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REVIEW ARTICLE

Tinnitus and arterial hypertension: a systematic review

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Abstract Tinnitus is considered a multi-factorial symptom. Arterial hypertension has been cited as a tinnitus etiological factor. To assess the scientific evidence on the associations between arterial hypertension and tinnitus. A systematic review was performed using PubMed, ISI Web, Lilacs and SciELO scientific databases. This review included articles published in Portuguese, Spanish, French and English correlating tinnitus with hypertension. Letters to editors and case reports were excluded. A total of 424 articles were identified, of which only 20 met the inclusion criteria. Studies that analyzed the incidence of hypertension in tinnitus patients tended to show an association, while those that evaluated the incidence of tinnitus in hypertensive patients did not. There is evidence of an association between tinnitus and hypertension, although a cause and effect relationship is uncertain. Changes in the cochlear microcirculation, resulting in hearing loss, may be an adjuvant factor in tinnitus pathophysiology

Keywords Tinnitus · Arterial hypertension

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Introduction

Tinnitus is the perception of sound that is not associated with an acoustic stimulus [1]. A study performed in 2010 by the Massachusetts Eye and Ear Infirmary (MEEI), estimates the prevalence of tinnitus to be at 25.3 % (approximately 50,000,000 individuals) of the United States' populace [2] where 7.9 % (approximately 16,000,000 individuals) of adults complained of frequent tinnitus. These data corroborate with a prior study which found that 35–50 million of North-American adults complained of tinnitus, with approximately 12 million requiring medical attention, and 2–3 million complaining of debilitating symptoms [3] .

One of the classifications used for tinnitus is that it can be divided into two groups: auditory or para-auditory [4]. The former group, which corresponds to the majority of the cases, represents "phantom" sound perception, being that there is no verification of the presence of sound itself. Whereas, in the latter classification, real sounds are generated by the anatomical structures neighboring the cochlea of which it is then capable of perceiving. Para-auditory tinnitus can then be subdivided into muscular and vascular categories. The tinnitus which can be considered auditory may be generated as consequence of damage to the external, middle and, more frequently, inner ear; the auditory nerve; and the central auditory pathways [4]. Of these last examples, they can be considered classified as "sensorineural" which can sum up the large majority of verified cases in clinical practice [4].

Systemic arterial hypertension (SAH) is defined as systolic blood pressure equal to or superior than 140 mmHg and diastolic blood pressure equal to or superior than 90 mmHg [5]. It is a highly prevalent disease that has been considered directly responsible for the great

majority of the ambulatory consultations in Cardiology [5, 6]. Although there are no epidemiological data for Brazil, most studies estimate of a 25 % occurrence in the adult population [5].

Concerning the possible effects of SAH at the inner ear, experimental studies have shown that genetically predisposed mice to SAH acquired hearing loss induced by noise at a higher rate than those mice without a genetic predisposition [7]. SAH may induce or aggravate pre-existent tinnitus through two, principle mechanisms: damage to the cochlear microcirculation; and to ototoxicity caused by diverse anti-hypertensive drugs, such as furosemide and beta-blockers [7, 8]. An electron microscope study revealed that the primary site of cochlear involvement in patients with SAH is the stria vascularis, followed by the Corti organ [8]. Other authors speculated about an increase in perilymphatic pressure due to the increase of extracellular volume generally associated with high sodium retention in SAH [9].

In acute hypertension cases, the mechanisms of vascular protection of the cochlea maintain stable the endocochlear's potential, and yet, in chronic hypertension, permanent damage may occur. In a study performed on mice, arterial hypertension has been linked to a decrease of the endocochlear's potential without damage to the permeability of the hemato-perilymphatic barrier to small molecules [10].

Ischemial events may induce vestibular (more frequently) and cochlear (including tinnitus) symptoms [11]. Among the more common signs of encephalic Vascular accidents (EVAs) hearing loss, sudden hearing loss, tinnitus, dizziness and central auditory processing impairment can be included. SAH has been associated with a higher risk of hearing loss with EVAs [11].

In a recently proposed theory [12], Ménière disease attacks may result from cerebrovascular events (SAH included) that affect the inner ear. The resulting temporary ischemia induces ischemia/reperfusion injuries, with release of large amounts of glutamate on the synaptic cleft. With subsequent reperfusion, calcium binds to AMPA (α-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) and NMDA (N-Methyl-D-aspartate) receptors, which may, in turn, result in severe injuries to the distal parts of the neurons.

