for demographic variables (i.e., age, gender, race, and ethnicity). We anticipated that those with higher medication use will have higher anxiety and depression, as medication's intent would be to address these problems. However, this was not observed in the current study. Further, these conditions psychological are often associated with other physical health problems and long-term chronic diseases (Trick et al., 2016), hence their potential to influence tinnitus effects. However, this association with tinnitus severity and medication use was also not observed after adjusting for demographic variables. As anticipated, individuals who had consulted their PCP for tinnitus, had significantly higher medication usage. Nevertheless, these associations need further exploration in follow-up studies.

In the study, cardiovascular agents (beta-blockers and lipid lowering drugs), antidepressants, electrolytes/minerals/metals/vitamins, respiratory tract/ pulmonary agents, and anxiolytics were the most commonly used drugs. This is comparable to reports of lipid lowering (high cholesterol) drugs, beta-blockers and antidiabetic drugs being the most commonly used drugs in US adults over the age of 60 years, whereas antidepressants, analgesics (pain relief) and lipid lowering drugs were among the most commonly used among adults aged 20-59 years (Martin et al., 2019). Similarly, our findings of common use of electrolytes/minerals/metals/vitamins reflected the common use of vitamins and dietary supplements by U.S. adults in previous reports (Rock et al., 2007; Kantor et al., 2016). As the use of respiratory track/pulmonary agents was more common in children and younger adults (Martin et al., 2019), higher use of these agents was surprising in the current study focused on individuals with tinnitus. Among various respiratory tract/ pulmonary agents, the use of antihistamines was highest in our population. Recent studies show a link between allergic rhinitis and eustachian tube dysfunction (reviewed in Juszczak and Loftus, 2020), a finding further supported by our study; such a link may explain the efficacy of antihistamines in alleviating tinnitus symptoms for some patients. Further, tinnitus may lead to anxiety and depression, and therefore, the use of anxiolytics and antidepressants in our study population was anticipated.

There was an association with type of medication used and demographic variables such as age, duration of tinnitus, work type, education and ethnicity. Additional results related to the association between medication class among those reporting higher levels of tinnitus severity, anxiety, depression, and insomnia. As anticipated, antidepressants and anxiolytics (i.e., anti-anxiety) use was higher among those with higher anxiety and depression. In addition, anxiolytic

drugs were also more commonly used by individuals with higher tinnitus severity and insomnia. While some antibiotics and cancer drugs are known to cause severe and irreversible hearing problems, certain common long-term medication use has also been associated with tinnitus. These common medications include some non-steroidal anti-inflammatory drugs (analgesics), loop diuretics (cardiovascular agents), tricyclic antidepressants and selective serotonin reuptake inhibitor antidepressants (Bisht & Bist, 2011). While our study did not aim to assess the contribution of long-term medication use on tinnitus onset and severity, this is an important question that needs to be evaluated in prospective studies.

Study Limitations and Future Directions

There are some limitations that need to be considered during result interpretation. Firstly, the study represents the medication use of individuals with tinnitus who were seeking help for their tinnitus via an internet-based psychological interventions. This may have resulted in some sampling bias as is the participants may not be representative of the general tinnitus population Secondly, there may be some recall bias when reporting the medication, although this may have been reduced as people were completing the questionnaire via the internet at home and thus most likely having access to their medications to crosscheck Thirdly, the current study is cross-sectional study and as a result the longitudinal changes in medication use were not considered. For these reasons, the study results should be interpreted cautiously and be considered as preliminary. Future studies should aim to compare medication profile of individuals with tinnitus to medication use of a comparable age and gender matched general population.

Conclusion

This study provides information regarding the medication use by individuals with tinnitus who are seeking psychological intervention. Healthcare professionals should be mindful of the medications that may be used and be prepared to investigate the general health of individuals relying on such medications. Audiologists and their patients may benefit from a careful review of such medications' use and potential side effects. Future studies need to evaluate the effect of these medications on tinnitus. Prospective studies investigating the effect of acute medication use in the past and long-term medication use over time as a cause of tinnitus or a factor increasing the severity of tinnitus are recommended.

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Conflict of Interest

None to declare.

Data Sharing

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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