The Efficacy of Conventional and Liquid-Based Cytology in Women Infected with HPV Type 16

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INTRODUCTION

Cervical screening as part of secondary prevention is recommended for all sexually active women. For many years, cytology-based screening has been the only method of screening. It was known as the Pap test. The implementation of molecular-based technique for detecting HPV DNA changed cervical cancer screening programmes. A number of randomized clinical trials have shown that HPV screening is more sensitive than cytological screening. But it is still debated which test should be performed first during cervical screening: the cytology or HPV test. Conventional cytology (CC) and liquid-based cytology (LBC) have different sensitivity, which could be dependent upon HPV viral load.

THE AIM OF THIS STUDY WAS TO COMPARE THE EFFICACY OF CONVENTIONAL CYTOLOGY AND LIQUID-BASED CYTOLOGY (BD SUREPATH) IN DETECTING KOILOCYTIC CHANGES (KC) IN HPV-POSITIVE WOMEN.

STUDY DESIGN

Study population and sampling

3370 women aged 18-65 (mean age 30±23 years) undergone cervical co-testing in “Garmonia” Medical Center (Yekaterinburg, Russia) in 2016-2018.

The study received ethical approval from the Ural State University Research Ethics Board (Protocol N 4, 15.05.2015). All participants provided written informed consent and all methods were performed in accordance with the relevant guidelines and regulations.

Cervical smears were collected with Rovers® Cervex-Brush® Combi with detachable head, which was placed into the BD SurePath collection vial, containing preservative fluid.

DNA extraction, HPV test and quantitative analysis of vaginal microbiota by real-time PCR

Total nucleic acid (NA) was extracted from swabs using the kit for NA isolation PREP-NA-PLUS (DNA-Technology, LLC).

HPV test was performed using real-time PCR HPV-Quant-21 kit (DNA-Technology, Russia), which allows genotyping of HPV for 21 types and evaluation of the absolute viral load (DNA copies/sample) and relative viral load (RVL, DNA copies/105 epitheliocytes).

Liquid based cytology (LBC) was performed according to the protocol for the BDSurePath® equipment. Cervical samples were evaluated according to the Bethesda system (2014).

Conventional cytology was performed using the standardized Romanowsky-Giemsa staining procedure.

Statistical analysis was carried out using the IBM SPSS Statistics version 21.0 software package.

Example of lab results of HPV Quant test for detecting 21 genotypes of HPV by means of quantitative real-time PCR

№	Name of research	Results		
		Relative, (X/SIC)	Quantitative, Lg (copies/sample)	Qualitative
1	HPV 31	not discovered	not discovered	
2	HPV 35	not discovered	not discovered	
3	HPV 16	not discovered	not discovered	
4	HPV 52	4.9	5.0	
5	HPV 33	not discovered	not discovered	
6	HPV 68	not discovered	not discovered	
7	HPV 45	not discovered	not discovered	
8	HPV 82	not discovered	not discovered	
9	HPV 51	not discovered	not discovered	
10	HPV 6	not discovered	not discovered	
11	HPV 44	not discovered	not discovered	
12	HPV 11	not discovered	not discovered	
13	HPV 18	4.2	4.3	
14	HPV 39	not discovered	not discovered	
15	HPV 58	not discovered	not discovered	
16	HPV 66	not discovered	not discovered	
17	HPV 26	not discovered	not discovered	
18	HPV 53	not discovered	not discovered	
19	HPV 59	not discovered	not discovered	
20	HPV 56	not discovered	not discovered	
21	HPV 72	not discovered	not discovered	
22	SIC		5.1	
23	Total HPV load	5.0	5.1	

Patient 32 years old, cytology – LSIL

RESULTS

Depending on the cytology type, patients were divided into two groups: those who undergone CC (N=1591) and LBC (N=1779).

HPV type 16 was the most prevalent. It was detected in 395 (11.7%) of 3370 women. Among them, 219 women were co-tested with CC (Group 1) and 176 — with LBC (Group 2). Koilocytic changes were detected in 103 (48.0%) patients from Group 1 and 130 (73.9%) patients from Group 2 (p<0,01). Figure 1

