ISSN: 2688-8238
DOI: 10.33552/OJOR.2025.07.000664
Online Journal of Otolaryngology and Rhinology
Iris Publishers

Research Article

Auditory Function and Female Sex Hormones (Narrative Review)

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Received Date: February 24, 2025

Published Date: March 12, 2025

Abstract

It seems that female sex hormones (estrogen and progesterone) affect hearing functions. Hence, this narrative review study was designed to determine the relationship between auditory function and female sex hormones. Based on the inclusion criteria, the full text of 52 articles published in 2000 to 2023 were extracted from Scopus, PubMed, Web of Science websites and became the sources of this research. The results of the studies showed that the entire human auditory and vestibular system is dimorphic, and the serotonergic system is sex-dependent. Estrogen protects the auditory system. Progesterone is a neuroinhibitory hormone and modulates the stimulatory role of estrogen. Due to the stimulating role of estrogen, men are more likely to have high-frequency hearing loss than women, and due to the inhibitory role of progesterone, women are more likely to have low-frequency hearing loss. There is also a possibility of hearing-balance disorders in pregnant women, especially in the third trimester of pregnancy and it may cause symptoms similar to Meniere's disease. There are different opinions about the impact of hormonal changes during menopause on hearing functions. However, the age of menopause coincides with the onset of presbycusis, and these two conditions occur simultaneously.

Keywords: Female sex hormones, Estrogen, Progesterone, Sensorineural hearing loss

Introduction

Female and male sex hormones (androgens) affect auditory function. The balance of all three sex hormones is beneficial for the health of men and women. Estrogen has a protective role, is produced by the ovaries, adrenal glands and fat cells, is beneficial against osteoporosis and maintains good cholesterol levels. Its amount is higher in young women and during fertility [1]. Estrogens affect the function of many female and male organs, including skeletal, cardiovascular, nervous, urinary-genital and mammary gland systems [2]. Estrogen facilitates the transmission of auditory nerve signals and plays a protective role in the auditory system [3]. It plays an important role in the physiology of hearing, the plasticity of neurons and the metabolic levels of neurotransmitters [4, 5]. Estrogens are mediated through estrogen receptors (ERs), and there are at least three to four distinct estrogen receptors [6]. The most common are ERα and ERβ, which are encoded by genes on chromosomes 6 and 14, respectively [7]. Estrogen receptors are found in the inner ear of mammals, including inner/outer hair cells and stria vascularis, spiral ligament, Reisner's membrane, and spiral ganglion cells [8]. However, in the adult human inner ear, cells containing estrogen receptors alpha (ERα) and beta (ERβ) are present only in the spiral ganglion and stria vascularis, respectively [6]. ERα can alter cochlear and vestibular sensory transmission, ERβ protects the auditory system against acoustic shock [8, 9].

Progesterone is produced by the ovaries during ovulation, is involved in balancing the stimulatory effects of estrogen (edema), helping the body use fat for energy, maintaining a healthy weight,

restful sleep, and protection against breast and uterine cancer. It can have a detrimental effect on hearing performance [2]. Progesterone is mainly secreted by the corpus luteum and is the main pregnancy hormone [4]. As the main source of progesterone, the placenta replaces the corpus luteum after the eighth week of pregnancy [10]. The two main progesterone receptors are A and B. Progesterone receptor expression is regulated by estrogens, so progesterone is almost always prescribed with estrogen therapy [5]. In hormone replacement therapy, progesterone leads to poorer hearing in older women and affects the peripheral and central auditory system and causes speech perception impairment in background noise [11].

