

Systemic Interferon Alpha-2a in the Treatment of Condylomata Acuminata

KONDİLOMATA AKÜMİNATA TEDAVİSİNDE SİSTEMİK İNTERFERON ALFA-2A

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Summary

Background: Human papilloma virus infections (HPVs) which involve skin and mucous membranes are widespread and occur all over the world. They can lead to benign and malignant epithelial tumors. In this study we aimed to evaluate the efficacy of systemic interferon alfa-2a in adult patients with anogenital warts.

Methods: Twenty four adult patients with perianal and inguinal warts were included in the study. The interferon alfa-2a was used subcutaneously in a dosage of 3 MIU/m² per day for two weeks, and then three days a week for further 4 weeks.

Results : Twenty out of 24 patients recovered completely in one to six months. One had partial response and in the rest there was no response.

Conclusion: Subcutaneous interferon alfa-2a, in the current dosage and treatment schedule can be used in recurrent and recalcitrant cases of anogenital wart. Since it may treat the occult lesions in which the conventional treatment modalities can not achieve, this therapeutic approach should be encouraged.

Key Words: Condylomata acuminata, Systemic interferon alpha, Treatment

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Özet

Amaç: Deri ve müköz membranları etkileyen human papilloma virus enfeksiyonları (HPV'ler) oldukça yaygındır ve tüm dünyada gözlenir. Bu enfeksiyonlar iyi ve kötü huylu tümörlere neden olabilirler. Bu çalışmada anogenital verrüsü olan yetişkin hastalarda sistemik interferon alfa-2a'nın etkisini değerlendirmeyi amaçladık.

Metod: Perianal ve inguinal verrüsü olan 24 yetişkin hasta çalışmaya alındı. İnterferon alfa-2a subkütan olarak 3 milyon ünite /gün dozunda ilk iki hafta hergün, sonraki dört hafta ise haftada üç gün olarak uygulandı.

Bulgular: Yirmidört hastanın yirmisi bir ile altı ay içinde tamamen iyileşti. Birinde kısmi iyileşme gözlenirken diğer üçünde ise yanıt alınamadı.

Sonuç: Çalışmamızda kullandığımız dozda ve tedavi şemasındaki subkütan interferon alfa-2a, tekrarlayan ve tedaviye dirençli anogenital verrü vakalarının tedavisinde kullanılabilir. Konvansiyonel tedavi yöntemlerinin ulaşmadığı gizli lezyonları da tedavi edebileceği düşünüldüğünde, bu tedavi yaklaşımının bu tür olgularda öncelikle tercih edilmesi önerilebilir.

Anahtar Kelimeler: Kondilomata aküminata, Sistemik interferon alfa-2a, Tedavi

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Warts in humans have been recognized for thousands of years and were caused by human papillomaviruses (HPVs) that more than 77 different types were identified and characterized. Many HPV types infect the mucous membranes, particularly, of anogenital region. Anogenital HPV infections are the most frequently diagnosed sexually transmitted diseases of viral origin. Large epidemiologic studies have revealed that infections with certain HPV types, such as HPV 16 and HPV 18, are an important risk factor for cervical cancer and noncervical anogenital cancer (1).

HPV types are grouped according to DNA sequence homologies and association with clinical lesions (cutaneous epidermodysplasia verruciformis-associated, cutaneous, cutaneous and/or mucosal, mucosal). But one type of HPV can cause different types of clinical lesions.

Different types of genital HPVs can infect the squamous epithelia and mucous membranes of the cervix, vagina, vulva, penis, and perianal region; and may lead to genital warts (condylomata acuminata), precancerous squamous intraepithelial lesions, or cancers (cervical, vulvar, vaginal,

penile, and perianal). Genital HPVs are easily transmitted. Long-term association with partner is not necessary for transmission. Since no antiviral treatment is available for HPVs, the clinician's role is to treat all detectable lesions in order to help the patient's immune system fight the virus and prevent transmission.

Materials And Methods

Patients included in this trial had recalcitrant/recurrent disease as judged by failure of multiple previous treatments (cryosurgery, radiosurgery, excision, some topical therapies except imiquimod). The diagnosis of condylomata acuminata (CA) was confirmed by biopsy. Patients were excluded from study if they had any of the followings; a) renal dysfunction, b) liver cirrhosis, c) autoimmune diseases, d) depression, e) pregnancy, f) leukopenia, trombocytopenia, g) immunosuppression, h) malignant degeneration in biopsied tissue, i) drug-using (e.g. cannabis).