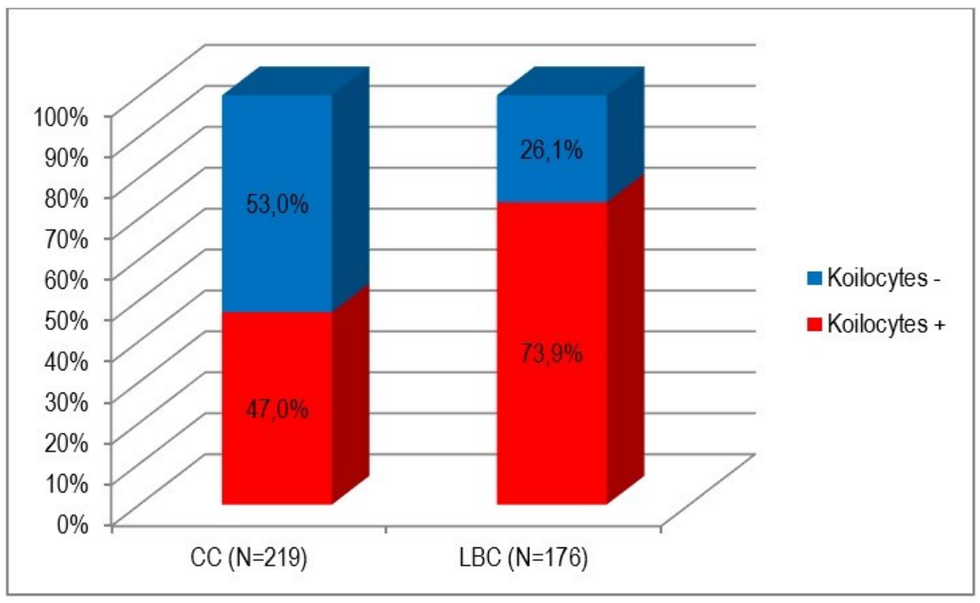

Figure 1. Koilocytic changes rate as detected by LBC and CC in HPV16-positive women

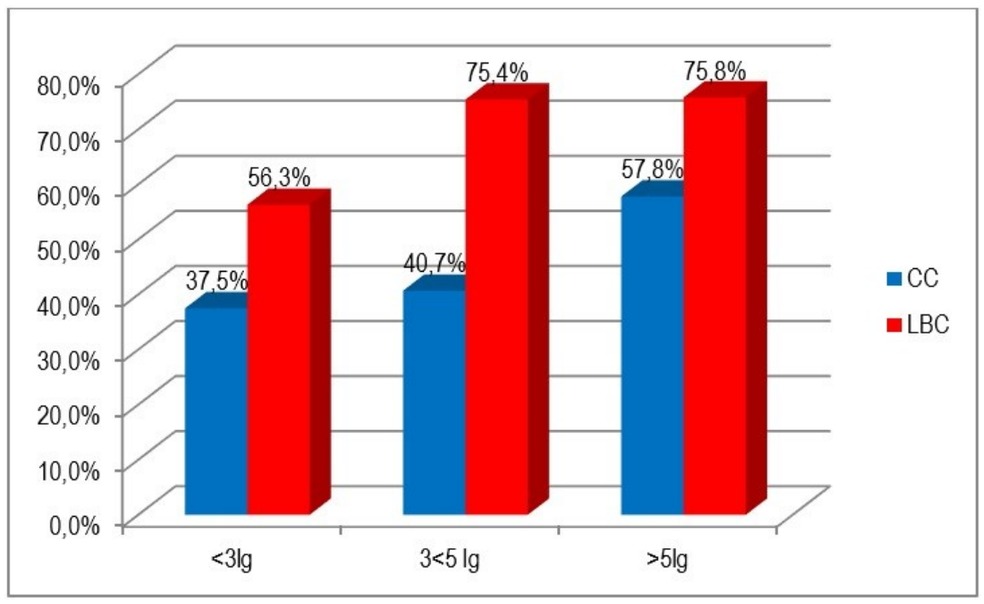

Figure 2. The detection rate of koilocytic changes in HPV-16-positive women depending on viral load and cytology type used (* - p<0.01)

The koilocytic changes rate in HPV-16-positive women depended on relative viral load and the cytology type. When RVL was $<10^3$ DNA copies/10^5 epitheliocytes, KC were detected in 37.5% samples using CC and in 56.3% using LBC. When relative viral load was $10^3<10^5$ DNA copies/10^5 epitheliocytes, the koilocytic changes were determined in 40.7% with CC and in 75.4% with LBC (p<0.01). When relative viral load was $>10^5$ DNA copies/10^5 epitheliocytes, the koilocytic changes were detected in 57.8% of samples using CC and in 75.8% using LBC (p<0.01). Figure 2

CONCLUSION

Both CC and LBC failed to detect koilocytes in every forth HPV-16-positive woman with high RVL. HPV test using HPV-Quant-21” kit is more effective for primary screening from this point of view.

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