



Research Article

ORAL USE OF CONTRACEPTIVE AND THE RISK OF PRIMARY OPEN ANGLE GLAUCOMA

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ABSTRACT

Background: Oral contraceptive (OC) is one of contraceptives that widely used by family planning participant. OC consists of estrogen and progesterone. OC is one of the risk factors for glaucoma. The mechanism between sex hormone and glaucoma unclear, but many studies reported sex hormone receptors found in retinal ganglion cells.

Material and Methods: Prospective, analytical observational with cross sectional study was conducted at University as Sumatera Utara Hospital from April to September 2018 after approved by the Ethics Committee for Health Research. 77 samples (154 eyes) with history OC ≥ 3 years were included in this study. Intraocular pressure (IOP), retinal nerve fiber layer (RNFL) thickness and iridocorneal angle was measured by using Non contact Tonometry, Optical Coherence Tomography and Gonioscopy for diagnosed primary open angle glaucoma (POAG).

Results: There was a significantly differences between duration of OC use, IOP, and RNFL thickness with POAG ($p = 0.0001$), and there was no significantly differences between age OC users and POAG ($p = 0.062$).

Conclusion: OC is a risk factor for incidence of POAG. So, Obstetrics and Gynecologist are advised to consult OC users to Ophthalmologist for evaluation.

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INTRODUCTION

Contraceptive comes from the counter word means 'fight' or 'prevent' and conception is a meeting between a mature egg cell and sperm which results in pregnancy.¹ Oral contraceptive is one of the contraceptives that are widely used by family planning participants.² According to the World Health Organization (WHO), in 2009 nearly 380 million couples running family planning programs and 65-75 million of them in developing countries used hormonal contraception, namely birth control pills.³ Oral contraceptive consisted of components of estrogen and progesterone (synthetic progesterone), or incorrect one of the components.⁴

Glaucoma disease is now the second leading cause of blindness globally after cataracts.⁵ Primary Open Angle Glaucoma (POAG) is one of classified of glaucoma. Primary open angle glaucoma is typically a chronic, slowly progressive optic neuropathy with characteristic patterns of optic nerve damage and visual field loss. Numerous clinical factors affect an individual's susceptibility to POAG, which is a multifactorial disease process.

These include elevated IOP, advanced age, race, thin central cornea, and a positive family history of glaucoma. Other factors that may contribute to disease susceptibility include corneal hysteresis, low ocular perfusion pressure, low cerebrospinal fluid pressure, abnormalities of axonal or ganglion cell metabolism, and disorders of the extracellular matrix of the lamina cribrosa.⁶

Mechanisms that cause sex hormones to be associated with risk factors for glaucoma that occur through estrogen and progesterone receptors found in ganglion cells in the retina and ciliary epithelial cells found to metabolize estrogen, progesterone and androgen.⁷ In addition, estrogen and progesterone are said to affect the outflow, therefore they can play several roles in IOP regulation.⁸

IOP measurement has an important role in case detection and management of primary open angle glaucoma. Ocular hypertension (OHT) is associated with an increased risk of developing glaucoma and reducing IOP has been shown to lessen progressive loss of the visual field. Accurate and precise measurement of IOP is, therefore, fundamental to management of glaucoma.⁹

Based on these studies, the aim of current study to investigate the risk factor of open angle glaucoma with history of oral

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contraceptive and evaluate duration oral contraceptive with incidence of open angle glaucoma.

MATERIALS AND METHODS

Subjects

This was a prospective, analytical observational with cross sectional study comprising seventy seven oral contraceptive users. These subjects were recruited consecutively at University as Sumatera Utara Hospital North Sumatera, Indonesia from April 2018 to September 2018. The subjects who use oral contraceptive referred from Obstetric Gynecologic Departement Ethical approval was obtained from Universitas Sumtera Utara Ethics Committee. A written consent was obtained from all subjects by the researchers.

All subjects underwent ophthalmologic examination included measured of best corrected visual acuity (BCVA), intraocular pressure by Non-Contact Tonometry (NT 530-Nidek), iridocorneal angle with gonioscopic (Volk Optical, Germany), and retinal nerve fiber layer thickness with Cirrus Optical Coherence Tomography (Optovue).

The inclusion criteria were the subjects who used oral contraceptives ≥ 3 years and open iridocorneal angle. Patients with a history of glaucoma, eye infections, and taking medication of steroid were excluded.