The main androgen hormone is testosterone, produced by the testicles, adrenal glands, and ovaries, which helps build muscle and increase energy [9]. Increased testosterone levels can lead to acne, unwanted facial and body hair, aggression, and polycystic ovaries [3]. Androgens, like all steroid hormones, are made from cholesterol, some of which is made in the adrenal cortex [7]. The strongest and most important of them is testosterone. The highest level of testosterone production is in the testes, which has two main functions: initiation of spermatogenesis, development and maintenance of secondary sexual characteristics [11]. The effect of androgens on hearing is unknown, however, the presence of androgen receptors (ARs) in the cochlea and auditory system neurons of adults has been confirmed [12, 13]. Hyperandrogenism may worsen high-frequency hearing thresholds in women with polycystic ovary syndrome [14-16]. However, hyperandrogenism in normal adult women does not seem to cause disturbances in otoacoustic emission levels or the medial olivocochlear reflex response [17].

The relationship between auditory function and female sex hormones can be questioned from three aspects: Does the sex hormone estrogen contribute to the protection of the auditory system? Is the human auditory system dimorphic? Is age-related hearing loss more likely in men than in women? Is there the possibility of hearing and balance disorders in pregnant women? Therefore, this narrative review study was designed with the aim of determining the relationship between auditory function and female sex hormones.

Materials and methods

The inclusion criteria for this study were original research articles published in English on the effects of female sex hormones on auditory function in women. Exclusion criteria included animal studies, research in children, and hearing loss caused by non-hormonal factors. After a thorough search based on the titles of the articles and reading their abstracts, the full texts of those that met the inclusion criteria for this study were obtained. The search sites for this study were Scopus, Medline, and Web of Science, published between 2000 and 2023. So, 98 articles were selected based on their titles, and after reading their abstracts, the full texts of 52 articles became the sources of this study.

Results

In women, hearing and balance system changes depend on the blood level of estrogen and progesterone. Changes in auditory function are evident during the ovarian cycle [10]. There are different opinions about the influence of sex hormones on brain auditory function and speech perceptual processing in women during the ovulatory cycle [9, 11]. The hearing thresholds changes based on different levels of sex hormones during the menstrual cycle [1]. Auditory conduction as measured by auditory brainstem response is better in the postovulatory phase compared to the preovulatory [19]. Also, brainstem auditory evoked potentials change in the mid-follicular and mid-luteal phases of the ovarian cycle [20]. Changes in estrogen and progesterone levels affect the postural stability of women, but not their optokinetic functions [21]. Dichotic listening in reproductive age is also influenced by the ovarian hormonal cycle. The perceptual speech processing of women is highly variable and fluctuates during the menstrual cycle [22-24].

Progesterone may have negative effects on the hearing of pre- and postmenopausal women. It has been reported that the auditory brainstem response threshold of postmenopausal women is higher than that of young men or women [25, 26]. Endogenous estrogen at physiological levels may slow the rate of hearing loss in older women [27], and estrogen therapy may be effective in protecting hearing in older women [28]. It has been reported that estrogen and progesterone levels in postmenopausal women with benign paroxysmal vertigo are lower than in non-menopausal women, which can cause inner ear microcirculation disorder and be a risk factor for Benign paroxysmal positional vertigo [29]. Although estrogen has benefits for the auditory system, it has unwanted side effects such as increased risk of uterine cancer [30, 31].

Some researchers have reported reversible sensorineural hearing loss at low frequencies during pregnancy [32, 33]. In one case, it was reported in one pregnancy [34] and in another case, it was reported in every pregnancy [35]. Another researcher has also stated that the possibility of sudden sensorineural hearing loss in pregnant women is rare [36]. However, it is more likely to occur in the third trimester of pregnancy when progesterone levels are at their highest. It seems that it can cause changes in the cardiovascular system, cause disturbances in cochlear blood circulation and fluid homeostasis that lead to hearing loss [37].

In a survey, it was found that the manifestations of otosclerosis are more during pregnancy. Hempenin, the resonance frequency of the middle ear decreases in the third trimester of pregnancy, which causes the amount of sound transmission from the middle ear to change [38]. Tinnitus has been reported to occur during pregnancy and appears to resolve spontaneously [35]. Autophony is another complaint during pregnancy and is also evident in women who have undergone estrogen replacement therapy [39]. There is also a possibility of Bell's palsy during pregnancy [40]. It seems that brainstem synaptic disorder caused by estrogen accelerates the occurrence of ischemic changes, which is usually more in the third trimester of pregnancy [41].

