Evaluation of the Relationship Between Histopathological Tissue Diagnosis and Endometrial Thickness in Cases with Postmenopausal Bleeding

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ABSTRACT

OBJECTIVE: The investigation of the relationship between the endometrial sampling results and the endometrial thicknesses measured by transvaginal ultrasonography (TV-USG) in patients with postmenopausal bleeding.

STUDY DESIGN: The results of 235 cases, where endometrial sampling has been made due to postmenopausal bleeding at the Diyarbakır Maternity and Pediatric Hospital between January 2013 and December 2013, have been evaluated retrospectively.

RESULTS: In the findings, the mean age is 57.83±8.06 years and the mean parity is 7.73±3.26. In 126 of the findings (53.6%), the endometrial thickness in TV-USG is <5 mm (group 1), and in 109 (46.4%) the endometrial thickness in TV-USG is ≥5 mm (group 2). It has been observed that 53 (22.6%) of the cases have been diagnosed with atrophic endometrium, 43 (18.3%) with endometrial polyp, 34 (14.5%) with deficient material, 28 (11.9%) with secretory endometrium, 19 (8.1%) with proliferative endometrium, 16 (6.8%) with simple endometrial hyperplasia, 12 (5.1%) with irregular proliferative endometrium, 7 (3%) with complex endometrial hyperplasia, 3 (1.3%) with endometrial adenocarcinoma and 3 (1.3%) with endometritis. In Group 1, any abnormal histopathological (endometrial polyp, hyperplasia and adenocarcinoma) findings have not been identified.

CONCLUSION: In cases with postmenopausal bleeding, endometrial sampling is important. Endometrial thickness measurement with TV-USG, which is a non-invasive technique, should be used as the first step in the evaluation of the cases. It appears that high parity ratios reduce the endometrium cancer risk.

Keywords: Postmenopausal bleeding, Transvaginal ultrasonography, Endometrial thickness, Histopathological diagnosis

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Introduction

According to the definition by the World Health Organization, menopause is the permanent failure to menstruate as a result of the loss of follicular activity.[1] Meanwhile, postmenopausal bleeding is the bleeding observed in women, who have gone into menopause, following a period of 6-12 months of amenorrhea.[2-3] It is a widespread gynecological ailment that composes 5-10% of all gynecological patients.[4] The underlying causes include atrophic vaginitis, cervicitis, endometritis, atrophic endometrium, myoma, endometrial polyp, endometrial hyperplasia and other genital organ cancers, primarily led by endometrium cancer.[5-8] Endometrium cancer is determined in 10-15% of the cases, while the sole complaint may be postmenopausal bleeding in 90% of the endometrium cancer cases.[9,10] Therefore, endometrial sampling is important in patients who have postmenopausal bleeding. While endometrial sampling may be performed under local anesthesia in office conditions, it may also be performed under general anesthesia in operating room conditions. Pipelle, Karman injector and dilation-curettage (D&C) are methods that are frequently used for these purposes. Endometrial sampling may also be performed hysteroscopically, by directly observing the endometrial cavity. Hysteroscopy is important especially in patients where endometrial sampling has been unsuccessful, whose material is inadequate for evaluation, who have cervical stenosis and repetitive postmenopausal bleeding.[11,12] All of these diagnostic procedures are invasive methods and have the tendency to lead to serious complications including uterus perfo-

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ration, although quite rare.[13] TV-USG, being a non-invasive method that can be easily applied as contrary to the available diagnostic methods, is used as the first evaluation in postmenopausal bleeding management.[14] Researches on predicting the pathologies of endometrial thickness in patients with postmenopausal bleeding are available in the literature.[6-7]

In this paper, the relationship between the endometrial sampling results and the results of endometrial thickness measurements by transvaginal ultrasonography of patients with postmenopausal ultrasonography has been examined.

Material and Method

Patients, who have applied at the Diyarbakır Maternity and Pediatric Hospital between January 2013 and December 2013 with postmenopausal bleeding and on whom endometrial sampling has been made, have been included in the research. Following evaluation by TV-USG, Karman injector guided endometrial sampling has been performed on all patients by paracervical blockage with Jetocaine at the intervention service. The final diagnosis has been established following histopathological evaluation. Among the histopathological findings that have been determined, endometrial hyperplasia, endometrial polyps and endometrium cancers have been accepted as abnormal. As based on the endometrial thickness values measured by TV-USG, the patients have been separated into two groups as <5 mm (group 1) and ≥ 5 mm (group 2). The relationship between the endometrial thickness and the abnormal histopathological findings has been examined. All data have been acquired retrospectively by accessing patient files through the hospital automation system. The histopathological tissue findings have been reviewed by a pathologist and the accuracy of the diagnoses has been confirmed.

