Hearing loss and circulating markers of endothelial dysfunction - 927 words

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Hearing loss is highly prevalent in older people, affecting 50% of Australians aged over 55 years, and 70% of people aged over 70 years. It is the third most common chronic disease experienced by older Australians, after chronic pain and restricted physical activity (J Aging Health. 2009;21:1098). With an aging population, the number of people affected by this disability continues to rise, as does the cost to both affected individuals, in terms of their quality of life, and to society. A number of other co-morbidities often accompany age-related hearing loss; it is associated with endothelial dysfunction and increased cardiovascular risk, and there is evidence of significantly higher rates of cardiovascular disease in people with hearing loss (Circulation. 2016;134:A19010). Hearing loss causes significantly negative effects on quality of life, mental health and physical function. Therefore, finding potentially modifiable risk factors and markers for hearing loss should be a public health priority. Our world-first study investigated the association between hearing loss and circulating markers for endothelial dysfunction, which are potentially modifiable through lifestyle and drug interventions.

Endothelial cells form the linings of every blood vessel in the body, almost every cell of which requires a blood supply. They comprise a one-cell-thick layer called the endothelium, and are also found, for example, on the inner walls of the heart and in the lymphatic vessels. The endothelium acts as a barrier between the blood and the rest of the body while allowing some chemicals and white blood cells to move from blood to tissue, or for waste and carbon-dioxide to move from tissue to blood. Endothelial cells also facilitate the movement of plasma and other cell components throughout the vascular system, and are responsible for maintaining homeostasis and the formation of new blood vessels, and for regulating inflammatory processes. Dysfunction of endothelial cells is associated with diabetes, inflammatory, cardiovascular and immune disease.

Methylarginines are well-recognised markers of endothelial dysfunction and cardiovascular disease. They have been found to be elevated in blood serum in diabetes, coronary artery disease, kidney disease, hypertension, and other diseases (Ann Med. 2000;32:293; Ann Med; 40:180; J Am Soc Nephrol. 2008;19:388). There is a 54% higher prevalence of hearing loss in people with a history of cardiovascular disease than in the general population (JSLHR. 2005;48:473). The research in this area over the past 6 decades has shown significant negative effects of cardiovascular disease on the peripheral and central auditory systems (Am J Audiol. 2010;19:9). Given the cochlea (inner ear) has a rich blood supply and is highly sensitive to disruptions in blood flow, it is possible that higher
circulating methylarginine concentrations could impair endothelial function, and therefore blood flow to the cochlea, contributing to hearing loss.

Until now, only one study has examined the relationship between hearing loss and serum concentrations of methylarginines (Ren Fail. 2008;30:877). In 40 patients with kidney disease it was found that high frequency hearing loss was predicted by higher methylarginine blood serum concentrations, providing support for the theory that hearing loss may be caused by vascular problems. Our study investigated whether there was a relationship between serum concentrations of methylarginines and hearing loss in a population-based cohort of older adults, hypothesizing that higher serum concentrations of the methylarginines, Asymmetric dimethylarginine (ADMA) and symmetric dimethylarginine (SDMA), would be associated with poorer hearing.

630 participants of the Hunter Valley Community Study for whom audiometric evaluations were conducted were selected for serum methylarginine concentration measurement. Pure tone audiometry was used to measure air and bone conduction thresholds at 0.5 – 4kHz for both ears using standard audiometric procedures in a sound treated facility. Blood serum, for measurement of ADMA and SDMA, was collected when the audiometric evaluations were performed. Using better ear pure tone average (PTA), the prevalence of hearing loss in this sample was 52%; 48% of participants had a mild loss, 3.5% had a moderate loss, and 0.2% had a severe or greater loss. Hearing loss prevalence increased with age. There were more women than men with mild hearing loss (particularly older women), more men than women with moderate hearing loss, and only women with severe hearing loss in the sample.

A statistically significant association was found between higher serum concentrations of ADMA and L-arginine, an ADMA precursor, and greater hearing loss for men, particularly those aged over 75 years. This indicates that endothelial dysfunction may be associated with hearing loss across different populations. This finding has potential clinical significance if the association between ADMA and hearing loss is causal, as serum methylarginine concentrations can be modified through pharmacotherapeutic and lifestyle interventions. In contrast, ADMA concentration was not associated with hearing loss for women, but a higher concentration of serum L-arginine, was associated with reduced hearing loss in older women (over 70 years). This finding may reflect gender differences in the role of L-arginine in hearing loss.

Further large population-based studies are required to confirm these findings and to investigate whether the relationship between serum methylarginines and hearing loss is causal. If there is found to be a causal relationship, it will be important to conduct further research on the effect of lowering blood serum methylarginines on hearing loss, or of bypassing this mechanism by introducing nitric oxide donors. Given the prevalence of endothelial dysfunction and cardiovascular disease in older people, prevention of hearing loss through this mechanism could significantly impact on the incidence of hearing loss in this population. It may also be beneficial to investigate whether higher serum methylarginine concentrations may be useful as a biomarker for predicting future hearing loss.
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