Pap Smear Screening Among the Postmenopausal Women

Berfu DEMİR[1], Ali HABERAL[2], Esmen OZTÜRKOĞLU[1a], Betül DÜNDAR[1], Bahar BASKAN[1a]
Emine SOBACI[1], Nejat ÖZGÜL[1]

Ankara, Turkey

OBJECTIVE: To evaluate the effectiveness of routine Pap smear screening in postmenopausal women.

STUDY DESIGN: 2060 women applied to menopause outpatient clinic were reviewed retrospectively. Demographic characteristics, the use of hormone therapy, and the history of previous Pap smear were analyzed.

RESULTS: The Pap smear results were as; normal in 1320, inflammation in 591, atrophy in 121, metaplasia in 22, ASCUS in 4, HGSIL in 1, and carcinoma in 1. While two of the ASCUS patients had two previous cervical smears which were normal; the other two HGSIL and carcinoma patient had not previous Pap smear. The patients who had ASCUS, colposcopy was applied and three of them were normal. The histopathological analysis of the cervical biopsy in the HGSIL case was squamous cell carcinoma.

CONCLUSION: Pap smear screening should be done to postmenopausal women in spite of low efficiency or false positive results.

Key Words: Pap smear, Postmenopausal women

Gynecol Obstet Reprod Med; 2010;16:168-72

Introduction

It is known that cervical cancer mortality has decreased over the last five decades due to the introduction of Papanicolau (Pap) test. As cervical cytology screening has become more prevalent preinvasive lesions of the cervix are detected far more frequently than invasive cancers. An unscreened woman's life time risk of cervical cancer is estimated as 3.5% and can be reduced to 0.8% with screening.[1,2] Most cervical cancers diagnosed in older women occur among unscreened or poorly screened women.[3,4,5,6] Still there is no consensus about screening postmenopausal women for cervical neoplasia. The atrophic changes in menopause are known to be reflected in cytology but relevance of other features in menopausal management is relatively unknown.[7] The benefits and risks of performing annual Pap test on postmenopausal women are not well-defined.[8] Since women spend one third of their lives in the postmenopausal period the issue of cervical screening has great public health importance. There are different data on the effect of exogenous hormone therapy (HT) on cervical cytological conditions in postmenopausal women.

The objective of this study is to determine the pattern of abnormal cervical cytology in postmenopausal women, to determine whether there is any benefit of using routine Pap smear in this group and to compare the histological findings in women who use hormone therapy (HT) with those who do not.

Material and Method

Total of 2060 women with Pap test who attend to menopause outpatient clinic were reviewed retrospectively. The age, parity, menopausal status and the use of HT, were recorded. Cytological analysis of all slides was performed at the Department of Pathology, Ministry of Health Ankara Etlik Zubeyde Hanım Women's Health Teaching and Research Hospital. The specimens were classified according to the modified Bethesda system[9] (normal, inflammation, atypical squamous cells of undetermined significance (ASCUS), atypical glandular cells of undetermined significance (AGUS), low-grade squamous intraepithelial lesion (LGSIL), high-grade squamous intraepithelial lesion (HGSIL) and squamous cell carcinoma. The information about the previous Pap smear re-

[1]Department of Obstetrics and Gynecology Etlik Zübeyde Hanım Women's Health Teaching and Research Hospital, Ankara

[2]Department of Obstetrics and Gynecology Baskent University, School of Medicine, Ankara

[a]At the time of the study this author was a resident at our hospital.

Address of Correspondence: *Berfu Demir*
Mustafa Kemal Mah. Ankara Sitesi
B2-12 TR-06520
Çankaya, Ankara
demirs@isbank.net.tr

Submitted for Publication: *29. 03. 2010*
Accepted for Publication: *08. 04. 2010*

sults and the screening intervals were also recorded. In the surgical menopause cases, Pap smear was taken if the case had not postoperative pathology report or patient's cervical pathology was CIN II and CIN III. The diagnostic (colposcopy, endocervical curettage, cervical biopsy, etc.) and therapeutic (loop electrosurgical excision procedure, radical surgery, or radiation therapy) cervical procedures performed to evaluate abnormal smears were also recorded.

The rates of cervical smear abnormalities were determined, and if HT was associated with an increased incidence of abnormal findings on Pap smear was investigated.

