Effect of cryotherapy and povidone-iodine preparation on eradication of DNA corresponding to highly oncogenic HPV in women with lesions in the uterine cervix

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Summary

In all 88 patients, 23-67 years of age (mean of 34.8 years) with abnormal cytology, lesions in the uterine cervix and presence of DNA corresponding to highly oncogenic HPV, two cycles of uterine cervix cryotherapy and local treatment with povidone-iodine resulted in eradication of the virus six months after detection of the virus.

Key words: HPV eradication; Infection; Cryotherapy; Povidone-iodine.

Introduction

Epidemiologic and molecular studies have proven that over 90% of carcinomas in the uterine cervix are linked to infection with highly oncogenic human papillomavirus (HPV) strains, including 15 HPV types: 16, 18, 45, 31, 33, 52, 58, 35, 59, 56, 39, 51, 73, 68, and 66 [1, 2]. Currently, around 80% of sexually active women are thought to experience a HPV infection at some point in their lifetime which, in most cases, is eradicated spontaneously. Only in 5%-10% of infections, particularly those involving highly oncogenic HPV strains, does the infection persist, which is defined as a persisting presence of DNA of the same type after a period of at least 6-12 months [3, 4].

In cases with additional risk factors, such as immunological dysfunction, other sexually transmitted infections, smoking, prolonged use of hormonal contraception, multiple deliveries, age of ≥ 42 years, the persisting infection leads to Pap test alterations of atypical squamous cells of undetermined significance (ASC-US), low-grade squamous intraepithelial lesion (LSIL) or high grade (HSIL) type and to CIN 1, 2, 3 histologic lesions [5-7].

Observational eight-year cohort studies on 1,001 and 2,404 patients demonstrated that CIN 1 lesions (regression, persistence or progression to higher CIN) can develop within six months while changes in Pap test results in women with positive HPV DNA can undergo regression or progression to HSIL in a period of 7.7 to 88 months, depending on the oncogenic potential of the virus [8, 9]. Other studies have proven that CIN 3 can develop even within two to three years due to exposure to HPV, particularly HPV types 16/18 [10, 11]. Development of an invasive carcinoma in the uterine cervix takes years or decades after HPV infection [12, 13].

Anti-viral vaccination using two prophylactic vaccines, Cervarix and Gardasil is effective not only due to the vaccine activity against HPV 16 and 18, the principal highly oncogenic HPV types, but can also provide cross protection against other highly oncogenic HPV types (31, 33, 45, 52 and 58) [14].

In general, it is not the HPV infection itself which is targeted by the treatment but the virus-induced precancerous and cancerous lesions. Various methods of CIN treatment are employed, sometimes excessively aggressive, although references indicate that even after conization relapses of CIN are encountered [7, 15]. Most probably, this reflects either a persisting HPV infection despite the elimination of the cervical lesion or another infection.

A recent report in 2011 appeared on the treatment of HPV infections using intravaginal administration of a zinc-citrate solution, which significantly eliminated the viral infection [16].

Another original paper pertains to carcinoma of the uterine cervix and the action of arsenic trioxide (As_2O_3) as a potential agent which would sensitize lesions to treatment. The target is supposed to involve zinc finger transcription factor YY1, the expression of which is increased in uterine cervix carcinomas and which plays a significant role in progression of HPV-positive carcinoma [17].

This study aimed to evaluate the effects exerted by repeated cryotherapy and pharmacotherapy, using povidone-iodine for the presence of DNA representing highly oncogenic HPV in female patients with abnormal cytology and lesions in the uterine cervix.

Materials & Methods

The treatment was performed in 88 women, ranging in age from 23 to 67 years, who demonstrated cytological alterations, clinical presence of cervical lesions or erosion type and presence of DNA corresponding to highly oncogenic HPV types.

Cervical cytology was estimated using the Bethesda system.

Viral genotyping was performed in the Laboratory of Molecular Genetics using reverse transpiration polymerase chain reaction (RT-PCR), capable of detecting 15 highly oncogenic types and 12 low oncogenic types of HPV.

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Following the estimation of HPV type the following procedures were performed:

– cryotherapy for 3 min, using liquid nitrogen applied via a cervical probe the size of which depended on the size of the vaginal portion of the cervix and type of vaginal opening, including lesions on the disc and external opening, including the transient zone and part of cervical canal;

– intravaginal povidone-iodine (betadine) was applied (which also acts as has an antiviral) every day for 14 nights to a depth guaranteeing the drug reached the uterine cervix;

– after two months the cryotherapy and local betadine treatment procedures were repeated;

– two months later tests were made to check for presence of HPV DNA.

Results

Cytological examination disclosed: in 62 cases ASC-US and in 26 patients LSIL with koilocytosis. No differences in cytological results were disclosed between women aged 23 and 47 years (69 patients) and those between 49 and 67 years (19 patients).

In 33 women (37%) individual HPV types were identified:

– HPV 16 (noted most frequently) was found in 11 (33%) patients; HPV 58 in five patients, HPV 31 in four patients, HPV 51 in four patients, HPV 18 in four, HPV 33 in three and HPV 52 in one patient and HPV 45 also in one patient.

In 18 women (20.2%) two types of the virus were detected:

– in five patients types 16+31, in four patients HPV 16+another highly oncogenic type (52, 18, 39, 31, 45).

In nine patients two of the following highly oncogenic types of HPV were detected: 52, 51, 45, 39, 59, 58, 56.

In 37 women (42.6%) multiple HPV types were detected, apart from those listed above, also types 68 and 66; with types 16 and 51 being the most frequent among the multiple infections.

Six months after HPV infection detection RT-PCR failed to detect HPV DNA in any of the patients and cytological examination performed three months after the diagnosis was normal in every one of the patients.

In seven women, aged 45 to 67, continuing cervical erosion of the vaginal portion led to patients being subjected to conization and histological evaluation of the excised preparation documented the diagnosis of glandular erosion with no traits of koilocytosis.

Discussion

The highly oncogenic HPV types are linked to the development of precancerous lesions and carcinoma of the uterine cervix. Despite differences in the distribution of HPV types on various continents, seven genotypes (type 16, 18, 45, 31, 33, 52 and 58) have been found in 87.4% of invasive carcinomas worldwide. Studies on precancerous lesions prove that after six months around 49% of women diagnosed with CIN 1 manifest a normal cervix, 45% continue to carry CIN, but in 7% of women progression is noted to higher CIN. Moreover, the treatment of precancerous lesions using loop excision of the transformation zone may be linked to the persistence of the viral infection [7, 18].

Until now, viral infections as such were not treated but the therapy was targeted at lesions resulting from the infection. Kim *et al*. [16] presented pilot results of conservative local management of HPV infection using zinc citrate solution, which proved to be highly promising.

In conclusion, the method presented above is effective, economic and it fulfils the expectations of patients who want to eradicate the virus and lesions in the uterine cervix instead of waiting for spontaneous eradication or a further unfavourable development.

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