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Evaluation of heart rate variability and night-time blood pressure measurements in patients with idiopathic sudden sensoryneural hearing loss

S. DEMIRELLI[1], H. DEGIRMENCI[2], S. FIRTINA[3], I. SALCAN[4], E. ERMIS[1], H. DUMAN[5], E. IPEK[1], H. HAMUR[2], G. CEYHUN[2]

[1]Department of Cardiology, Erzurum Education and Research Hospital, Erzurum, Turkey
[2]Department of Cardiology, Erzincan Universty, Erzincan, Turkey
[3]Department of Cardiology, Maresal Cakmak Military Hospital, Erzurum, Turkey
[4]Department of Ear, Nose and Throat, Erzincan University, Erzincan, Turkey
[5]Department of Cardiology, Rize University, Rize, Turkey

Abstract. – OBJECTIVE: The aim of this study is to investigate the role of the autonomic nervous system in the etiology of idiopathic sudden sensorineural hearing loss (ISSHL) by measuring heart rate variability (HRV) and night-time blood pressure levels.

PATIENTS AND METHODS: A total of 58 patients, 31 ISSHL patients (group 1) and 27 healthy volunteers (control group; group 2), were included in this study. Clinical and ambulatory blood pressure measurements and Holter electrocardiography were performed in both groups. After these evaluations, HRV parameters and night-time blood pressure values were determined.

RESULTS: Mean systolic blood pressure (SBP) and mean diastolic blood pressure (DBP) measured at night-time were higher in group 1 compared to group 2 ($p < 0.05$). Heart rate variability parameters were lower in group 1 than in group 2.

CONCLUSIONS: In patients with ISSHL, elevated blood pressure at night-time and reduced heart rate variability suggest that autonomic nervous system dysfunction might play a role in the etiopathogenesis of the disease. The measurements of ambulatory blood pressure and heart rate variability can reveal more enlightening data in the determination of the etiology of ISSHL and guiding the treatment.

Key Words:
Sensorineural hearing loss, Night-time blood pressure, Heart rate variability, Autonomic nervous system.

Introduction

Idiopathic sudden sensorineural hearing loss (ISSHL) was first described in 1944 as a sudden onset, generally unilateral hearing loss of at least 30dB in at least three consecutive frequencies that develops within 72 hours[1]. The diagnosis is made by exlusion of any other pathology causing sudden sensorineural hearing loss. In 28-57% of patients, vestibular symptoms, fullness in the ear, tinnitus, variable degrees of vertigo and balance disorder can be seen[2]. Although various causes of ISSHL have been suggested such as viral infections, vascular occlusion, autoimmunity, cochlear membrane damage, toxic and vascular reasons, viral infections and vascular pathologies stand in the forefront among these causes[3]. One of the factors that can contribute to the vascular pathology is impairment in the autonomic nervous system. Impairment in the autonomic regulatory mechanisms can result in changes in blood flow to the cranial structures indirectly by causing some dysfunction in the cardiovascular system, which may result in impaired nutrient supply and oxygenation in the inner ear and other structures. Two of the methods that are used to evaluate the effects of autonomic irregularities on the cardiovascular system are 24 hours Holter electrocardiography and ambulatory blood pressure measurement. These two techniques allow us to effectively evaluate the heart rate variability and blood pressure fluctuations. Especially the arterial blood pressure measurements at night-time can provide valuable data in terms of autonomic dysfunction in ISSHL etiology, because the night-time measurements are not affected by the factors such as exercise, smoking, caffeine consumption and stress which can have some influence on autonomic regulation. Additionally, heart rate variability (HRV) is another parameter

Corresponding Author: Selami Demirelli, MD; e-mail: demirelli23@yahoo.com

which can show improper autonomic regulation. It has been demonstrated that HRV decreases in diseases such as diabetes mellitus and myocardial infarction[4,5]. Especially in patients with ISSHL, determination of autonomic dysfunction can aid in elicitation of etiopathogenesis. The autonomic nervous system works to keep our body in a state of equilibrium against the environmental, psychological and physical stress conditions. The cranial nuclei and secretory glands (both are components of autonomic nervous system) in humans, which are responsible for maintaining our circadian rhythm, are strongly affected by some factors such as chronic sleep deprivation and exposure to light at nights in today's civilized life[6]. Inadequate or excessive regulatory responses in our autonomic nervous system can trigger different pathological processes in many organ systems. ISSHL can as well be a such process. Therefore, in this study we have evaluated heart rate variability and blood pressure changes in patients with ISSHL as determinants of autonomic dysfunction.