Statistical analyses were performed using the SPSS for Windows (release 10.0, Chicago, IL, USA). Comparisons were done using student t test or Mann Whitney U test according to the distribution of the parameters. $p<0.05$ was considered to be statistically significant.

Results

A total of 2060 women were evaluated in this study. Demographic characteristics were as follows: age: 54.2±6.3 years, parity: 3.5±1.9, and the menopausal period was 6.5±5.7 years. 84% of the cases (n=1748) were grouped in spontaneous menopause, while the other 15.1% were included in the surgical menopause group. The Pap smear results in the total 2060 cases were as; normal in 1320 (64.1%), inflammation in 591(28.7%), atrophy in 121 (5.9%), metaplasia in 22 (1.1%), ASCUS in 4 (0.2%), HGSIL in 1 (0.05%), and carcinoma in 1 (0.05%). The incidence of cytological abnormalities was calculated as 0.3% (n=6), ASCUS in 4 (0.2%), HGSIL in 1 (0.05%) and squamous cell carcinoma in 1 (0.05%). All the patients who had cytological abnormalities on Pap smear were in the spontaneous menopause group and had macroscopic findings on the speculum examination. The demographic characteristics and pelvic examination results of the women having cytological abnormalities are given in Table 1.

While two of the women with cytological abnormalities had two previous Pap smears, which were normal and were not taken within 2 years, the others were not screened before. Women with ASCUS were evaluated with colposcopy. The type of management was determined throughout the final pathology (Table 2).

The number of prior Pap smears was 1 in 519 of the cases (25,2%), 2 in 224 cases (10.9%), ≥3 in 163 cases (7.9%) the remaining 56% (n: 1154) had no Pap smear.

Sixty six percent (n=1351) of the women were receiving HT. Endocervical cells were present 41.1% in cases not receiving HT, this ratio was 40% in cases receiving HT (p=0.93). The 3 of the 6 cases with cytological abnormalities were receiving HT and there was not any statistically significant difference about the use of HT (p=0.24).

Table 1: Clinical findings of the cases with cytological abnormalities

	Age (year)	Parity	Men. period (year)	Menop.type	Pap smear
1	57	3	9	Spontaneous	ASCUS
2	53	6	1	Spontaneous	ASCUS
3	53	2	5	Spontaneous	ASCUS
4	48	3	4	Spontaneous	ASCUS
5	62	7	7	Spontaneous	HGSIL
6	54	2	2	Spontaneous	Squamous cell carcinoma

Table 2: Additional diagnostic and therapeutic interventions results of the cases with cytological abnormalities

	Pap Smear	Colposcopy	LEEP	Cervical biopsy	Treatment
1	ASCUS	(+) Normal	(-)	(-)	Observation
2	ASCUS	(+) Normal	(-)	(-)	Observation
3	ASCUS	(+) Normal	(-)	(-)	Observation
4	ASCUS	(+) Suspicious	(+) Chronic cervicitis	(-)	Observation
5	HGSIL	(+) Suspicious	(-)	(+) Squamous carcinoma	Radical hysterectomy with cell pelvic lympadenectomy
6	Squamous cell carcinoma	(-)	(-)	(+) Squamous carcinoma	Radical hysterectomy with cell pelvic lympadenectomy

Discussion

There were 2060 Pap smears evaluated in this study, but only two were invasive cancer. The percentage of abnormal Pap smears was 0.3%, which is lower than that of the other reports. In the report by Benard et al., the rate of abnormal Pap tests in the age group 50-64 years was 1.1%.[10] When ASCUS taken as abnormal, the percentage of abnormal smear results rise to 4.5%. In the European Union countries with a screening program (Belgium, Denmark, Finland, France, Germany, Ireland, Italy, Netherlands, Sweden and the United Kingdom), the percentage of abnormal Pap tests varied from 1.5% to 8% with the age range 20 to 65 years. But age specific data for the abnormal smears were not reported.[11] The low percentage abnormal Pap smear data (0.3%) in this study may be explained with the following facts observed in the patient records: most of the women had monogamy in their life and the frequency of the coitus decreased, or ceased after the menopausal period.

