Audiology

Bilateral transverse sinus stenosis in patients with tinnitus

Stenosi bilaterale del seno trasverso in pazienti affetti da acufene

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SUMMARY

Tinnitus is a frequent complaint in patients affected by intracranial hypertension (IH). Recently, some studies have reported an association between idiopathic intracranial hypertension (IIH) and bilateral transverse sinus stenosis (BTSS). We investigated the relationship between BTSS and monosymptomatic tinnitus, regardless of its clinical characteristics, in subjects without clinical evidence of IH. We selected 78 subjects (all women, mean age 49.5 ± 10.36) affected by tinnitus, without clinical history of audiological and otological pathologies, enrolled among outpatients of the Institute of Audiology and Phoniatrics in Catanzaro, Italy, over a 2 year period. All subjects underwent psychometric evaluation, psychoacoustic assessment, neurological and ophthalmological examination, cerebral magnetic resonance venography (MRV) and brain magnetic resonance imaging (MRI). MRV identified BTSS in 17.9% (14 patients). In the BTSS group, tinnitus was bilateral/central in 21%, and monolateral in the remaining patients (50% left; 29% right ear). It was more frequently pulsating in the BTSS group, but 64.9% of BTSS subjects described their tinnitus as stable. No features of tinnitus showed statistical significance in association with BTSS. In BTSS subjects, we found values suggesting IH by lumbar puncture (LP) in 40% of cases. In these patients, LP gave immediate improvement of tinnitus. The association between BTSS and tinnitus, regardless of its features, must be considered when other causes of tinnitus are excluded.

KEY WORDS: Idiopathic intracranial hypertension (IIH) • Magnetic resonance venography (MRV) • Bilateral transverse sinus stenosis (BTSS) • Tinnitus

RIASSUNTO

L’acufene è un sintomo frequente nei pazienti affetti da ipertensione endocranica (IE). Recentemente è stata riportata in numerosi studi l’associazione tra ipertensione endocranica idiopatica (IEI) e stenosi bilaterale del seno trasverso (SBST). Ciò ci ha spinto ad indagare la possibile relazione tra SBST ed acufene monosintomatica, indipendentemente dalle sue caratteristiche cliniche, in soggetti senza evidenza clinica di IE. Abbiamo esaminato 78 soggetti di sesso femminile (età media 49.5 ± 10.36) affetti da acufene, con anamnesi negativa per patologia audilogica o otologica, selezionati tra i pazienti afferenti all’Unità operativa di Audioligia e Foniatria di Catanzaro in un periodo di circa due anni. Tutti i soggetti sono stati sottoposti a valutazione psicometrica e psicoacustica, visita neurologica ed oftalmologica, venografia cerebrale con risonanza magnetica e risonanza magnetica dell’encefalo. L’esame venografico cerebrale ha documentato un quadro di SBST nel 17.9% del campione (14 soggetti). Nel gruppo di pazienti con SBST l’acufene è stato riferito bilaterale/centrale nel 21% dei casi, monolaterale nei rimanenti (50% orecchio sinistro, 29% destro). L’acufene era più frequentemente di tipo pulsante nel gruppo con SBST rispetto ai soggetti senza SBST, anche se il 64,9% dei soggetti con SBST ha descritto il proprio acufene come stabile. Nessuna caratteristica dell’acufene ha mostrato significatività statistica tale da poter essere considerata come indicativa dell’associazione con SBST. Infine nei pazienti del gruppo SBST sottoposti a puntura lombare abbiamo documentato valori riferibili ad IE nel 40% dei casi. In questi soggetti la puntura lombare ha determinato un drastico miglioramento dell’acufene. L’associazione tra SBST ed acufene, indipendentemente dalle sue caratteristiche cliniche, deve essere considerata quando siano state escluse le altre cause.

