

Liquid based and conventional cytology associated with HPV genotyping: a preliminary study of 200 cases

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Objectives:

Liquid based cytology (LBC) is today largely utilized in diagnostic and screening cytology, offering the opportunity of complementary genetic analysis of samples. The aim of this study is to compare conventional and LBC in cervical cancer and to evaluate HPV genotyping offered by LBC technology using the CellSolutions system in diagnostic and patient management.

Materials and Methods:

We analyzed both conventional and LBC in 200 patients using the CellSolutions protocol. We established with the departments of Gynecology/Obstetric, Pathology and Virology between September 2012 and January 2013. Cervical samples using the Rovers cervix-Brush were splitted, obtaining a conventional smear on one side of the brush and a liquid cytology on the other side. LBC were processed using the CellSolutions System obtaining a thin layer of cells. Conventional and liquid smears were stained with Papanicolaou. Cervical cytology was interpreted by 2 pathologists (LD, BA) using the Bethesda System¹. HPV genotyping was performed in ASCUS, ASCH and patients with cervical surgery (conisation, laser treatment).

Results:

In 77% of patients (n=154) there was no dysplastic lesion. Among these, 11% (n=22) had metaplasia, 4% (n=8) inflammation and 1% (n=2) Gardnerella. ASCUS was observed in 8,5% (n=17), ASCH In 1,5% (n=3), LSIL in 5% (n=10), HSIL in 5,5% (n=11). In 2,5% (n=5) conventional and liquid smears were uninformative because of inadequate sampling. High percentages of positive cytology in this study is due to, first, the peculiar population of our center (mainly pregnant women), and second, to inclusion's criteria used in this study (cervical surgery). Minor discordances in cell quantity between both technics were found in 6,5% (13 cases). Morphological discordances between conventional and LBC smears were found in 8 cases (**Tab. 1**). In five of these 8 cases HPV genotyping was performed and was a powerful adjunct for the diagnosis. In 8% (16 cases) hemorrhage on conventional cytology prevents diagnostic but not on LBC (**Fig.1**). Differences between cytological results using the two methods could be due to splitting bias. In ASCUS, HPV genotyping showed high-risk HPV (HR-HPV) (type 16,18,51,52,58,68) in 29,5% (n=5), low-risk HPV (LR-HPV) (type 44) in 5,9% (n=1), both HR-HPV (type 16,18,31,33,39,51,52,58,68) and LR-HPV (type 6,44,54,70) in 11,7% (n= 2) and was negative in 52,9% (n=9). In ASCH, HPV genotyping showed HR-HPV+LR-HPV in 100% (n=3 cases). In patients who had surgery, genotyping shows HR-HPV in 30,8% (4 cases), HR-HPV+LR-HPV in 38,4% (4 cases), no cases with LR-HPV and no HPV in 30,8% (4 cases)(**Tab. 2**).

HPV Type	ASCUS	ASCH	Surgery
HR	29.5% (n=5)	0%	30.8% (n=4)
LR	5.9% (n=1)	0%	0%
HR+LR	11.7% (n=2)	100%(n=3)	38.4% (n=5)
NONE	52.9% (n=9)	0%	30.8%(n=4)

Tab. 2 HPV status according to the context of HPV test request. Abbreviations: HR= high-risk virus; LR= low-risk virus; HR+LH= high and low risk virus coinfection.

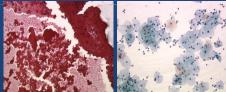


Fig. 1 Same case on conventional (left) and LBC (right)

Cases	Conventional smear	LBC	HPV genotyping
n=2	APK	neg	np
n=1	Gardnerella	ASCUS	HPV 16
n=1	ASCUS	LSIL	HPV 33,6,44
n=1	APK	ASCUS	neg
n=1	neg	APK	np
n=1	LSIL	ASCUS	HPV 16,39,6
n=1	APK	ASCUS	neg
n=8	HEMORRAGIC	neg	np

Tab. 1 Discordant cases on conventional and LBC and HPV genotyping. LBC= liquid based cytology; APK= atypical parakeratosis; NEG= negative; np= not performed.

Conclusions:

This study showed excellent cytological correlation between LBC and conventional smear using the CellSolutions system. HPV genotyping was possible in all tested cases (20,5%) and was particularly useful in the management of patients with ASCUS, discriminating patients who had no virus or regressive HPV disease (52,9%) from patients who had a positive HPV test for LR-HPV (5,9%), HR-HPV (29,5%) or both (11,7%) who were directly manage by colposcopy and cervical biopsy.

References:

1 - The Bethesda System for Reporting Cervical Cytology. Diane Solomon, Ritu Nayar. 2003.