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A comparative study of conventional and liquid-based cervical cytology

Konwencjonalna i płynna cytologia – badania porównawcze

Mehmet Şükrü Budak[1], Mehmet B. Senturk[2], Cihan Kaya[3], Sedat Akgol[4], Muhammed H. Bademkiran[1], Ali Emre Tahaoğlu[1], Ayhan Yildirim[5], Hüseyin Büyükbayram[6]

[1] Clinic of Obstetrics and Gynecology, Diyarbakır Maternity and Children's Disease Hospital, Diyarbakır, Turkey
[2] Department of Obstetrics and Gynecology, Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Turkey
[3] Clinic of Obstetrics and Gynecology, Van Özalp State Hospital, Van, Turkey.
[4] Clinic of Obstetrics and Gynecology, Veni Vidi Hospital, Diyarbakır, Turkey
[5] Clinic of Pathology, Diyarbakır Maternity and Children's Disease Hospital, Diyarbakır, Turkey
[6] Department of Pathology, Dicle University Medicine Faculty, Diyarbakır, Turkey

Abstract

Objectives: *The aim of our study is the comparison of the results of conventional smear (CC) technique and liquid-based cytology (LBC) technique used as cervical cancer screening methods.*

Material and methods: *The results of 47954 patients submitted to smear screening in our gynecology clinic between January 2008 and December 2014 have been studied. The smear results have been divided into two groups CC and LBC according to the technique used.*

Results: *When considering the distribution within CC group, the results were as follows: intraepithelial cell abnormalities 2,0% (n=619), insufficient sample for analysis 2,1% (n=660), Atypical squamous cells of undetermined significance (ASC-US) 1.8% (n=554), Low grade squamous intraepithelial lesion (LGSIL) 0.1% (n=35), High grade squamous intraepithelial lesion (HGSIL) 0.1% (n=16), Atypical squamous cells – cannot exclude HGSIL (ASC-H) 0.029% (n=9), Atypical glandular cells- not other wise specified (AGC-NOS) 0.012% (n=4), squamous carcinoma 0.003% (n=1). When considering the distribution in LBC group, the results were as follows: intraepithelial cell abnormalities2.1% (n=357), insufficient sample for analysis 0.9% (n=144), ASC-US 1.8% (n=296), LGSIL 0.2% (n=38), HGSIL 0.1% (n=8), ASC-H 0.1% (n=10), AGC-NOS 0.017% (n=3), squamous carcinoma 0.011% (n=2).*

Conclusions: *Although the rates of epithelial cell abnormalities are similar for both tests, LSIL results are more frequently observed in LBC technique. In LBC technique, the number of insufficient sample for analysis is quite low compared to CC group and thus constitutes an advantage.*

Key words: **cervical intraepithelial neoplasia** / **conventional smear** / / **liquid-based smear** /

Corresponding author:
Cihan Kaya
Cumhuriyet Mh No 3 Özalp Van, Türkiye
phone: 90 506 484 5469
fax: 90 432 712 2302
e-mail: drcihankaya@gmail.com

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Streszczenie

Cel pracy: *Celem badania było porównanie wyników konwencjonalnej (CC) i płynnej cytologii (LBC) stosowanej w skriningu raka szyjki macicy.*

Materiał i metoda: *Przeanalizowano wyniki od 47954 pacjentek objętych cytologicznym badaniem skriningowym w naszym oddziale ginekologicznym w okresie od stycznia 2008 do grudnia 2014. Wyniki cytologiczne podzielono na dwie grupy CC i LBC w zależności od techniki pobierania.*

Wyniki: *W grupie CC wyniki przedstawiały się nastepująco: nieprawidłowości komórek śródnabłonkowych 2,0% (n=619), nieodpowiednia próbka do analizy 2,1% (n=660), ASC-US 1.8% (n=554), LGSIL 0.1% (n=35), HGSIL 0.1% (n=16), ASC-H 0.029% (n=9), AGC-NOS 0.012% (n=4), rak płaskonabłonkowy 0.003% (n=1). W grupie LBC wyniki przedstawiały się następująco: nieprawidłowości komórek śródnabłonkowych 2.1% (n=357), nieodpowiednia próbka do analizy 0.9% (n=144), ASC-US 1.8% (n=296), LGSIL 0.2% (n=38), HGSIL 0.1% (n=8), ASC-H 0.1% (n=10), AGC-NOS 0.017% (n=3), rak płaskonabłonkowy 0.011% (n=2).*

Wnioski: *Chociaż odsetek nieprawidłowości komórek śródnabłonkowych jest podobny dla obu testów, wyniki LSIL są częściej obserwowane w technice LBC. W metodzie LBC liczba próbek nieodpowiednich do analizy jest dość niska w porównaniu do grupy CC, stąd jest to jej niewątpliwa zaleta.*

