

## The effect of chronic use of combined Oral contraceptive pills on pap smear

Abdaladeem Yousif Jasem\* and Shaimaa Mohsen\*

### الخلاصة

دراسة مستقبلية لاختبار احتمالية التأثير السلبي للحبوب المانعة للحمل المزدوجة الهرمون في زيادة مخاطر التغيرات الخلوية لعنق الرحم ( تغيرات لا سرطانية أو ما قبل السرطانية )، حيث أجرينا دراسة حالات مسيطر عليها في مستشفى الديوانية التعليمي للنسائية و الاطفال، وقد تم اختيار اثنان و تسعون سيدة يستعملن الحبوب المانعة للحمل المزدوجة الهرمون لفترة طويلة ( 5 سنوات أو أكثر ) واعتبرت هذه مجموعة الحالات المدروسة ، بينما اختيرت مائة و عشرون سيدة لا يستعملن الحبوب المانعة للحمل كمجموعة السيطرة لتقييم النتائج ، كلا المجموعتين ( مجموعة الحالات و مجموعة السيطرة ) تمت مماثلتها من حيث العمر ، عدد الأطفال ، الحالة الاقتصادية و الاجتماعية ، و عدد شركاء ممارسة الجنس ( شريك واحد لكل امرأة لكون جميع الحالات هن نساء مسلمات )، تمت هذه المماثلة لكي نتجنب تأثير العوامل الاخرى على مسحة عنق الرحم فيما عدا الحبوب المانعة للحمل ، كذلك فان جميع السيدات غير مدخنات للسكائر، وأن مدة استعمال الحبوب في مجموعة الدراسة هي 5 سنوات او اكثر ( جميع السيدات لديهن استعمال طويل للحبوب المانعة للحمل )، إن النتائج التي حصلنا عليها هي نتائج مقارنة لبعض الدراسات الاخرى الخاصة بهذا الموضوع ، وقد أظهرت نتائجنا وجود علاقة ذات أهمية بين الاستخدام الطويل للحبوب المانعة للحمل المزدوجة الهرمون وبين التغيرات الخلوية النسيجية لعنق الرحم .

### Abstract

To assess the probability that combined oral contraceptive pills increase the risk of cervical epithelial changes ( like dysplasia or other changes ),we conducted a case controlled study in Diwaniyah maternity & pediatric teaching hospital; ninty –two women with chronic use of combined oral contraceptive pills ( using pills for 5 years or more ) were chosen as a study group ,while one hundred –twenty women with no history of using the pills ( non-users ) were selected as a control group for evaluation,both the control & study groups were matched by age,parity,socio-economic status & number of sex partners ( all with a single partner being a muslim).

\*Department of Obstetrics &Gynecology ,College of Medicine ,AlQadisia University

This is to rule out any other effects on the pap smear except for the use of combined oral contraceptive pills, all women were non-smokers, the duration of using the pills was 5 years or more in the study group ( all are chronic users which means using the pills for more than 5 years ), our findings were close to some other studies ; it showed an association between chronic use of combined oral contraceptive pills & cervical cellular changes.

## **Introduction**

Pap smear; is a simple test that can help prevent cancer of the uterine cervix, it really saves lives, if all women at risk have regular pap smears ; 90 % of cervical cancers would be prevented, during a pap smear a sample of cells taken from the cervix is tested, the samples may be collected by a cotton bud, a small brush or a tiny wooden spatula (Ayer's spatula ), more than one sample may be taken at a time from different parts of the cervix including the endocervix, it should be labeled carefully.

What the results of pap smear mean; negative test means it is showing normal cells , positive test means abnormal cells which may be due to inflammation ( chronic irritation ) because of local infection by yeasts or human papilloma virus or herpes virus, or changes of cells as an early sign of cancer or it may detect cancer itself..

Reliability of the test; the test is mostly reliable which means that if the test is positive then abnormal cells are present in about 90% of the time but it doesn't mean cancer ( like mentioned before ; may be inflammation ) , while if the Pap smear is negative there still can be some abnormal cells that are missed by the test ; that's why it should be repeated at least every year during the reproductive age ( from 18 years & more...), also should be taken after the woman has gone through menopause...

Some studies were looking for the relationship between oral contraceptive pills & cervical epithelial changes ( 1-3 ), it was concluded from some of them that there is a weak correlation between the use of combined oral contraceptive pills for more than 5 years & the risk of cervical smear changes (dysplastic or neoplastic ) ( 4,5 ), Molina & co-workers did not find any risk for neoplasia in women who used the pills

( 6,7 )Screening for cervical dysplasia or neoplasia with pap smear is very useful for prevention of cervical cancer but it seems that other factors might be major affecters for cervical neoplasia like infection with HPV ( human papilloma virus ) with changes in cervical mucus (8-10).

This study is conducted to evaluate the effect of oral contraceptive pills on cervical mucus & the epithelial changes it may cause ( dysplastic or neoplastic ), so we conducted a case control study involving patients with moderate to high grade changes in the cervical epithelium at pap smears & were compared with control cases ; all of which were collected from Diwaniyah maternity & paediatric teaching hospital..

### **Materials and methods**

Between January 2009 & February 2010 ; cases eligible for this case – controlled study were selected from women aged 20-50 years attending the gynecological clinic in Diwaniyah pediatric & maternity teaching hospital who were referred from different health centers in Diwaniyah city,several pap smears were taken from each patient which determined the presence of dysplastic changes ( mild , moderate or severe ), all the slides were reviewed by cytopathologist...of all the 212 women that were chosen in this study ; 34 women had moderate – severe dysplasia on pap smears, while 178 women had normal pap smears, all cases were matched by age , socio-economic state , & number of sex partners ( all had one sex partner because they were all muslim ) , the variables included in the analysis were indices by age,parity, number of miscarriages,smoking state & duration of use of oral contraceptive pills..

