

## Effect of Combined Oral Contraceptive Pills on Auditory Function

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**Abstract Background:** A lot of contraceptive methods are used by women for birth control such as oral contraceptive pills, contraceptive patch, vaginal contraceptive ring, contraceptive injection and the intra uterine device. One of these methods is oral contraceptive pills which may be combined or single. Combined oral contraceptive pills (COCP) contain estrogen and progesterone hormones, these are like pregnancy hormones preventing fertilization from taking place. **The aim:** Hearing loss was observed in females who are using COCP, so this study was designed to explore the nature of auditory disorders in those females and to correlate the degree and configuration of hearing loss with the type and duration of COCP. **Subjects & method:** This study included 30 females who were using COCP and 15 control females. Participants underwent a full history taking, basic audiological evaluation, DPOAE and neuro-otological ABR. **Results:** 26% of the study group (8 females) had hearing loss and 20% had tinnitus (6 females). 6 females had SNHL and 2 had conductive hearing loss. **Conclusion:** 26% had hearing loss and 20% had tinnitus. No correlation between the duration of using COCP with hearing loss. [Gehan Abd El-Rahman El-Zarea; Ali Abd–Eldaiem Ali; Mohamed Mohamed Frahat; Amr Mohamed Galal Arisha. **Effect of Combined Oral Contraceptive Pills on Auditory Function.** *N Y Sci J* 2017;10(6):17-21]. ISSN 1554-0200 (print); ISSN 2375-723X (online). <http://www.sciencepub.net/newyork>. 3. doi:[10.7537/marsnys100617.03](https://doi.org/10.7537/marsnys100617.03).

**Keywords:** COCP, Hearing loss, Side effect, DPOAE, Tinnitus.

### 1. Introduction and Rationale

A lot of contraceptive methods are used by women for birth control such as oral contraceptive pills, contraceptive patch, vaginal contraceptive ring, contraceptive injection and the intra uterine device. All are effective methods of contraception that may be a good option for women. One of these methods is oral contraceptive pills which may be combined or single<sup>1</sup>.

Combined oral contraceptive pills (COCP) taken orally, preventing fertilization from taking place. This occurs through gonadotrophin secretion inhibition by the pituitary acting on the hypothalamus. The progesterone agent present in the pills suppresses leutinizing hormone (LH) secretion and the estrogen agent is responsible for the follicular stimulating hormone (FSH) secretion suppression. **2.** COCPs are currently used by more than 100 million women worldwide<sup>3</sup>. Estrogen interacts either directly or indirectly with estrogen receptors alpha (ER $\alpha$ ) and beta (ER $\beta$ ) **4.** Both ER $\alpha$  and ER $\beta$  are present in the inner ear of humans and animals, and both subtypes seem to be active in the hearing process **5.**

There is no visible nuclear staining of progesterone receptors (PR's) in the striavascularis, organ of Corti or spiral ganglion in either human or rat inner ears, indicating that progesterone could not have a direct effect on the hearing modulation in the inner ear via its nuclear receptors. However, PR's have been shown in both osteoblasts and osteoclasts in the bone of humans, rats and mice. These findings lead us to conclude that there is no direct effect of progesterone

on hearing<sup>6</sup>.

Bittar claimed that the use of COCP may lower hearing thresholds, without altering stapedial reflex **7.** On the other hand, the use of COCP does not cause significant hearing loss, however it favors tinnitus symptoms **8.** Also COCP seems to have an effect on otoacoustic emissions (OAE), in a study on post-menopausal women using Hormonal Replacement Therapy (HRT) which consists of estrogen combined with progestin (progesterone) women revealed decline in OAE levels **9.**

### Subjects, Equipments And Method:

The subjects were divided into two groups:

