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Effect of menstrual cycle on outer hair cells (OHC's) and efferent auditory pathway in females – An Indian study

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ABSTRACT

Menstrual cycle occurs in females every months for ones where the endometrium which is the thick lining of the uterus wall where the fertilized egg is attached during pregnancy, this will shed every month. Sodium, chloride, and water reabsorption capacity increases by high-level progesterone during this period. When there is a change in water and sodium reabsorption which may in term affect the functioning of the auditory system especially peripheral auditory system. Otoacoustic emissions (OAE's) arise from outer hair cells (OHC's) which is situated on the basilar membrane that is seen inside the inner ear. The changes in the hormonal levels during the menstrual cycle has a clinically less significant effect on the suppression of TEOAE's, one of the type of OAE. The current study targeted the testing during three different phases of the menstrual cycle (Day 1 to Day 28) - Follicular phase, Ovulation phase and Luteal phase. The amount of suppression (3dB) caused during different phases of the menstrual cycle for each individual frequencies was compared and analyzed. The study shows that TEOAE, CSTEOAE's and suppression did not exhibit any statistically significant differences at all the frequencies between the different phases of the menstrual cycle. There are no significant correlation findings between menstrual cycle and outer hair cell function, and menstrual cycle and efferent auditory pathway functioning, considering the complaints of hearing and balance problem during the menstrual cycle period by.

1. Introduction

As we know that the female body undergoes a series of changes for pregnancy this also termed as the menstrual cycle. This occurs in females every months for ones where the endometrium which is the thick lining of the uterus wall where the fertilized egg is attached during pregnancy, this will shed every month this is known as the monthly menstrual bleeding which is also known or called as menstruation or menstrual period that is seen in early teenage years to the end of the menstrual period end which is known as menopause. It is said that the menstrual cycle is measured from 1 day of the menstrual bleeding to the 1 day of the next menstrual cycle bleeding. It is normal to have a longer or shorter menstrual cycle ideally the average menstrual cycle is although of 28 days.

On the 8th day of the menstrual cycle, the bleeding ends and the Hypothalamus secretes Gonadotrophin-releasing hormone (GnRH). This GnRH releases Follicle Stimulating Hormone (FSH). The FSH stimulates and helps the growth of Ovarian Follicle. As the Ovarian Follicle matures GnRH again stimulates the Pituitary Gland. The Pituitary Gland releases Luteinizing Hormone (LH). On the 14th day, there is a sudden peak in the blood level of LH. This sudden peak of LH triggers Ovulation by follicle rupture. The follicle contains egg surrounded by Oestrogen secreting cells. From the ruptured follicle, the egg moves through the fallopian tube. The ruptures follicle turns into Corpus Luteum, the

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cells that secrete Progesterone. This progesterone makes the uterus wall thick. After 5 days the egg reaches the cavity of the uterus. And the egg which reaches the uterus and which is not fertilized by the sperm, then on the 20th day of the menstrual cycle the egg begins to dissolve in the blood. As a result of the 28th day, the thickened endometrium along with blood is shed out of the uterus opening along with the dissolved egg. The bleeding ends on the 8th day. Between first day and 14th day, there is high estrogen secretion and between the 14th day and 22nd day, there is high progesterone secretion. The blood levels of both estrogen and progesterone fall between 22nd and 28th days.

Sodium, chloride, and water reabsorption capacity increases by high-level progesterone. When there is a change in water and sodium reabsorption which may in term affect the functioning of the auditory system especially peripheral auditory system. Most changes in the female body happen during the luteal phase. The changes that occur are as follows: Fluid retention, weight gain, changes in glucose uptake, increased energy demands, hydrops of the labyrinth and a slower gastrointestinal transit time. These are the changes that are observed during this phase.[1] Previous studies have indicated the effect of fluctuation reproductive hormones like estrogen and progesterone, especially during ovulation, on the auditory function.[2] A study that was reported that when testing was done during the menstrual cycle there was significance that they observed that was the "right ear advantage" which was observed to decrease in the premenstrual period compared to that of the postmenstrual period.[3] The changes in the hormonal activity which raised during the menstrual cycle may lead in the commitment of the homeostasis of the labyrinthine fluids due to the influence of the enzymatic processes and in triggers the neurotransmitters.[4] The changes which are seen during the menstrual cycle, this can in terms influence the functioning of the cochlear active mechanism this can been measured or evaluated by taking the means of the amplitude of otoacoustic emissions.[5] In the normal menstrual cycle, the frequency of the emission of the response captured decreases before menstruation and increases after the flow starts. The lack of ovulation, whether natural or induced by contraceptive medication, reduces the fluctuation of the characteristics of spontaneous otoacoustic emission during the cycle.[6]