Measurement of Intraocular Pressure

A non-contact tonometer (NT 530-Nidek) was used to measure the eye pressure. After the measurement is triggered, the tonometer send an air pulse to the eye with a pressure profile. The time dependent pressure profile and peak pressure were evaluated in advance.¹⁰

Retinal Nerve Fiber Layer Analyses

All patients had their RNFL measured by Cirrus HD-OCT (Optovue). Cirrus HD-OCT (Optovue) improves on time-domain systems, allowing performance of up 27000 axial scans per second. Cirrus HD-OCT imaging, the Macular Cube 200 x 200 Combo protocol was used. The protocol consists of two perpendicular line scans centered at the fovea followed by a cube scan also centered at the fovea. The line scans were 6 mm in the transverse direction, had a 2 mm acial depth, and was composed of 200 x 200 axial scans. The Cirrus RNFL map represents a 6x6 mm cube of A-scan data centered over the optic nerve in which a 3.4 mm diameter circle RNFL data is extracted to create what is refered. It to as the TSNIT map (temporal, superior, nasal, inferior) is displayed as a false color scale with the thickness values by quadrants and clock hours, and the RNFL peaks give a sense of the anatomic distribution of nerve fiber axons represented by the superior and inferior bundles that emanate from optic neve. SD OCT had a sensitivity of 83% and a specificity of 88%.^{11,12}

Statistical Analysis

The collected data write in the research publication and keep in the computer and analysed by using statistical software. To analyse between duration oral contraceptive with risk factor of primary open angle glaucoma, chi square test was used. Statistical analyses were performed with SPSS (IBM SPSS Statistic for Windows, Version

19.0) and the level significance was p<0,05 in all statistical test.

RESULT

The study was conducted at Universitas Sumatera Utara Hospital from April 2018 to September 2018 in seventy seven subjects with history oral use of contraceptive.

Table 1 The demographic parameters from 77 subjects with history oral use of contraceptive

Characteristics	Total	%
Age		
17 – 25 years	3	3,9
26 – 35 years	56	72,7
36 – 45 years	17	22,1
46 – 55 years	1	1,3
Duration Oral Contraceptive		
3 – 5 years	50	64,9
5 – 9 years	22	28,6
≥ 10 years	5	6,5
Right Visual Acuity		
6/6 – 6/7,5	15	19,5
6/9,5 – 6/21	28	36,4
6/24 – 6/48	28	36,4
≤ 6/60	6	7,8
Left Visual Acuity		
6/6 – 6/7,5	10	13,0
6/9,5 – 6/21	33	42,9
6/24 – 6/48	25	32,5
≤ 6/60	9	11,7
Right Intraocular Pressure		
10 – 21 mmHg	58	75,3
>21 mmHg	19	24,7
Left Intraocular Pressure		
10 – 21 mmHg	60	77,9
>21 mmHg	17	22,1
Right RNFL		
Normal	63	81,8
Borderline	6	7,8
Outside normal	8	10,4
Left RNFL		
Normal	60	77,9
Borderline	5	6,5
Outside normal	12	15,6
Diagnosis		
Non glaucoma	50	64,9
Ocular Hypertension	5	6,5
Normo Tension Glaucoma	3	3
Primary Open Angle Glaucoma	19	24,7

From the table 2, there was significantly differences correlation between duration oral use of contraceptive and right intraocular pressure (p < 0, 05).

Table 2 Correlation between Duration Oral Use of Contraceptive and Right IOP

Duration Oral Contra-ceptive	Left Intraocular Pressure				p.
	Normal (10-21mmHg)		Increase IOP (> 21 mmHg)		
	n	%	n	%	
3 – 5 year	46	92,0	4	8,0	0,001*
6 – 9 year	13	59,1	9	40,9	
≥ 10 year	2	40,0	3	60,0	
Total	61	79,2	16	20,8	

Table 3 Correlation between Duration Oral Use of Contraceptive and Left IOP

Age of User Oral Contraceptive	Diagnosis				p.
	Non Glaucoma		POAG		
	n	%	n	%	
17 – 25 years	3	100,0	0	0,0	0,062
26 – 35 years	43	76,8	13	23,2	
36 – 45 years	9	52,9	8	47,1	
46 – 55 years	0	0,0	1	100,0	
Total	55	71,4	22	28,6	

From the table 3, there was significantly differences correlation between duration oral use of contraceptive and left intraocular pressure ($p < 0,05$).

Table 4 Correlation between Duration Oral Use of Contraceptive and Right RNFL Thickness

Duration Oral Contraceptive	Right RNFL Thickness						p.
	Normal		Border-line		Outside Normal		
	n	%	n	%	n	%	
3-5 year	46	92,0	2	4,0	2	4,0	0,009
6-9 year	14	63,6	4	18,2	4	18,2	
≥ 10 year	3	60,0	0	0,0	2	40,0	
Total	63	81,8	6	7,8	8	10,4	

From the table 4, there was no significantly differences correlation between duration oral use of contraceptive and right RNFL thickness ($p > 0,05$).

