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A clinical correlation between hypozincemia and tinnitus

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Summary. We examined a group of 115 patients suffering from tinnitus and have attempted to find a statistically significant correlation between the tinnitus experienced and low blood zinc levels (hypozincemia). No particular correlation could be made between the nature of the tinnitus experienced and hypozincemia except for the continuation of head noises, these being more frequently associated with hypozincemia when they are intermittent. Two hypotheses of pathogenesis are proposed to explain this phenomenon and are based on the importance of zinc to the syntheses of enzymes and proteins.

Key words: Tinnitus – Hypozincemia – Zinc

Introduction

Zinc belongs to that group of trace elements which are present in minute quantities in living cells but nevertheless play an important role in metabolism. Iron is the first such element to have been identified, while the second and third (respectively) are iodine and fluorine [10]. The sixth of these elements is zinc.

In 1934, Todd first drew attention to the role of zinc in stimulating growth in the rat [13]. It was, however, a revelation in 1966 when Prasad and his colleagues (6) described – first in Iran and then in Egypt – cases of dwarfism accompanied by hypogonadism linked with zinc deficiencies. For several years, these observations have been considered to be only curiosities confined to certain tropical countries where various types of metabolic deficiencies are prevalent. Nevertheless, the development and improvement of reliable methods for determining zinc levels in the blood serum and erythrocytes have demonstrated that marginal and less spectacular deficiencies (now described as "hypozincemias") do exist in other countries throughout the world.

Zinc is present in 80 different enzymes, hence the diversity of the pathology now encountered. There is known to be a lowered zinc level in some cases of growth insufficiencies, oligo-asthenospermia, ageusia and anosmia, torpid wound healing, alcoholism, enteropathic acrodermatitis, sickle-cell anemia and Wilson's disease [3, 9].

Shambaugh [10] has recently suggested the existence of a progressive neurosensory deafness that resembles presbycusis but is associated with a hypozincemia. Supplementary zinc given to his patients presenting such deafness resulted in a 20% improvement in auditory thresholds and a 25% decrease in any tinnitus present.

On the basis of these experiences, we have sought to verify and possibly quantify Shambaugh's theory of hearing loss and zinc deficiency by looking for an association between the existence of tinnitus and the presence of a hypozincemia.

Materials and methods

Clinical material. A total of 115 patients with tinnitus were studied: 53 women (46%) and 62 men (54%). All patients were examined between 1984 and 1986 at the ENT Outpatient Clinic of the Louvain University Hospital of St. Luc. A preliminary report describing these patients has previously been released [5]. The mean age of the group was 50.35 years (standard deviation, 12.63 years). The youngest patient was aged 18 and the oldest 73 years.

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Tinnitus was localized to the right ear by 31 patients (27%) and by 40 to the left ear (35%). It occurred bilaterally in 44 patients (38%). The tonality of the tinnitus was described as shrill (whistling) by 63 patients (55%) and low-pitched (buzzing) by 29 (25%). It was not clearly describable or was mixed in 23 patients (20%).

The mean time of occurrence of the tinnitus was 42.8 months (standard deviation, 55.6 months) with extremes of 1–312 months at the time of consultation. Noises were continuous in 80 patients (70%), intermittent in 23 (20%) and lacked precision for 12 patients (10%).

Tinnitus was considered to be incapacitating in 31 patients (27%). This high incidence in our cases can probably be explained by the university nature of our patient population. The etiology of the tinnitus was linked to acute or repeated acoustic trauma in 29 patients (25%). Degenerative changes in the inner ear, independent of origin, were found in 11 cases (10%). Ten cases (9%) showed evidence for petrosal trauma (radiological fracture of the petrous bone or labyrinthine concussion).

Nine patients (8%) had various stages of otosclerosis. Seven patients (6%) had vascular or pressure dysfunctions of the labyrinth (inclusive of Meniere's disease). Six patients (5%) had chronic otitis media. Three patients (3%) had radiological evidence for cervical arthrosis. Two patients (2%) had medication-related ototoxicity, while two other patients (2%) had sudden deafness from some other causes.

One patient each (0.6%) had viral labyrinthitis, jugular vein turbulence, post-stapedectomy changes, arterial hypertension, and a diffuse severe atheromatosis of the neck vessels (demonstrated by dopplerogram). Nevertheless, it was not possible to establish any etiology after extensive testing in 31 cases (27%). A certain proportion of these latter patients were probably suffering from miscellaneous cerebral vascular disorders that are difficult to demonstrate by non-invasive procedures.

