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THE EFFECTS OF ORAL CONTRACEPTIVES ON CHOROIDAL THICKNESS IN INDIAN POPULATION

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ABSTRACT:

Background: To evaluate effects on choroidal thickness by oral contraceptives
Methods: In this observational prospective study, 40 eyes of 20 women consuming monophasic OCP (0.15mg Levonorgestrel (LNG)& 0.03mg ethinylestradiol) for 1 year were compared to 40 eyes of of 20 women in control group who did not take OCP. Choroidal thickness was evaluated using SD-OCT. Evaluation was done on day 3 of menstrual cycle in all participants. The BMI of all women were recorded.
Results: Choroidal thickness was significantly thin in OCP group ($p<0.001$)
Conclusions: OCP use can cause changes in choroidal thickness over a period of 1 year. Women using OCP over longer period , can have eye problems. OCT needs to be done to follow up. Long term research studies are needed, using OCP preparations of different proportions. It is necessary to determine when CT alterations may be symptomatic or clinically significant and if it is reversible.

Keywords: CT, OCT, Oral contraceptives

BACKGROUND

Oral contraception is one of the known and most common method of contraception employed by women of India to prevent or delay pregnancy. It is available as the combined pills, progesterone only pills and emergency contraceptive pills. The use combined oral contraceptive has been implicated not only for contraception but for other gynaecological conditions and premenstrual syndrome. With increased use of Oral contraceptive pills (OCP) among women studies have reported the incidence of ocular risk and side effects which is estimated to be 1 in 230 000. It is later observed that ocular tissues, such as the choroid, retina, lens, conjunctiva, cornea, and the Meibomian gland carry the receptors for progesterone and estrogen[1]. Its been proven that sex hormones affect choroid[2-4]. There can also be changes due to environmental, hormonal or genetic factors[5]. Choroidal thickness can decrease with ischemia, age, degenerative diseases, chronic inflammatory processes[6]. As OCP generally contain progesterone & estrogen, choroid is at risk. There is minimal data regarding effect on choroidal thickness by OCP , in previous literatures[7]. Through this study , our aim is to determine the effect on choroidal thickness by OCP, to address the side effects and complications to women who use the oral contraceptive pills & to advise routine followup of ocular examination when using OCP's.

METHODS

Aim

To evaluate choroidal thickness using Spectral domain- OCT in females using a uniform OCP and comparing them with females who never

use OCP. 40 eyes of 20 healthy females who have taken OCP more than a year (OCP group) were compared to 40 eyes of healthy females who did not use OCP (control group). The participants were Indian women, in the age group of 22 to 39 years. Those who never used OCP have regular 28 to 30 days menstrual cycle. Evaluation was done on day 3 of menstrual cycle in all participants.

Design

An observational prospective study

Setting

This study was conducted in Sree Balaji Medical College and Hospital , Chrompet, Chennai, India. Patients consulting the ophthalmology outpatient clinic were recrutited in the study and SD-OCT was done. Choroidal thickness measurement was taken from 2.5mm temporal to fovea, subfovea, 2.5mm nasal to fovea. The candidates underwent complete ophthalmological examination which includes medical history, testing of visual acuity, GAT, cycloplegic refraction, slitlampbiomicroscpy, and examination of fundus.

Inclusion criteria: Patients with best corrected vision >/= 20/25, spherical refraction upto +/- 3D, cylindrical refraction upto +/- 1.5D, and with normal ocular findings. BMI of all participants were measured in both groups. Exclusion criteria: Participants who had ocular trauma, prior ocular surgery, macular degeneration, glaucoma, cystoids macular edema, glaucoma and uveitis were excluded in this study. Cardiovascular events, pregnancy, thyroid disorders, diabetes mellitus, Cushing disease, hypertension, chronic liver disorders, thromboembolic events, cancer, kidney disease, psychotic disorders, pancreatitis, adrenal hyperplasia, and those on steroids, antidepressants, mood stabilizers, tobacco and caffeine were excluded as well.