PAROLE CHIAVE: Ipertensione endocranica idiopatica • Venografia con risonanza magnetica • Stenosi bilaterale del seno trasverso • Acufene

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Introduction

Tinnitus is a common condition that affects a broad range of patients, with some uncertainties about its prevalence and incidence, and a great variety of aetio-pathogenetic and diagnostic issues. Prevalence data range from 3 to 30%, without consistent findings with regard to relationship between prevalence and age or gender. Idiopathic intracranial hypertension (IIH) is a condition characterized by raised intracranial pressure without any identifiable pathology in the brain and with normal cerebrospinal fluid (CSF) composition. IIH may occur with and without papilloedema. It predominantly affects overweight women, and while headache is the most common symptom, disturbance of vision and tinnitus are also very frequent complaints. In particular, tinnitus is reported in 55%-60% of patients, is usually pulsatile and often occurs in one ear only. Non-pulsatile or bilateral tinnitus can also occur in some cases.

Recently, a connection between bilateral transverse sinus stenosis (BTSS) and IIH with or without papilloedema has been described. Cerebral MR venography studies have found BTSS in the majority of IIH patients, with or without papilloedema, whereas BTSS has been reported in only a few subjects with normal CSF pressure.

Considering this and the well-known relationship between intracranial and cochlear fluids, hypothesizing that an alteration of venous cerebral circulation, especially BTSS, could be the basis of onset and maintenance of monosymptomatic tinnitus in subjects without clinical evidence of elevated intracranial pressure, we investigated the frequency of association between tinnitus and BTSS and the possibility to define some specific features of tinnitus that allow us to suspect BTSS.

Materials and methods

The study population consisted of 78 patients affected by tinnitus (ages 27 to 69, mean age 49.5 ± 10.36), enrolled according to selection criteria, among those admitted to Institute of Audiology and Phoniatrics in Catanzaro, Italy, over a 2 year period, starting from February 2008. We selected only females as it affects predominantly women. Tinnitus was diagnosed and assessed according to criteria described later.

All patients underwent otolaryngological and neurological examination, standardized clinical general examination and, as IIH affects predominantly overweight women, we also included evaluation of body mass index (BMI: weight in kilograms divided by the square of height in meters). Examination and interviews were conducted by the same physicians.

Given the availability in literature of data about the prevalence of BTSS in normal subjects and, in this particular case, personal data already published in a previous paper, the authors decided to make utilize these previous data without violating of ethical and economic precepts by carrying out expensive imaging exams in normal subjects.

Inclusion criteria

Female sex, tinnitus for at least two months, monosymptomatic, regardless of its characteristics, and an age between 25 and 70 years.

Exclusion criteria

Clinical history of audiological and otological pathologies (other clear causes for tinnitus, Ménière’s disease, acoustic neuroma, noise-induced hearing loss, assumption of drugs inducing tinnitus, etc.), otological surgery, were excluded. In order to exclude presbycusis, individuals with a pure-tone average over 30 dB HL for 2-4-8 kHz were not included in the study. Presence of papilloedema and abnormalities in neurological examination.

Assessment of tinnitus

We carried out careful evaluation of tinnitus that included both evaluation by questionnaires for psychometric assessment and hyperacusis as well as psychoacoustic assessment.

Our protocol included: i) A thorough history with detailed interview; ii) questionnaire for hyperacusis; iii) physical examination; iv) pure-tone thresholds with air and bone conduction and speech audiometry; v) tinnitus test battery: tinnitus loudness and pitch matching; minimal masking levels and acoustic-immittance measurements with tympanometry and acoustic-reflex thresholds (only if tolerated comfortably by patient and always after the results of the hyperacusis questionnaire). We did not perform the residual inhibition test because of its controversial clinical and scientific value.

Neuroimaging studies

All patients included in this study underwent brain gadolinium-enhanced magnetic resonance imaging (MRI) to exclude acoustic neuroma or other neoprotective causes for tinnitus. Patients with normal MRI underwent MRV of the brain with a 1.5 T scanner (GE Medical systems, Milwaukee, WI), using three dimensional phase-contrast (PC) techniques. All brain MRV were analyzed by the same neuroradiologists who were blinded to patient history. We classified the transverse sinus stenosis (TSS) as absent or present. BTSS was considered when the signal flow was lacking (flow gap) in the midlateral portion of both transverse sinuses.

