FIRST-VOID URINE AND PHYSICIAN-TAKEN SMEAR SHOW SIMILAR SENSITIVITY FOR THE DETECTION OF CIN2+ LESIONS

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Aim

To study the correlation between HPV detection using self-collected urine samples, brush-based self-samplers and physician-taken smears and to compare HPV detection in morning first-void urine to HPV detection in first-void urine from any hour during the day.

Introduction / Background

In a hrHPV-oriented screening program, self-sampling can raise the number of women participating. Results of hrHPV-testing in brush-based self-samplers are highly representative when compared to testing on cytology.

Another, less invasive, method for self-sampling can be found in collecting urine. Exfoliated cells from the cervix and vagina are secreted with the vaginal mucus, contaminating the urine that passes. The detection of HPV DNA in urine for disease surveillance and cervical cancer screening has been widely evaluated over the last years.

It was found that first-void urine contains higher concentrations of human DNA and HPV DNA than midstream urine. Whether the first fraction of urine of the first void of the day contains a higher concentration of DNA than the first fraction of any void of the day remains to be determined.

Methods

Women planned to undergo a colposcopy after an abnormal PAP-smear result (N=91) were sent a device (Colli-Pee™, Novosanis, Wijnegem, Belgium) (Figure 1) to collect first-void urine on the morning of their colposcopy (U1). A second first-void urine sample (U2), a physician-taken cervix smear (PTS) and a brush-based self-sample (SS) and at least one cervical biopsy were collected during colposcopy.

DNA from smears was isolated with the NucliSENS easyMAG (250µl input, 100µl eluate) and from the urine samples with the MagNAPure 96 (1000µl input, 50µl eluate). DNA from all samples was tested with the analytically sensitive SPF10-DEIA-LiPA25version1 assay and the clinically validated GP5+/6+-EIA with LMNX genotyping. Biopsies were evaluated by a specialized pathologist.

Figure 1: Colli-Pee™, device used to collect first-void urine.

Results

Morning (U1) and afternoon (U2) urine samples, physician-taken smear (PTS) and brush based self-samples (SS) from 91 patients were analysed.
All CIN3 lesions (N=6) were hrHPV positive in PTS, SS, U1 and U2 with both the SPF10-assay and the GP5+/6+-assay (Table 1).
The sensitivity for CIN2+ detection in PTS, SS, U1 and U2 with the SPF10 was 96.4%, 92.9%, 92.9% and 96.4% respectively (p>0.05). With the GP5+/6+ assay, the sensitivity was 78.6% in PTS, 82.1% in SS, 92.9% in U1 and 85.7% in U2 (p>0.05).

On genotype level, a substantial to almost excellent agreement was found between all samples (kappa 0.663-0.912), for both SPF10 and GP5+6+. When comparing the genotypes found in PTS to those found in urine samples, 12.6% of the samples were discordant when tested with SPF10 and 19.8% of the samples when tested with GP5+/6+.
For the comparison between SS and urine, discordant results were found in 10.0% and 14.3% of the samples, respectively.
When comparing PTS to SS, 11.0% of the samples were discordant with SPF10 and 16.5% with GP5+/6+. Between U1 and U2, 3.2% were discordant with SPF10 and 6.6% with GP5+/6+.

Histological diagnosis	PTS		SS	
	SPF10	GP5+/6+	SPF10	GP5+/6+
Negative (N=46)	56.5%	47.8%	56.5%	50.0%
CIN 1 (N=17)	82.4%	82.4%	82.4%	76.5%
CIN 2 (N=22)	95.5%	72.7%	90.9%	77.3%
CIN 3 (N=6)	100.0%	100.0%	100.0%	100.0%
Total (N=91)	N=67	N=58	N=66	N=59

Histological diagnosis	U1		U2	
	SPF10	GP5+/6+	SPF10	GP5+/6+
Negative (N=46)	58.7%	45.7%	63.0%	52.2%
CIN 1 (N=17)	82.4%	76.5%	82.4%	70.6%
CIN 2 (N=22)	90.9%	90.9%	95.5%	81.8%
CIN 3 (N=6)	100.0%	100.0%	100.0%	100.0%
Total (N=91)	N=67	N=60	N=70	N=60

Conclusions

- CIN2+ detection using HPV testing in first-void urine seems feasible, with sensitivity similar to the sensitivity of the physician-taken smears and brush-based self-samples.
- No advantage in testing morning first-void urine over first-void from later during the day was found.

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