The main purpose of this systematic review is to analyze the diverse studies that evaluate the association between tinnitus and SAH in humans.

Materials and methods

A systematic review of published articles on tinnitus and SAH was performed using the databases of PubMed, ISI Web (Web of Knowledge), SciELO and LILACS. For the search in PubMed and ISI Web, the strategy of advanced search used the following keywords extracted from the Medical Subject Headings (MeSH): "Tinnitus"[Mesh] AND "Hypertension"[Mesh] AND "humans"[MeSH Terms] AND (English[lang] OR Spanish[lang] OR French[lang] OR Portuguese[lang]) AND "adult"[MeSH Terms].

For the LILACS and SciELO databases, we utilized the keywords indexed in the Health and Sciences Keywords using the following strategy: Tinnitus AND Hypert$. The basic research form was used with the term AND to relate the words (hypertension and tinnitus) and the trunking sign$ was used to search for words with the same root word of the keyword "hypertension".

The choice of using the keyword "hypertension" instead of "arterial hypertension" was justified to create a more comprehensive review, considering the fact that some articles only employ the term "hypertension" as a keyword.

Included in the search was a series of patient studies in which the patients were 18 years or older, published in English, Portuguese, French or Spanish which associated tinnitus and Hypertension. Letters to the Editor and Case Reports were not included in the search.

Data extraction from the selected papers was carried out by two reviewers, organized under the following subject titles: Authors, year of publication, sample size, type of study, instruments used, and principle results of associations between tinnitus and SAH.

The selected articles were classified into two subgroups: articles analyzing the prevalence of Tinnitus in SAH patients, and articles analyzing the prevalence of SAH in Tinnitus patients.

Results

A systematic review produced a total of 424 articles, of which 232 were found in PubMed, 168 in ISI Web, 19 in LILACS and 5 in SciELO databases, respectively. The articles had publications dates ranging from 1948 to 2013. Access to the articles was conducted online through CAPES website by the researchers using BIREME so as to obtain copies of the published journals. Additionally, some published articles were made available through the personal library of the authors of this report.

Amongst the papers located, 20 met the systematic review's criteria and were included in the study [2, 13–31]. The other 404 were excluded for the following reasons: articles dealing with references which were in common in more than one database; multiple references in scientific journals and congress records; case reports; letters to the editor; studies dealing with intracranial hypertension; and

studies which did not have an objective of correlating an association between Tinnitus and SAH.

Among the 20 articles that met the inclusion criteria, there was a randomized clinical trial [13], four cohort studies [14–17], twelve cross-sectional studies [2, 18–28] and three series of case studies [29–31]. Among the population studies, ten articles analyzed the presence of SAH in patients with inner ear symptoms (including tinnitus) [2, 13, 14, 18, 20, 21, 23, 26, 29, 30] and ten analyzed the prevalence of tinnitus in patients with SAH [15–17, 19, 22, 24, 25, 27, 28, 31]. Table 1 shows the main interest parameters of the selected articles.

Of the 20 studies found, eight analyzed a possible association between tinnitus and SAH [2, 14–17, 22–24], while twelve were merely descriptive [13, 18–21, 23–31]. In considering the eight studies analyzing the possible association, evidences of a positive association were found in three studies evaluating the presence of SAH in patients with tinnitus [2, 14, 23]. Yet among the other five studies, only one showed a positive association of tinnitus in SAH patients treated with diuretics [15], while one study even found a negative correlation, or in other words, that patients without SAH had tinnitus more frequently than those with SAH [17].

In considering the descriptive studies, five evaluated the presence of SAH in patients with tinnitus [13, 18, 20, 21, 26], five analyzed the presence of tinnitus in patients with SAH [19, 25, 27, 28, 31], and two evaluated the presence of SAH as causing pulsatile tinnitus [29, 30]. The prevalence of SAH in the five studies conducted in patients with tinnitus ranged from 15.2 to 49 %. The prevalence of tinnitus in the five studies evaluating patients with SAH, ranged from 7.8 to 52 %. Finally, the prevalence of SAH as a possible cause of pulsatile tinnitus in the two remaining studies was found to be between 3.45 and 5 %.