Study group (30 female subjects) this group is consisted of 30 female subjects. Control group (15 female subjects) this group consisted of 15 healthy volunteer women, who did not use contraceptive hormones or any other medications. They were selected from relatives accompanying patients. Equipment are sound treated room (locally made) according to international specifications, two channel calibrated audiometer Interacoustics, model AC40. Immittancemeter Interacoustics model GSI 39. Otoacoustic Emission Analyzer Madsen model (Celesta 503). Evoked Potential Audiometer model (Smart Intelligent Hearing System). The subjects of study and control groups were submitted to history taking, otological examination, basic audiological evaluation including pure Tone Audiometry air conduction hearing threshold level for octave frequencies between 250 to 8000 Hz and bone

conduction hearing threshold level for octave frequencies between 500 to 4000 Hz. The threshold was taken as the faintest sound that the patient responds to 50% of the time **10, 11**. Immitancemetry including tympanometry and acoustic reflex tympanometry done at varying pressure ranging from +200 to -400 mm H<sub>2</sub>O, to evaluate the middle ear pressure and its compliance. Acoustic reflex thresholds elicited both ipsilaterally and contralaterally using pure tones of 500 to 4000 HZ. Distortion Product otoacoustic emission (DPOAE) the stimulus consisted of two equal intensities, pure-tone signals at two different frequencies, i.e., f<sub>1</sub> and f<sub>2</sub> (f<sub>1</sub> < f<sub>2</sub>), that were generated simultaneously by the equipment with an f<sub>2</sub>/f<sub>1</sub> ratio of 1.22. The two primaries were chosen so that their geometric mean was at the same test frequency used to obtain hearing thresholds and at a primary level of 70 dB SPL. The two signals were conducted separately in two transducers and, then, by silicon rubber tube to the probe housing so the two signals were conducted entirely independently and then acoustically mixed only in the external ear canal. Auditory Brain Stem Response (ABR) Recording were carried out with the subject lying down after

good skin preparation over forehead and mastoids to reduce electrode impedance below 5 Kilo ohms. Disposable electrodes were attached to the scalp. Ipsilateral electrodes montage was used with the recording electrode on the forehead, the reference electrode on the ipsilateral mastoid, and the ground electrode on the contralateral mastoid. Rarefaction click was used with the duration of 100 usec. It was presented at an intensity of 90 dB nHL and at repetition rate of 21.4 per second as low repetition rate and 71.4 per second as high repetition rate, a total of 1024 sweeps were obtained from the stimulated ear. Recordings were made with a band-pass filter of 100-3000 Hz in a time window of 12.5 ms. A minimum of 2 traces were recorded for each run to ensure the reproducibility of the waves. Latencies were considered to be prolonged when the latencies exceeded the mean 2SD of the normal controls. ABR to click stimuli was analyzed for morphology, repeatability, absolute latencies of wave I, III, and V as well as inter peak (I- III, III-V, and I- V) latencies at low repetition rate and wave V at high repetition rate.

**Table (1): Mean & SD of contralateral acoustic reflex between study and control groups.**

Contralateral acoustic reflex threshold Hz	Group				P value
	Study		Control		
	Mean	±SD	Mean	±SD	
500	82.9 dBnHL	±3.8	82.0 dBnHL	±2.7	0.66
1000	84.6 dBnHL	±3.3	84.5 dBnHL	±2.3	0.90
2000	90.0 dBnHL	±8.5	86.3 dBnHL	±2.5	0.19
4000	90.8 dBnHL	±10.3	87.6 dBnHL	±2.4	0.94

**Table (2): Basic audiological evaluation (PTA, SRT & WDS)**

PTA Frequency Hz	Groups				P value
	Study		Control		
	Mean	SD	Mean	SD	
250	16.1 dBHL	±5.1	13.3 dBHL	±2.9	*0.03*
500	16.9 dBHL	±5.4	15.0 dBHL	±4.4	0.25
1000	19.6 dBHL	±5.8	13.8 dBHL	±3.4	*0.01*
2000	20.3 dBHL	±8.6	13.0 dBHL	±3.5	*0.01*
4000	22.8 dBHL	±10.3	13.0 dBHL	±4.1	*0.01*
8000	22.8 dBHL	±12.3	13.6 dBHL	±4.3	*0.03*
Speech audiometry SRT dBnHL	16.5 dBHL	±6.2	13.1 dBHL	±3.2	0.08
250	16.1 dBHL	±5.1	13.3 dBHL	±2.9	*0.03*
500	16.9 dBHL	±5.4	15.0 dBHL	±4.4	0.25
1000	19.6 dBHL	±5.8	13.8 dBHL	±3.4	*0.01*
2000	20.3 dBHL	±8.6	13.0 dBHL	±3.5	*0.01*
4000	22.8 dBHL	±10.3	13.0 dBHL	±4.1	*0.01*
8000	22.8 dBHL	±12.3	13.6 dBHL	±4.3	*0.03*
Speech audiometry SRT dBnHL	16.5 dBHL	±6.2	13.1 dBHL	±3.2	0.08
WDS (%)	98.9 dBHL	±1.2	98.4 dBHL	±1.1	0.21