Patients and Methods

Patient Population

Patients admitting to our Ear, Nose and Throat Outpatient Clinics with the complaint of sudden hearing loss between 2014-2015 were included in this study. ISSHL was defined as the sudden onset hearing loss of at least 30dB in at least three consecutive frequencies in audiometry test that developed progressively within 72 hours and presented in one or both ears in the absence of any other etiological factors as determined by patient history, physical examination, laboratory evaluation and imaging. A total of 79 patients with the diagnosis of ISSHL were evaluated, and those with hypertension, cardiac, vascular, metabolic, neurologic, otologic, and psychologic disease, and those receiving any medical treatment were excluded. A total of 58 patients, 31 with ISSHL and 27 healthy volunteers, were included in the study. An ethical approval was obtained from Erzincan University local Ethics Committee and the study was conducted according to the Declaration of Helsinki. All patients were informed before the study and their consents were obtained.

Study Design

In this study patient group and control group was designated as group 1 and group 2, respectively. In order to investigate the secondary causes of hearing loss patients were assessed by Earnose-Throat, Neurology, Internal Medicine and Psychiatry Outpatient Clinics. Those patients with a diagnosis of ISSHL were also evaluated by cardiology clinic. Conventional echocardiographic evaluation was performed to exclude cardiac pathologies. A 24 hours blood pressure monitoring was obtained by ambulatory blood pressure measurement and 24 hour electrocardiographic Holter was used to determine the HRV. All of the evaluations were performed by two cardiologists.

Measurement of Clinical Blood Pressure

Blood pressure measurements were performed according to the standard blood pressure measurement rules, manually using a sphygmomanometer after a rest of 5 minutes in sitting position. Those with a mean value of ≤ 140/90 mm Hg of three consecutive measurements were included in the study.

Evaluation of Ambulatory Blood Pressure

24 hours ambulatory systolic (SBP) and diastolic blood pressure (DBP) measurements were taken automatically by anoscillometric portable monitor (SpaceLabs, Medical Inc, Model: 92512, Redmond, WA, USA) from the non-dominant arm. The measurements were taken once in every 20 min between 07:00-22:00 (day-time) and once in every 30 min between 22:00-07:00 (night-time). The cuff sizes were chosen in accordance with the arm circumference of the individuals. All patients and healthy controls were advised to carry on their routine daily activities and to avoid excessive exercise, smoking, alcohol and caffeine containing drinks. Ambulatory blood pressure data was recorded digitally. The blood pressure values during sleep and awake state were recorded.

Determination of Time Related Variability in Heart Rate

A 24 hours Holter electrocardiography monitoring was undertaken. The 'Holter WIN-PV plus' software was used during monitorization. All the Holter recordings were evaluated manually to avoid interference of any artefacts and then 'time domain' variability in heart rate parameters were calculated automatically. The following parameters were chosen for evaluation: 24 hours SDNN (the standard deviation of all normal R-R intervals), SDNN-i (the mean of standard devia-

tions of all R-R intervals within the 5 min of the recordings), SDANN (the standard deviation of the means of all R-R intervals within the 5 min of the recordings), pNN_{50} (the ratio of adjacent R-R intervals that demonstrate a difference of more than 50 milliseconds), RMSSD (the square root of the difference between the consecutive R-R intervals), NN (the distance between two QRS segments). Patients were instructed not to take any medications and caffeinated drinks up to 48 hours before the application of Holter electrocardiography.

Conventional Echocardiographic Evaluation

The transthoracic echocardiographic evaluations were performed by a Vivid 7 Dimension® (GE Vingmed Ultrasound AS N-3190 Horten, Norway) echocardiography device with the use of a 2.5 MHz transducer. Patients were evaluated in left lateral decubitus position after a 5 min rest. The pericardium, heart valve morphology and wall motion were evaluated by M mode and 2 dimensional echocardiography.