Statistical evaluation

In the evaluation of the findings obtained in the research, the IBM SPSS Statistics 22 (IBM SPSS, Turkey) software has been used for statistical analyses. In addition to descriptive statistical methods (Mean, Standard deviation) during the evaluation of the research data, the Student t-test has been used in the comparisons of parameters displaying a normal distribution between two groups, and the Mann Whitney U test has been used in the comparisons of parameters that did not display a normal distribution among the two groups. In the meantime, in the comparisons of the qualitative data, the Fisher's Exact Chi-Square test and the Continuity (Yates) Correction have been used. Significance has been evaluation at the level of $p<0.05$.

Results

The research has been carried out with 235 cases in total between January 2013 and December 2013. The ages of the cases vary between 40 and 83 years, the mean is 57.83±8.06. The parity numbers range between 0 and 18, the mean is 7.73±3.26 and the median is 8. While the mean parity is 6.43±3.60, and the median is 6 in cases with endometrial carcinoma, the mean parity is 7.77±3.25, and the median is 8 in those who do not have endometrial carcinoma. The endometrial thickness in TV-USG is <5 mm in 126 of the cases (53.6%), while endometrial thickness is ≥5 mm in 109 cases (46.4%). The age and parity distributions of the cases, as based on the groups, have been summarized in table 1. The average age of Group 1 is higher than that of Group 2 in a statistically significant manner ($p<0.01$). Meanwhile, there is no statistically significant difference between the parity means of Group 1 and Group 2 ($p>0.05$).

The distribution of the diagnoses of the cases, as based on endometrial thickness in TV-USG, has been summarized in table 2. Secretory endometrium has been observed in 14.% of the cases in Group 1, and 9.2% of the cases in Group 2, and there is no statistically significant difference between the two groups ($p>0.05$). The ratio of observing proliferative endometrium in Group 2 (13.8%) is higher than that in Group 1 (3.2%) at a statistically significantly level ($p<0.01$). The ratio of observing irregular proliferative endometrium in Group 2 (11%) is higher than that in Group 1 (0%) at a statistically significantly level ($p<0.01$). The ratio of observing atrophic endometrium in Group 1 (42.1%) is higher than that in Group 2 (0%) at a statistically significantly level ($p<0.01$). The ratio of observing inactive endometrium in Group 1 (13.5%) is higher than that in Group 2 (0%) at a statistically significantly level ($p<0.01$). The ratio of observing endometrial polyp in Group 2 (39.4%) is higher than that in Group 1 (0%) at a statistically significantly level ($p<0.01$). The ratio of observing simple endometrium hyperplasia in Group 2 (14.7%) is higher than that in Group 1 (0%) at a statistically significantly level ($p<0.01$). The ratio of observing complex endometrial hyperplasia in Group 2 (6.4%) is higher than that in Group 1 (0%) at a statistically significantly level ($p<0.01$). The ratio of inadequate material in Group 1 (27%) is higher than that in Group 2 (0%) at a statistically significantly level ($p<0.01$). There is no statistically significant difference between Group 1 and Group 2 with respect to observing endometrial adenocarcinoma and endometritis ($p>0.05$).

Table 1: Evaluation of age and parity number on group basis

	Group 1 (<5mm)	Group 2 (≥5mm)	p
	Mean±SS (median)	Mean±SS (median)	
[1]Age	59.36±7.63 (57)	56.06±8.20 (54)	0.002**
[2]Parity	7.90±3.10 (8)	7.53±3.43 (7)	0.245