There are gender differences in hearing performance due to differences in estrogen levels in men and women. For example, the latency time of brainstem auditory evoked potentials is shorter in women [31]. The rate of hearing loss in elderly men is also higher

than in women of the same age, and the range of otoacoustic emissions in women is greater. These advantages are also observed in girls compared to boys [27]. It seems that the difference in hearing performance of women compared to men and the dimorphic structure of the auditory system is formed during development and before birth and is due to the influence of androgens [25].

Discussion

In this research, 52 articles were studied. The findings showed that the function of the human auditory system varies by gender. The hormone estrogen is a neuroprotective hormone, while the role of the hormone progesterone is inhibitory and can have a modulating and even destructive role. Therefore, it seems that men are more susceptible to hearing loss in any age group than women, and the descending audiogram pattern is more common in them. While, due to the inhibitory role of progesterone, the likelihood of hearing loss with an ascending pattern and a decrease in low frequencies is higher in women. Conditions that cause hormonal changes in women, such as the menstrual cycle or pregnancy, also cause symptoms of hearing and balance disorders, which resolve anyway. During menopause, women's hormonal status stabilizes and their blood estrogen/progesterone levels become similar to men's, and since there is also a possibility of age-related hearing loss, it cannot be explicitly reported that menopause can cause hearing disorders. Other research that has been conducted in this field includes the following:

Emami, et al. (2018) conducted a study with the aim of determining changes in hearing function in follicular and luteal phases using pure tone audiometry (PTA), tympanometry, distortion product otoacoustic emissions (DPOAE) and auditory brainstem responses (ABR). They included 20 healthy female volunteers in the age group of 19 to 30 years with normal menstrual cycles and no hearing problems in their case-control study. Hearing evaluation was done on the 13th day of the menstrual cycle (follicular phase) and then on the 22nd day (luteal phase). All participants had normal results in the follicular phase. In the luteal phase, four abnormalities were observed as follows: decreased PTA at 250 Hz (mean = 15 dBHL), increased DPOAE amplitude (mean = 3 dBspl), decreased middle ear pressure (mean = 110 dapa), and delayed ABR peak (average IPLs I-III = 0.4 and average IPLs III-V = 0.6 ms). Their findings showed that in some women, changes in ovarian hormones may cause hearing fluctuations, and increased progesterone in the luteal phase can lead to abnormal results in hearing performance. However, increased estrogen modifies its consequences in the follicular phase [42].

Emami, et al. (2022) done a cross-sectional study with the aim of comparing the average ABR interpeak delay times in menopausal women compared to non-menopausal women. Their case group included 60 menopausal women with normal hearing (45-55 years old) and non-menopausal women with similar characteristics as the control group. Their findings showed that the average interpeak delay times of ABR waves 1 to 3, 3 to 5 and 1 to 5 did not differ in the two groups. They concluded that menopause does not cause abnormal hearing results [43]. Emami, et al. (2022) showed that menopause is not the cause of cochlear dysfunction. In a cross-sectional case-control study, they compared postmenopausal women with normal hearing to a matched non-menopausal group. Both groups were assessed by DPOAEs and no significant difference was observed between the mean response amplitudes of the two groups [44].

Williamson, et al. (2020) reported that sexual hormones such as estrogen, progesterone, and aldosterone play critical roles in maintaining auditory function through maintenance of cochlear neurons, up/down regulation of critical molecules (eg, IGF-1 and BDNF), and intracochlear production. Potentially, with disease or aging, hormone expression begins to decrease drastically, which ultimately affects cochlear structures and cochlear cell integrity [45]. Urbaniak, et al. (2015) observed that in women with hearing disorders or balance system lesions, compared to normal women, the administration of hormonal contraceptives for at least 2 months caused a decrease in plasma estradiol levels during the stages of the menstrual cycle (41.2%) which can cause thromboembolism [46].