Słowa kluczowe: **śródnabłonkowa neoplazja szyjki macicy** / **cytologia konwencjonalna** / / **cytologia płynna** /

Introduction

Cervical cancer is a frequently observed in women all over the world and is at the second place after breast cancer [1-3]. The importance of this cancer depends its high mortality risk. The cause of frequency is related to the inefficient screening programs in developing countries. The American Society for Colposcopy and Cervical Pathology (ASCCP) recommends initial cervical screening for women 21 year-old, Pap test every three years for women 21-29 years old and prefers Cotesting (pap test and HPV testing) every five years for women over 30 years old. Appropriate recommendations such as; routine screening, repeating tests, colposcopy or excisional procedures are also defined for dealing with abnormal gynecological smear in this guideline [4]. The utilization of CC technique developed by George Papanicolau in 1940s for the first time, an important decrease in rates of mortality associated to cervical cancer has been observed [5, 6]. In CC technique, material is collected from the cervix, abnormal cells are covered by blood, mucus and other residues during the fixation on glass slides and this leads to increased false negative rates [7]. LBC test developed in 1960s and 1970s to decrease the rates of false negative constitutes as an alternative to the CC technique [8]. The LBC technique developed has been approved for the first time by American Food and Drug Administration (FDA) as a cervical cancer screening test in 1996 [7-9]. This technique has decreased the number of insufficient sample number and has permitted a simultaneous Human Papilloma Virus (HPV) screening [7, 10]. Although LBC technic seems to have advantages on detecting cervical abnormalities, the cost of this technic is still a major concern [11].

Our objective was to compare the results of CC technique and LBC technique used as a cervical cancer screening technique.

Material and methods

The results of 47954 patients submitted to smear screening in Diyarbakir Maternity and Children's Disease Hospital between January 2008 and December 2014 have been studied retrospectively. In both screening tests, cervical samples have been taken by gynecologists using vaginal speculum and cervical brush. The tests were performed seperately to different patients in different time period. The other test was not repeated if a test has been made for the same patient.

The samples were taken from the ecto- and endocervix by 360° rotating the cervical brush. After spreading the material rapidly on glass slidesusing CC technique, it has been fixed using polyethylene glycol. In LBC technique, the cervical brush has been totally immerged in the disposable collecting bottle. ThinPrep 2000 Hologic (Marlborough, USA) has been used as LBC technique. All the slides for CC and LBC have been stained with Pap staining. The stained slides have been examined using the microscope (×10, ×40 objective), for evaluating the cellularity, the bacterial flora, and for morphological details. LBC has been considered as significant if the slide contained more than 5000 epithelial cells. A comparison has been performed between smear results evaluated according to Bethesda 2001 classification [12].

IBM SPSS Statistics 22 (IBM SPSS, Turkey) has been used for statistical analyses. In the comparison of cytological results of materials collected using both techniques, Chi-Square Test and Continuity (Yates) Correction have been used. The significance has been evaluated at $p<0,05$ level.

Results

A total of 47 954 smears have been analyzed, among which 31 092 (64,8%) have been analyzed using CC technique, while 16 862 cases (35,2%) have been analyzed using LBC technique. There was no satatistically significant differences between study groups considering; age, gravidity, parity, smoking habit, nubmber of sexual partner and fist age of sexual intercourse. (Table I). When considering the distribution of the cases in CC group, the following results have been obtained; intraepithelial cell abnormalities 2,0% (n=619), insufficient sample for analysis 2,1% (n=660), ASC-US 1.8% (n=554), LGSIL 0.1% (n=35), HGSIL 0.1% (n=16), ASC-H 0.029% (n=9), AGC-NOS 0.012% (n=4), squamous carcinoma 0.003% (n=1). When considering the distribution in LBC group, the following results have been

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Table I. Demographic charecteristics of the study population.

	CC	LBC	P value
Age	27.6 ±5.7	29.0 ±4.4	0.27
Gravidity	2.61±2.31	2.75±2.04	0.691
Parity	2.34± 1.47	2.05± 1.06	0.416
Number of sexual partner	1.36±1.87	0.83±1.3	0.116
Smoking habit	11867 (38.20%)	6804 (40.40%)	0.778
First age of sexual intercourse	19±2.33	21±2.08	0.98

Table II. Cervical cytology results of study groups.

	CC (n=31092) n(%)	LBC (n=16862) n(%)	P value
Insufficient for evaluation	660 (%2.1)	144 (%0.9)	0.001**
Epithelial cell abnormality	619 (%2.0)	357 (%2.1)	0.350
ASC-US	554 (%1.8)	296 (%1.8)	0.834
LGSIL	35 (%0.1)	38 (%0.2)	0.002**
HGSIL	16 (%0.1)	8 (%0.047)	1.000
ASC-H	9 (%0.029)	10 (%0.1)	0.175
AGN-NOS	4 (%0.012)	3 (%0.017)	0.976
Squamous carcinoma	1 (%0.003)	2 (%0.011)	-

obtained: intraepithelial cell abnormalities 2.1% (n=357), insufficient sample for analysis 0.9% (n=144), ASC-US 1.8% (n=296), LGSIL 0.2% (n=38), HGSIL 0.1% (n=8), ASC-H 0.1% (n=10), AGC-NOS 0.017% (n=3), squamous carcinoma 0.011% (n=2).