Statistical Analysis

All of the data was recorded in the Statistical Package for Social Sciences 20.0 software programme (SPSS Inc., Chicago, IL, USA). Parametric variables were expressed as mean ± standard deviation whereas non parametric data were expressed as percentages. A distribution test was used in comparison of demographic and clinical features. A Chi square test was used to compare ratios of parametric data when the distribution was normal and a *t*-test was used in comparing parametric data with non-parametric data. A Student *t*-test and Mann-Whitney U-test were used to compare numeric variables that are normally distributed and not normally distributed, respectively. A p value of < 0.05 was designated as statistically significant in all analyses.

Results

The comparison of the groups in terms of demographics, clinical features and blood pressures is shown in Table I. There was no statistically significant difference between the groups in terms of age, gender and heart rate. Also there was not any significant difference between groups in terms of day-time and clinical systolic and diastolic blood pressures. But the night-time systolic blood pressure was significantly higher in Group 1 compared to Group 2 (Group 1; 130.6 ± 5.1; Group 2; 124.1 ± 5.1, respectively, $p < 0.05$) (Figure 1). Also night-time diastolic blood pressure values was significantly higher in Group 1 compared to Group 2 (respectively Group 1; 83.2±3.8; Group 2; 80.2 ± 4.7, $p < 0.05$) (Figure 2).

The comparison of the groups in terms of heart rate variability in relation to time parameters is shown in Table II. NN was significantly lower in Group 1 compared to Group 2 ($p < 0.05$). SDNN was significantly lower in Group 1 compared to Group 2 ($p < 0.05$). SDANN and SDNN-i was significantly lower in Group 1 compared to Group 2 ($p < 0.05$). RMSSD was significantly lower in Group 1 compared to Group 2 ($p < 0.05$). pNN_{50} was significantly lower in Group 1 compared to Group 2 ($p < 0.05$).

Table I. Comparison of the groups in terms of demographics, clinical features and blood pressures.

Parameters	Group 1 (n: 31)	Group 2 (n: 27)	*p*-value
Age (years)	48 ± 17	49 ± 14	0.985
Gender (male/female)	20/11	17/10	0.675
Heart rate (beat/minute)	81 ± 8.3	78 ± 7.7	0.095
SBP (mmHg)	121.8 ± 9.6	122.3 ± 5.8	0.881
DBP (mmHg)	80.1 ± 6.2	78.9 ± 3.9	0.643
24-hour SBP (mmHg)	123.4 ± 7.1	120.8 ± 6.6	0.123
24-hour DBP (mmHg)	79.6 ± 7.9	78.9 ± 4.5	0.760
Day-time SBP (mmHg)	122.6 ± 6.2	122.4 ± 4.8	0.642
Day-time DBP (mmHg)	79.2 ± 5.8	79.4 ± 3.2	0.867
Night-time SBP (mmHg)	130.6 ± 5.1	124.1 ± 5.1	0.001
Night-time DBP (mmHg)	84.2 ± 3.8	80.2 ± 4.7	0.010

SBP: Systolic blood pressure, DBP: Diastolic blood pressure.

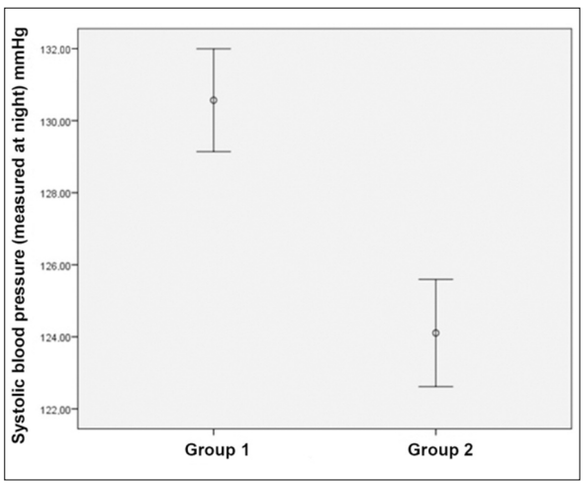

Figure 1. Comparison of the groups in terms of night-time systolic blood pressure.