Table 2: Evaluation of diagnoses as based on endometrium thickness in TV-USG

	TV-USG Endometrial Thickness			
	Group 1 (<5mm) n (%)	Group 2 (≥5mm) n (%)	Total n (%)	p
Secretory Endometrium	18 (%14.3)	10 (%9.2)	28 (%11.9)	0.315
Proliferative Endometrium	4 (%3.2)	15 (%13.8)	19 (%8.1)	0.006**
Irregular Proliferative Endometrium	0 (%0)	12 (%11)	12 (%5.1)	0.001**
Atrophic Endometrium	53 (%42.1)	0 (%0)	53 (%22.6)	0.001**
Inactive Endometrium	17 (%13.5)	0 (%0)	17 (%7.2)	0.001**
Endometrial Polyp	0 (%0)	43 (%39.4)	43 (%18.3)	0.001**
Inadequate Material	0 (%0)	16 (%14.7)	16 (%6.8)	0.001**
Endometritis	0 (%0)	3 (%2.8)	3 (%1.3)	0.098
Simple Endometrium Hyperplasia	34 (%27)	0 (%0)	34 (%14.5)	0.001**
Complex Endometrial Hyperplasia	0 (%0)	7 (%6.4)	7 (%3)	0.004**
Endometrial Adenocarcinoma	0 (%0)	3 (%2.8)	3 (%1.3)	0.098

Discussion

The frequency of endometrium cancers increases with age. 80% of the cases are in the postmenopausal period, and the average observation age is 60.[15] In the researches that have been conducted, it has been stated that the frequency of endometrium cancer in patients with postmenopausal bleeding is in the range of 3.7% and 17.9%.[16] Abdulah et al.[17] have determined this ratio as 3.3% in patients with postmenopausal bleeding, while Kaya et al.[18] have determined it as 6.5%. In our study, this ratio has been determined as 1.3%. When examined as based on the groups, this ratio is 0% in group 1 and 2.8% in group 2. The results obtained in our research are lower than the results in both of the two studies that are mentioned above and in the literature. Meanwhile, the ratios in Group 2 are similar to the results of Abdullah et al. The fertility rate in our region is high and the mean parity of our cases is 7.73±3.26. This ratio may be the cause underlying the low endometrium cancer frequency in our study. In the study they have conducted, Pınar et al.[19] have stated that the risk of endometrial cancer in nulliparous women increased 2-3 times as compared to women who have given birth.That research supports our data.

Among the causes of postmenopausal bleeding in our study, proliferative-secretory endometrium is the most frequently encountered pathology at a ratio of 25.1%, it is followed by atrophic endometrium with a ratio of 22.6%. In the research conducted by Abdullah et al.[17], the ratio of proliferative-secretory endometrium is 52.6%. Meanwhile, Kucur et al.[20] have stated this ratio as 31%. The results of our research are similar to those of Kucur et al. Meanwhile, the most frequent finding has been determined to be atrophic endometrium in another research.[21]

Endometrial polyps are the important cause of postmenopausal bleeding. The malignity development ratio in polyps observed in the postmenopausal term has been stated to be 1.5%.[22] In their research, Bani-Irshaid et al.[22] have stated the frequency of endometrial polyps observed in 486 cases as 5.1%.On the other hand, in the series they have conducted, Selçuk et al.[24] have determined this ratio as 14.3%. In the series by Kaya et al.[18], this ratio has been found to be 33.4%. The ratio in our research is 18.3% and similar to that of Selçuk et al.

Since endometrial hyperplasias are pre-cancerous lesions, their diagnoses and treatment are important. In the research they have conducted on cases with postmenopausal bleeding, Caspi et al.[25] have determined this ratio as 11%. In the series by Selçuk et al.[24], this ratio has been determined as 5.4%. Meanwhile, Abdullah et al.[17] have stated this ratio to be 8.8% in the series they have conducted. In our research, the ratio of endometrial hyperplasia in patients with postmenopausal bleeding is 9.8%. The results of our research are similar to those of Caspi et al. and Abdullah et al.

In the Nordic Multicenter study on 1168 cases, Karlsson et al.[7] have stated that endometrial cancer has not been observed in any cases with an endometrial thickness of less than 5 mm. Nasri et al.[26], in their study, have reported that they have determined inactive endometrium as a histopathological finding in all cases with an endometrial thickness of 1-5 mm. Meanwhile, Selçuk et al.[17] have stated that they have not determined any abnormal histopathological findings in any cases with an endometrial thickness of less than 5 mm. In our research, any abnormal histopathological findings have not been determined in any of the cases with an endometrium thickness of less than 5 mm. In this respect, the results of our research are similar with those of the three researches mentioned above. The statement made by the ACOG (American Congress of Obstetricians and Gynecologists) in 2009 on that endometrial sampling is unnecessary in postmenopausal bleeding cases with an endometrial thickness of 4 mm and less supports our findings.[21]

Conclusion

Endometrial sampling is important due to pre-cancerous lesions and endometrial cancer risk underlying postmenopausal bleedings. The procedures applied for diagnostic purposes are invasive methods and may have important complications. Considering all of these factors, we believe that the use of endometrial thickness measurement by TV-USG, which is a non-invasive and easily applied method, would be beneficial as the first evaluation tool in this patient group. In the meantime, it appears that high parity ratios reduce the risk of endometrium cancer.

