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Auditory and Vestibular Findings in Females Receiving Hormonal Contraceptives: Review Article

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ABSTRACT

There is evidence of interaction between hormonal contraceptives (estrogen and progesterone) and the inner ear functions, which can result in hearing loss and vestibular dysfunction. Hormonal contraceptives can cause alteration in inner ear fluids homeostasis, affecting the endolymph regulation and transmission of the audiovestibular impulse from the inner ear to higher centers. In addition, it leads to enhancement of the effect of angiotensin II, which causes vasoconstriction and reduction in inner ear blood flow. Consequently, hormonal contraceptives can cause tinnitus, hearing loss, vertigo, and aural fullness. The objectives of this review article are to discuss the types, and mechanism of action of hormonal contraceptives, and their effects on the audiovestibular system and inner ear homeostasis.

Keywords: Audiovestibular manifestation, contraceptive hormones, hearing loss, vertigo, Tinnitus, Review, Zagazig University.

INTRODUCTION

Hormonal contraception is a known method of endocrine system-based birth control. There are many methods that have been developed, but oral and injectable are the most popular methods. The majority of hormonal contraceptives have a failure rate of 0.3% or below, making hormonal contraception highly effective. They are predominantly used for contraception, in addition to being given for menstrual diseases such as dysmenorrhea, menorrhagia, and hirsutism [(1)].

Types of Contraceptive Hormones

- ***Combined:*** It is the most widely used hormonal contraceptive method and it contains (progesterone and estrogen). It can be used in four different forms:

1) Tablets most frequently for 21 days, then a seven-day stop, or as emergency tablets:

2) Injections are used as a single injection per month; 3) Vaginal rings are worn for three weeks before being removed and replaced with a new ring after a one-week interval; and 4) The contraceptive patch is put on the skin and worn continuously. The user wears a set of three patches for a week each, followed by a one-week rest [(2,3)].

- ***Progestogen-only:***

It is in the form of four types: 1) Mini pills which contain low-dose of progestrone. Progestogen-only medications, in contrast to combined oral contraceptive pills (COCPs), are taken without interruptions or as emergency contraception [(4)]**;** 2) Intrauterine systems (IUS) or intrauterine devices (IUD); 3) Intramuscular injections (IM) of medroxyprogesterone acetate MDPA are taken every 3 months [(5)]**;** and 4) Progesterone-only contraceptive implants are implanted under the skin of the upper arm [(6)].

Mechanisms of Action of Contraceptive Hormones

- ***Gynecological Mechanism:*** It inhibits the ovulation by preventing the gonadotropins release. In addition, it can cause endometrial atrophy, which inhibits implantation. Additionally, it increases the viscosity and decreases the amount of cervical mucus, which inhibits sperm penetration [(7)].

- ***Audiovestibular Mechanism:*** Hormonal contraceptives may affect the homeostasis of labyrinthine fluids, due to their impact on the activity of neurotransmitters and enzymatic activities. Inner ear homeostasis is the process that keeps tissues and fluids in the inner ear chemically balanced. The inner ear can only work effectively if its cell membranes' ion motions are properly controlled. This involves the conductance of nerve impulses, modulation composition of the endolymph and perilymph, and hair cell activity. Sodium (Na+) and potassium (K+) are the major ions, but calcium (Ca2+), chloride (Cl-), and other ions also have an important role [(8)]. For the hair cells to work properly there must be specific ion concentrations in the endolymph and perilymph fluids. These fluids act as the metabolic support system [(9)].

In addition, they increase the coagulative factors IX, X, XI, prothrombin, and fibrinogen levels while decreasing the anticoagulative factor levels, which may lead to vascular obstruction of the internal auditory artery and result in sudden audiovestibular impairment [(10)]. Moreover, the effects of estrogen and progesterone increase the body's reaction to chemical vasopressor mediators like nicotine and phenylephrine, which increase the effect of angiotensin II causing vasoconstriction and a decrease in inner ear blood flow [(11)].

Another theory is based on estrogen receptors (ERs) which are present in the hair cells, ganglion cells, stria vascularis, dark cells, and spiral ligament of the inner ear. The entry of metabolites into these cells might

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be altered by estrogen. Moreover, on neuronal tissue, it has a direct excitatory impact and can change the concentrations of neurotransmitter receptors [(12)]. Moreover, estrogen inhibits neurons' capacity to synthesize gamma-aminobutyric acid (GABA). As a result, estrogen influences the transmission of audiovestibular impulses from the inner ear to higher centers, which can lead to cochlear abnormalities and tinnitus. Moreover, the stria vascularis contains receptors that may affect the inner ear's fluid and electrolyte balance [(13)].

Progesterone can influence and regulate endolymph and affect the central and peripheral auditory systems, due to it acts indirectly by interaction with steroid-binding sites on GABA-A receptors acting as a GABA-A agonist, which are widely distributed throughout the audiovestibular apparatus. Progesterone also has an inhibitory effect by lowering serotonin levels, which indirectly affects signal processing [(14,15)].

The high levels of progesterone may cause blood crasis, and alter the dynamics of the blood and consequently alter the endovascular flow by increasing the reabsorption of sodium, chloride, and water in distal renal tubules. Vertigo can occur due to altered endolymph PH and impaired electrolyte balance [(16)].

Auditory and Vestibular Findings:

Estrogen and progesterone-containing pills can change hearing thresholds, resulting in progressive hearing loss [(17)]. Contraceptive medications are possibly ototoxic chemicals **[(11)]**. In addition, it could result in alterations in salt and water reabsorption, these changes may disrupt the peripheral auditory system's functionality, which may then affect homeostasis and result in hearing loss [(18)].

