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## Full Length Research Article

# EFFECT OF PROGESTERONE ON THE INTERPRETATION OF CERVICAL SMEAR

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### ABSTRACT

Papanicolaou screening is the standard of care for detection of abnormal cervical cell. Cervical cells are susceptible to change as a result of hormonal exposure and this has the potential to affect cytologic interpretation. The purpose of this study was to examine the accuracy of cervical cytology finding in women using progesterone only contraception as compared to women who used no contraception. Material and methods- A total of 162 women were screened over a period of 3 years. Cytology and histology were done to find out sensitivity and specificity. Result- With no contraception user cervical smear sensitivity was 10% higher than with patient who use progesterone only contraception.

## INTRODUCTION

Cervical cancer causes 5% of cancer death in women worldwide (Cotran *et al.*, 2014). In the last few decades the use of pap testing to screen for cervical neoplasia has led to a decrease in death due to cervical cancer. George Papanicolaou in 1940s first developed this method. Pap screening remains the standard of care for detecting of abnormal and atypical cervical cells. Early detection and treatment of cervical neoplasia depends upon the accuracy of cervical interpretation. The sensitivity of the pap test has been shown to fall between 50-75%. (Renshaw *et al.*, 2002). Exogenous hormones has been noted to affect cervical cellular characteristics (Harris *et al.*, 2009, Kaptain *et al.*, 2002, Valente *et al.*, 1998). Effect of progesterone on cervical cells includes crowding of cells, curling of cells and presences of navicular cells (glycogen filled squamous cells with thickened borders) (Kaptain *et al.*, 2002). These changes may lead to difficulty with cytologic interpretation.

## MATERIALS AND METHODS

A total of 162 cases were studied over a period of 3 years from

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May 2011 to May 2014. This study was done at Patna Medical College and Hospital, Patna. Patients were between the age group of 21-40 with mean age of 31. Out of the 162 cases, 112 were using no contraception. 50 cases were using progesterone only contraception. Progesterone only contraception included injectable depot medroxyprogesterone or progesterone only contraceptive devices. The patient themselves reported their contraceptive use. Patients using other forms of contraceptions were not included in this study. Cervical smear were taken from these patients in the gynaecology outdoor and sent to the Pathology department. These slides were stained by papanicolaou stain and interpreted. The abnormal cervical smear were called back for colposcopic directed biopsy. Abnormality was considered to be cases diagnosed as ASCUS and above.

### Bethesda system of classification was used for interpretation

ASCUS-Atypical squamous cell of undetermined significance.

This term as assigned by pathologist to cytologic smear where the cellular features are not clear as to whether they are inconsequential or problematic in nature (Ferris *et al.*, 2004)

LSIL-Low grade squamous intraepithelial lesion.

The cell nucleus is at least three times larger than normal cells with irregular nuclear shaping, wrinkling of cell membrane and multiple nuclei (Ferris *et al.*, 2004).

**HSIL**-High grade squamous intraepithelial lesion.

Features similar to LSIL with greater nucleus to cytoplasmic ratio (Ferris *et al.*, 2004)

**CIN**- Cervical intraepithelial neoplasia.

**CIN 1**- Is assigned to histologic samples where a mild degree of dysplasia or abnormality is present.

**CIN 2**- Is consistent with moderate degree of dysplasia.

**CIN 3**- Is for severe dysplasia/ neoplasia in situ.

**Squamous Cell Carcinoma (SCC)** - Neoplasia of cervical squamous cell both in situ or invasive.

The total cases who were not using any form of contraception were 112. Of these 53 had a normal pap smear.

The rest 59 were called for colposcopy directed biopsy. Only 47 reported back.

**Table 1. Cytological and Histological result of non contraceptive users (47 cases).**

Histology result	Cytology	Cytology	Cytology	Cytology
	Ascus	Lsil	Hsil	ScC
Negative	7	2		
Cervicitis		7	3	
Cin 1	3	14	2	
Cin 2	1		5	2
Sq.cell ca				1

The total cases who were using progesterone only contraception were 50. Out of these 8 had normal smear.