CSF measurements

10 patients with BTSS underwent lumbar puncture to eval-
uate CSF opening pressure\(^4\). The test was not performed in the remaining 4 patients because they denied consent.

**Statistical analysis**
Statistical analyses were performed using Primer® software. The statistical assessment of differences between classes was performed using Fisher’s exact test and the chi-square test. A p-value < 0.05 was considered statistically significant. We also evaluated the Mantel-Haenzel odds ratio and performed multivariate logistic analysis using a multiple logistic regression model.

**Results**
We studied 78 subjects, all females, affected by tinnitus, regardless of its clinical characteristics, carefully ruling out specific causes.

**Imaging studies**
MRV identified the presence of BTSS in 14 subjects (17.9%); this was significantly different from that in subjects with normal CSF pressure (1.8%; \(p = 0.000734;\) odds ratio [OR] = 0.0996\(^\circ\)). In 17 patients (21.7%), the test did not highlight any specific alteration, while in the remaining 47 (60.2%) MRV detected various degrees of transverse sinus (TS) alterations (hypoplasia or asymmetry) that did not reach the level of stenosis or bilateral extension (Table I).

Next, we investigated the site (Table II), type (Table III), pitch (Table IV) and loudness (Table V) of tinnitus.

**Tinnitus site**
In the BTSS group, tinnitus was bilateral/central in only 21% of cases, while it was monolateral in the remaining patients (50% left ear; 29% right ear). In the no-BTSS group, tinnitus was localized bilaterally/centrally in 39%, on the left ear in 48.4% and on the right side in 12.5% of cases. Compared to the BTSS group there was a higher frequency of bilateral/central localization of tinnitus in the global no-BTTS group, as well as in normal subjects (\(p = 0.008717, \text{OR} = 2.4052\)) (Table II).

**Tinnitus temporal characteristics**
Concerning the temporal characteristics of tinnitus, it was more frequently pulsating in the BTSS group compared to the no-BTSS group (\(p = 0.000244, \text{OR} = 0.2532\)) (Table III). On the other hand, we found that the majority of subjects in the BTSS group (64.9%) described their tinnitus as stable, rather than pulsatile.

**Tinnitus pitch**
We separated all subjects into three classes of tinnitus pitch: over 3 kHz, under 3 kHz and those not able to identify a frequency for their tinnitus. Tinnitus with pitch over 3 kHz was more frequent in both groups of patients, but the distribution, reported in Table IV, did not show any significant differences.

**Other psycho-acoustic tests ( Loudness, MMLs, LDLs)**
No differences in tinnitus were seen in other psycho-acoustic tests. In particular (mean values), tinnitus loudness was 8.1 dB SL in the BTSS group and 7.6 dB SL in the no-BTSS group; MMLs were 11.7 dB SL for the former, 12.2 dB SL for the latter. Analysis of LDLs revealed values over 90 dB for all frequencies tested in both groups, according to the results of the hyperacusis questionnaire which did not show the presence of loudness sensitivity problems.

**Psychometric tests**
The results of the tinnitus handicap inventory (THI)\(^{12}\) and grading of psychometric evaluation are reported in Table V. Compared to the no-BTSS group, subjects with BTSS

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**Table I.** MRV venography results. MRV identified the presence of BTSS in 17.9% of subjects (\(p = 0.000734\) vs. no-BTSS subjects; OR = 0.0996).

| Group   | Subjects | %  | Mean age |
|---------|----------|----|----------|
| BTSS    | 14       | 17.9 | 54 ± 8.8 |
| No-BTSS | 64       | 82.1 | 48.5 ± 11.92 |

**Table II.** Tinnitus site. Compared with the BTSS group, there was a higher frequency of bilateral/central localization of tinnitus in the no-BTSS group, as well as in normal subjects (\(p = 0.008717, \text{OR} = 2.4052\)).

| Group   | Bilateral/Central | Left | Right |
|---------|-------------------|------|-------|
| BTSS    | 3 (21%)           | 7 (50%) | 4 (28.5%) |
| No-BTSS | 25 (39%)          | 31 (48.4%) | 8 (12.5%) |