Table 5 Correlation between Duration Oral Use of Contraceptive and Left RNFL Thickness

Duration Oral Contraceptive	Right RNFL Thickness						p.
	Normal		Border-line		Outside Normal		
	n	%	n	%	n	%	
3-5 year	46	92,0	2	4,0	2	4,0	0,001*
6-9 year	12	54,5	4	13,6	4	31,8	
≥ 10 year	2	40,0	0	0,0	2	60,0	
Total	60	77,9	6	6,5	8	15,6	

From the table 5, there was significantly differences correlation between duration oral use of contraceptive and left IOP ($p < 0,05$).

Table 6 Correlation between Age of User Oral Contraceptive and POAG

Duration Oral Contraceptive	Diagnosis				p.
	Non Glaucoma		POAG		
	n	%	n	%	
3 – 5 year	41	82,0	9	18,0	0,001*
6 – 9 year	13	59,1	9	40,9	
≥ 10 year	1	20,0	4	80,0	
Total	55	71,4	22	28,6	

From the table 6, there was no significantly differences correlation between age and primary open angle glaucoma ($p > 0,05$).

Table 7 Correlation between Duration Oral Use of Contraceptive and POAG

Duration Oral Contraceptive	Right Intraocular Pressure				p.
	Normal (10-21mmHg)		Increase IOP (> 21 mmHg)		
	n	%	n	%	
3 – 5 year	43	86,0	7	14,0	0,040*
6 – 9 year	13	59,1	9	40,9	
≥ 10 year	4	80,0	1	20,0	
Total	60	77,9	17	22,1	

From the table 7, there was significantly differences correlation between duration oral use of contraceptive and open angle glaucoma ($p < 0,05$).

DISCUSSION

Potential pathological link between oral contraceptive and glaucoma has been proposed. Oral contraceptive have some risks and side effects with regard to several organs, one of which is the eye.¹³ Oral contraceptive consists of estrogen and progesterone or one of them. Caused of circulations of

estrogen in RGC play an important role in the pathogenesis of glaucoma. Estrogen exposure contributes to increased optic nerve susceptibility to glaucomatous damage.¹⁴ Among the glaucoma, open angle glaucoma is a subtype of glaucoma is associated with female sex hormones. The common mechanism between primary open angle glaucoma and oral contraceptive has been proposed. However contradictory reported was still noted in study Vessy *et al*, that there was no consistent evidence of important increases in risk of eye diseases in users of oral contraception, exception of retinal vascular lesions. Moschos *et al* also shows that Faust and Tyler noted that there was no difference in prevalence of glaucoma between patients receiving oral contraceptives and control group, whereas lens pathology was observed at 4% of control individuals compared to 1.5% of patients under contraception.^{15,16} Tables 2 and 3 show significantly differences correlation between duration oral use of contraceptive and intraocular pressure. This is in corresponding with Karleia Steiner say that Optometrists' Clinic Inc. explains glaucoma as a condition resulting from damage to the eye because of elevated intraocular pressure. It is caused by increased fluid production coupled with decreased drainage that causes injury to retinal fibers and the optic nerve.¹⁷

Table 4 show no significantly differences correlation between duration oral use of contraceptive and right RNFL thickness. But in table 5 show significantly differences correlation between duration oral use of contraceptive and left RNFL thickness. Madendag Y *et al* also found that women who used oral contraceptive were significantly slimmer average RNFL versus the control group.¹³ Table 6 show no significantly differences correlation between age of oral use contraceptive and primary open angle glaucoma. Until now there have been no studies that shows correlation between age of oral use contraceptive and primary open angle glaucoma. But in Foris *et al* show that the incidence of open angle glaucoma and the rate of associated blindness both increase with age, particularly those older than 40 years old, with up to 15% of individuals affected by their 60s. Though mean IOP also slowly increases with age, the incidence of open angle glaucoma is still higher in the aging population, even when this is estimated. The glaucoma foundation also say that approximately one percent of all Americans have this form of glaucoma, making it the most common form of glaucoma in America. It occurs mainly in the over 50 age group.^{18,19}

Table 7 show significantly differences correlation between duration oral use of contraceptive and open angle glaucoma. The same study was conducted by Wang *et al* and Bhanwra S *et al* show that the use of oral contraceptives for 3 years or more was associated with twice the risk for self-reported glaucoma.^{14,20} From this study we found 22 subjects (22,6%) who suffered from primary open angle glaucoma. The previous Wang *et all* study found that women who used oral contraceptives for more than three years had a twofold risk of developing primary open angle glaucoma later in life.¹⁴

CONCLUSION

The present study concludes that ocular damage such as open angle glaucoma seen in subjects with history oral use of contraceptive and have correlation between duration of oral use of contraceptive and incidence of open angle glaucoma, so

further long studies are needed for evaluate another side ocular complication, hence obstetric gynecologist are advised to refer the subjects to ophthalmologist for evaluation.

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Conflict of Interest

The authors declare that there are no conflicts of interest.

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