Correlation Analysis Among Different Stages of Physiological Cycles and Sudden Sensorineural Hearing Loss in Female

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Abstract

Key Points 1. Women in different periods of physiological cycles, the levels of sex hormones in their body will change significantly, which had correlated to SSNHL. 2. There were significant differences in the average hearing threshold of subjects in different periods, and the average hearing threshold in follicular periodwas significantly lower than that in menstrual period , luteal period and menopause 3. There was a correlation between the subjects at different periods and the severity of SSNHL and the SSNHL severity was the slightest in the follicular period according to the mean rank value. 4. The analysis of SSNHL typing of subjects at different periods were variously . 5. The results of this study can explain the effect of sex hormone on SSNHL to a certain extent, and we will further explore the relationship between sex hormone levels and SSNHL, in order to provide more support for the diagnosis and treatment of SSNHL.

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5. The results of this study can explain the effect of sex hormone on SSNHL to a certain extent, and we will further explore the relationship between sex hormone levels and SSNHL, in order to provide more support for the diagnosis and treatment of SSNHL.

Keywords : Menstrual Cycle;Sudden Deafness;Sex Hormone

The authors report no fundand conflicts of interest.

INTRODUCTION

Sudden deafness, also known as sudden sensorineural hearing loss (SSNHL), which generally thought to be the blood disorders in the inner ear, the dysfunction of the hair cells, or physiological structural damage of the inner ear [1]. Up to now, various hypotheses had been proposed.The sex hormone hypothesis believes that changes in sex hormone levels may increase the risk of thrombosis and block the cochlear microcirculation,

leading to the occurrence of SSNHL[2-4]. The menstrual cycle is a normal physiological cycle for women. In different stages of the menstrual cycle, the body's sex hormone levels vary significantly. However, there have not any clear report on the study of the differences in women's hearing at different menstrual stages. This study collected and analyzed the results of auditory examinations of female subjects in different menstrual cycles.By comparing the average hearing threshold value, the severity and typing of SSNHL, explored the correlation between the occurrence and severity of SSNHL and the menstrual cycle stage.

2. Materials and methods

2.1Ethical considerations

Based on the study designed, after the review of Ethics Committee, the health, right and privacy of subjects are fully protected; potential risk and harm to the subjects are controllable to minimal. This study was approved by Research Ethics Committee of the second hospital of [Blinded for review]

2.2 General information

According to inclusion and exclusion criteria,389femalesubjects were selected anddivided into fourgroups:32 people in the "Menstrual period group" (1-6days of the menstrual cycle), 57 people in the "Follicular phase group" (7-15days of the menstrual cycle), 144 people in the "Luteal phase group" (16-28 days of the menstrual cycle) and 156 people in the "Menopausal group".

2.2 Checking Method

Pure tone audiometry checking was used to have the pure tone thresholds by the professional technician. Then record and calculated the average hearing threshold. According to the *"Otorhinolaryngology Head and Neck Surgery"* [5] and*" Guidelines for Diagnosis and Treatment of Sudden Deafness"* [1], determined the severityand the typing of SSNHL.

2.3Statistics

Data analysis was performed using IBM SPSS Statistics 25 software. One-way analysis of variance was used for the average hearing threshold in different periods, and Tukey method was used for multiple comparisons. The severity of SSNHL in different periods was ordered data.Therefore the Kruskal-Wallis test in rank sum test was adopted. The typing was categorical data, using R × C table chi-square test, and further using Post hoc testing for in-depth analysis, according to adjusted standardized residuals to determine the differences among the groups. All diagrams were generated using Graph Prism 6.0 software.

3. Results

3.1 One-way analysis of variance for the average hearing threshold of subjects in different periods

The results showed that the average hearing threshold of menstrual, follicular, luteal and menopausal subjects were: 51.09 dBHL, 35.44 dBHL, 42.69 dBHL, 47.39 dBHL;$F(3, 774)=8.773$,$P<0.001$, indicating that there was a significant difference in the average hearing threshold of subjects in different periods.Further multiple comparisons testshowed that the average hearing threshold of subjects in follicular phase was significantly lower than that in menstrual period ($P<0.001$), luteal phase ($P=0.036$) and menopause ($P<0.001$). That is, subjects in follicular phase had better hearing than other periods (Figure 1 ,Table 1).