Discussion

The association between tinnitus and SAH is controversial. The loss of blood pressure control has been found to potentially create alterations within the cochlear microcirculation [7, 8]. The majority of the studies agree that these alterations can lead to hearing loss and thus progress to tinnitus of sensorineural origin [7–10]. This relationship can be corroborated by study findings which show that 85–96 % of tinnitus patients have hearing loss [1, 2, 4].

In considering the association of SAH with pulsatile tinnitus, there were two studies in which low prevalence of SAH as a possible tinnitus etiology was found [29, 30]. In this case, SAH attribution was probably considered to be a factor through the process of excluding other vascular findings. SAH can generate alterations in blood pressure dynamics within the cochlear blood flow thus resulting in vascular noises which can be perceived by the hair cells, frequently with sudden onset, in this case related to hypertensive peaks [29]. Some anti-hypertensive drugs, such as verapamil and enalapril, have also been seen to cause pulsatile tinnitus which can regress upon drug termination [29]. These drugs reduce peripheral vascular resistance, leading to hyperdynamic circulation and, eventually to pulsatile tinnitus.

One may speculate whether the presence of SAH is, in itself, a real etiological factor or just a mere coincidence, considering that tinnitus is more frequently found in the elderly, a population where SAH also frequently occurs. On the other hand, the majority of the studies consider tinnitus as a multifactorial symptom [2, 4]. Therefore, the increase in arterial blood pressure and its effects on cochlear microcirculation could contribute to other changes generated by aging, noise exposure and metabolic disorders, just to cite some of the etiological factors more frequently associated with sensorineural hearing loss and consequently, tinnitus.

According to some reports, in some patients [28], an aggravation of tinnitus occurs with a rise in blood pressure and an improvement after adequate control over blood pressure has been regained, findings which reinforce the role of SAH as an etiological factor in at least some tinnitus subtypes. In another study of patients having severe SAH who had undergone surgical treatment (neurectomy), tinnitus also improved with blood pressure control [31].

It has been observed that there is a clear difference in the evidence of the association between tinnitus and SAH as concerning the different types of studies: those studies analyzing the prevalence of SAH in patients with tinnitus tended to show an association; while those studies evaluating the prevalence of tinnitus in patients with SAH did not. It could be speculated, in light of these data, that tinnitus could be a causative factor of SAH, but it is more probable that the frequent association between tinnitus, anxiety and depression may instead be contributing factors to SAH. Another possible interpretation is that SAH could be more of a co-factor than actually that of triggering the tinnitus. As previously discussed in this text, recurrent blood pressure fluctuations could affect the cochlear microcirculation, thus aggravating pre-existing conditions, such as hair cells damage caused by noise exposure and metabolic diseases.

Studies which analyzed the association of tinnitus and SAH concerning periodicity and onset of tinnitus were not located. A single study evaluated the prevalence of tinnitus according to anti-hypertensive drugs usage by patients, denoting a statistically significant difference in relation to treatment with diuretics, in that those patients treated with diuretics presented a higher prevalence of tinnitus [15].

