

A CYTO-HISTOLOGICAL STUDY OF ENDOCERVIX AMONG THE ORAL CONTRACEPTIVE USERS

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SUMMARY

The use of oral contraceptives causes hyper activity of endocervical glands in the form of hyperplasia and hypersecretion which leads to dysplasia and metaplasia. Since there is always to risk of change of dysplasia to neoplasia, a close follow-up is advised when the woman is taking oral contraceptives for prolonged period of time.

Introduction

According to present estimate, over 80 million women around the world use 'the pill' (W.H.O., 1978). The high level of acceptance of steroid contraceptive represents a potential health problem. Numerous studies have established an association between oral contraceptives and cardiovascular diseases, thromboembolic phenomenon and sterility but particular anxiety has also been expressed about the possible effects of the use of steroid contraceptive on the risk of developing neoplastic disease. Therefore, the present study was undertaken with the view to study—

(i) Cytohistological changes in the cervix with the use of oral contraceptives.

(ii) The effect of duration of use of

oral contraceptive on cervical epithelium.

(iii) To correlate the use of oral contraceptives and endocervical dyskariogenesis.

Material and Method

In the present study 120 cases of test group (40 cases taking sequential type and 80 cases taking combined type of oral contraceptives) were compared with 120 cases of control group (who were not taking oral contraceptives). After taking detailed history, a routined general and systemic examination was done in each case. Speculum and vaginal examination was done to see any discharge, inflammation of vagina and cervix and erosion of cervix. Scrap smears were taken from squamo-collumnar junction of cervix by means of Ayre wooden spatula. The metarial on this spatula was gently but rapidly spread over previously numbered glass slides which were immediately dip-

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ped in 95 per cent ethyl alcohol for fixation. The staining of the fixed smears was carried out according to standard Papanicolaou's technique.

Biopsies from eroded areas were taken whenever indicated and fixed with 10 per cent formaline solution and their histopathological examination was done. The criteria for cytological analysis were those described by Papanicolaou (1954), Watchel (1969), Wahi *et al* (1969) and Novak (1974). The cases were classified into 7 groups-normal, chronic cervicitis, dysplasia of mild, moderate and severe grade, carcinoma in situ and invasive carcinoma.

Observations

Table I shows the cytohistological changes in endocervix with the use of oral contraceptives. In this study normal histology of cervix was found in 40 cases (33.33 per cent), chronic cervicitis in 50 cases (41.67 per cent), mild dysplasia in 14 cases (11.67 per cent), moderate dysplasia in 10 cases (8.33 per cent) and severe dysplasia in 4 (3.33 per cent). In the control group, the mild, moderate and severe dysplasia was found in 10 per cent, 5.0 per cent and 1.67 per cent cases respectively. Carcinoma in situ was present in 1.67 per cent cases in each of test and control group. In addition to normal histology of cervix, the following findings were seen in chronic cervicitis and dysplasia.

Hypersecretion: Endocervical glands were increased in number dilated and lined by columnar epithelium. The hypersecretory activity of endocervical glands were observed in 25 per cent test group and 15 per cent of control group. It was characterised by presence of secretions in endocervical glands at places filling the

TABLE I
Cyto-histological Changes in Endocervix Among Oral Contraceptive Users and Non-users

	Normal	Chronic cervicitis	Dysplasia			Car-cinoma in situ	Car-cinoma	Total
			Mild	Moderate	Severe			
Test Group	40 (33.33)	50 (41.67)	14 (11.57)	10 (8.33)	4 (3.33)	2 (1.67)	0	120 (100)
Control Group	54 (45.0)	42 (35.0)	12 (10.0)	6 (5.0)	2 (1.67)	2 (1.67)	2 (1.67)	120 (100)

Note: Figures in parentheses denote percentage.

lumen. At places there was collection of chronic inflammatory cells.

Micro-glandular hyperplasia: It was observed in 55 per cent of cases of test and 35 per cent cases of control group. It was patchy in distribution and located near squamo-columnar junction, polypoid and varicose in nature. It was characterised by basal cell hyperplasia of glands along with piling up of the cells lining the glands at places forming small papillies.

Stromal oedema: This was found in 30 per cent cases of test and 15 per cent cases of control group. It was characterised by oedematous changes and loosening of the stroma and associated with opening of new blood vessels and increase vascularity.

Squamous metaplasia: It was characterised by squamous lining of the endocervical glands in place of tall columnar epithelium. It was associated with chronic inflammatory changes and atypia of cervical epithelium.

Mild dysplasia: It was found in 11.67 per cent cases of test group and 10.0 per cent cases of control group. Mostly the lesions showed mild to moderate type of chronic cervicitis with varying degree of basal cells hyperplasia, epithelial hyperplasia, keratosis and parakeratosis. In few cases mild type of atypia were seen. In a few cases the cervical gland showed epiderodization and polyp formation.

Moderate Dysplasia: It was found in 8.33 per cent cases of test and 5.0 per cent cases of control group. As compared to mild dysplasia, the areas of dysplasia was wider and there was increased keratosis and parakeratosis along with leucocytic infiltration of epithelium.

Severe dysplasia: It was observed in 3.33 per cent cases of test group and 1.67 per cent cases of control group. The

lesions gave an appearance of intra-epithelial carcinoma in deeper layers with variable amount of differentiation in superficial layers of the epithelium.

Carcinoma in situ: In the neoplastic area, the epithelium was full of malignant cells but the basement membrane was not broken and there was no invasion of stroma. Leucocytic infiltration was associated with it. Carcinoma in situ was present in 1.67 per cent cases of each test and control groups.