**Table III.** Tinnitus type. Pulsatile was more frequent for tinnitus in the BTSS group compared to the no-BTSS group (\(p = 0.000244, \text{OR} = 0.2532\)).

| Group   | Pulsatile | Stable |
|---------|-----------|--------|
| BTSS    | 5 (35.9%) | 9 (64.9%) |
| No-BTSS | 8 (12.5%) | 56 (87.5%) |

**Table IV.** Tinnitus pitch. Distribution of population in different pitch subgroups. Tinnitus with pitch over 3 kHz was more frequent in each group of patients.

| Group   | > 3 kHz | < 3 kHz | Not certain |
|---------|---------|---------|-------------|
| BTSS    | 11 (78.5%) | 3 (21.4%) | - |
| No-BTSS | 45 (70.3%) | 12 (18.7%) | 7 (8%) |

**Table V.** THI grading. Distribution of population in different THI classes. For BTSS, the average value was 15.14 (± 10.12), while for no-BTSS was 15.68 ± 12.99 (\(p\), not significant).

| Group   | 1 (0-16) | 2 (18-36) | 3 (38-56) | 4 (58-76) | 5 (78-100) |
|---------|----------|-----------|-----------|-----------|-----------|
| BTSS    | 6 (42.8%) | 8 (57.1%) | -         | -         | -         |
| No-BTSS | 37 (67.2%) | 12 (21.8%) | 6 (10.9%) | -         | -         |
reported more frequently (57.1%) tinnitus that was easily masked by environmental sounds and easily forgotten with activities, that may occasionally interfere with sleep but not with daily activities. In the majority of no-BTSS subjects (67.2%), tinnitus was heard only in a quiet environment and very easily masked and had no interference with sleep or daily activities. Only few of these subjects fall in THI grade 3 (10.9%). These results did not show any statistically significant differences. The results of hyperacusis questionnaire did not show the presence of loudness sensitivity problems, according to LDLs performance.

**BMI**
Because of their frequent association with IH, and, hereupon, with BTSS, we also investigated for the presence of overweight and obesity (Table VI) and found no statistical significance when matched between different groups.

**CSF measurements**
We found values suggesting IH in 40% of BTSS patients (4/10) (Table VII). Only one (# 13) of these patients referred tinnitus as pulsatile and bilateral. In the other patients, tinnitus was localized on the left and was stable. In all of 4 IH cases, LP led to immediate improvement of tinnitus.

**Multivariate analysis**
We also performed multivariate logistic analysis using a multiple logistic regression model considering tinnitus type and site in order to clarify the association of these variables with the presence of BTSS. The main conclusion of this analysis is that the tinnitus site (OR = 2.40) seems to be associated with the presence of BTSS. Considering the other variables, the results were inconclusive.

