

Original Research Article

Study of cervical cytology in users of progestagen-only contraceptives**Prof. Dr. Tawfik Abdel Salam Tawfik¹, Prof. Dr. Mervat Aly El-Din Hamza², Dr. Ziad Sami Abou-Zeid³, Hebatallah Said Abd El-Fattah Salem⁴**¹Professor of Obstetrics and Gynecology, Faculty of Medicine, Alexandria University, Egypt.²Professor of Pathology, Faculty of Medicine, Alexandria University, Egypt.³Lecturer of Obstetrics and Gynecology, Faculty of Medicine, Alexandria University, Egypt.⁴Visiting resident at El-Shatby Maternity University Hospital, Department of Obstetrics and Gynecology, Faculty of Medicine, Alexandria University, Egypt.***Corresponding author**

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Abstract: Early detection of cervical precancerous lesions by cervical cytologic examination has dramatically decreased the risk of cervical malignant disease. There is always a major concern about the relationship between hormonal contraception and cervical malignancy. The objective of this study is to define the relationship between the use of progestagen-only contraception and the occurrence of abnormal cervical cytology. In Methods Cervical cytologic smears were taken from 250 women attending El-Shatby family planning-clinic including 200 progestagen-only contraceptive users as cases group and 50 non-hormonal contraceptive users as control group. In results cytologic examination revealed epithelial cell abnormalities in 44 (22%) smears including ASCUS in 31 (15.5%), LSIL in 11 (5.5%) and HSIL in 2 (1%) of cases. Control group showed 9 (18%) positive smears including ASCUS in 6 (12%), LSIL in 3 (6%) smears. There is no statistically significant difference between both groups. In conclusion the Progestagen-only contraceptives are not associated with increased risk of abnormal cytologic findings and preinvasive disease of the cervix.

Keywords: cervical precancerous lesions, progestagen, malignancy.

INTRODUCTION

Cervical cancer is the most common gynecologic cancers affecting women worldwide especially in developing countries [1]. Cervical intraepithelial neoplasia is a premalignant lesion that can progress to cervical cancer [2]. Invasive cancer of the cervix has been considered a preventable cancer because it has a long pre-invasive state, cervical cytology screening programs are available, and the treatment of pre-invasive lesions is effective [3-5]. Cytologic screening of cervical smears is the most effective screening test for cervical cancer ever developed [6].

However, in developing countries, 80% of cervical cancer cases are incurable at the time of detection due to lack of screening programs [7]. Dealing with limited resources in developing countries, practically speaking, the screening programs should focus on high-risk group of patients [8].

An association of cervical cancer with several risk factors including human papilloma virus infection, smoking, sexual factors and hormonal contraceptive use have been shown in some studies [9-13].

Hormonal contraceptives are the most popular and most effective nonsurgical methods for spacing and fertility control in the world [14]. However, there is concern about the link between hormonal contraceptives and the risk of cancer cervix [15, 16].

In this study, we investigated the effects of progestagen-only contraception on the prevalence of abnormal Pap smear and the risk of developing cervical intraepithelial neoplasia.

PATIENTS AND METHODS

A case-control study was conducted over the period from January 2014 to April 2015. The study included 250 women recruited from the family-planning clinic of El-Shatby Maternity University Hospital. The study group included 200 women who had been using progestagen-only contraceptives for more than a year. Depo medroxy progesterone acetate (DMPA) 150 mg injections was used by 101 cases, Progestagen-only pills (POPS) were used by 78 cases, etonogestrel single-rod implant (Implanon®) was used by 20 cases and Levonorgestrel intrauterine device (Mirena®) was used by only 1 case. The control group included 50 women who were non-hormonal contraceptive (barrier method) users or non-contraceptive users. The age range for both

groups was limited between 20 and 40 years. Women who were previously diagnosed with cervical cancer or with known premalignant lesions or previously treated by conservative surgery or ablation for CIN and who have been using combined hormonal contraception were excluded. After approval of the medical ethics committee and signing a written informed consent all selected case were subjected to the following:

- History taking (Menstrual, Obstetric, Sexual, Medical, Surgical)
- Complete general and gynecological examination.
- Pap smear was taken using Ayre’s spatula. Cytologic evaluation was done and the results were classified according to Bethesda system 2001 [17].
- Follow up for patients having abnormal Pap smear: ASCUS cases were followed up by repeated Pap smear after 3 months. LSIL and HSIL smears were evaluated by VIA (Visual inspection of the cervix with acetic acid) and VIA directed cervical biopsy.

RESULTS

This study comprised 200 women using progestagen-only contraceptives as cases compared to 50 non-hormonal contraceptive users as control. The age ranged from 20-40 years in both groups with a mean of 32.41 ± 5.28 and 30.82 ± 6.61 in cases and control group respectively with no significant statistical

difference. Parity ranged from 1-5 with a mean of 2.45 ± 0.93 and 1-6 with a mean of 2.06 ± 1.19 with no significant statistical difference. The duration of marriage ranged from 2-25 years with a mean of 9.79 ± 6.03 and from 1.5–25 years with a mean of 8.05 ± 7.13 in the cases and control groups respectively also with no significant statistical difference.