Postmenopozal Kanamalı Olgularda Histopatolojik Doku Tanısı ile Endometriyal Kalınlık Arasındaki İlişkinin Değerlendirilmesi

AMAÇ: Postmenopozal kanaması olan hastaların endometriyal örnekleme sonuçları ile transvajinal ultrasonografide (TV-USG) ölçülen endometriyal kalınlık arasındaki ilişki incelenmesidir.

GEREÇ VE YÖNTEM: Diyarbakır Kadın Doğum ve Çocuk Hastalıkları Hastanesi'nde postmenopozal kanama nedeniyle Ocak 2013 ile Aralık 2013 tarihleri arasında endometriyal örnekleme yapılan 235 olgunun sonuçları retrospektif olarak değerlendirildi.

BULGULAR: Olguların yaşlarının ortalaması 57,83±8,06 yıl ve parite ortalaması 7,73±3,26'dır. Olguların 126'sında (%53,6) TV-USG'de endometriyal kalınlık <5 mm (grup 1), 109'unda (%46,4) TV-USG'de endometriyal kalınlık ≥5 mm (grup 2) şeklindedir. Olguların 53 (%22,6) atrofik endometriyum, 43 (%18,3) endometriyal polip, 34 (%14,5) yetersiz materyal, 28 (%11,9) sekretuar endometriyum, 19 (%8,1) proliferatif endometriyum, 16 (%6,8) basit endometriyal hiperplazi, 12 (%5,1) düzensiz proliferatif endometriyum, 7 (%3) kompleks endometriyal hiperplazi ve 3 (%1,3) endometriyal adenokarsinom 3 (%1,3) endometrit tanısı aldığı görülmüştür. Grup 1'de anormal histopatolojik (endometriyal polip, hiperplazi ve adenokarsinom) bulgu saptanmamıştır.

SONUÇ: Postmenopozal kanamalı olgularda endometriyal örnekleme önem arz etmektedir. Non-invazif bir teknik olan TV-USG ile endometriyal kalınlık ölçümü olgu değerlendirilmesinde ilk basamak olarak kullanılmalıdır. Yüksek parite oranları endometriyum kanser riskini azaltıyor gözükmektedir.

Anahtar Kelimeler: Postmenopozal kanama, Transvajinal ultrasonografi, Endometriyal kalınlık, Histopatolojik tanı