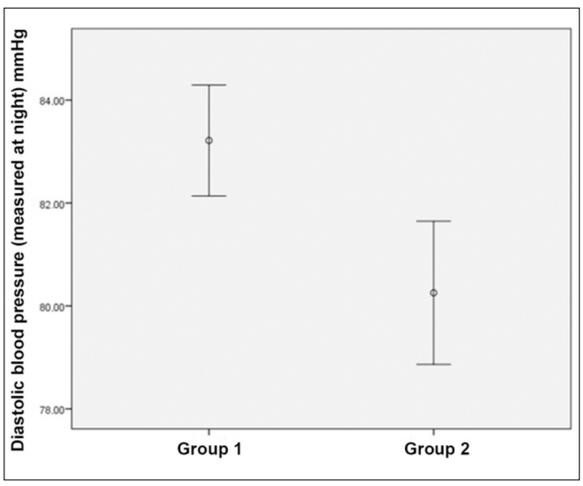

Figure 2. Comparison of the groups in terms of night-time diastolic blood pressure.

Discussion

In this study we demonstrated an increased night-time systolic and diastolic blood pressures and decreased time related variability in heart rate in patients with ISSHL. Approximately half of the patients with ISSHL have the symptoms that result in an impairment in quality of life such as balance disorder, fullness in the ear, tinnitus and vertigo[2]. It is very important to understand the underlying etiology in order to guide the treatment. Vascular pathologies were accused initially in the etiology of ISSHL. The reason for considering a vascular pathology as an offender is that it occurs suddenly just like myocardial infarction and frequently coexists with a systemic vascular disease[7,8]. It can be the case that vascular physiopathology can lead some irregularity in the blood flow to the cranial structures which can then contribute to the development of ISSHL. Also autonomic nervous system (ANS), being the main regulator of the cardiovascular functions, can play a key role in the vascular physiopathology of the ISSHL. The regulatory function of the ANS is briefly as follows: the day-night time cycle occurring as a result of sun rise and sunset allows us to maintain our circadian rhythm regularly in normal circumstances. Circadian rhythm activates many regulatory processes through neurohormonal effects such as immune system, musculoskeletal system, cardiovascular system, metabolism and regulation of reparative and reconstructive activities in other organ systems. These processes reveal their effects through the nuclei and endocrine glands within the ANS. It has been shown that the impairment in the circadian rhythm and chronic sleep deprivation result in abnormalities in the autonomic functions which cause different pathologic processes in

Table II. Comparison of the variability in the heart rate between the groups.

Parameters	Group 1 (n: 31)	Group 2 (n: 27)	*p*-value
NN (ms)	510 ± 39.1	549 ± 74.4	0.030
SDNN (ms)	81 ± 5.3	89 ± 8.0	0.036
SDANN (ms)	71 ± 3.0	83 ± 2.2	< 0.001
SDNN-i (ms)	63 ± 3.4	71 ± 2.3	< 0.001
RMSSD (ms)	60 ± 4.1	66 ± 3.0	0.032
pNN50 (%)	11.5 ± 1.2	13 ± 0.7	0.012

NN; the distance between two QRS segments, SDNN; the standard deviation of all normal R-R intervals, SDNN-i; the mean of standard deviations of all R-R intervals within the 5 min of the recordings, SDANN; the standard deviation of the means of all R-R intervals within the 5 min of the recordings.

many organ systems[9,10]. Nowadays we are exposed to excess levels of environmental light within the modern urban living. Although it is dark after the sunset, we are exposed to excess light in our workplaces, houses and many social places until late times at night. This excess light results in inadequate synthesis and delayed peaking of melatonin hormone which is responsible for regulation of our circadian rhythm, leading disturbances in our circadian rhythm[11]. It is now well established that disturbances in the circadian rhythm can play some important role in the etiology of several diseases such as immune system dysfunction, metabolic disorders, cardiovascular diseases and cancer[12,16]. Möller-Levet et al[17] investigated the genetic basis of the effects of inadequate sleep on the circadian rhythm in their gene study. It was revealed that the most important effects were the disturbances in the inflammatory, stress and oxidative responses. Current results show that the disturbances in the circadian rhythm can lead to initiation of many pathologic processes through the genetic pathways in different organ systems.