3.2The comparison of SSNHL severity of subjects in different periods

Ranked tests of ordered data (Kruskal-Wallis test) were calculated amongsubjects with normal,mild,moderate,moderately severe, severe and extremely severe deafness in different periods. The results showed that$\chi^2 = 38.587$, df = 3, P <0.001, indicating that the severity of SSNHL varies amongsubjects in different periods. The meanrank value showed that the SSNHL in the follicular phase has the least severe, that is, the hearing of subjects in the follicular phase wasbetter than other periods (Table 2).

3.3 Comparison of SSNHL typingofsubjectsin different periods

According to the frequency and degree of hearing loss, the subjects in each periods were divided into fourtypes:Low-frequency sudden deafness, High-frequency sudden deafness, Flat descending sudden deafness and Total sudden deafness, and R × C chi-square test was performed.

The results showed that 6.3% of the expected cell counts were lower than 5, and the minimum expected count was 3.04, which met the requirements of chi-square test. Pearson $\chi^2 = 38.568$, df = 9, $P < 0.001$, indicating that the composition of SSNHL typingvariesamongsubjects in different periods. There was a correlation between the periods and the SSNHL typing, and the correlation strength Cramer's V = 0.182, $P < 0.001$. Analysis of the significance of the difference according to the ASR of Post hoc testing.

The results show that: 1)subjects inmenstrualperiodhad more Flat descending sudden deafness and fewer High-frequency sudden deafness; 2) subjects in follicular periodhad more Low-frequency sudden deafness and fewer High-frequency sudden deafness; 3) subjects in luteal phase had more High-frequency sudden deafness; 4) menopause subjects had more Total sudden deafness; while,there was no significant differences in the comparison among other periods(Table 3).

4.Discussion

4.1 Synopsis of key findings

The incidence of SSNHL has been on the rise in recent years. Due to the lack of large-scale epidemiological investigations, the annual incidence can only be estimated to be about 5-20 / 100,000 people[6]. A multicenter study of SSNHL in China showed that there was no significant difference between the male and female ratios and the vast majority of cases were unilateral onsetwhile very few bilateral incidences[7]. And some subjectshad self-healing tendency[8]. The pathological mechanisms of SSNHL are not very clear at present. The cause was difficult to clear identification and and the treatment's lack of specificity and pertinence.

The menstrual cycle is the normal physiological cycle for female. Due to the special stages of menstrual cycle, pregnancy and menopause, the hormone levels of female individuals are more complicated and variable than those of male.Female in different stages of their menstrual cycles, the levels of sex hormones such as estrogen and progesterone fluctuate more drastically, so their hearing changes are also more complicated and problematic[9], while the study of it lack of all-around research all the time.

The comparison of the average hearing threshold of subjects at different periods showed that estrogen levels reach the peak during the follicular phase, and the average hearing threshold was significantly reduced at this time. Meanwhile, the severity of SSNHL in this period was also the slightest.The corpus luteum secretes large amounts of progesterone after formation, which results in a significant increase in the average hearing threshold of the subjects, causing the severity of SSNHL to be significantly worse than other periods.Theseallconfirmed the effect of sex hormones on hearing.

Our study showed that the composition of SSNHL typingvariesamongsubjects in different periods.Therefore, when treating women in different periods, different treatment methods should be used to deal with the

different consequences of different hormone levels.On the one hand, hormone therapy can be utilized to regulatesubjects' unbalanced sex hormone levels.

The results also showed that there was a correlation between the periods and the SSNHL typing,and the composition of SSNHL typingvariesamongsubjects in different periods. These confirmed the protective effect of estrogen on hearing, and also suggested that there may be other complex synergies or antagonism between estrogen and progesterone, which require further research[10].

All results of this study suggest to a certain extent that there may be a correlation between the menstrual cycle and SSNHL, indicating that fluctuations in sex hormones can affect women's hearing. This may provide some support for further elucidating the internal mechanism of SSNHL, thereby contributing to the diagnosis and treatment of SSNHL in women.

4.2 Comparison with other studies

Some scholars had suggested that changes in hormone levels can affect the body's hearing in various ways[11]. Sex hormones had a regulatory effect on the central nervous system[12], which can affect multiple systems such as breathing, circulation, and endocrine, causing complex physiological changes in the body, such as increasing the risk of thrombosis and blocking microcirculation in the cochlea, and further affecting hearing leads to the occurrence of SSNHL[13].On the other hand, changes in sex hormone levels can cause lymphatic osmotic pressure disorder and sodium and potassium ion retention, which may affect the inner ear like Meniere[3].