**Table (3): Mean & SD of DPOAE amplitude at different frequencies in both groups.**

OAE Frequency	Group				P value
	Study		Control		
Hz	Mean	±SD	Mean	±SD	
500	2.3 dB	±1.7	2.2 dB	±1.3	0.84
1000	4.1 dB	±1.5	4.8 dB	±1.3	0.20
2000	3.2 dB	±1.7	3.3 dB	±0.8	0.90
4000	2.7 dB	±6.1	6.4 dB	±1.1	*0.01*
8000	1.00- dB	±10.7	4.7 dB	±1.3	0.06

**Table (4): Mean & SD in ABR wave latencies (absolute & inter-peak) in both groups.**

ABR wave latencies (absolute & inter- peak)	Group				P value
	Study		Control		
	Mean in ms	±SD	Mean in ms	±SD	
Wave I	1.67ms	±0.11	1.66ms	±0.11	0.83
Wave III	3.67ms	±0.09	3.68ms	±0.15	0.46
Wave V	5.70ms	±0.09	5.70ms	±0.10	0.79
Inter-peak I –III	2.00ms	±0.11	2.02ms	±0.15	0.69
Inter-peak III-V	2.03ms	±0.11	2.01ms	±0.14	0.33
Inter-peak I-V	4.03ms	±0.10	4.03ms	±0.12	0.93
Wave V (high repetition)	5.91ms	±0.08	5.95ms	±0.11	0.40

### Statistical analysis

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 23. Data was summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data.

### 3. Results

This study was performed in Audiology unit, ENT department, at AL- Hussin university hospital, from April 2016 to October 2016. Forty five females were enrolled in this study. Thirty females (30) using COCP were examined (study group). Fifteen females (15) who hadn't hearing complaint were also examined and constituted the control group.

### 4. Discussion

Combined oral contraceptive pills are currently used by more than 100 million women worldwide 4. The Pills are used for birth control, they have also been used to treat other medical conditions, such as PCOS, endometriosis, amenorrhea, menstrual cramps, adenomyosis, menorrhagia (excessive menstrual bleeding), menstruation related anemia and dysmenorrhea 12. Our current study was designed to evaluate the hearing profiles of females who are taking COCP. Forty five females participated in this study, and their age range was 20-40 years. The study group consisted of 30 females. The basic audiological evaluations remained the keystone of the audiological diagnosis to define the degree, type and configuration

of hearing loss 13. In this study, twenty percent (6 females) of 30 females had bilateral SNHL that ranged from mild to moderate hearing loss and it affected all frequencies, with the high frequencies being the most affected, resulting in a down sloping audiometric configuration. Seven percent (2 females) had bilateral conductive hearing loss. Seventy three percent (22 females) had normal hearing sensitivity. Twenty percent (6 females) was complaining of tinnitus. Some researchers have proposed that women with hormonal changes may experience alterations in auditory functions, such as in menopause woman, woman with hormonal contraceptive, or even during the ovarian cycle. Previous studies suggested that even the physiological fluctuation in reproductive hormones (estrogen and progesterone) during the ovarian cycle may influence auditory function 14. Also, a lot of studies have shown that pills that contain estrogen and progesterone can alter hearing thresholds causing gradual hearing loss 15. One report claimed that the cause is that contraceptive drugs are potentially ototoxic substances 16. Another report claimed the cause of this is that contraceptive drugs may produce changes in sodium and water reabsorption that take place during the ovarian cycle and this may affect the function of the peripheral auditory system, which could in turn affect homeostasis, causing hearing loss 17.

