

Evaluation of isotretinoin gel and oral zinc sulphate in the treatment of plane warts

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Summary

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Background: Plane warts represent a common dermatological problem encountered in daily practice with no uniformly effective treatment modality.

Patients and methods: This study was conducted at the Department of Dermatology and Venereology of Baghdad Teaching Hospital / Medical City from April 2005 to June 2006. Fifty patients enrolled in the study and 36 completed it. Patients were instructed to apply isotretinoin gel once daily and keep on regular follow up every 2 weeks for one month to assess the response and side effects. At the end of the first month those with complete cure were instructed to stop therapy and keep on regular follow up to detect any recurrence. Patients with no response were divided into 2 groups. One group continued on isotretinoin gel alone. In the second group oral zinc sulphate was added and both groups were reevaluated after one month.

Results: 22 patients out of 36 (61.7%) showed complete cure after one month of isotretinoin gel therapy. In the group that continued on isotretinoin gel for another month cure rate was 42.8% (3 patients out of 7) while in the other group where oral zinc sulphate was added the cure rate was 71.4% (5 patients out of 7). The total number of patients with complete cure throughout the study was 30 patients (83.3%). The results also showed that the cure rate for warts located on the face is much higher than cure rate for those located in the limbs and hands.

Conclusions: The result of this study showed that isotretinoin gel is a new effective and well tolerated therapy for the treatment of plane warts. Adding oral zinc sulphate seems to increase the cure rate especially for those patients who did not respond to isotretinoin.

Keywords: Plane warts, isotretinoin gel, zinc sulphate

Introduction

Plane warts occur mostly in children and young adults [1]. The face and back of the hands and the shins are the sites of predilection [2]. Usually presented as 2-4 mm flat topped papules that are slightly erythematous or brown on pale skin and may be hyperpigmented on darker skin [3].

There are many modalities for the treatment of plane warts, the form of therapy used depends on the number of lesions, site, age of the patient and the previous therapies used and their success and failure [3].

Isotretinoin gel contains isotretinoin as its active ingredient in a concentration of 0.05%. Isotretinoin is 13-cis retinoic acid, which is naturally occurring metabolite of retinoic acid [4]. In dermatology,

isotretinoin is particularly useful in the treatment of severe forms of acne vulgaris when it's taken systemically [4]. Zinc is essential for immune system and zinc deficiency leads to lymphopenia and reduction of the immunity [5]. The aim of the present study is to evaluate the efficacy and tolerability of isotretinoin gel in the treatment of plane warts and the effect of adding oral zinc sulphate to the therapy.

Patients and Methods

This study was conducted in the department of dermatology and venereology of Baghdad Teaching Hospital / Medical City from April 2005 to June 2006. The study was designed as an open therapeutic trial. Fifty patients were enrolled in this study, their ages ranged from 3 to 38 years (mean 16, SD±8) years. The number of their warts ranged from 5 to 80 (mean 25, SD±15) and duration of warts ranged from 1 to 40 months (mean 8, SD±8) they mainly located on the face and hands. Only 36 patients completed the study. The remainder defaulted for

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unknown reasons. Full history was taken from each patient regarding age, medical history, drug history, dermatologic history and any previous treatment modality. All the patients did not have history of any skin or medical diseases and did not receive previously any treatment for warts. Physical examination was done on each patient to assess the number, location and size of the lesions.

The course of treatment and possible adverse effects were explained to the patients and their consent were obtained. Isotretinoin gel used in this study was manufactured by Stieffil laboratories, Ireland, under the trade name, Isotrex Gel.

The patients were given the instructions of use of the drug. They were asked to apply the drug once daily at night and were advised to stop the therapy temporarily or consult the doctor if severe reaction occurred.

Patients were also instructed to minimize sun exposure during therapy and to use sun screen and to avoid contact with the eyes and mucous membranes and to avoid concomitant use of abrasive, peeling or caustic agents.

Follow up and evaluation: All patients were re-examined at the end of the second week and at the end of the fourth week to assess the response to the treatment and side effects. The patients who showed complete disappearance after the first month were asked to stop therapy and remain on monthly follow up for 6 months. Patients who showed partial response or no response at all were divided into 2 equal groups. One group continued on isotretinoin alone. In the other group oral zinc sulphate was added to the therapy at a dose of 10 mg/kg/day up to 600 mg in 3 divided doses.

Patients in both groups were re-evaluated after another month of treatment.

At the end of the second month all patients with complete response were asked to stop therapy and keep on regular follow up for 6 months to detect any recurrence. Chi-Square test was used to compare the results.