The distribution of the cases between both groups and the statistical comparison have been summarized in Table 2. The insufficient material rate in CC group has been found to be significantly higher (p:0,01) than in LBC group. LGSIL rate has been found to be higher in LBC group than CC group (p:0,02). No significant difference has been observed in the observation of other abnormalities rates between the study groups.

Discussion

The sensitivity and specificity of screening tests are crucial to determine commonly seen diseases [11]. In this context, appropriate screening for cervical cancer is still being investigated by researches [13]. Respectable number of studies are performed for comparison of CC and LBC in the literature [14]. The presence of more material in the sample collected increases the rate of success and rate of getting abnormal cytology results. The common statement about the sensitivity of CC is low, between 70-80%, and this is associated to insufficient sample collection and preparation [15]. However, LBC technique presents with higher sensitivity rates (85-95%) when compared to CC technique [16]. This can be explained with cellular structure is better preserved and drying artifacts are reduced in LBC technic than CC technic. LBC also enhances adequacy by increase in cellularity [17]. In a previous study inadequate rates for CC and LBC rates were 4.3% and 0.68%, respectively [18]. The presence of insufficient material for evaluation in CC group is2.1% and 0.9% for LBC group in our study and this is conform to the results of previous studies [11, 19, 20].

In our study, the rates of epithelial cell abnormalities were 2,0% and 2,1% in CC and LBC groups respectively and these rates are lower than those reported in literature [11, 20, 21]. These low rates may be associated to the reduced number of polygamy in our region. Also, many studies have demonstrated that the frequency of cervical cancer incidence increases with the number of different partner [22-24].

Although there is a common agreement on LBC detecting abnormalities in inadequate samples, there is still concerns on LBC technic if it is the best for detecting high grade lesions, or not. According to previous literature, LBC technic has a high detection rate of intraepithelial cervical abnormalities and decrease in atypical squamous cells of undetermined significance [25]. This technic also give an advantege in detection of preinvasive and invasive glandular lesions [26]. In a meta-analysis comparing LBC samples with CC samples, Abulafia et al.mentioned that LBC samples were more sensitive and more specific than CC samples in detecting cervical dysplasia [27]. However Davey et al analysed 56 studies comparing LBC samples with CC samples

and reported that there was no evidence for liquid-based cytology reducing the proportion of unsatisfactory slides, or detecting more high-grade lesions than CC [21]. The study by Strander et al. mentioned that 40 % more high-grade lesions were identified as a result of LBC sampling than CC sampling (1.20% vs 0.85%) [19]. In contrast, the study by Sigurdsson et al. reported that LBC is no more sensitive than CC for the detection of high grade cervical intraepitelial lesions irrespective of age [28].

In our study, ASC-US rates were the same between study groups.These results were similar to study of Ilter et al. [11] and the study of Davey et al. [21]. However Monsonego et al. reported, 29% more ASCUS cases were detected on the Thin Prep slides than on the CC [16].

There was no difference between study groups considering HGSIL rates in our study. The rates obtained in our study were similar to those given in literature [13, 22]. However, in previous studies LBC samples are more prone to detect these lesions than CC samples [28].

In our study, LBC was more succesful in detecting LGSIL cases than CC technic.This rates were also similar to previos studies [11, 21]. Monsonego et al. also reported 39% more LSIL [16].

The retrospective evaluation of cytology results constitutes as a limitation in present study.However the presence of case number and including the data of demographically paired patients increases the strength of the study.

In conclusion, our study suggest that LBC gives advantage in detecting insufficient material rate and LGSIL than CC technic. As a speculation, cost analysis studies which demonstrate to find out superior cervical screening method can be usefull for low-income countries.

Oświadczenie autorów:

1. Mehmet Şükrü Budak – concept, study design, analysis and interpretation of data, acquisition of data, revised article critically.
2. Mehmet B. Sentruk – concept, acquisition of data, revised article critically.
3. Cihan Kaya – concept, assumptions, study design, article draft, analysis and interpretation of data, corresponding author.
4. Sedat Akgol – acquisition of data, analysis, revised article critically.
5. Muhammed H. Bademkiran – revised article critically.
6. Ali E. Tahaoglu – acquisition of data, analysis, revised article critically.
7. Ayhan Yildirim - acquisition of data, analysis, revised article critically.
8. Hüseyin Buyukbayram – analysis and interpretation of data.

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