Chronically deprived sleep and continued exposure to light during the dark period after the sunset, when we normally need to switch to the sleep state, can cause impairments in the regulatory effects of autonomic nervous system on the cardiovascular system. Thus, irregular vascular function can lead to chronic reduced blood supply and oxygenation of the structures that are responsible for hearing functions and plays some role in the etiology of the ISSHL. Our study is important in terms of having the potential to show the direct effect of the autonomic nervous system in the physiopathology of ISSHL by measuring the night-time blood pressure variability. During day-time a lot of changes occur in the cardiovascular system both related and not related to ANS which are generally due to exogen factors like smoking, caffeinated drinks, alcohol consumption and psychological stress. Night-time blood pressure measurements were found to be higher in the patient group. This suggests that impairment in the regularity functions of the ANS on blood pressure can play a role in the etiology of the ISSHL. Mutoh et al[10] in their mammalian animal study, demonstrated an increase in the sympathetic activity and a decrease in the vagal tonus together with elevated blood pressure in the animals exposed to light. The disturbance in autonomic regulation can explain the increase in the sympathetic activity and elevation in the blood pressure values. From this point of view, the clinical blood pressure measurement as a sole diagnostic test in our daily practice can be inadequate to determine the etiology. Additionally, the decrease in the variability of the heart rate in the ISSHL group also suggests that ANS can play a role in the etiopathogenesis of ISSHL. Both the reduction in the heart rate variability and the relative elevation in the night-time blood pressure measurements can be important signs of regulatory dysfunction in the ANS. Schulz et al[18] previously discussed about autonomic regulatory dysfunction at the vascular physiopathology of ISSHL. In our study we found changes in both the blood pressure values and the heart rate variability. But they showed variabilities only at the blood pressure of ISSHL patients, not at the heart rates. Studies especially evaluating the heart rate variability and with larger numbers of patients may enlighten the exact data about heart rate variability. Although the blood pressure measurements in the patient group were found to be higher compared to the control group, these values are not adequate for diagnosis of hypertension, but they can predict a possible ANS dysfunction. There are studies[19] demonstrating the development of autonomic dysfunction in situations such as depression and anxiety. Also in states of emotional stress, sympathetic activity is reported to increase whereas parasympathetic activity decreases[20]. This can be a contributing factor to night-time blood pressure elevation, reduction in the heart rate variability and the occurrence of ISSHL. Especially in elderly patients heart rate variability is reported to decrease as a result of ANS dysfunction[21,22]. Also in the elderly ISSHL can be seen. But there was no difference between the patient group and the control group in terms of age in our study.

Electrical signals are carried from the nerve endings located in the inner ear to the brain. A pathology in these nerve endings or in the pathways that carry the signals to the brain can lead to autonomic dysfunction and sensory neural hearing loss. In this situation night-time blood pressure variability can occur too[23-25]. For this reason the concomitant occurrence of ISSHL and autonomic dysfunction can lead some elevation in night-time measured blood pressures and decrease in heart rate variability. But it is hard to say whether ISSHL is due to autonomic dysfunction or vascular pathology.

Conclusions

Impaired autonomic nervous system functions can play an important role in the etiology of the ISSHL. Determination of blood pressure changes and heart rate variability in cardiovascular system can be an important tool in the clinical practice to evaluate autonomic dysfunction. In clinical practice, instead of a single measurement to predict the existence of autonomic dysfunction, a 24 hours follow up of the blood pressure can provide us more informative data. Chronic irregularities in the autonomic nervous system and their role in the physiopathology of many diseases have been reported in various studies. We think that larger scale clinical studies designed in detail can demonstrate the role of autonomic nervous system dysfunction in the etiology of ISSHL.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