**Discussion**
Tinnitus is a common and poorly understood disorder, whose aetiopathogenesis is still under debate, and represents an enormous challenge for both otologists and neurotologists. In the present study, we hypothesize that an alteration of venous cerebral circulation, especially BTSS, might be one of the pathophysiological bases of the disease, even in absence of clinical evidence of elevated intracranial pressure. The rationale for this hypothesis relies on the potential effects of vascular abnormalities (i.e. BTSS) on the fragile homeostasis that exists between intracranial and labyrinthine fluids. In fact, several lines of clinical evidence indicate that pressure variations of intracranial fluids influence labyrinth hydromechanics causing otoologic reversible symptoms such as hypoacusis, vertigo or tinnitus. A connection between intracranial and labyrinthine fluids has been reported, albeit inconstant; the perilymph is, in fact, in direct relationship with the intracranial fluids district throughout the cochlear aqueduct; conversely, the endolymph communicates indirectly with the intracranial fluids district throughout the endolymphatic sac; the pressure homeostasis between endolymph and perilymph is maintained by the Reissner’s and other labyrinthine membranes. Different connections are represented by the perivascular and perineural spaces, even if this is possible only in the presence of high intracranial pressure or anatomical lesions. Moreover, experimental demonstration of the connections between the intracranial and labyrinthine fluids has been reported in animal models, showing the absence of modifications within labyrinthine fluids if the cochlear and vestibular aqueducts were closed. The cochlear aqueduct seems to act as a low pass filter, avoiding strong and dangerous transmission of intracranial pressure variations to the labyrinthine fluids. On the other hand, it is important to underscore that the anatomical features of the cochlear aqueduct may per se lead to potential loss of efficacy, due to the progressive but variable degree of sealing throughout life. The percentage of this closure among life is reported to be very different in the literature. Nonetheless, mechanisms of reabsorption and, therefore, of pressure regulation, of cerebrospinal fluid (CF) are well known. It occurs mainly at the level of arachnoid granulations that are located, to a large extent, in transverse sinuses. The functions of these structures are CF reabsorption and its transportation in the bloodstream. A transverse sinus stenosis could influence CF reabsorption with indirect consequences on labyrinthine hydromechanics.
All these considerations, together with those on pathophysiological mechanisms of IIH, already discussed in the introduction, prompted us to consider a possible association between the BTSS and abnormal homeostasis among intracranial and cochlear fluids. The first aim of our study was to evaluate the frequency of association between BTSS and tinnitus. For this purpose we selected subjects affected by monosymptomatic tinnitus, without clinical signs of IIH. In this first step of our study, we choose to reinforce the sample to evaluate if there is some basis for our hypothesis by enrolling only female patients due to the higher incidence of IIH among women. We planned to extend our evaluation to a cohort with males in a second step.

BTSS is reported in 1.8% of subjects with normal CSF pressure. As mentioned in the methods section, we decided to utilize personal data already published in a previous paper for ethical and economical reasons. In our cohort, we found a significantly higher percentage (17.9%) of bilaterally abnormal transverse sinuses, therefore hypothesizing that this condition might be one of the causes of tinnitus. Given the frequent association between BTSS and IIH, we investigated if IH was present in our BTSS cases, even if without clinical evidence. Indeed, 4 of 10 subjects that underwent LP presented values suggesting IIH. Moreover, in these 4 subjects LP determined recovery from tinnitus. This allowed for two considerations: the first on therapeutic effect on tinnitus from IH treatment, and the second on need to investigate the suspect of IH in presence of monosymptomatic tinnitus without evident causes. Our second aim, consequential to the first, was to characterize some features of tinnitus linked to BTSS based on the findings of MRV. Our results highlighted that the common association between some features of the tinnitus (e.g. pulsatility, low frequency pitch) and its “vascular” origin appears to be more unlikely. Pulsatility, in fact, was reported in only 35.9% of our BTSS group, and in just one of patients with a diagnosis of IH after LP. Thus, it cannot be considered as a criterion for the suspect of association with BTSS. This result could be explain by the subjective nature of information about tinnitus, despite careful interviews. However, in the literature there are reports that agree with this finding. No other feature of tinnitus showed statistical significance in association with BTSS.

With reference to site of tinnitus, there is agreement between our results and literature data about the prevalence of localization on the left in both groups, as well as the more frequent bilateral localization in the no-BTSS group compared to the BTSS one. Therefore, a potential limitation of our study is when to indicate MRV in the clinical management of patients suffering from tinnitus. MRV, as described earlier, is a fast non-invasive tool that does not necessitate the use of contrast agents. Nonetheless, at present, there are no clinical and/or instrumental features that can be used as a specific marker to address tinnitus patients to further MRV imaging studies.

On the basis of the described significant association with BTSS, we hypothesize that this venous alteration can be considered as one potential pathophysiological mechanism of tinnitus. Based on our selection criteria that excluded IIH symptoms, this conclusion is also valid in subjects without clinical evidence of IIH. As a consequence, monosymptomatic tinnitus maybe an important symptom if IIH without papilloedema is suspected, regardless of its features. The therapeutic effect of LP on tinnitus in subjects with IH reinforces the hypothesis of a direct influence between labyrinthine and intracranial fluids, confirming observations reported in the literature. This allows us to underscore that tinnitus, when linked to venous stenosis and IIH, may benefit from pharmacological drugs for IH.

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