In addition, there is a correlation between hearing impairment and the usage of contraceptive hormones, which was discovered in a young woman who presented with sudden SNHL. These hormones when used for long periods may cause sensory neuronal hearing loss in high frequencies [(11)]. Research on postmenopausal women receiving hormone replacement therapy (HRT), which composed of estrogen and progesterone, appears to have an impact on otoacoustic emission (OAE) [(19)].

Hearing loss with contraceptive hormones can be attributed to the effect on bone metabolism of the ear ossicles mainly stapes (otosclerosis) resulting in CHL, due to the direct inhibition of the activity of the osteoclast which have inhibitory influence on bone resorption and production of cytokines like interleukin and tumor necrotic factor (TNF) [(12)].

The impact of these hormones on the fluid balance of the labyrinth may be a cause of dizziness. The action of these hormones on the homeostasis of labyrinthine fluids can lead to irritative peripheral vestibular dysfunction. Estrogen can cause water retention, which can push water into the inner ear's sensitive parts and result in vestibular symptoms [(20)].

Mitre *et al.* [(21)] in a vestibular testing VNG study for 30 females control group and 30 females who received hormonal contraceptives, found more peripheral vestibular dysfunction in the study group. They reported that in the control group, 23.3% of the female had irritative peripheral vestibular syndrome (IPVS), while 76.7% of them had normal vestibular tests. Whereas 16.7% of the study group had normal vestibular tests, and 83.3% had the irritative peripheral vestibular syndrome.

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REFERENCES

1. **Teal S, Edelman A (2021):** Contraception Selection, Effectiveness, and Adverse Effects: A Review. JAMA., 326(24):2507-18.
2. **Galzote R, Rafie S, Teal R, Mody S (2017):** Transdermal delivery of combined hormonal contraception: a review of the current literature. International Journal of Women's Health, 9:315-21.
3. **Albawardi I, Alqahtani A, Aljamea D *et al* . (2022):** Hormonal Contraception Use and Depression among Women in Saudi Arabia. Journal of Multidisciplinary Healthcare, (15):1677-88.
4. **Hall K, Trussell J, Schwarz E (2012):** Progestin-only contraceptive pill use among women in the United States. Contraception, 86(6):653-8.
5. **Nelson A, Massoudi N (2016):** New developments in intrauterine device use: focus on the US. Open Access Journal of Contraception, 7:127-41.
6. **Rocca M, Palumbo A, Visconti F, Di Carlo C (2021):** Safety and benefits of contraceptives implants: A systematic review. Pharmaceuticals, 14(6):548. Doi: 10.3390/ph14060548
7. **Regidor P (2018):** The clinical relevance of progestogens in hormonal contraception: present status and future developments. Oncotarget, 9(77):34628-38.
8. **Köppl C, Wilms V, Russell I, Nothwang H (2018):** Evolution of endolymph secretion and endolymphatic potential generation in the vertebrate inner ear. Brain, Behavior and Evolution, 92(1-2):1-31.
9. **Reichenbach T, Hudspeth A (2014):** The physics of hearing: fluid mechanics and the active process of the inner ear. Reports on Progress in Physics, 77(7):076601. Doi: 10.1088/0034-4885/77/7/076601.
10. **Dos Santos P, de Oliveira A, Alves C, Souza Filho C, Ladeia A, Petto J (2022):** Renin-Angiotensin-Aldosterone System in Women Using Combined Oral Contraceptive: A Systematic Review. Revista Brasileira de Ginecologia e Obstetrícia, 44(7):710-8.
11. **El-Zarea G, Ali A, Frahat M, Arisha, A (2017):** Effect of Combined Oral Contraceptive Pills on Auditory Function. New York Science Journal, 10(6):17-21.
12. **He Z, Ren D (2018):** Sex hormones and inner ear. Sex Hormones in Neurodegenerative Processes and Diseases, 329-46. Doi: 10.5772/intechopen.7415
13. **Bittar R, Cruz O, Lorenzi M, Marone S, Miniti A (2001):** Morphological and functional study of the

cochlea after administration of estrogen and progesterone in the guinea pig. The International Tinnitus Journal, 7(1):41-5.

14. **Birzniece V, Bäckström T, Johansson I *et al*. (2006):** Neuroactive steroid effects on cognitive functions with a focus on the serotonin and GABA systems. Brain Research Reviews, 51(2):212-39.
15. **Price K, Zhu X, Guimaraes P, Vasilyeva O, Frisina R (2009):** Hormone replacement therapy diminishes hearing in peri-menopausal mice. Hearing Research, 252(1-2):29-36.
16. **Madani G, Connor S (2009):** Imaging in pulsatile tinnitus. Clinical Radiology, 64(3):319-28.
17. **Sarmento T, Luiz A, Campos R, Moura H, Cristina S, Augusto C (2013):** Effect of hormone replacement therapy on the auditory brainstem response of postmenopausal women. International Tinnitus Journal, 18(2):122-8.
18. **Arruda P, Silva I (2008):** Study of otoacoustic emissions during the female hormonal cycle. Braz J Otorhinolaryngol., 74(1):106-11.
19. **Robert N (2016):** Hormone replacement therapy and its effects on human hearing. Hearing and Hormones,57:191-209.
20. **Apisa P, Auletta G, Furia T *et al*. (2019):** Audio-Vestibular Alterations during the Phases of the Menstrual Cycle in Patients with Cochlear Implant. Archives of Clinical and Biomedical Research, 3(6):386-96.
21. **Mitre E, Figueira A, Rocha A, Alves S (2006):** Audiometric and vestibular evaluation in women using the hormonal contraceptive method. Brazilian Journal of Otorhinolaryngology, 72(3):350-4.