The OCP used is the most commonly suggested combined OCP containing 0.15mg LNG & 0.03mg ethinyl estradiol which contain equal quantity of progesterone & estrogen for the entire cycle. SD-OCT was used to measure choroidal thickness. The procedures were done by using the same instrument and by the same examiner. The enhanced depth image scan was utilized to measure choroidal thickness. 3 points namely, subfoveal, 4mm temporal and nasal to the fovea were measured. The study was done in the period between December 2019 to December 2020

Results:

There were no disparities in respect to age or BMI between the control group & OCP group . (Table 1)

TABLE 1- Demographic data for control group & OCP group

PARAMATER	OCP GROUP (n=40)	CONTROL GROUP (n=40)
Age, years	**30.41 +/- 4.4**	**30.39 +/-3.3**
Gender	**female**	**female**
Number of subjects	**20**	**20**
Ethnicity	**Indians**	**Indians**
Study location	**Chennai**	**Chennai**
BMI kg/m²	**23.1+ 2.1**	**22.9 +2.2**

In our study, OCP group had significant thinning of subfoveal choroid, temporal choroidand nasal choroid with average choroidal thickness of 227.32µ compared to control group of265µ which was statistically significant with $p<0.001$(TABLE 2)

TABLE 2-Comparison of choroidal thickness in females using OCP and control group in our study:

PARAMETER	OCP GROUP (n=40) Mean +/- SD	CONTROL GROUP (n=40) Mean +/- SD	p-value

TEMPORAL CHOROID	220.86 ± 6.56	250.83 ± 15.56	< 0.001
SUBFOVEAL CHOROID	235.98 ± 9.14	274.39 ± 14.50	< 0.001
NASAL CHOROID	225.12 ± 7.22	261.43 ± 15.80	< 0.001
AVERAGE CHOROID	227.32 +/- 8.99	265.55 +/- 5.55	< 0.001

Discussion

Progesterone and estrogen receptors are found in ocular tissues like lens, cornea, meibomian glands, conjunctiva, retina and choroid. Expression of progesterone and estrogen receptors in eye is the reason for the ocular effects as found in previous literature[3]. OCPs are also used in endometriosis, hirsutism, menorrhagia, fibroid uterus, acne and PMS , other than for contraception[8].Combined OCP can cause dry eye, corneal edema, increased CCT,contact lens intolerance & discomfort[9].Considerable raise in CCT was also repotrted in women using OCP[10]. Neuro ophthalmological complications include parietal syndrome, retrobulbar neuritis, 6th nerve palsies, hemianopia, and papillary edema[11]. Vascular complications like intraocular hemorrhages, CRAO, CRVO, AION, aneurysms, macular edema also occur[12]. There has also been association with venous thromboembolism, cardiovascular events, breast cancer and ischemic strokes[13,14]

Sex hormones fluctuate during OCP intake. Estrogen peak at the time of follicular phase and cause impairment of tear stability, production , inflammation and dryness[15]. Cornea is thin at the start and thick at the end of menstrual cycle[17]. There was a fall in choroidal thickness in healthy reproductive aged women during their midluteal phase of menstrual cycle[16]. Estrogen deficiency in menopausal woman caused a further thinning of choroidal thickness, as recorded by SD-OCT[18].Previous study by Madendag [7] in 2017 proposed that combined OCP doesnot affect choroidal thickness as progesterone opposes estrogen.Manjunathreported a mean subfoveal choroidal thickness of 272+/-81µm which showed thin choroid more nasally, thinner choroid more temporally and thick choroid subfoveally[19]

In our study, we noted that average choroidal thickness decreased in the group taking OCP compared to control group .Temporal choroidal thickness 220 µ was comparatively less than that of subfoveal 235 µ and nasal 225 µ choroidal thickness.

CONCLUSION

We conclude from our study that women who use OCP more than a year can develop eye problems involving central vision due to involvement of retina. Long term research studies are needed, using OCP preparations of different proportions. It is necessary to determine if CT alterations may be symptomatic or clinically significant and if it is reversible. Routine follow up of these cases should be done with OCT. Physicians should consider ocular history of patients before prescribing oral contraceptives. Limitations to our study was short duration & less number of subjects. Large database study including retinal nerve fiber thickness (RNFL) , macular volume , macular thickness should be evaluated in patients using OCP's in Indian population to know more in detail about the effects of OCP in retina.

ABBREVIATIONS

SD-OCT: Spectral Domain Ocular Coherence Tomography; OCP: Oral Contraceptive Pills; CT: Choroidal Thickness; BMI: Body Mass Index; GAT: Goldmann Applanation Tonometry; CCT: Central Corneal Thickness; PMS: Pre Menstrual Syndrome; CRAO: Central Retinal Artery Occlusion; CRVO: Central Retinal Vein Occlusion; AION: Anterior Ischemic Optic Neuropathy

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