Table 1 Overall view of the selected studies

Authors and year	Study design	Sample size (*n*)	Type of sample	Primary outcome (tinnitus × SAH)
Dehkordi et al. (2011) [13]	Randomized clinical trial	80	SAH in patients with tinnitus	SAH in tinnitus patients = 21.3 %
Lasisi et al. (2010) [14]	Longitudinal cohort	1302	Tinnitus in the elderly. SAH in patients with and without tinnitus	Tinnitus patients more prone to have SAH (OR = 2.1; $p = 0.05$)
Borghi et al. (2005) [15]	Longitudinal cohort	476	Tinnitus in patients with uncontrolled SAH	Tinnitus in patients with uncontrolled SAH = 17.6 %. Tinnitus more frequent in patients that use diuretics (27.2 %, $p < 0.05$)
Mondelli et al. (2009) [16]	Retrospective cohort	392	SAH in middle-aged patients with hearing loss, with and without tinnitus	No statistically significant difference in tinnitus prevalence between patients without (37.93 %) and with (43.75 %) SAH, $p = 0.2483$
Baraldi et al. (2004) [17]	Transversal cohort	70	SAH in the elderly with hearing loss, with and without tinnitus	Tinnitus more frequent in patients without SAH (65.8 × 34.2 %, $p = 0.009$)
Sogebi (2012) [18]	Transversal	127	Tinnitus in ENT Service patients, SAH in patients with and without tinnitus	SAH in the tinnitus group = 15.2 %
Chávez-Delgado et al. (2012) [19]	Transversal	385 (181 with HAS)	Tinnitus in SAH patients	Tinnitus prevalence = 32 % in patients with SAH
Fujii et al. (2011) [20]	Transversal	14.423	Tinnitus in patients >45 years old, SAH in patients with and without tinnitus	Odds ratio for SAH in tinnitus patients = 1.36 (men) and 1.52 (women), no *p* value
Shargorodsky et al. (2010) [2]	Transversal	14.178	Tinnitus in general population, SAH in patients with and without tinnitus	Odds ratio SAH prevalence in tinnitus patients = 1.48, $p < 0.01$
Ferreira et al. (2009) [21]	Transversal	100	SAH in patients with tinnitus	SAH in tinnitus patients = 49 %
Marchiori (2009) [22]	Transversal	154	Tinnitus in patients with SAH	Odds ratio = 0.346 ($p = 0.556$)
Negrila-Mezei et al. (2011) [23]	Transversal	471	Tinnitus in ENT Service patients, SAH in patients with and without tinnitus	Odds ratio = 3.9318, $p < 0.0001$
Fasce et al. (2002) [24]	Transversal	1100	Tinnitus in patients with and without SAH	Tinnitus prevalence = 9.10 % in patients without SAH and 9.40 % in SAH patients, *p* value not significant
Brohem et al. (1996) [25]	Transversal	50	Tinnitus in SAH patients	Tinnitus prevalence = 38 %
Fukuda et al. (1990) [26]	Transversal	50	SAH in patients with tinnitus	SAH prevalence = 16 %
Colafêmina et al. (1985) [27]	Transversal	50	Tinnitus in SAH patients	Tinnitus prevalence = 52 %
Weiss et al. (1972) [28]	Transversal	6.672	Tinnitus in patients with and without SAH	Tinnitus prevalence ranges from 9 to 11.9 % in systolic SAH and from 7.8 to 9.1 % in diastolic SAH
Herraiz et al. (2007) [29]	Case series	80	SAH in patients with pulsatile tinnitus	SAH as pulsatile tinnitus cause = 5 %
Sismanis (1998) [30]	Case series	145	SAH in patients with pulsatile tinnitus	SAH as pulsatile tinnitus cause = 3.45 %
Johnson et al. (1948) [31]	Case series	76	Tinnitus in patients with severe SAH	Tinnitus prevalence = 30 %

Another study cited the diverse drugs used for SAH treatment without, however, realizing any kind of statistical analysis concerning possible ototoxicity [22]. There is no reference to the effect of beta-blockers, also considered potentially ototoxic drugs. The ototoxicity of some anti-hypertensive medications may be an adjuvant factor in tinnitus pathophysiology [29].

In one study, some patients reported the onset or aggravation of tinnitus after abrupt falls of the systolic blood pressure (to levels below 140 mmHg) [28]. This finding seems to corroborate with the hypothesis that recurrent alterations in the dynamics of cochlear micro-circulation may lead to temporary changes of hearing thresholds and, subsequently lead to tinnitus.

Various studies also analyzed the prevalence of hearing loss [16, 17, 19, 21, 25, 26], however, without having performed a statistical analysis of the association of tinnitus, hearing loss and SAH.

Conclusion

Tinnitus is a very bothersome symptom for many patients and early therapeutic intervention is desirable so as to minimize its impact on quality of life. To achieve this, a more detailed understanding of possible tinnitus aetiologies and their injury mechanisms can provide important clues for the clinician.

Clinical evidence exists indicating an association between SAH and tinnitus which reinforces the hypothesis that alterations in the cochlear microcirculation, as causal or adjuvant factors in tinnitus pathophysiology, occur, including in cases of pulsative tinnitus. Therefore, more detailed data on this subject, tending towards multi-causality of tinnitus, are needed so that preventative measures can be taken. More detailed analysis, including the use of group controls, evaluations of the characteristics of the tinnitus, the degree of discomfort created by the tinnitus, (using a valid scale or questionnaire) and potential ototoxicity of anti-hypertensive medications could result upon the provision of more information.

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Conflict of interest The authors declare no conflict of interest.

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