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Genotype-specific prevalence and distribution of human papillomavirus genotypes in underserved Latino women with abnormal Papanicolaou tests

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Objective: Knowledge about the prevalence and distribution of human papillomavirus (HPV) genotypes in cervical premalignant and malignant lesions is crucial to guide development of clinical management strategies and prophylactic vaccines. The aim of this study was to determine HPV genotype-specific prevalence and distribution in an underserved cohort of Latino women.

Methods: From 12/2009 to 4/2011, 808 SurePath cervicovaginal specimens were collected from women who were referred from charity clinics for abnormal Papanicolaou (Pap) tests. The patients' average age was 36.5 years (range 19-85 years). The specimens were tested for HPV genotypes by DNA microarray and sequencing assays.

Results: The HPV infection rate was extremely high [93% for any HPV and 64% for high-risk (HR)-HPV, with frequent multiple-strain infection (39%). Younger age (<30 years) was associated with frequent HR-HPV infection, multiple strain infections and cytologic abnormalities. When compared to previous reports, HPV 16 remained the most common genotype (44.6%) in women with high-grade squamous intraepithelial lesion (HSIL), however, a significant increase in HPV 31 (17.9%) and 45 (10.7%) and a decrease in HPV 35, 52, 33 and 66 were observed.

Conclusions: The HPV genotype-specific prevalence and distribution pattern in this cohort of underserved Latino women differed significantly from previously published data in the United States. Understanding the potentially changing trends in HPV distribution pattern will help guide the development of appropriate preventive and therapeutic strategies for both underserved and general populations.

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Cidofovir and Imiquimod in the treatment of VIN3: HPV E2 DNA methylation as a predictive biomarker of response

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Introduction: Results of a randomized controlled trial of treatment of VIN3 with cidofovir and imiquimod are reported (RT3 VIN). Complete response occurred in 61% and 57% of patients treated with imiquimod and cidofovir respectively. Treatment is associated with significant side effects and if ineffective, on-going symptomatology and risk of malignant progression. A predictive biomarker of treatment response is an attractive prospect and the potential of HPV characteristics as such biomarkers were investigated. HPV E2 DNA methylation significantly correlated with clinical outcome in both treatments arms and has good potential as a biomarker.

Methods: DNA from 167 cases of histologically confirmed VIN3 from the RT3 VIN clinical trial was studied. HPV positive cases were identified using Greiner PapilloCheck® and HPV 16 type-specific PCR. The HPV characteristics tested included: Integration status, DNA methylation status and gene expression levels. Data were correlated with clinical outcome using SPSS.

Results: HPV E2 DNA methylation >4% predicted response to treatment with cidofovir with a sensitivity of 88.2% and a specificity of 84.6%. Conversely, for treatment with imiquimod E2 DNA methylation <4% was found to predict response with a sensitivity of 70.6% and specificity of 62.5%.

Conclusion: Opposing levels of HPV E2 DNA methylation demonstrate potential as a predictive biomarker for the treatment of VIN with cidofovir and imiquimod and warrants further investigation. These drugs appear to work best in two different sub-groups of the disease; their targeted use could significantly reduce the dependency on surgery in management of this disease.

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