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Original Article

Liquid-based endometrial cytology associated with curettage in the investigation of endometrial carcinoma in postmenopausal women

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ABSTRACT

Objective: The aim of this study was to investigate the diagnostic accuracy of liquid-based endometrial cytology in postmenopausal women, in comparison with histology.
Materials and methods: There were 790 postmenopausal women scheduled for hysteroscopy enrolled in this study. After providing informed consent, all patients proceeded sequentially through endometrial cytology, hysteroscopy, and then dilatation and curettage (D&C). Cytology sampling was performed by brushing the uterus cavity using SAP-1 and the sample was prepared to liquid-based smear using SurePath technology. The slides were stained by Papanicolaou method. All cytological diagnoses were correlated with the D&C histological diagnoses.
Results: Cytohistological correlations were possible in 567 (71.8%) patients: the D&C was inadequate in 204 (25.8%) patients; the cytology was inadequate in 32 (4.1%) patients; and both were inadequate in 13 (1.6%) patients. SAP-1 provided more sufficient material for cytology than D&C can for histology ($p < 0.001$). Taking atypical hyperplasia and endometrial carcinoma as a positive result, the diagnostic accuracy of liquid-based endometrial cytology was 81.5%; sensitivity was estimated at 75.9%, specificity at 83.3%, positive predictive value at 59.1% and negative predictive value at 91.6%.
Conclusion: Liquid-based endometrial cytology can be considered a useful method in the detection of endometrial pathology in postmenopausal women.

Introduction

Endometrial carcinoma is the most common malignancy of the female genital tract in developed countries [1]. It often occurs in postmenopausal women and abnormal vaginal bleeding is the primary symptom. There are several methods to identify the endometrial pathology, such as transvaginal ultrasonography (TVS), hysteroscopy and endometrial biopsy, sonohysterography and endometrial cytology [2–5]. TVS is known as the first step in the evaluation of women with postmenopausal bleeding. However, TVS suffers from low specificity, due to its low positive predictive value (PPV) and high false-positive rate [6]. Hysteroscopy and dilatation and curettage (D&C) is a second-line method that has been considered as the 'gold standard' in the diagnosis of endometrial pathology.

Historically, endometrial cytology has not been widely used for accuracy issues, which is probably due to the common presence of excess blood and overlapping cells [7]. Recent development of liquid-based cytology techniques can overcome these obstacles and increase the diagnostic accuracy [8–10]. We conducted the current study to compare the results of liquid-based endometrial cytology with hysteroscopy and D&C to assess its diagnostic accuracy in a group of 790 postmenopausal women.

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Materials and methods

Patients enrolled in this trial were 790 postmenopausal women who received hysteroscopy from March 2009 to February 2015. This multicenter study was performed in the Department of Gynecology of Peking University First Hospital, Beijing Tsinghua Changgung Hospital, Beijing Cancer Hospital, and Beijing Daxing District Hospital. After providing informed consent, all the patients proceeded sequentially to endometrial cytological sampling, hysteroscopy, and diagnostic and/or therapeutic D&C. The median age of the patient group was 54 years (range, 41–89 years). The majority of the cases, 334 women (42.3%), hysteroscopy was required for abnormal endometrium assessed by transvaginal ultrasonography as follows: thickened endometrium ($\geq$ 5 mm) or intrauterine occupational disease. There were 193 women (24.4%) referred for postmenopausal uterine bleeding; 228 women (28.9%) were referred for both postmenopausal bleeding and abnormal endometrium. Twenty-two women (2.8%) were tamoxifen users. Eight women (1.0%) received hysteroscopy follow-up who were diagnosed with simple or complex endometrial hyperplasia. Five women (0.6%) women were referred for atypical glandular cells found in ThinPrep Cytologic Test (TCT) (Table 1). There was no financial interest or any arrangement with the companies producing the instruments used in the study.