Twenty four patients (22 men, 2 women) were included in the study. The ages of patients ranged between 21 and 62 years, and they had the lesions for at least six months (ranged between 6 months and two years). There was history of recurrence in one patient after surgical removal of his lesions one year ago. All of the lesions were moist and located in perianal and inguinal regions (Table 1). There were not HIV and VDRL positivity in any patient and they all denied homosexuality.

Table 1. Characteristics of patients

Characteristics	No. of patients
Male	22
Female	2
Age (Years)	
Median-range	36/21-62
Localization	
Inguinal	4
Perianal	22
Response	
Completely recovered	20
Partial response	1
No response	3
Recurrence*	0

Photographs were taken before therapy and then at monthly intervals for six months (Figure 1). Patients recovered were examined every month after the recovery during twelve months.

In routine weekly hematologic evaluations performed before and during the therapy, no abnormality was found. Any symptomatic side effect was recorded daily by the patient.

The interferon alpha-2a was used subcutaneously in a dosage of 3 MIU/m² per day for 14 days, and then three days per week for further four weeks. Patients self-administered the drug in the anterior thigh after the third day of therapy (in the first two days, they were trained about injection). They were all controlled weekly during the treatment, and monthly thereafter.



Figure 1. The typical lesions of a male patient before (a) and after (b) the treatment.

Results

Twenty out of 24 patients recovered during one to five-month periods. (mean: 94 days) One had almost 20 percent improvement, and the other three, one of whom had a surgical removal history, had no improvement. All of the patients had transient flue-like symptoms which had disappeared spontaneously without discontinuation of treatment. No other side effects were encountered.

None of the 20 recovered patients had recurrence during the twelve-month follow-up period.

Discussion

While warts are frequently considered trivial or a cosmetic problem, genital warts may be painful or irritating, cause social embarrassment, and in some patients, may be multifocal and there may simultaneously have infection in the cervix uteri, anal region and even may be associated with a cancer risk. Therefore, the clinical approach to HPV-associated pathologies need to be multidisciplinary and lesions at different sites should be screened and treated at the same time to achieve the best clinical response.

Although we did not perform anosopic examination before and after therapy, in some studies, it has been shown that at least 50% of men and women with perianal warts have internal lesions in the anal canal (2). It may be missed or hard to treat these internal lesions with local therapies. Therefore, some types of systemic treatment should be preferred to topical therapy in these perianal recalcitrant cases. In the light of this knowledge, systemic interferon of which parenteral administration should theoretically treat all HPV infections, was used in different studies. Highly variable outcomes were obtained in different treatment regimens (3-9). These results are explained especially by different biologic effects of different treatment regimens (3).

Interferons (IFNs), part of the natural defense system, have antiviral, antitumor and immunomodulating properties. It has been shown that antigen presentation capability is also enhanced after IFN treatment in responders. The lack of this effect in nonresponders may be due to the overexpression

of HPV early (E7) gene in contrast to responders, where HPV late (L1) gene expression predominates (10,11).

Antiviral and antiproliferative properties of IFNs are seen at high doses, while immunomodulatory effects are prevalent at low doses and decrease with increasing doses. (12) Therefore optimal doses and optimal regimens should be used to obtain the best results. In our study, we used 3 MIU/m²(approximately 5 MIU) IFN alpha-2a per injection. This dose is neither low nor high. Because natural killer cell activity-inducing effect of IFNs tends to disappear if treatment is prolonged, we used IFN three days per week after 14 days of continuous treatment (12,13). Twenty out of 24 patients (83,3%) were completely cleared during one to five-month periods, and there were no recurrences twelve months following the clearing of the last lesions.

As a result, it can be thought that it may be cheaper to use imiquimod instead of interferon, but it can not be applied into the anal canal, besides it is not available in every country. Therefore, parenteral IFN alpha, it was interferon alpha-2a in our study, should be tried preferentially as first-line drug (especially in perianal region) for recurrent/recalcitrant disseminated condyloma acuminata (RDCA) because of the chance of cure requirements mentioned above. We suggest that the point is to find the ideal dose and regimen for parenteral interferon in the treatment of RDCA and naturally we suggest the dose and regimen used in this study which showed high remission rates and no recurrences.

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