Third Explanation is that estrogen and progesterone affect body response to chemical vasopressor mediators, such as nicotine and phenylephrine. Hence, potentiate the effect of angiotensin II by direct action on cochlear vessel

receptors, leading to vasoconstriction and decreasing cochlear blood flow<sup>18</sup>. On the other hand, some studies suggested a protective effect of estrogen. **Mitre et al.**, concluded that hearing loss does not seem to be related to the use of oral hormonal contraceptives, since both the study and the control groups did not show alterations in their audiometric tests. Their study was carried out by taking history, audiometry examination for 30 women who used the oral hormonal contraceptive pills. In the study group, 100% of the sample (30 women) did not complain of hearing loss<sup>19</sup>. In addition, 100% of the sample (30 women) had audiometric test within the normal range. It was explained by that current contraceptive pills are mainly made up of low doses of estrogen and progesterone, thus reducing the occurrence of side effects. About third of the cases complained of tinnitus; 73.3% (22 women) complained of dizziness; 76.7% (23 women) reported sporadic headaches and 23.3% (7 women) complained of insomnia. The occurrence of tinnitus in the risk group was significant which was in agreement with this study, so tinnitus should be regarded as a warning signal that might require discontinuation of therapy<sup>20</sup>. Results also point that headache and insomnia complaints may not be related to the use of contraceptive medication, because there was no difference between the number of women in the risk group and in the control group who had these symptoms, as well as headache was reported were as sporadic and not as chronic-recurrent (migraine). In some scientific findings, migraines are closely related to the use of hormones. Also, the duration of using pills in this study was at least 6 months duration, we concluded that no relation between the duration of using the pills and appearance of hearing loss. **Mitre et al.**, made their study with duration of using the pills 6 months duration at least and concluded no relation between the duration of use and hearing loss which was in agreement with this study<sup>19</sup>. Two cases were diagnosed as bilateral moderate conductive hearing loss with flat configuration in this study. The two cases was complaining of bilateral hearing loss and tinnitus not before using the pills, both had family history of hearing loss, one case complained of hearing loss after second pregnancy and the other case after third one. Both had intact tympanic membrane with absent acoustic reflex at 500Hz to 4000 Hz. One of them used COCP 1 year duration and the other 9 months duration, none of them was complaining of vertigo or ear discharge the most probable diagnosis was clinical otosclerosis. Clinical otosclerosis is a familial disease which is more frequent among women in their reproductive years. The condition usually is aggravated by pregnancy. Endocrinologic variables may influence the time of onset and the course of the

disease<sup>21</sup>. It is suspected that oral contraceptives might stimulate the onset of the disease. Six hundred nulliparous women between the ages of 16 and 30, who used a variety of oral contraceptive pills for 12–36 months, were examined. The hearing of these women was thoroughly investigated. The first audiometric examination of the 600 women revealed three cases (0.5%) of clinical otosclerosis and this was in agreement with this study. It seems that COCP act as a triggering factor in a genetically susceptible female. Also, hyperprolactinemia could oppose estrogen protection effect<sup>22</sup>. In this study, DPOAEs were done as rapid, objective and non-invasive audiological procedures to study the cochlear function (outer hair cell function). Since distortion product otoacoustic emissions provide frequency-specific information based on discrete frequency stimuli, they often compared to audiometric configurations. In individuals with sensorineural hearing loss, distortion product otoacoustic emissions are often eliminated only for the stimulus frequency regions that coincide with the impaired region<sup>23</sup>. The response amplitudes were the same in the study group when compared with the DPOAE amplitude recorded from the control group except at 4000 Hz. **Yellin & Stillman** examined thirteen healthy females<sup>24</sup>. They ranged in age from 25 to 49 years. Hearing thresholds were screened at 15 dB HL between 500 and 4000 Hz and demonstrated sensitivity within normal limits for all subjects. Results confirm that DPOAE amplitudes are stable. Over the course of the study, DPOAE amplitudes showed no systematic changes, suggesting that OAEs are unaffected by hormonal changes known to affect auditory measures in females. In this study, the results of ABR measurements showed that 100% had normal latency in the study group compared to the control group. There was no statistically significant difference in the absolute latency of all waves. Also, there was no difference in the inter-peak latencies. Also latency of wave V at high repetition rate which is an indication of retro-cochlear pathway was normal.

## Conclusion

**From the current study, the following can be concluded:**

- 1) Current COCP are mainly made up of low dose of estrogen and progesterone so they reduce the occurrence of side effects.
- 2) COCP might act as a triggering factor in genetically susceptible females for audio-vestibular dysfunction.
- 3) COCPs have an impact on auditory system in sort of tinnitus & hearing loss.
- 4) About one quarter of the females in study group had hearing loss and about 20% had tinnitus.
- 5) About 75% of total percentage of hearing loss

was SNHL and 25% was conductive hearingloss.

6) No correlation between the duration of using COCP and hearingloss.

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