Results

The patients were seen after 2 weeks and after 4 weeks from the onset of therapy to assess the response to treatment and side effects. The results showed that 22 patients out of 36 (61.2%) achieved complete cure while 14 patients (38.8%) showed partial response or no response at all (table no. 1).

Those with complete cure (22 patients) were asked to stop the therapy and keep on regular follow monthly follow up for 6 months to detect any recurrence.

Those patients with partial or no response (14 patients) were divided into 2 equal groups each consisted of 7 patients. The first group continued on isotretinoin gel alone for another month and three patients (42.8%) showed complete cure (table 2).

In the second group where oral zinc sulphate was added to topical isotretinoin, 5 patients showed complete cure (71.4%) (table no. 2). The P-value between the 2 groups is 0.589, which is statistically insignificant probably due to small sample size of the groups.

So the total number of patients who achieved complete cure throughout the study was 30 patients (83.3%).

All patients with complete cure were followed for 6 months and 4 patients (13.3%) developed recurrence within the first 2 months of cessation of therapy and they were all who were treated with isotretinoin gel alone. Different body areas demonstrated different response to the therapy. The cure rate for lesions located on the face was (90%), while for those located on the hands and limbs the cure rate was (50%) (table no.3), P-value 0.04, which is statistically significant. Regarding the local side effects, they occurred in 28 patients (77.7%). These included mild erythema and itching and did not necessitate stopping the therapy in any of these patients. The face was more sensitive to develop these side effects compared with other areas (table no.3). All patients who received oral zinc sulphate developed mild gastric pain that did not require cessation of therapy.

Table (1) : response rate after 2&4 weeks of isotretinoin gel therapy.

	After 2 weeks	After 4 weeks
Full response	0 (0%)	22 (61.2%)
Partial response	21 (58.3%)	10 (27.7%)
No response	15 (41.6%)	4 (11.1%)
total	36 (100%)	36 (100%)

Table (2) : response rate after a second month of therapy in 2 different groups

Type of treatment	Responded patients	Partial response	No response
Isotretinoin gel alone (7 patients)	3	2	2
Isotretinoin gel and oral zinc sulphate (7 patients)	5	2	0
Total no. 14 patients	8	4	2

Table (3) :response rate and side effects according to body area.

Body area	No.of patients responded	No. of patients with side effects
Hands and forearms (7 patients)	4 (55%)	3 (33%)
Face (29 patients)	26 (90%)	25 (86.6%)

Discussion

Plane warts are a common dermatological problem seen most commonly in children and usually on face and dorsum of the hands [1]. Although their tendency for spontaneous resolution, patients usually seek help for their problem, fearing of spread of the disease and disfigurement they cause, since the disease affects the exposed parts usually. Many treatment modalities are available but no single treatment is uniformly effective [3]. Isotretinoin gel which has been tested in this study proved to be an effective topical agent in the treatment of plane warts, especially those located on the face. Although many patients developed local side effects, including erythema, peeling and itching, these were mild and did not require stopping the therapy in any patient. All the side effects disappeared after a few days of starting of therapy. The pharmacological action of isotretinoin gel in the treatment of warts is supposed to be mostly related to its peeling effect that leads to destruction of warts [5] and also probably to its irritant effect that leads to induction of inflammation and resolution of the warts [5], since the patients who develop these side effects showed a high cure rate compared with those who did not experience these local reactions. The results of this study using isotretinoin gel alone were comparable with previous studies using tretinoin cream in treating plane warts [6]. Also the results of this study using isotretinoin gel were comparable with previous studies using topical zinc sulphate solution 10% in treating plane warts. But recurrence was not detected within 6 months of follow up in that study [7]. Oral zinc sulphate had been used successfully in the treatment of recalcitrant common viral warts [8]. In this study adding oral zinc sulphate at a dose of 10 mg / kg / day for one month seems to increase the cure rate in comparison with patients who continued on isotretinoin gel alone.

The mechanism of action of oral zinc sulphate is believed to be attributed to enhancement of immunity against human papilloma virus by its immunomodulating effect, since it has been used successfully to treat many skin conditions with altered immune response, for example cutaneous leishmaniasis [9,10].

Four patients of those with apparent cure (13.3%) developed recurrence of their warts after stopping the therapy. All these recurrences happened within two months of cessation of treatment. All recurrent cases were among those who were treated with isotretinoin gel alone without adding oral zinc sulphate.

So adding oral zinc to the therapy did not only seem to increase the cure rate but also seems to decrease the possibility of recurrence, probably by augmenting the immune response against the virus both in clinically evident lesions and in latent stage.

In conclusion isotretinoin gel is a new effective and well tolerated topical therapy for the treatment of plane warts especially those located on the face. Adding oral zinc sulphate to the therapy seems to increase the cure rate and decrease the recurrence rate.

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