Most invasive cervical cancer is diagnosed after the age of 45 years.[12] However, there is very low risk of cervical cancer for women aged 50 and older in countries with organized screening programs.[13] Kietperakool et al. carried out a study to define the factors in predicting occult invasive carcinoma in women undergoing see and treat approach; 121 postmenopausal women was evaluated in that study and the result was that the postmenopausal status is not a predictor of having such lesion.[14] In the results reported by Benard ET al., 57% of the 465 women with invasive cancers were diagnosed among women aged 50 years or older. 32% of those had no Pap smear before.[10] Gustaffson et al. reported that age specific incidence rates of the invasive cervical cancer showed the same pattern for many Western European countries (a peak age at 44-47 years for Denmark, Germany, the Netherlands, Sweden).[15] Although some countries seem to have a slightly different distribution (A peak age at 53.5 years and 48 years for Finland, and United Kingdom, respectively). It may be difficult to get satisfactory samples from older women due to conditions such as atrophy, physiological retraction of transformation zone and cervical stenosis. There is an evidence that screening is associated with potential harms, including anxiety and discomfort during cytology sampling of some older women and invasive procedures and anxiety due to false positive cytology results[8,13] Several studies have shown a low efficiency of cytological screening in women over the age of 50, the vast majority of cervical cancers in older women occur in those who are not previously screened or who do not have three consecutive normal cytology results.[6,8,16,17] Published reviews suggest that 50-70% of women in whom invasive cervical cancer develops failed to get a Pap smear within the five years before diagnosis or have never been screened at all.[18,19] According to this study results, none of the cases completed the screening program (66% were not screened before and the others have only two documented consecutive, technically satisfactory normal cervical cytology tests). Although rate of the abnormal Pap smear was low in this study population, cases with pathological smears were diagnosed among the unscreened or previously screened postmenopausal women.

ASCUS constitutes majority of the cytological abnormalities in postmenopausal women.[8,20] In a report by Rader et al., the incidence of ASCUS in women over 55 were given as 1.8% and they indicate that these women were three times more likely to be receiving HT than similar aged women with normal Pap smear.[21] Keating et al. and Flyn et al. reported that the perimenopausal and postmenopausal women appear to have elevated ASCUS to SIL ratios, despite a decreased abnormality rate with increasing age.[22,23] In the presented study, the incidence of ASCUS in postmenopausal women is 0.2%, this ratio is far low than the other studies which found this incidence as 1.8% and as 2.9% .[21,22] This result may be explained due to taking Pap smear after applying local estrogen and/or antimicrobial treatment in the women who have moderate to heavy cervicovaginal atrophy or vaginitis at the speculum examination according to the menopause study protocol.

According to the our results, HT is not associated with cytological abnormalities in postmenopausal women. This result is in agreement with some others. Sawaya et al. reported that the incidence of cytological abnormalities was non-significantly higher in hormone treated women compared with non hormone treated women, because of a non significant (58%) greater incidence of ASCUS.[8] In a randomized controlled trial, the incidence of cytological abnormalities, cervical cancer and to determine the effect of HT on cervical cytology among postmenopausal women (aged 50-79 years) was evaluated. The study concluded that HT was associated with increased incidence of any cytologic abnormality, although it had no impact on the incidence of HSIL or cervix cancer.[24]

There is general consensus that the incidence of cervical cancer in older women almost entirely confined to the unscreened women and the benefits of screening are clear in unscreened postmenopausal women. Screening in the unscreened population can reduce morbidity and mortality from cervical cancer. But, risk based screening intervals or age limits on screening are important clinical topics for the Pap smear screening. Mindy Smith et al.[25] used reducing the frequency of Pap tests for low-risk women to once every 3 years, as recommended by the US Preventive Services task Force and the Canadian Task Force.[26,27] American Cancer Society Guideline indicate that; 'women who are age 70 and older with an intact cervix and who have had three or more documented, consecutive, technically satisfactory normal/negative cervical cytology test and no abnormal/positive cytology tests within the 10 year period prior to age 70 may elect to cease cervical cancer screening'.[13]