References

1. Research on the menopause in the 1990s: report of a WHO scientific group. WHO Tech Report Series 1996;866:1-107.
2. Breijer MC, Timmermans A, van Doorn HC, Mol BW, Opmeer BC. Diagnostic strategies for postmenopausal bleeding. Obstet Gynecol Int 2010;2010:850812.
3. Kaur M, Singh R, Sharma M. Endovaginal sonographic evaluation of postmenopausal uterine bleeding. Journal of Clinical and Diagnostic Research 2010;(4):2175-82.
4. Astrup K, Olivarius NDF. Frequency of spontaneously occurring postmenopausal bleeding in the general population. Acta Obstet Gynecol Scand 2004;83:203-7.
5. Burbos N, Musonda P, Giarenis I, Shiner AM, Giamougiannis P, Morris EP et al. Predicting the risk of endometrial cancer in postmenopausal women presenting with vaginal bleeding: the Norwich DEFAB risk assessment tool. Br J Cancer 2010;102:1201-6.
6. Granberg S, Wikland M, Karlsson B, Norstrom A, Friberg LG. Endometrial thickness as measured by endovaginal ultrasonography for identifying endometrial abnormality. Am J Obstet Gynecol 1991;164:47-52.
7. Karlsson B, Granberg S, Wikland M, Ylöstalo P, Kiserud T, Marsal K,Valentin L. Transvaginal ultrasonography of the endometrium in women with postmenopausal bleeding: a Nordic multicenter study. Am J Obstet Gynecol 1995; 172:1488-94.
8. Oriel KA, Schrager S. Abnormal uterine bleeding. Am Fam Physician 1999;60:13;71-80.
9. Sousa R, Sylvester M, Sousa LAE, Falcao F. et al. Transvaginal ultrasonography in postmenopausal bleeding. A Prospective Study. Acta Obstet Gynecol Scand2001;80:856-62
10. Epstein E, Skoog L, Valentin I. Comparison of Endorette and dilatation and curettage for sampling of the endometrium in women postmenopausal bleeding. Acta Obstet Gynecol Scand 2001;80:959-64.
11. Buchanan EM, Weinstein LC, Hillson C. Endometrial cancer. Am Fam Physician 2009;80:1075-80.
12. Lin HH, Wu MY, Shyu MK, Chen D, Tsai JL, Hsieh CY. Clinical study of 381 postmenopausal bleeding patients. J Formos Med Assoc 1993;92:241-4.
13. Dijkhuizen FP, Mol BW, Brölmann HA, Heintz AP. The accuracy of endometrial sampling in the diagnosis of patients with endometrial carcinoma and hyperplasia: a meta-analysis. Cancer 2000:89:1765-72.
14. Dijkhuizen FP, Brolmann HA, Potters AE, Bongers MY, Heinz AP. The accuracy of transvaginal ultrasonography in the diagnosis of endometrial abnormalities. Obstet Gynecol 1996;87:345-9.
15. Soliman PT, Oh JC, Schmeler KM, Sun CC, Slomovitz BM, Gershenson DM et al. Risk factors for young premenopausal women with endometrial cancer. Obstet Gynecol 2005;105:575-80.
16. Hurd WW. Abnormal Bleeding. In: Berek JS, Adashi EY, Hillard PA, editors. Menopause. Novak's Gynecology. Pennsylvania. Williams & Wilkins Company;1996.
17. Abdullah LS, Bondagji NS. Histopathological Pattern of

Endometrial Sampling Performed for Abnormal Uterine Bleeding Bahrain Medical Bulletin 2011;33(4):1-6

18. Kaya O, Dane C, Kaya E, Semiz MM, Cetin A, Saygı G. Predictive Value of Endometrial Thickness in Detecting Endometrial Malignancy in Patients with Postmenopausal Bleeding. The Medical Bulletin of Haseki Training and Research Hospital 2014;52:164-7
19. Pınar G, Algier L, Dogan N, Kaya N. Determination of the Risk Factors in Individuals with Gynecological Cancer. International Journal of Hematology and Oncology 2008; 18(4):208-216
20. Kucur SB, Sencan H, Yuksel KB, Gozukara I, Keskin N, et al. Evaluation of Endometrial Biopsy Results in Our Clinic. Analysis of 744 Cases. Med Bulletin of Zeynep Kamil 2014;45:146-50
21. American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 426: The role of transvaginal ultrasonography in the evaluation of postmenopausal bleeding. Obstet Gynecol 2009:113:462-4.
22. Anastasiadis PG, Koutlaki NG, Skaphida PG, Galazios GC, Tsikouras PN, Liberis VA. Endometrial polyps: prevalence, detection and malignant potential in women with abnormal uterine bleeding. Eur J Gynaecol Oncol 2000;21(2):180-3
23. Bani-Irshaid I, Al-Sumadi A. Histological findings in women with postmenopausal bleeding: Jordanian figures. Eastern Mediterranean Health Journal 2011;17(7):582-62
24. Selcuk S, Asoglu MR, Celik C, Tug M, Cam C, Karateke A. The Relationship Between Endometrial Thickness And Histopathological Results in Patients With Postmenopausal Vaginal Bleeding. Med. Bulletin of Zeynep Kamil 2011;42(1):7-11
25. Caspi E, Perpinial S, Reif A. Incidence of malignancy in Jewish 13. women with postmenopausal bleeding. Israel Journal of Medical Sciences 1977;13(3):299-304.
26. Nasri MN, Shepherd JH, Setchell ME, Lowe DG, Chard T. Sonographic depiction of postmenopausal endometrium with transabdominal and transvaginal scanning. Ultrasound Obstet Gynecol 1991;1:279-83.