Table 1 describes the results of Pap smears showing no statistically significant difference between normal and abnormal cases between groups.

The incidence of abnormal Pap smears in the POC users group did not greatly vary between different methods of POC as shown in table -2

Table 3 describes the correlation between duration of use of POC and abnormal Pap smears showing no statistically significant difference between normal and abnormal smears.

Table 4 describes the follow-up of ASCUS smears after 3 months by Pap smear. There was no statistically significant difference in the follow-up results between groups.

Table 5 shows the results of histopathological analysis of VIA directed punch biopsy of cases with LSIL and HSIL smears. No statistically significant difference between the study groups.

Table 1: Comparison between the two studied groups according to Pap smear results

	Cases (n=200)		Control (n=50)		χ^2	P
	No.	%	No.	%		
Smear						
Negative	156	78.0	41	82.0	0.383	0.536
Normal	102	51.0	23	46.0		
Reactive atypia	54	27.0	18	36.0		
Positive	44	22.0	9	18.0		
ASCUS	31	15.5	6	12.0		
LSIL	11	5.5	3	6.0		
HSIL	2	1.0	0	0.0		

Table 2: Relation between cytology results and mode of contraception in cases group

Cytology results	POPS (n=78)		DMPA (n = 101)		Implanon® (n=20)		Mirena® (n=1)	
	No.	%	No.	%	No.	%	No.	%
Normal	68	87.2	71	70.3	16	80.0	1	100.0
Abnormal	10	12.8	30	29.7	4	20.0	0	0.0
ASCUS	10	100.0	17	56.7	4	100.0	0	0.0
LSIL	0	0.0	11	36.7	0	0.0	0	0.0
HSIL	0	0.0	2	6.7	0	0.0	0	0.0
χ^2 (Mc p)	8.611 (0.059)							

Table 3: Relation between cytology results and duration of use in cases group

	Cytology Results		Test of sig.	p
	Normal (n=156)	Abnormal (n=44)		
Duration of use				
Min. – Max.	1.0 – 16.0	1.0 – 13.0	t=1.852	0.107
Mean ± SD	2.61 ± 2.69	4.10 ± 3.30		
Median	2.0	3.0		

Table 4: Comparison between the two studied groups according to follow up of ASCUS

	Cases (n = 31)		Control (n=6)		□ □	^{FE} p
	No.	%	No.	%		
Follow up of ASCUS						
Persistent	11	35.5	3	50.0	0.450	0.653
Regressed to normal	20	64.5	3	50.0		

Table 5: Comparison between the two studied groups according to punch biopsy (histopathology)

	Cases (n=13)		Control (n=3)		□ □	p
	No.	%	No.	%		
Punch biopsy						
False positive	7	53.8	0	0.0	2.872	^{FE} p= 0.251
Mild dysplasia	4	30.8	2	66.7		
Moderate dysplasia	2	15.4	1	33.3		

DISCUSSION:

Precancerous cervical lesions have become an important concern of women's healthcare in recent years. The Pap test is an excellent screening test, easy to do and interpret and evaluate to detect premalignant changes [18].

Cervical cancer is associated with several risk factors including human papilloma virus infection, smoking, sexual behavior and hormonal contraceptive consumption [9-12]. Hormonal contraceptives is the most popular method of contraception worldwide. The relationship between preinvasive cervical cancer and progestogen-only hormonal contraceptives is controversial [16].

The results of Pap smear in this study showed epithelial cell abnormalities in 44 cases (22%) and 9 controls (18%). These findings suggest that progestagen-only contraceptives do not increase the risk of cervical precancerous lesions nor invasive carcinoma.

In agreement with our study, Darwish *et al.*; [19] in a study performed on progestagen-only contraceptives users including minipills, Levonorgestrel-sub dermal implants and DMPA in comparison to non-hormonal contraceptive users found that 19% of the study group and 17.6% of the control group had cervical cytologic changes in their Pap test with no significant statistical difference.

Lessard *et al.*; [20] in a study on levonorgestrel intrauterine device (Mirena®) and Mascarenhas *et al.*; [21] in a study on etonogestrel contraceptive implants (Implanon®) investigated the changes in cervical cytology using these contraceptive methods and also found non-significant incidence of cytological abnormalities.

An additional finding in this group of patients is the cellular changes associated with progestagen-only contraceptive use that simulate precancerous lesions. Seven cases (53.8%) of the study group showed cytological abnormality without concurrent dysplasia seen in histopathological examination indicating a falsely positive result in the Pap smear. These findings minimize the diagnostic efficacy of cytology in such cases and highlight the value of colposcopically guided cervical biopsy to reach a definite diagnosis in cytologically abnormal cases.

Clark *et al.*; [22] and Collins *et al.*; [23] noted similar findings in their study of false-positive cervical cytology results among women using either progesterone only or combined contraception.

CONCLUSIONS

Progestagen-only contraceptives use is not associated with increased risk of abnormal cytologic findings and preinvasive disease of the cervix. Preliminary observations reported need more validation by screening larger scale of progestagen-only contraceptive users. Cervical cancer screening strategies need to be applied to women in developing countries as

a simple diagnostic and preventive method to decrease the burden of cancer cervix.

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