The presence of Human Papillomavirus in older women is an independent risk factor for cervical disease. Chan et al. reported that there are two peaks of HPV infection and consequent cervical cancer.[28] The first infection peak at ages 26-30 was followed by a CIN 2/3 and an invasive cervical cancer peak respectively 5-15 years and 15 years later. The second infection peak at ages 46-50 was followed by an invasive cervix cancer peak 20 years later. In the second peak age group there weren't any CIN 2/3 cases detected. The most plausible explanation of this situation is that women at second peak (ages 50-65) group are not having Pap smears under current opportunistic screening programs, so that the chance of treating the lesions in preinvasive stages was eliminated.[28] Onuki et al. studied the age related prevalence of HPV and found that the prevalence of HPV varied greatly according to woman's age; highest among women aged 20-29 years and lowest over 60 years of age.[29] HPV testing at 50 years old may identify the small proportion of women still at risk who could continue screening and minimize the potential increase in the incidence of cervical cancer.[30]

Future studies should focus on determining the optimal screening strategy in postmenopausal women. The incidence of preinvasive disease of the cervix is low over the age of 50 and is seen almost exclusively in inadequately screened women there appears to be little benefit in taking Pap test orderly in the postmenopausal women, especially if they have had regular negative Pap test.

Postmenopozal Kadınlarda Pap Smear Taraması

AMAÇ: Postmenopozal kadınlarda Pap smear taramasının etkinliğini değerlendirmek.

GEREÇ VE YÖNTEM: Menopoz polikliniğine başvuran 2060 kadın retrospektif olarak incelendi. Hastaların demografik özellikleri, hormon tedavisi kullanıp kullanmadıkları ve daha önce Pap smear alınma öyküsü kaydedildi.

BULGULAR: Pap smear sonuçları 1320 hastada normal, 591 hastada inflamasyon, 121 hastada atrofi, 22 hastada metaplazi, 4 hastada ASCUS, 1 hastada HGSIL ve 1 hastada karsinom olarak rapor edildi. Pap smear sonucu ASCUS olarak rapor edilen dört hastadan ikisinin daha önce normal olarak rapor edilmiş Pap smear sonuçları varken, diğer iki HGSIL ve karsinom olgusunda Pap smear taraması yapılmamıştı. ASCUS olgularına kolposkopi yapıldı ve üç tanesinde normal kolposkopi bulguları mevcuttu. HGSIL olgusuna yapılan servikal biyopsi sonucu ise yassı hücreli karsinom olarak rapor edildi.

SONUÇ: Postmenopozal kadınlara düşük etkinliğe veya yanlış pozitif sonuçlara rağmen Pap smear taraması yapılmalıdır.

Anahtar Kelimeler: Pap smear, Postmenopozal kadınlar

References

1. McCrory DC, Matchar DB, Bastian L, Datta S, Hasselblad V, Hickey J et al. Evaulation of cervical cytology. Evidence Rep Technol Assess. 1999;(5):1-6.
2. Ries LAG, Kosary CL, Hankey BF, Miller BA, Clegg L, Edwards BK. SEER Cancer Statistics Review, 1973-1996. Bethesta, Md: National Cancer Institute, 1999.
3. Sung HY, Kearney KA, Miller M, Kinney W, Sawaya GF, Hiatt RA. Papanicolaou smear history and diagnosis of invasive cervical carcinoma among members of a large prepaid health plan. Cancer 2000;88:2283-9.
4. NIH Consensus Statement. Cervical Cancer. Washington, DC. US Dept of Health and Services,1996.
5. Van Wijngaarden WJ, Duncan ID: Rationale for stopping cervical screening in women over 50. BMJ 1993;306: 967-71.
6. Cruickshank ME, Angus V, Kelly M, McPhee S, Kitchener HC. The case for stopping cervical screening at age 50. Br J Obstet Gyaecol 1997;104: 586-9.
7. Thomas A, Correa MM, Kumar KR. Clinical profile and cervical cytomorphology in symptomatic postmenopausal women. Indian J Pathol Microbiol 2003; 46(2):176-9.
8. Sawaya GF, Grady D, Kerlikowske K. The positive predictive value of cervical smears in previously screened postmenopausal women: The Heart and Estrogen/progestin replacement study (HERS). Ann Intern Med 2000; 133:942-50.
9. The 2001 Bethesda System. Terminology for reporting results of cervical cytology. JAMA 2002; 287(16): 2114-9.
10. Benard VB, Eheman CR, Lawson HW. Cervical screening in the National Breast and Cervical Cancer Early Detection Program. 1995-2001. Obstetrics and Gynecology 2004;103(3): 564-71.
11. van Ballegooijen M, van den Akker-van Marle E, Patnick J, Lynge E, Arbyn M, Anttila A et al. Overview of important cervical cancer screening process values in European Union countries, and tentative predictions of the corresponding effectiveness and cost-effectiveness. Eur J Cancer 2000;30:2177-88.
12. Schiffman MH. Recent progress in defining the epidemiology of human papillomavirus infection and cervical neoplasia. J Natl Cancer Inst 1992;84:394-98.
13. Saslow D, Runowicz CD, Solomon D, Moscicki AB, Smith RA, Eyre HJ, Cohen C. American Cancer Society Guideline for the early detection of cervical neoplasia and cancer. CA Cancer J Clin 2002;52:342-62.
14. Kietpeerakool C, Sukkawattananon W, Srisomboon J, Khunamompong S, Siriaunkgul S, Nimmanhaemindak K. Factors predicting occult invasive carcinoma in women