Otoacoustic emissions (OAE's) arise from outer hair cells (OHC's) which is situated on the basilar membrane that is seen inside the inner ear. OAE's are broadly divided into four types based on the stimulus. They are i). Spontaneous OAE's ii). Transient Evoked OAE's (TEOAE's), iii). Distortion Product OAE's (DPOAE's) and iv). Stimulus Frequency OAE's. As suggested by recent studies OAE's are accurate in identifying ears with normal auditory functioning and ears with hearing loss.[7,8] OAE's provide information about OHC's mechanism.[9,10] OAEs can be present spontaneously or may be evoked by presenting sound(s) to the ear. By presenting a noise (in addition to the eliciting stimulus) to one or both ears during testing it usually causes a change in the measurement OAE levels. This is because of the change that is most often seen due to the decrease in OAE levels, this effect is been termed as "suppression." Although OAE suppression is not used in audiometric evaluations, research has indicated that the use of OAE's are useful for diagnosing certain pathologies, such as auditory neuropathy (e.g., Starr et al., 1996).[11] Contralateral suppression of TEOAE's which help in identifing the working of the efferent auditory pathway. This efferent auditory neurons which project bilaterally to the outer hair cells of the cochleae and in terms controls cochlear gain and also helps in enabling the modulation of auditory-nerve activity.[12,13] The efferent auditory neurons feedback of the cochlea which is play an important roles in deciphering signals such as speech signals in noisy environments and protecting the cochlea from traumatizing exposures to sound.[14,15] Menstrual cycle variations in sodium and water absorption and reabsorption affect the active mechanism of the cochlea; the amplitude of OAE may be used to assess such variations in each phase of the cycle. Previous studies of fluctuations in spontaneous OAE frequencies appear to follow the same pattern of estradiol concentration fluctuations during the cycle. In the normal menstrual cycle, the frequency decreases before menstruation and increases immediately after a new cycle begins. Natural or medication-induced anovulation reduces the characteristic OAE fluctuations during the cycle.[16] The changes in the hormonal levels during the menstrual cycle has a clinically less significant effect on the suppression of TEOAE's.

2. Materials and Methods

This is an analytic study with a cross-sectional design that was conducted. 30 female individual of the age range of 18 to 22 years were selected by systematic random sampling. All the 30 individuals reported that they had a regular menstrual cycle. None of the individuals had undergone the treatment of hormonal contraceptive or other drug treatment that could affect or alter their auditory function such as Cisplatin, aminoglycoside, hemodialysis etc. They also reported not having any history of endocrine pathology, hypertension or otological conditions in any manner. Individuals neither had any external ear, middle ear or inner ear abnormalities (anatomical and physiological). Individuals with hearing sensitivity within normal limits and 'A' type tympanogram with correlating ipsilateral and contralateral acoustic reflexes of middle ear muscle were included in the study. SPSS version 17 software was used for statistical analysis.

Test stimuli and instrumentation - Pure tones of 250 Hz, 500 Hz, 1 KHz, 2 KHz, 4 KHz and 8 KHz were

Table 1: Different phases of menstrual cycle and activities during the phases

Menstrual Cycle	Day	Activity
Menstruation	01	Bleeding begins
Follicular Phase	03	Fall in blood level of progesterone and oestrogen
Menstruation	08	Bleeding ends
Ovulation phase	14	Ovulation/Lining of Uterus thickens and high blood level of oestrogen
	20	Egg begins to dissolve
Luteal phase	22	High blood level of progesterone
	28	Bleeding begins

used for tracking the auditory thresholds using Grason – Stadler (GSI-61) Clinical Audiometer. Tympanogram was obtained using 226 Hz probe tone and acoustic reflexes were obtained using 226 Hz probe tone and 500 Hz, 1000 Hz, 2000 Hz and 4000 Hz pure tones delivered from GSI-Tympstar Pro clinical tympanometer. Clicks generated by Otodynamics DP – Echoport ILO with ILO version 7 were delivered for obtaining TEOAE's at 1000 Hz, 1400 Hz, 2000 Hz, 2800 Hz and 4000 Hz. The number of sweeps was 260, delivered at 65 dB pe. Using the same instrument contralateral suppression of TEOAE's (CSTEOAE's) was conducted by delivering broadband noise (BBN) of 60 dB SPL in the non-test ear (contralateral ear).