Invasive carcinoma: It was found only in one case of control group. The cervical epithelium was full of neoplastic cells infiltrating deep down stroma. Well developed epithelial pearls were also seen at places.

Table II shows relationship of cyto-histological changes with the type of oral contraceptive used. In this study, 40 cases (33.33 per cent) were taking sequential type of oral contraceptives while 80 cases (66.67 per cent) were taking combined type of oral contraceptives. In sequential type of pill users, 14 (35.0 per cent) cases showed normal cytology, 16 (40.0 per cent) cases showed inflammatory smears while mild, moderate and severe dysplasia was present in 6 (15.0 per cent), 2 (5.0 per cent) and 2 (5.0 per cent) cases respectively. In combined type of pill users, 26 cases (32.5 per cent) showed normal smears, 34 cases (42.50 per cent) showed cervicitis, 8 cases (10.0 per cent) showed moderate dysplasia and 2 cases (2.5 per cent) showed severe dysplasia. There were 2 cases of carcinoma in situ in this group.

Table III shows the relationship of morphological changes with the duration of use of oral contraceptives. The pills were taken by 53.33 per cent of cases for 7-18 months. The prevalence and severity of cervical dysplasia was found to

TABLE II
Relationship of Cyto-histological Changes in Endocervix With the Type of Oral Contraceptive

Type of oral contraceptive	Normal	Chronic cervicitis	Dysplasia		Carcinoma in situ	Invasive carcinoma	Total
			Mild	Mode-rate			
Sequential type	14 (35.0)	16 (40.0)	6 (15.0)	2 (5.0)	—	—	40 (33.33)
Combined type	26 (32.5)	34 (42.50)	8 (10.0)	8 (10.0)	2 (2.5)	—	80 (66.67)
Total	40 (33.33)	50 (41.67)	14 (11.67)	10 (8.33)	2 (1.67)	—	120 (100.0)

Test $X^2 = .07$, $df=2$, $p > .05$.

Note: Figures in parentheses denote percentage.

increase very significantly with the duration of use of oral contraceptives ($p < .001$). The moderate to severe dysplasia was seen mostly in women who took oral contraceptives for more than 20 months. One case of carcinoma in situ was found in a woman who took the pills for 37 months. In contrast the prevalence of chronic cervicitis was found more in women who took oral contraceptives for 6-12 months.

Discussion

In the present study, the hyperplasia of endocervical glands was 55% among the oral contraceptive users (test group) as compared to 35% among non-users (control group). Similar high prevalence of hyperplasia was also reported by Gall *et al* (1969) as 84% and Nichols and Fidler (1971) as 44%. However, the latter found only 11% cases of hyperplasia among non-users. This variation may be due to other associated factors like infections, low socio-economic status, longer marital life etc.

The hypersecretion of the endocervical glands was found in 25% cases of test group and 15% cases of control group. The similar findings were also observed by Maqueo *et al* (1966) and Gall *et al* (1969). The stromal oedema was seen in 30% cases of test group and 15% cases of control group. Similar findings were also reported by Gall *et al* (1969) and Nichols and Fidler (1971).

The prevalence of all grades of dysplasia was found 23.3% among oral contraceptive users and 16.6% among non-users, while Rao *et al* (1973) reported the prevalence of dysplasia as 7.5%. The higher prevalence of dysplasia in oral contraceptive users may be due to higher levels of hormones similar to that of

TABLE III
Relationship of Cyto-histological Changes in Endocervix With the Duration of Use of Oral Contraceptives

Duration of use (in months)	Normal	Chronic cervicitis	Dysplasia			Carcinoma in situ	Invasive carcinoma	Total
			Mild	Moderate	Severe			
0-6	18 (56.25)	14 (43.75)	0	—	—	—	—	32 (26.66)
7-12	14 (31.82)	24 (54.54)	4 (9.09)	2 (4.54)	—	—	—	44 (36.67)
13-18	8 (33.33)	8 (33.33)	4 (16.67)	4 (16.67)	—	—	—	24 (20.0)
19-24	—	4 (33.33)	4 (33.33)	2 (16.67)	2 (16.67)	—	—	12 (10.0)
25-36	—	—	2 (33.33)	2 (33.33)	2 (33.33)	—	—	(5.0)
36+	—	—	—	—	2 (100.0)	—	—	2 (1.67)
Total	40 (33.33)	50 (41.67)	14 (11.67)	10 (8.33)	6 (3.33)	—	—	120 (100)

Test — X^2 — 14.9, df—2 $p < .001$.

Note: Figures in parentheses denote percentage.

pregnancy. The cytological changes were more in combined type of oral contraceptive users than those of sequential type, but the differences were not found significant statistically. The similar trend was also observed by Engineer *et al* (1980).

In the present study, the prevalence and severity of cervical dysplasia was found to increase significantly with the duration of use of oral contraceptives ($p < .001$). The chronic cervicitis and mild dysplasia developed after short duration of use than severe dysplasia and carcinoma in situ. Ory (1977) reported the relative risk of cervical carcinoma in situ among oral contraceptive users in comparison to non-users as 1.3 for 1-12 months duration of use, 2.5 for 13-29 months of use and 2.6 for 29-30 months of use. The similar trend was also reported by Peritz *et al* (1977).

Thus the use of oral contraceptives causes hyperactivity of endocervical

glands in the form of hyperplasia and hypersecretion which leads to dysplasia and metaplasia. Since there is always to risk of change of dysplasia to neoplasia, a close follow-up is advised when the woman is taking oral contraceptives for prolonged period of time.

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