Williamson, et al. (2019) stated long-term effects of hormone therapy can increase thresholds of ABR and decrease ABR gap-in-noise amplitude levels. Consequently, hormone therapy does not seem to be a safe alternative to protect the auditory nervous system [47]. Kathleen, et al. (2009) also reported that estrogen administration alone or in combination with progesterone provides bone protection, which is a potent stimulant of prolactin secretion and affects calcium metabolism. Hyperprolactinemia associated with pregnancy and lactation may also be responsible for the association of an increased risk of otosclerosis in multiple pregnancies [48]. Al-Mana, et al. (2009) reported that hearing function changes slightly during the ovarian cycle and hearing sensitivity increases during ovulation. They subjected 16 normal-hearing women to simultaneous hearing evaluation and hormone level measurements during the ovulatory cycle. They observed that a significant positive correlation of Transient evoked otoacoustic emissions (OAEs) and ABR responses (wave V latency and III-V interval) and a significant negative correlation of medial olivocochlear suppression with oestradiol levels in the follicular phase [49].

Frisina et al. (2013) conducted a review study with the aim of investigating the relationship between hormones and the function of the auditory system. The results showed that progesterone has negative effects on the hearing of elderly women, while the effect of estrogen is positive. Aldosterone also slows down the progress of hearing loss and has positive effects on stria vascularis [50]. Abdel-Salam, et al. (2018) reported that human menopausal gonadotropin (HMG) is one of the most common drugs used for ovarian stimulation, and there are no reports on its effects on the auditory and vestibular system. They conducted their study with the aim of investigating HMG on the hearing status of patients who intended for intracytoplasmic sperm injection (ICSI). They evaluated 30 patients using PTA, DPOAEs and vestibular evoked myogenic potential (VEMP) immediately before treatment and on the 10th day of treatment. After the treatment, they observed side effects such as hearing loss, tinnitus, dizziness and ear pain. Also, they observed significant hearing loss on the 10th day of treatment in the frequency range of 1000 to 8000 Hz, while the speech

comprehension scores were not impaired. DPOAE amplitude was significantly reduced at all F2 frequencies. They determined that auditory and vestibular sequelae may result from HMG treatment, indicating the importance of close monitoring of auditory functions in these patients [51].

Ghaemi, et al. (2018) described increased levels of estrogen and progesterone affect the function of the larynx and lead to edema and swelling in the mucous membrane of the vocal cords. Estrogen increases the thickness of the epithelium of the vocal cords, and progesterone leads to changes in the transitional layer, making it dry and sticky. The best voice quality occurs during ovulation, when estrogen levels are at their highest. During the premenstrual phase, when estrogen is at its lowest level, vocal fold fatigue, hoarseness, and weakness of higher base frequencies develop. Progesterone levels increase especially in the third trimester, which may lead to vocal asthenia and hoarseness in pregnant women [52].

Conclusion

The entire human auditory and vestibular system is dimorphic, and the serotonergic system is sex-dependent. Estrogen protects the auditory system. Progesterone is a neuroinhibitory hormone and modulates the stimulatory role of estrogen. Due to the stimulating role of estrogen, men are more likely to have high-frequency hearing loss than women, and due to the inhibitory role of progesterone, women are more likely to have low-frequency hearing loss. There is also a possibility of hearing-balance disorders in pregnant women, especially in the third trimester of pregnancy and it may cause symptoms similar to Meniere's disease. There are different opinions about the impact of hormonal changes during menopause on hearing functions. However, the age of menopause coincides with the onset of presbycusis, and these two conditions occur simultaneously.

Acknowledgement

This research lacks financial support and cooperation from institutions or individuals.

Conflict of Interest

None.

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