Individuals were made aware of the testing procedure. For personal concerns of the participants, their identities were coded and these codes were decipherable only by the authors of this paper. Participants were instructed to sit still and not to shake their head or move any body part or swallow saliva during the testing. Hearing thresholds, tympanometry, TEOAE's and CSTEOAE's were carried on each participant during three different phases of the menstrual cycle (Day 1 to Day 28). They are as follows

1. Follicular phase: It is the third day after menstruation, indicating that the estrogen and progesterone are at the lowest level in the body.
2. Ovulation phase: After the ovulation times tested with the ovulatory kit which indicated that the estrogen is in high in the body.
3. Luteal phase: On the seventh day after the ovulation, which indicates that the progesterone is high in the body.

The same audiologist performed each test, all the time.

The TEOAE values reveal the functioning of outer hair cells (OHC's) while the CSTEOAE values reveal the functioning of the efferent auditory pathway. TEOAE's and CSTEOAE's were present only if the signal-to-noise ratio (SNR) at each frequency was 3 dB i.e. if the OAE signal was 3 dB was above the noise floor by 3 dB. The difference between SNR's of TEOAE's and CSTEOAE's is the amount of suppression caused by the presence of narrowband noise in the contralateral ear. If the difference in the SNR's of TEOAE's and CSTEOAE's is more than or equal to 3 dB only then the suppression is said to be present. The amount of suppression caused during different phases of the menstrual cycle for each individual frequencies was compared and analyzed. The difference is the value of suppression would indicate the effect of hormones released during that particular phase on the contralateral pathway. The comparison of the suppression of OAE's across different menstrual phases was done using R – ANOVA statistical analysis test. Paired 't' test was done for at 95% confidence level and keeping the statistical power at 5.

3. Results and Discussion

All the participants had normal hearing sensitivity, 'A' type tympanogram with correlating ipsilateral and contralateral acoustic reflexes of middle ear muscle. TEOAE's was present in all the participants. The suppression of TEOAE's was also observed to be present in all the participants. The mean and standard deviation for TEOAE's, CSTEOAE's and Suppression at 1000 Hz, 1400 Hz, 2000 Hz, 2800 Hz and 4000 Hz, for Follicular Phase, Ovulation Phase and Luteal Phase are given below in the table, for the right ear and left ear separately.

There was no statistically significant difference, as revealed by R – ANOVA statistical analysis test, between TEOAE, CSTEOAE and Suppression values obtained across three different phases of menstrual cycle. The p-value obtained was not less than 0.005. Thus the null hypothesis was accepted.

The presence of TEOAE's and CSTEOAE's indicated normally functioning outer hair cells, while the presence of suppression indicated normal functioning of efferent auditory pathway.[17] While the absence of statistical significance between the TEOAE's obtained across three phases of menstrual cycle revealed no influence of increased blood levels of progesterone and oestrogen on afferent auditory pathway, the absence of statistical significance between the CSTEOAE's and the suppression values obtained for three different menstrual phases indicated that the increased blood level of progesterone during follicular phase and oestrogen during ovulation phase had no effect on the functioning of the efferent auditory pathway. The

Table 2: Mean and standard deviation for follicular phase

	Right Ear														
Hz	TEOAE					CSTEOAE					Suppression				
	1 k	1.4 k	2 k	2.8 k	4 k	1 k	1.4 k	2 k	2.8 k	4 k	1 k	1.4 k	2 k	2.8 k	4 k
Mean	15.01	21.66	22.82	19.00	15.21	9.74	12.59	11.94	7.34	7.53	5.74	9.44	10.84	11.61	7.91
SD	3.82	4.65	4.77	4.35	3.9	3.12	3.54	3.45	2.70	2.74	2.39	3.07	3.29	3.40	2.81
	Left Ear														
Hz	TEOAE					CSTEOAE					Suppression				
	1 k	1.4 k	2 k	2.8 k	4 k	1 k	1.4 k	2 k	2.8 k	4 k	1 k	1.4 k	2 k	2.8 k	4 k
Mean	14.13	20.19	19.15	16.77	12.26	9.48	12.18	10.23	7.55	6.74	4.65	8.00	8.92	9.22	5.54
SD	3.75	4.49	4.37	4.09	3.50	3.07	3.48	3.19	2.74	2.59	2.15	2.82	2.98	3.03	2.35