It is generally believed that estrogen can excite neurons, improve nerve conduction, affect cochlear microvascular circulation and cochlear intra- and extra-lymphatic fluid[14], and protect the hearing organs[15]. Progesterone receptors had not been observed in the cochlea, but progesterone can antagonize the excitatory effects of estrogen through other steroid receptors[16].Due to the excitatory and protective effects of estrogen on the central nervous system[17,18], auditory function would be more sensitive at the peak of estrogen, which shows that the hearing threshold of female with normal cycles in the follicular phase is significantly lower than that in the later luteal phase[19]. The pure tone audiometry results of our study also confirmed this aspect.Progesterone does the opposite, mainly to suppress and counteract the excitability of estrogen[20].

Some studies had found that Otoacoustic emission (OAE) also fluctuates during the menstrual cycle, and the amplitude of Spontaneous otoacoustic emission (SOAE) during the follicular phase is greater than other stages. A study on the frequency change of SOAE showed that in the follicular phase SOAE migrated to a higher frequency location, and in the luteal phase SOAE migrated to lower[21].This also highly suggests the influence of estrogen and progesterone on SOAE.Dennis[22] compared and analyzed thedifferences in hearing between the sexes. The results showed that women's hearing sensitivity was higher, especially for high frequencies, the Auditory brainstem response (ABR) thresholdwas shorter, SOAE and Click evoked otoacoustic emissions (CEOAE) werealso stronger than men.The researchers attributed this gender difference in hearing to different hormone exposures.Our study showed that the composition of SSNHL typingvariesamongsubjects in different periods.Therefore, when treating women in different periods, different treatment methods should be used to deal with the different consequences of different hormone levels.On the one hand, hormone therapy can be utilized to regulatesubjects' unbalanced sex hormone levels. On the other hand, it can also target estrogen receptor (ER) and estrogen response element (ERE) in estrogen signaling pathway to develop new treatments[23].Studies on postmenopausal female had shown that estrogen therapy can delay their hearing loss, while progesterone had no protective effect on hearing[24]. In elderly women using hormone replacement therapy, the group using both estrogen and progesterone had worse hearing than the group using estrogen alone, and the auditory perception ability in noise environment was also lower[25], indicating that progesterone would suppress the periphery (ears)and the central (brain) auditory system, and had an antagonistic effect on estrogen[26].

4.3Study strength

This study analyzed the correlation between different physiological cycles and SSNHL in female, and came up with some interesting results. We found that there were significant differences in the incidence, severity, and typing of SSNHL in female at different stages of the menstrual cycle, which may be related to changes in sex hormones.

4.4 Study limitations

Our study had no in-depth study on the internal mechanism and principle, nor had it completely removed the confounding factors related to mental psychology[27].There were still some shortcomings remain to be improved.First, all the cases were collected from the otolaryngology electrical audiometry room.Without professional gynecologist in clinic, it was impossible to accurately determine the physiological cycle stage for each patient.Allwe can do was groupedthe subjects by menstrual date asked by themselves. Second, because of lack of extra expense and compliancein subjects, blood samples could not be collected and accurate levels of sex hormones could not be measured. We hope to present the current preliminary results to peers in order to obtain the approval of the corresponding research structure and thus apply for funding. If we obtain financial support, we can make up for the above deficiencies, accurately assess the relationship between different physiological cycles and SSNHL, and furthur explore the correlation between sex hormone levels and SSNHL, thereby providing stronger support for the diagnosis and treatment of SSNHL.

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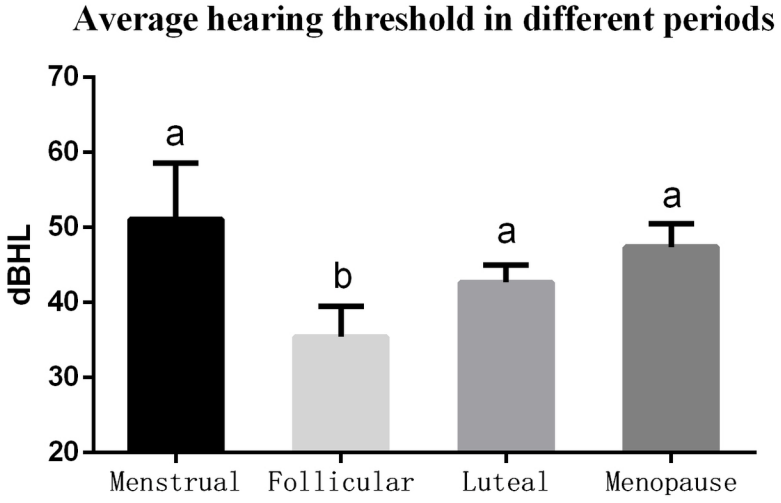

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