A NEW STRATEGY TO PREVENT AND TREAT PRECANCEROUS CERVICAL LESIONS AMONG HPV-POSITIVE WOMEN

UMA NOVA ESTRATÉGIA PARA PREVENIR E TRATAR LESÕES CERVICAIS PRÉ-CANCEROSAS EM MULHERES POSITIVAS PARA O HPV

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There is a group of women in which usual human papillomavirus (HPV) viral clearance does not occur and this is considered high risk for early development of precancerous lesions of the cervix[1]. Experts speculate four circumstances that may be related to the clearance and persistence of HPV.

The viral genotype is the best-known variable that determines the capacity of cellular integration and associated oncogenic risk. Genotypes 16 and 18 are critical types[2].

The second variable is the histological structure of the ectocervix. HPV needs cells in mitotic activity to integrate[3]. Cells in metaplastic re-epithelization process in the transformation zone of the cervix are ideal targets for anchoring HPV. Consequently, well-epithelized cervix with squamous epithelium and limited or non-existent transformation areas do not provide a suitable environment for inclusive colonization of HPV.

Further, recent data clearly demonstrates vaginal microbiota imbalance may determine the pathogenesis of HPV cervical cancer. This circumstance is attracting more and more interest, due to the growing evidence of the direct relationship between the alteration of the microbiota (with decrease in lactobacilli and increased diversity), and the greater frequency and severity of the HPV-dependent cervical lesions[4]. The alteration of the vaginal microbiota can affect the other circumstances, deteriorating the epithelial integrity of the cervix and affecting the vaginal immune status.

Finally, there is the immune status of the host. It is known that immunocompromised patients have a high risk of developing HPV related lesions[5]. Recent data has shown a significant correlation between the immune status of women and the persistence of high-risk HPV genotypes[6]. Then, improving the local immune status, in the area of action of HPV, can be presumed a good strategy to facilitate the clearance of the virus.

Therefore, we hypothesize that interfering positively in the three modifiable circumstances outlined earlier could be a new strategy to prevent and treat precancerous lesions on HPV-positive women.

Based on this concept, the effect of a vaginal gel based on natural ingredients with repithelizing, moisturizing and microbiota balancing actions (Papilocare, Procare Health, Spain) on both cervical epithelization and vaginal microbiota in HPV-positive women without cytology/colposcopy lesions was evaluated in an exploratory, prospective and observational study.

Twenty-one patients were treated for 21 days. Changes in cervical epithelization degree were evaluated by standard colposcopy and measured by Likert scale (from 5, indicating no cervical ectopy, to 1, i.e., severe ectopy and bleeding). Changes in the microbiota composition were evaluated by 16S ribosomal ribonucleic acid (rRNA) gene pyrosequencing, and proportion of both bacterial phyla and species was assessed. The ectopy degree was significantly improved (mean score baseline 3.79 vs. final 4.47, T-test, $p<0,006$). Of all, 52.6% of the patients improved their cervix epithelization degree, and the score of 5 was observed in 63% of the patients. Also, reduction on vaginal diversity and increased proportion of *Firmicutes phylum*, which lactobacilli belongs, were observed. Specifically, significant increase of *Lactobacillus crispatus* and *iners* was shown (T-test, $p<0.005$)[7].

In conclusion, Papilocare has demonstrated significantly improvement to the epithelization degree, and in the vaginal microbiome status, reducing diversity and significantly increasing the concentration of specific species of *Lactobacillus*. These results suggest interfering in the modifiable factors of HPV persistence may provide positive results on normalizing HPV-dependent cervical lesions.

Conflict of interests

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