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Ushering in the Era of Circulatory Otologic Biomarkers

The article by Hana and Bawi in the current issue of this Journal entitled "Prestin, Otolin-1 regulation and human 8-oxoG DNA glycosylase1 gene polymorphisms in noise-induced hearing loss" is an interesting article that has important implications for occupational and clinical medicine.[1] This work explores biomarkers for noise-induced hearing loss in the blood of a population of individuals with unprotected, chronic, occupational noise exposure and compares them with controls. Hana and Bawi demonstrated that blood levels of two inner-ear proteins, prestin and otolin-1, are elevated in noise-exposed individuals. As such, it represents an application of the novel concept of measuring otological biomarkers in circulation to better understand and diagnose inner-ear disorders. In fact, it represents the first application of this concept to noise-induced hearing loss in the occupational setting.

The concept of blood-based biomarkers for inner-ear disorders was first introduced by this author in 2014, initially for vertigo.[2] As proof of concept, it was demonstrated that patients with benign paroxysmal positional vertigo had significantly higher levels of an inner-ear protein, otolin-1, than controls. I subsequently proposed extending this concept to acquired sensorineural hearing loss.[3] Biomarkers in circulation are powerful indicators of normal and pathological biological processes.[4] These biomarkers are easy to collect, sensitive enough to detect the disease of interest, and specific enough to differentiate normal from abnormal. They are routinely utilized in the clinical practice. For example, routine blood tests allow assessment of heart, kidney, liver, and bone health. They provide information on progression of disease and response to therapy and play important roles in development of new pharmaceuticals. In otology, at present, there are few blood tests that can be utilized to aid with diagnosis. Examples include blood tests for genetic testing for connexin 26/30 and pendrin for evaluating hearing loss.[5] Another example is measurement of inflammatory markers, such as heat shock protein, in diagnosis of autoimmune inner-ear disease.[6] These tests either have limited clinical applications or are not specific to the inner ear. No inner-ear-specific serum biomarkers have been approved for use in clinical otology. The inner ear has been found to possess a number of unique proteins that mediate its specialized functions. For example, outer hair cells (OHCs) are effector cells in the cochlea responsible for enhancing hearing sensitivity. Their function is made possible by a membrane protein, prestin.[7] Since OHCs are early targets for noise-induced damage and ototoxins, and because of the specificity of prestin to the OHCs, I hypothesized that prestin may have a role as serological biomarker for OHC damage and hearing loss.[8] I and my colleagues subsequently provided experimental support for this hypothesis in noise-induced[9] and cisplatin-induced[10,11] models of sensorineural hearing loss.

The study by Hana and Bawi[1] represents a practical application of the concepts we forwarded and further lends support for the proposed concepts and is important for potential application of blood biomarkers for early diagnosis and monitoring of inner-ear disorders. This work, because of its nature, was faced with many challenges, including difficulty controlling noise-exposure history and, therefore, should be considered as a preliminary proof of concept in the clinical setting. Nevertheless, this manuscript may contain potentially valuable data with significant implications due to the high prevalence of noise-induced hearing loss in the general population. It also breaks new ground, as it demonstrates potential impact of chronic noise damage, which is known to extend beyond the OHCs (represented by prestin) to other inner-ear structures (represented by otolin-1).

Much work lies ahead before we can reliably utilize this novel tool in the clinical setting. For example, blood levels of these biomarkers appear to vary after acute injury.[10-12] Thus, the temporal course of change in the blood levels of the biomarkers needs to be fully elucidated both in the acute and chronic settings after inner-ear injury and additional clinical data are needed to verify their value. What is clear, however, is that the era of circulatory otologic biomarkers is upon us. What is truly exciting is that these biomarkers not only can help us detect and treat acquired sources of hearing loss but also may help us gain insights into long mysterious disorders such as Meniere's disease and sudden sensorineural hearing loss.

Disclosures

Single author.

Compliance with ethical principles

Not required.

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