Comparison between groups were examined by Mantel-Haentzel, Chi-square & Mann- whitney tests..

### **Results**

All the 212 women are married,& the range of age is 20 -50 years ,all of them have one sex partner ( the husband ) , & most of them had the first experience of sexual intercourse when they were 20 years of age , both the case group ( study group ) & control group were very close regarding sexual habits, none of them were smoker to exclude the effect of smoking on the results of the pap smear,

The longer the duration of the use of combined oral contraceptive pills the more increased the risk of cervical dysplastic changes , 24 of women in the study group ( pill users )& 10 of women in the control group ( non users ) had cervical cytological changes ,a total of 34 women had positive smears, of these 24 females were chronic users of COCP while 10 females were non-users of COCP, the women with negative smears were 178 ( 68 of them were chronic users of COCP while 110 women were non-users of COCP ).. so it means that 26% of the chronic users have positive smears while 8.3 % of the non-users have positive smears ..

with 95% confidence interval ( CI ) ; 0.11- 0. 36 , it was considerable that consumption of oral contraceptive pills have risky effect on cervical smears ...

( OR ) was 3.88 with 95 % CI ; 0. 11 – 0 .- 36 ) ,

To investigate the role of oral contraceptive pills use & the duration of consumption : logistic regression was performed in which the effect of contraceptive pills use was adjusted separately for the cofactor of duration, other co- variables like age , level of education , parity & sexual behavior were very close in both the study group & the control group , all of women in both groups were non – smokers ..

The multi variable logistic regression showed that contraceptive use was 3.88 times more risky for cervical dysplasia , this risk was significant when adjusted with oral contraceptive use , Chi square = 20.063 , df = 1 , p < 0.01 , OR = 3.88 , 95 % CI = 0.11- 0.36 The logistic regression was estimated by forward wald method , OR = 3.88 the odd ratio is a simulation to the relative risk which means that:

Chronic users are 3.88 times more at risk of cervical changes than non-users.

**Table 1**

patient		Cervical changes		total
		positive	negative	
users	positive	34	58	92
Non-users	negative	13	107	120
total		47	165	212

## Discussion

The results of the study were of importance , because it showed that the use of combined oral contraceptive pills puts those women at risk of cervical dysplasia,also we concluded that the duration of consumption of the pills did not affect this association when we excluded it from the equation , this is parallel to some other studies which concluded a weak positive association between oral contraceptive use & risk of cervical dysplasia ( 5,6 ) ( 10-12 ),we controlled all co – variables that may affect the results of the cervical smear except for the human papilloma virus ( HPV ) , in our town extra – marital relations are rare so the HPV infection is expected to be rare , also another co-factor was excluded which is smoking because it is rare among Iraqi women due to social & cultural context ,the most important limitation of our study is the lack of information about HPV infection , in order to get a more reliable results we advise a wider study in the future that may include the duration of oral contraceptive consumption ,,also we should consider HPV infection when facilities are available ,we suggest to perform a future study on the relationship between oral contraceptive pills & cervical cancer ..

cervical changes could be premalignant so pay great attention to them when found on pap smear,

patient cooperation was poor especially in sample collection..

## Recommendations

It is advisable to change the method of contraception every 2-3 years ..

## References

1. sandmire ,H.F. , A.L. Austin & M.W.Becthel , 1976 cervical carcinoma in OCP & IUD users & non- users , American journal of obstetrics & gynecology ; 125 : 339- 45 .
2. Brinton , L.A., 1991, OCP & cervical neoplasia , contraception , 43 : 581- 95
3. Schlesselman , J.J. , 1989 carcinoma of the cervix & breast in relation to the use of OCP , contraception , 40 : 1 – 38 .

4. George , J.G., L.T., H. Nelson & R. Frutcher, 1977, contraception & cervical changes , American journal of obstetrics & gynecology ,128 : 761- 6 .
5. Melamed , M.R. & B.J. Flehinger, 1973 , early incidence of pre-cancerous cervical lesion in women using OCP , gynecological oncology , 1 : 290- 8 .
6. Worth A.J. & D.A. Boyes , 1972 , a study on birth control pills & pre-clinical carcinoma of the cervix , British journal of obstetrics & gynecology 79 : 673- 9 .
7. Molina., R.D.B.Thomas , et, al., 1988 , OCP & cervical carcinoma , cancer Research , , 48 : 1011- 15 .
8. Morrison, C.P.Prokoryn et al .., 2003, OCP use in association with changes in thin Prep PAP smear that mimic low grade squamous intra-epithelial lesions, cancer : 97: 75 – 82 .
9. Stubblefield, P.G., 1984. Oral contraceptives and neoplasia. J. Reprod. Med., 29S: 524
10. WHO collaborative study of neoplasia and steroid contraceptives, 1985. Invasive cervical cancer and combined Oral contraceptives. B.M.J., 290: 961-5.
11. Brinton, L.A., W. Reeves, M.M. Brenes and et al., 1990. Oral contraceptive use and risk of invasive cervical cancer. Int. J. Epidemiol., 19: 4-10.
12. Ursin, G., R.K. Peters, B.H. Henderson and et al., 1994. Oral contraceptives use and adenocarcinomaof cervix. Lancet, 344: 1390-4.