References

1) Rauch SD. Intratympanic steroids for sensorineural hearing loss. Otolaryngol Clin North Am 2004; 37: 1061-1074.
2) Chen CY, Halpin C, Rauch SD. Oral steroid treatment of sudden sensorineural hearing loss: a ten year retrospective analysis. Otol Neurotol 2003; 24: 728-733.
3) Baloglu O, Olgun G, Saraç S. Treatment of idiopathic sudden sensorineural hearing loss. Hacettepe Tıp Dergisi 2007; 38: 26-32.
4) Kleiger RE, Miller JP, Bigger JT. Decreased heart rate variability and its association with increased mortality after acute myocardial infarction. Am J Cardiol 1987; 59: 256-262.
5) Kudat H, Akkaya V, Sozen AB, Salman S, Demirel S, Ozcan M, Atilgan D, Yilmaz MT, Guven O. Heart rate variability in diabetes patients. J Int Med Res 2006; 34: 291-296.
6) Stevens RG, Brainard GC, Blask DE, Lockley SW, Motta ME. Adverse health effects of night time lighting: comments on American Medical Association policy statement. Am J Prev Med 2013; 45: 343-346.
7) Byl FM Jr. Sudden hearing loss: eight years' experience and suggested prognostic table. Laryngoscope 1984; 94: 647-661.
8) Perlman HB, Fernandez C. Experiments on temporary obstruction on the internal auditory artery. Laryngoscope 1959; 69: 591-613.
9) Davies SK, Ang JE, Revell VL, Holmes B, Mann A, Robertson FP, Cui N, Middleton B, Ackermann K, Kayser M, Thumser AE, Raynaud FI, Skene DJ. Effect of sleep deprivation on the human metabolome. Proc Natl Acad Sci 2014; 111: 10761-1076.
10) Mutoh T, Shibata S, Korf HW, Okamura H. Melatonin modulates the light-induced sympathoexcitation and vagal suppression with participation of the suprachiasmatic nucleus in mice. J Physiol 2003; 547: 317-332.
11) Jones TM, Durrant J, Michaelides EB, Green MP. Melatonin: a possible link between the presence of artificial light at night and reductions in biological fitness. Philos Trans R Soc Lond B Biol Sci 2015; 370: 1667.
12) Cappuccio FP, Cooper D, D'Elia L, Strazzullo P, Miller MA. Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. Eur Heart J 2011; 32: 1484-1492.
13) Stevens RG, Blask DE, Brainard GC, Hansen J, Lockley SW, Provecio I, Rea MS, Reinlib L. Meeting report: the role of envrionmental lighting and circadian disruption in cancer and other diseases. Environ Health Perspect 2007; 115: 1357-1362.
14) Bass J, Turek FW. Sleepless in America: a pathway to obesity and the metabolic syndrome? Arch Intern Med 2005; 165: 15-16.
15) Spiegel K, Tasali E, Leproult R, Van Cauter E. Effects of poor and short sleep on glucose metabolism and obesity risk. Nat Rev Endocrinol 2009; 5: 253-261.
16) Jia Y, Lu Y, Wu K, Lin Q, Shen W, Zhu M, Huang S, Chen J. Does night work increase the risk of breast cancer? A systematic review and meta-analysis of epidemiological studies. Cancer Epidemiol 2013; 37: 197-206.
17) Möller-Levet CS, Archer SN, Bucca G, Laing EE, Slak A, Kabiljo R, Santhi N, Von Schantz M, Smith CP, Dijk DJ. Effects of insufficient sleep on circadian rhythmicity and expression amplitude of the human blood transcriptome. Proc Natl Acad Sci 2013; 110: 1132-1141.
18) Schulz S, Ritter J, Oertel K, Witt K, Bär KJ, Guntinas-Lichius O, Voss A. Quantification of autonomic regulation in patients with sudden sensorineural hearing loss. Auton Neurosci 2013; 178: 9-14.
19) Meric C, Gartner M, Collet L, Chery-Croze S. Psychopathological profile of tinnitus sufferers: evidence concerning the relationship between tinnitus features and impact on life. Audiol Neurotol 1998; 4: 240-252.
20) Russo J, Katon W, Sullivan M, Clark M, Buchwald D. Severity of somatisation and its relationship to

psychiatric disorders and personality. Psychosomatics 1994; 6: 546-556.

21) Kayikçio lu M, Payzin S. Heart Rate Variability. Turkish Cardiol Ass Res 2001; 29: 238-245.

22) Kleiger RE, Miller JP, Bigger JT. Decreased heart rate variability and its association with increased mortality after acute myocardial infarction. Am J Cardiol 1987; 59: 256-262.

23) Arts HA. Sensorineural hearing loss in adults. In: Cummings CW, Flint PW, Haughey BH, et al, eds. Otolaryngology: Head & Neck Surgery. 5th ed. Philadelphia, PA: Mosby Elsevier, 2010; chap. 149.

24) Noise-Induced Hearing Loss. National Institute on Deafness and Other Communication Disorders 2014; 14: 4233.

25) Chau JK, Lin JRJ, Atashband S, Irvine RA, Westerberg BD. Systematic review of the evidence for the etiology of adult sensorineural hearing loss. Laryngoscope 2010; 120: 1011-1021.