The 42 having abnormal cytology were called for colposcopy directed biopsy. 31 came back for biopsy.

**Table 2. Cytological and histological result of progesterone only contraception users. (31 cases)**

Histology result	Cytology	Cytology	Cytology	Cytology
	Ascus	Lsil	Hsil	ScC
Negative	7	3		
Cervicitis	1	15	1	
Cin 1	1	1		
Cin 2			1	
Sq. Cell ca				1

**Interpretation**

Patients using no contraception-

False positive cases-12                      False negative cases-4

True positive cases-24                      True negative cases-7

Sensitivity of cervical pap-85.71%

Specificity of cervical pap-36.84%

Patients using progesterone only contraception-

False positive cases-19                      False negative cases-1

True positive cases-3                      True negative cases-8

Sensitivity of cervical pap-75%

Specificity of cervical pap-29.62%

So progesterone causes the sensitivity of pap smear interpretation to fall by 10%.

**Limitation**

The sample collection was done by different practitioner and interpretation of the samples were also done by different pathology professionals. So there was no way to assure that all the various practitioner and pathology professionals followed the same standard of expertise.

**DISSCUSSION**

Exogenous progesterone changes cervical cellular characteristics. (Dalstein *et al.*, 2003, Valente *et al.*, 1998). Effect of progesterone exposure includes curling or crowding of squamous cells, destruction of cells and unusual morphology of cells (navicular or boat shaped) (Kaptain *et al.*, 2002). Progesterone has thought to promote atrophy of the epithelial cells as well as to decrease the cellular maturation pattern (Bosch *et al.*, 1995, Meyer *et al.*, 2001). All these changes affect the cytological interpretation of the cells.

**Conclusion**

Pap smear remains the standard of care for detection of cervical neoplasia. So, accuracy of cytologic interpretation is necessary. Factors which alter the accuracy needs to be identified and explored. Progesterone can be one of the factors affecting cervical cellular characteristics, hence, pap smear interpretation.

**REFERENCES**

Bosch FX, Manos MM, Munoz N, et al. Prevalence of human papillomavirus in cervical cancer: a world wide perspective. *J Natl Cancer Inst.* 1995; 87:796-802.

Cotran RS, Kumar V, Collins T. Robbins pathologic basis of disease. 6<sup>th</sup> edition.

Dalstein V, Riethmuler D, Pretet JL et al. Persistence and load of high risk HPV are predictors for development of high-grade cervical lesions: A longitudinal French cohort study. *Int J Cancer*: 2003; 106:396-403.

Ferris DG, Cox JT, O'Connor DM, Wright VC, Foerster J. Modern Colposcopy 2<sup>nd</sup> edition 2004.

Harris TG, Miller L, Ulasingam SL, et al. Depot-medroxyprogesterone acetate and combined oral contraceptive used and cervical neoplasia among women with oncogenic human papillomavirus infection. *Am J Obstetric Gynecology* 2009; 489e1: 481-489.

Kaptain S, Bloom L, Weir MM. Hormonal effects of depo-provera in cervical smears. *Cancer*. 2002; 96(2):74-82.

Long HJ, Laack NN, Gostout BS. Prevention, diagnosis and treatment of cervical cancer. *Maya Clinical Procedures*. 2007; 82(2):1566-1574.

Meyer T, Arndt R, Beckmann ER, Padberg B, Christophers E, Stockfleth E. Distribution of HPV 53, HPV 73 and CP8304 in genital epithelial lesions with different grades of dysplasia. *Int J Cancer*. 2001; 11:198-204

Renshaw AA. Measuring sensitivity in gynaecologic cytology. *Cancer*. 2002; 96(4):210-217.

Valente PT, Schantz HD, Trabal JF. Cytologic changes in cervical smears associated with prolonged use of depot medroxyprogesterone acetate. *Cancer Cytopathology*. 1998; 84(6):328-334.

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