The device used for endometrial cytological sampling was the SAP-1 device (Saipujiuzhou, Beijing, China; Figure 1). This device was patented and received permission to be used in China. The SAP-1 sampler measures 3 mm in diameter and 250 mm in length. It consists of a flexible latex loop with spines on the side and a smooth tip to prevent injury to the myometrium. There is an outer protective sheath outside the loop to prevent contamination from cervical and vaginal cells. Before using the device, the stem was withdrawn into the sheath, and it was inserted into the uterus cavity through the endocervical canal. The loop was then released and rotated clockwise and anticlockwise, thus collecting tissue on the edges of the curette. It was then withdrawn into the sheath to prevent cervical contamination. After the device was removed from the uterus, the loop with the specimen was exposed and immersed in a SurePath (BD Diagnostic, Burlington, NC, USA) vial and vigorously rotated to allow the cells to release. The vial was labelled with the patient information and transported to the Department of Cytopathology. With a succession of centrifugation and suspension to obtain mucolysis and hemolysis, blood and mucus were separated from the endometrial cells. Finally, the vial was processed using AutoCyte PREP automated slide processor (Tri-Path; Becton–Dickinson, Franklin Lakes, NJ, USA). The slides were stained with routine Papanicolaou stain.

Hysteroscopy was performed using a 5-mm optic with saline solution distension after the cytological sampling. Histologic sampling was performed by D&C. Endometrial samples were routinely fixed in neutral buffered formalin, embedded in paraffin, and stained with hematoxylin–eosin.

Cytological and histological diagnosis was done by two pathologists blindly. The slides were considered unsatisfactory samples when there were fewer than five evaluable endometrial clusters (endometrial cytology) or severe fragmentation or scarcity of the endometrial tissue (D&C). If the first cytological or histological slide was inadequate, a second one would be prepared. When the second one was also an unsatisfactory sample, the diagnosis was considered as *inadequate*.

The cytological criteria used in the cellular interpretation were according to a previously published diagnostic system [11]. The cytological findings were divided into four categories: normal endometrium, benign endometrial abnormality, atypical endometrial cell, and suspected endometrial carcinoma (Figure 2). Negative and benign endometrial abnormality was considered as negative results, and atypical endometrial cell and suspected endometrial carcinoma were considered as positive results. The histological diagnosis was given according to the World Health Organization criteria of 2003 [12]. All cytological diagnoses were correlated with the D&C histological diagnosis.

Statistical analysis was carried out using SPSS 10.0 for Windows (SPSS Inc. Chicago, IL, USA). A double access table was created to evaluate the sensitivity of cytology (true positive/all positive

Table 1
Distribution of patients according to inclusion criteria.

Inclusion criteria	No. of patients	Endometrium thickness (mm), mean ± standard deviation (range)
Thickened endometrium	334	8.15 ± 3.15 (5–23)
Thickened endometrium + AUB	228	7.50 ± 2.50 (5–20)
AUB	193	2.20 ± 1.12 (1–4)
Tamoxifen users	22	7.15 ± 3.85 (4–18)
Simple or complex endometrial hyperplasia follow up	8	9.25 ± 5.00 (5–20)
Atypical glandular cells found in TCT	5	6.12 ± 3.75 (5–12)

AUB = abnormal uterine bleeding; TCT = ThinPrep Cytologic Test.

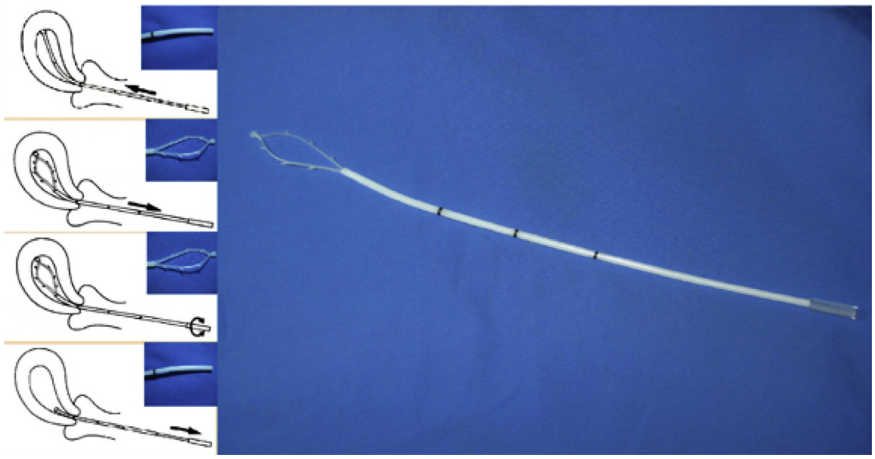

Figure 1. The SAP-1 device.