Audiometric testing. Audiometric testing resulted in a classification of our patients according to seven types of audiograms. These types are described in Fig. 1 and include the numbers of patients in each type.

We also studied the auditory nature of each person's tinnitus by means of audiometric testing in a sound-proof booth. The frequencies of the tinnitus could be defined in 53 cases: 4 patients perceived head noises at 250 Hz; 2 patients at 500 Hz; 2 patients at 750 Hz; 1 patient at 2000 Hz; 3 patients at 3000 Hz; 8 patients at 4000 Hz; 21 patients at 6000 Hz; 4 patients at 8000 Hz and 3 patients at 10000 Hz; 5 patients at a white noise. No patient perceived tinnitus

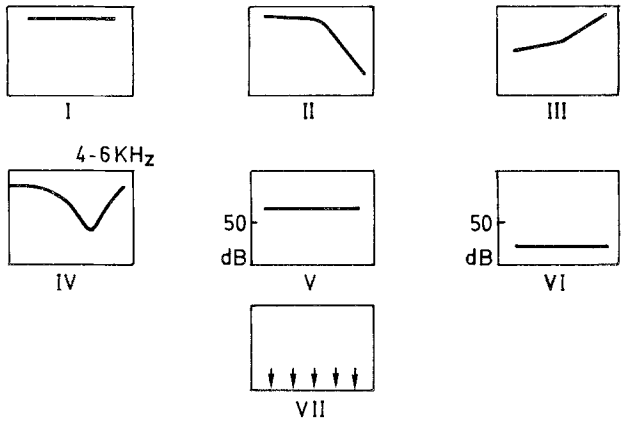

Fig. 1. Types of audiograms in 115 patients with tinnitus

I. Normal audiogram (5 patients)
II. Decreased hearing thresholds at high frequencies (38 patients)
III. Decreased hearing thresholds at low frequencies only (5 patients)
IV. Dip in perception at one or both of the 4000 Hz and 6000 Hz frequencies (29 patients)
V. Perceptional hearing loss below 50 dB at most frequencies (21 patients)
VI. Perceptional hearing loss above 50 dB at most frequencies (15 patients)
VII. Anacusis (cophosis) (3 patients)

at 1000 Hz. The intensity was measurable in 45 cases. The mean was 8.77 dB supra-threshold (standard deviation, 6.90).

Assessment of zinc levels. Blood was removed from all patients with tinnitus and was tested with the spectrophotometric method of Pekarek et al. [5] for determining globular and serum zinc levels. Normal serum zinc varies between 90 and 123 µg/dl (mean: 100.3 µg/dl; standard deviation, 13.44) and globular zinc between 1000 and 1500 µg/dl.

A control group of 15 patients not having tinnitus was used. This group consisted of 8 men and 7 women (average age, 50 years) and – except for the absence of tinnitus – had a clinical profile similar to the patients with tinnitus.

Results

From our total number of patients with tinnitus (n = 115), 79 patients (68.7%) were found to have serum hypozincemia. The serum zinc level in these patients was 84.19 µg/dl (standard deviation, 12.44) and is depicted in the histogram in Fig. 2.

In comparison with the mean level of zinc for the control group (126.27 µg/dl), there did exist a highly significant difference between the two groups ($P >$