Table 3: Mean and standard deviation for ovulation phase

	Right Ear														
Hz	TEOAE					CSTEOAE					Suppression				
	1 k	1.4 k	2 k	2.8 k	4 k	1 k	1.4 k	2 k	2.8 k	4 k	1 k	1.4 k	2 k	2.8 k	4 k
Mean	14.29	21.06	21.36	18.37	15.20	10.11	11.93	10.91	8.25	8.12	4.18	9.04	10.69	10.11	7.15
SD	3.78	4.58	4.62	4.28	3.89	3.17	3.45	3.30	2.87	2.8	2.04	3.00	3.26	3.17	2.67
	Left Ear														
Hz	TEOAE					CSTEOAE					Suppression				
	1 k	1.4 k	2 k	2.8 k	4 k	1 k	1.4 k	2 k	2.8 k	4 k	1 k	1.4 k	2 k	2.8 k	4 k
Mean	14.85	19.86	19.18	17.74	12.27	10.98	12.07	10.43	8.09	6.60	3.87	7.62	8.75	9.41	5.67
SD	3.85	4.45	4.37	4.21	3.50	3.31	3.47	3.22	2.84	2.56	1.96	2.76	2.95	3.06	2.38

Table 4: Mean and standard deviation for luteal phase

	Right Ear														
Hz	TEOAE					CSTEOAE					Suppression				
	1 k	1.4 k	2 k	2.8 k	4 k	1 k	1.4 k	2 k	2.8 k	4 k	1 k	1.4 k	2 k	2.8 k	4 k
Mean	14.86	20.65	21.50	18.14	14.73	10.11	11.46	11.19	7.26	6.74	4.74	8.61	9.67	10.88	8.59
SD	3.85	4.54	4.63	4.25	3.83	3.17	3.38	3.34	2.69	2.59	2.17	2.93	3.14	3.29	2.93
	Left Ear														
Hz	TEOAE					CSTEOAE					Suppression				
	1 k	1.4 k	2 k	2.8 k	4 k	1 k	1.4 k	2 k	2.8 k	4 k	1 k	1.4 k	2 k	2.8 k	4 k
Mean	14.30	19.65	18.92	14.49	9.70	9.98	12.03	10	6.75	4.61	4.30	7.61	8.92	7.88	5.48
SD	3.78	4.43	4.34	3.80	3.11	3.15	3.46	3.16	2.79	2.14	2.07	2.75	2.98	2.80	2.34

possible reason that we could for obtaining no significance in TEOAE's obtained during three different phases of the menstrual cycle is that of the OAE's being pre-neural during the statically analysis[18] and hormones usually affect the nerves. The probable reason for not obtaining a statistically significant difference in suppression across different phases of menstrual cycle could be the small sample size chosen for the study and also the reason that hormones had very less or no effect on the efferent auditory pathway. Similar studies were carried out by Arruda & Silva in 2008[5] and Adriztina in 2016[19] which revealed the same results as their study says that there is no statistical significance in suppression values that they obtained across different phases of menstrual period or menstruation.

4. Conclusion

TEOAE is a test, which is used for evaluating the integration or the functioning of outer hair cell of the cochlea. CSTEOAE is a test which is used for evaluating the function of the efferent auditory pathway of the auditory system. The result of our study shows that TEOAE, CSTEOAE's and suppression did not exhibit any statistically significant differences at all the frequencies between the different phases of the menstrual cycle. In other words, we did not find any correlation between menstrual cycle and outer hair cell function, and menstrual cycle and efferent auditory

pathway functioning. We suggest that similar studies should be carried out using larger sample size.

5. Source of Funding

None.

6. Conflict of Interest

None.

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