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Characteristics of tinnitus found in anemia patients and analysis of population-based survey

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ABSTRACT

Objective: This study analyzed the characteristics of tinnitus identified in anemia patients with cohort- and population-based studies in a single institute and suggests a management algorithm. **Methods:** Fifty patients who were treated for anemia and referred for tinnitus treatment were included in a single institute retrospective study. Characteristics of tinnitus were investigated in a correlation analysis with demographic and audiologic parameters. For the population-based study, data from the Korea National Health and Nutrition Examination Survey collected between 2010 and 2011 were analyzed. The study population consisted of 11,402 individuals aged 20–97 years with complete tinnitus-related data. The prevalence of tinnitus in anemia patients was investigated using the questionnaire, and associations between tinnitus and blood/urine parameters were evaluated by binary logistic regression analysis.

Results: In a single-institute study, patients with non-pulsatile tinnitus were significantly older and their initial hemoglobin was higher than those with pulsatile tinnitus ($p = 0.001$, 0.008 , respectively). In pulsatile tinnitus, age and difference between initial and post-treatment hemoglobin were significantly associated with a subjective improvement in tinnitus ($p = 0.002$, 0.016 , respectively). There were no significant audiologic or hematologic parameters associated with the improvement of non-pulsatile tinnitus. In the population-based study, there was no significant correlation between anemia and tinnitus ($p = 0.064$). In a multivariate analysis, age was the only parameter associated with tinnitus in participants with anemia.

Conclusion: The therapeutic strategy and prognosis of tinnitus in anemia patients differ according to the characteristics of tinnitus and the severity of anemia.

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1. Introduction

Tinnitus is the perception of sounds that occurs in the absence of external acoustic stimulus. The pathomechanism of tinnitus is thought to be complicated and therefore remains debatable [1]. Among several risk factors, such as increased age, female gender, and hearing loss, anemia is especially related to pulsatile tinnitus due to an altered hemodynamic

status although the prevalence of pulsatile tinnitus in anemia patients has not been reported in previous studies [2,3]. Anemia results in decreased oxygen carrying capacity of the blood, which carries an associated risk of insufficient oxygen delivery and cellular hypoxia [4]. The compensatory increased flow state and turbulence are perceived as tinnitus in the ear, and the recognition of a hyperdynamic circulatory state as the cause of the tinnitus avoids unnecessary diagnostic tests and is essential in determining appropriate treatment [5].

Until recently, there has been a lack of reports on the association between anemia and non-pulsatile tinnitus despite the possible influences on the pathologic alterations in the inner ear system [6,7]. Several case reports indicated that anemia may be associated with sudden hearing loss by aforementioned mechanism, while none have shown a direct correlation between anemia and non-pulsatile tinnitus [8–10]. A recent epidemiologic study of which the questionnaire survey was targeted to investigate non-pulsatile tinnitus also failed to show a significant correlation between anemia and subjective tinnitus [11,12].

It is important to compare and analyze the characteristics of tinnitus found in anemia patients because there is a paucity of reports with detailed descriptions on this specific entity and due to the differences in diagnostic procedures, treatments, and prognosis. This study investigated the characteristics and prognosis of tinnitus in all subsequent subjects with anemia identified to have tinnitus at our tinnitus clinic. This study also evaluated the associations between anemia and tinnitus and elucidated the epidemiologic parameters associated with tinnitus in anemia patients.

2. Materials and methods

2.1. Patients and evaluation in a single institute cohort study

This study was approved by the Institutional Review Board of our center (IRB No. 16-2016-73). The clinical data were retrospectively reviewed for the patients who were diagnosed with anemia and tinnitus at Seoul National University Boramae Medical Center from March 2005 to December 2016. Among them, 50 adults who were diagnosed with anemia were included in this study.

When the patient first visited our clinic, a detailed history of tinnitus was obtained, and 10 numerical rating scales were administered to score the subjective severity of tinnitus. This scale was adopted from our previous report in which the severity of tinnitus was assessed by subjective intensity and frequency on a scale of 0 (no tinnitus) to 10 (intolerable tinnitus) [13]. Tinnitus improvement was assumed when tinnitus severity was rated lower than 40% of the initial value. After thorough otoendoscopic examination in each patient, audiological evaluations were performed. The mean hearing level (MHL) was calculated as the average of the hearing thresholds at 0.5, 1, 2, and 3 kHz in a pure tone audiogram. A tinnitogram was performed to identify the frequency and level of a tone that is reported to be the closest approximation to a patient's tinnitus perception. Blood samples for complete blood count were taken at the initial and follow-up evaluation after treatment of anemia.

Anemia was defined as a hemoglobin (Hb) level below 13.0 g/dl in men and below 12.0 g/dl using the World Health Organization Hb threshold [13]. For patients with pulsatile tinnitus, computed tomography was performed if needed.

Treatment of tinnitus was as follows: (1) appropriate tinnitus counselling (tinnitus retraining therapy and sound therapy) was performed to all the patients, (2) medication was given to the patients with moderate to severe tinnitus. Anemia was treated according to the etiology (e.g., medical supplement in iron deficiency anemia and surgical excision of myoma, etc.). Method section was modified according to the reviewer's comment.

2.2. Population-based study

This study also investigated data from the sixth Korea National Health and Nutrition Examination Survey (KNHANES) collected from 2010 to 2011. The KNHANES is an ongoing nationwide survey of a noninstitutionalized population of South Korea with a high level of standardization and quality control. The data were collected and managed by the Centers for Disease Control and Prevention of Korea. Each year, a panel selected 192 enumeration districts and 20 households in each district sampled to reflect the entire Korean population. The sampling was weighted by adjusting the post-stratification, non-response rate, and extreme values by statisticians. These samples represent the civilian, non-institutionalized South Korean population using stratified, multistage clustered sampling based on National Census Data by the National Statistical Office.

Written informed consents were obtained prior to the survey from all participants. The presence of tinnitus was based on responses to the following question: "Have you heard any ringing, buzzing, roaring, or hissing sounds without an external acoustic source in the past year?" The response options were "Yes", "No", and "I cannot remember". The participants who answered "I cannot remember" were excluded. All tympanic membranes (right and left) were examined for signs of prior ear disease by trained otologists and were categorized into three groups: normal, abnormal, and could not examine. Pure-tone audiometry for hearing thresholds was measured at 500, 1000, 2000, 3000, 4000, and 6000 Hz in both ears in a soundproof booth. Hearing loss was defined as more than an average of 40 dB hearing loss at 500, 1000, 2000, and 3000 Hz on pure-tone audiometry.

Blood was examined for red blood cell (RBC) count, Hb levels, hematocrit, white blood cell (WBC) count, serum blood urea nitrogen (BUN), creatinine, glucose, aspartate aminotransferase, alanine aminotransferase, triglyceride, total cholesterol, high-density lipoprotein (HDL), and alkaline phosphatase (ALP); urine was examined for pH, specific gravity, and for protein, glucose, ketone, blood, bilinogen, cotinine, and creatinine levels.

2.3. Statistical analysis

Continuous variables were presented as the means \pm standard deviation (SD). In a single institute data analysis, the

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