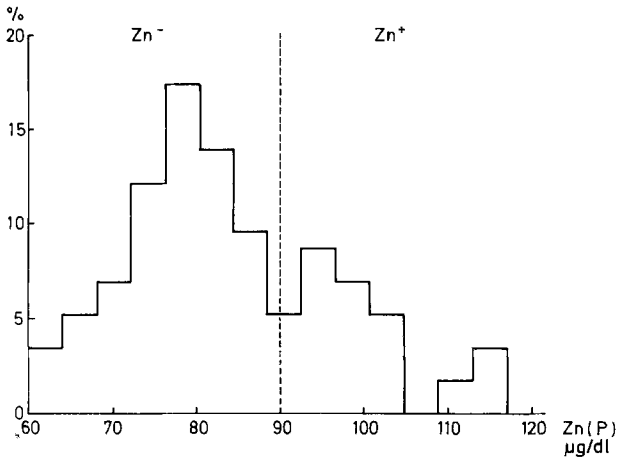

Fig. 2. Histogram of serum zincemia in patients with tinnitus

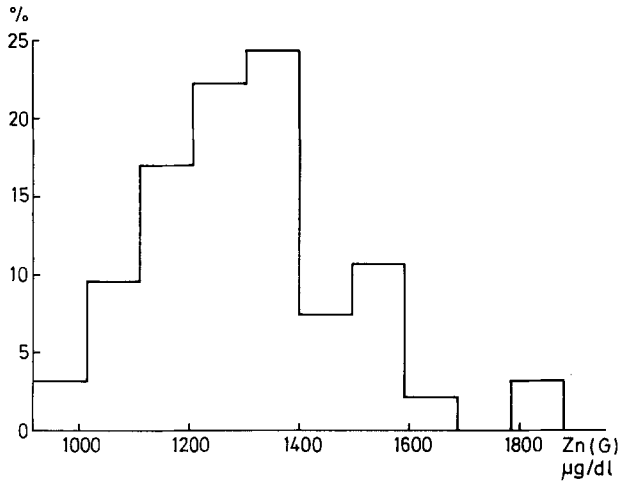

Fig. 3. Histogram of globular zinc in patients with tinnitus

0.95). The mean globular zinc level for our sampling group ($n = 94$) was 1304 µg/dl (standard deviation, 182.09) (Fig. 3). This value is within the normal limits for globular zinc determined by our laboratory.

We next sought to find a possible correlation between the hypozincemia and the various characteristics presented by our patients with tinnitus: age, sex, side of involvement, etiology, audiometric type, and characteristics (frequency, intensity, severity).

However, we were unable to find any statistically significant correlations between these parameters and hypozincemia, with the exception of the continuity of the tinnitus: intermittent tinnitus was most frequently found in the presence of a hypozincemia ($P > 0.95$). Additionally, attempted multiple correlations considering two characteristics in relationship to a constant characteristic of hypozincemia also showed no meaningful correlations.

Discussion

In this report, we have studied serum hypozincemia found in a population of 115 patients suffering from tinnitus. Of the serum zinc determined, only 10% corresponded to the free and therefore readily interchangeable fraction of zinc present. The remaining 90% was protein-linked.

Serum zinc accounts for only 1% of total body zinc. The remaining 99% is found within intracellular structures and is only partially and imperfectly represented by globular zinc [11]. Serum is therefore only an overall reflection of the pattern of the intricate exchanges of zinc present within the individual as a whole.

In addition to its role in endocrine function, cellular immunity, platelet function, and the response to stress, zinc plays a part in the constitution of almost 70 metallo-enzymes, as well as in protein synthesis [11]. It is probably in the latter two physiological roles that an explanation might be found for an association between tinnitus and hypozincemia. As such, two pathophysiological theories may be envisaged. The first is cochlear, particularly since the cochlea is one of the body organs rich in zinc [10]. In this site, zinc plays a part in the electrochemical and acid-base equilibrium of the endolymph. It is specifically involved in the formation of carbonic anhydrase, one of the metallo-enzymes previously described [11]. This latter enzyme is found in the marginal cells of the stria vascularis [13], where it transforms the dissolved carbon dioxide (CO_2) and water (H_2O) into bicarbonate (HCO_3) ions and hydrogen (H^+) that penetrate into the endolymph and influence the endocochlear potential [12]. In addition, the Na^+-K^+ pump is controlled by Na-K ATPase and is inhibited by zinc [4, 7]. As the result of a zinc deficiency, the Na-K exchanges can be altered to provoke a further modification of the endocochlear potential. Tinnitus could then conceivably result from this alteration of cochlear electrophysiology.

Further, a zinc deficiency might influence the integrity of the cellular microskeleton by interfering with the calcium-calmodulin system [7]. Shambaugh [8] has indeed suggested a degenerative pathology of Corti's cells through the lack of zinc assimilation by the kinocilia here. The second theory of tinnitus and hypozincemia pertains to neuronal dysfunction. Zinc plays a part in the synthesis of myelin [11] while zinc deficiency has been reported to play some role in certain neurological pathologies, such as the Guillain-Barré syndrome [11]. Through its action in the metallo-enzymes and its influence on proteinogenesis, zinc might then interfere in the synthesis of neuronal

neurotransmitters [11] and thus play a significant part in the occurrence of tinnitus [1].

In conclusion, we have described our studies concerning the association between hypozincemia and the presence of tinnitus. However, the present state of our knowledge prevents us from making any firm conclusions. Yet, should zinc be to the cochlea what iron is in the red blood cell, iodine for the thyroid, fluorine for bone; then it would be possible for this trace element to possess great importance and have still-to-be-defined implications in the occurrence of neuro-otologic pathologies.

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