undergoing a 'see and treat' approach. Asian Pac J Cancer Prev. 2008;9(2):209-12.

15. Gustafsson L, Ponten J, Bergstrom R and Adami HO. International incidence rates of invasive cervical cancer before cytological screening. Int J Cancer 1997;71:159-65.
16. Van Wijngaarden WJ, Duncan ID. Rationale for stopping cervical screening in women over 50. BMJ 1993; 306(6883):967-71.
17. McKenzie CA, Duncan ID. The value of cervical screening in women over 50 years of age time for a multicentre audit. Scott Med J. 1998; 43(1):19-20.
18. Janerich DT, Hadjimichael O, Schwartz PE, Wheeler CM, Barnes W, Lowell DM et al. The screening histories of women with invasive cervical cancer, Connecticut. Am J Public Health 1995;85:791-4.
19. Hildesheim A, Hadjimichael O, Schwartz PE, Wheeler CM, Barnes W, Lowell DM et al. Risk factors for rapidonset cervical cancer. Am J Obstet Gynecol 1999; 180 (3pt1): 571-7.
20. Saminathan T, Lahoti C, Kannan V, Kline TS. Postmenopausal squamous cell atypias: a dignostic challenge. Diagn Cytopathol 1994; 11(3):226-30.
21. Rader AE, Rose PG, Rodriguez M, Mansbacher S, Pitlik D, Abul-Karim FW. Aytipical squamous cells of undetermined significance in women over 55. Comparison with the general population and implications for management. Acta Cytol 1999; 43(3):357-62.
22. Keating JT, Wang HH. Significance of a diagnosis of atypical squamous cells of undetermined significance for Papanicolau smears in perimenopausal and postmenopausal women. Cancer 2001;93(2):100-5.
23. Flynn K, Rimm DL. Diagnosis of ASCUS in women over age 50 is less likely to be associated with dysplasia. Diagn Cytopathol 2001; 24(2):132-6.
24. Yasmeen S, Romano PS, Pettinger M. Incidence of cervical cytological abnormalities with aging in the women's health initiative: a randomized controlled trial. Obstet Gynecol. 2006;108(2):410-9.
25. Smith M, French L, Barry HC. Periodic Abstinence From Pap (PAP)Smear Study: women's perceptions of Pap smear screening. Ann Fam Med 2003;1;203-8.
26. US Preventive Services Task Force. Screening for cervical cancer: Recommendations and rationale. Am Fam Physician 2003;67M1759-66.
27. Canadian Task Force on the Periodic Health Examination. 2 1987 update CMAJ 1988; 138: 618-26.
28. Chan PK, Chang AR, Yu MY. Age distribution of human papilloma virus infection and cervical neoplasia reflects caveats of cervical screening policies. Int J Cancer. 2010;126(1):297-301.
29. Onuki M, Matsumato K, Satoh T. Human papillomavirus infections among Japanese women:age-related prevalence and type-specific risk for cervical cancer. Cancer Sci. 2009;100 (7): 1312-6.
30. Cruickshank ME. Is cervical screening necessary in older women? Cytopathology 2001;12: 351-3.