

Original Article

Efficacy of oral Isotretinoin in viral wartsManjulata Dash¹, Soubhagya Ranjan Tripathy², Tanmay Padhi³, Nikhil Ranjan Das⁴

Viral warts are commonly seen in dermatology OPD involving all age groups. Available treatment modalities have their own limitation like unacceptable side effects or inadequate efficacy. The present study was conducted to assess the efficacy of oral isotretinoin in the management of viral warts. Male agricultural workers in their 2nd to 4th decade were the most commonly subgroup of patients. Verruca vulgaris was the most common clinical subtype seen in 52.77% of the cases. Out of all body sites, upper limbs were affected in 37.5% followed by lower limbs in 31.94% and face in 10.18%. After isotretinoin therapy, complete response was seen in 87.09% of verruca plana, 60.78% of palmoplantar warts, 57.17% of verruca vulgaris and 30% of genital warts. However, 17.64% of palmoplantar wart and 14.91% of verruca vulgaris did not show any response. The common adverse effects observed were Chelitis (78.70%) followed by xerosis (36.57%), hair loss (3.70%) and hypertriglyceridemia (3.24%).

[J Indian Med Assoc 2018; 116: 16-9]

Key words : Viral wart, isotretinoin.

Warts are benign epithelial proliferation of the skin and mucous membrane resulting from infection with human papilloma virus.

Cutaneous warts spread either by direct contact from person to person or indirectly by contact with contaminated surfaces or objects, transmission being facilitated by minor breaks in the epidermal barrier.

Prevalence varies across different populations and age ranges, but is highest in children and adolescents at an estimated 3-5%¹. The natural progression of warts indicates approximately 23% of warts regress spontaneously within 2 months, 30% within 3 months and 65% to 78% within 2 years². Warts typically continue to increase in size and distribution and may become more resistant to treatment over time³. Individuals with treatment-resistant warts potentially may be reservoirs for HPV transmission. In addition, warts can be painful depending on their location (eg, soles of the feet and near the nails).

Of the various therapeutic options available treatment depends on factors as the location, size and type of wart as well as the patient's wishes. The various treatment modalities include destructive methods like topical salicylic acid, trichloroacetic acid and cantharidins or wart removal by surgical excision, laser ablation or electrocautery. Various immune modulators and antivirals used are Interferon alfa, Imiquimod, DCP and DNCB, Cidofovir, Antisense oligo nucleotides. The chemotherapeutic modalities in-

clude Bleomycin, 5-Fluorouracil, Podophyllin, Podophylotoxin. Other modalities used with variable outcomes include topical tretinoin, Oral Isotretinoin, Glutaraldehyde, Formaldehyde soaks and cimetidine available to practitioners faced with patients presenting with problematic warts.

Isotretinoin is a first generation retinoid and structurally it is 13-cis retinoic acid. Though used primarily for treatment of acne vulgaris it can be used in the treatment of viral warts as it can debulk warts by inhibiting the epidermal growth and differentiation⁴ they are also potent immune modulators⁵ and can down regulate HPV transcription in effected cells.

AIMS AND OBJECTIVES

The aim of the study was to evaluate therapeutic efficacy of oral Isotretinoin in different types of warts and also to study clinical profiles of patients with viral warts and various adverse effects oral Isotretinoin.

MATERIALS AND METHODS

Our study was a cross-sectional study based at a tertiary care Centre conducted between October 2015 to October 2017.

Inclusion criteria — All patients reporting to OPD with lesions clinically suggestive of warts were included.

Woman in the reproductive age group who had at least two negative urine or serum pregnancy tests and using two methods of contraception including at least one primary methods (tubal ligation, partner's vasectomy, intrauterine devices, birth control pills, and injectable/implantable/insertable hormonal birth control products) at least one month prior to Isotretinoin therapy and one month after discontinuation of therapy were included in the study.

Department of Dermatology, VSS Institute of Medical Sciences & Research (VIMSAR), Burla, Sambalpur, Odisha 768017

¹MD, Associate Professor & Head and Corresponding author

²MD, Junior Resident

³MD, Associate Professor

⁴MBBS, Junior Resident

Exclusion criteria — Patients with Abnormal biochemical profiles, pregnant woman and those taken any topical or systemic treatment within 3 months of enrolment were excluded from the study.

Special instruction —

(I) Women in the reproductive age groups were counselled not to conceive during the period of one month before therapy and one month after completion of therapy.

(II) All the patients enrolled into the study were advised to apply white petrolatum jelly (Vaseline) over the lips to avoid lip dryness.

Methods — A detailed history was elicited from patients selected for the study regarding

- (I) Demographic details
- (II) Duration of lesion
- (III) Symptoms if any
- (IV) H/O contact in anogenital warts
- (V) Previous treatment if any

Detailed general, physical and systemic examinations were conducted.

Dermatological examination — It includes

- (I) Location of lesion whether on skin or genitalia noted.
- (II) No of lesions, distribution and types of warts were noted both before and after treatment.
- (III) Serial digital photographs were taken both before and during the course of treatment.

Laboratory investigation — This include

(1) Routine laboratory investigation —

- (I) Complete Haemogram
- (II) LFT
- (III) RFT
- (IV) Serum lipid profile
- (V) Fasting blood sugar

(2) Biopsy of skin if required

(3) VDRL for syphilis and ELISA for HIV in genital warts

(4) Any specific investigation, if required

Laboratory investigations were performed before treatment and every four weeks during the treatment period.

The patients were administered 0.5 mg/kg/day of isotretinoin for three months. The response to therapy was either any of the following. Complete response - when there was complete disappearance of warts.

Partial response - when there was more than 50% reduction in the no of warts.

No response - when there was no or partial improvements.

OBSERVATION

During the study period, out of 64,347 patients coming to the OPD, 592 were clinically diagnosed as wart with a prevalence of 0.92% (Table 1&2).

In the present study, most of the patients had Verrucae vulgaris 114 (52.77%) followed by Palmo-plantar wart

51(23.61%), followed by Verrucae plana 31(14.35%) and Genital wart 20(9.25%). In our study, majority of patients were male 143(66.2%), with male to female ratio 1.95. Most of the patients were in the age group 21-30 years. Mean and median age were found to be 27.89±10.03 years and 24.5 years. Out of patients, 72.68% patients were from rural area and 27.32% patients from urban area. Majority of patients belonged to lower socio-economic status 77(35.64%) patients had upper lower 55(25.46%) status and 35(16.20%) had lower middle status.

Majority of patients were found to be 79(36.57%) illiterate, 51(23.61%) patients studied up to primary level while

47(21.75%) patients had studied up to secondary level. Majority of patients were farmers 88 (40.74%) followed by an employed 46(21.24%) followed by office workers 42(19.44%) and housewives 33(15.27%) (Table 3).

Most of the patients had lesions over upper extremities 63(29.16%) followed by lesions over lower extremities 57(26.38%) and face 22(10.18%) (Table 4).

In the present study majority of the patients had disease onset of >6 months comprising of 81 patients (37.50%) (Table 5).

Majority of patients 106 (49.07%) had average no of lesions 10-30 followed by <10 lesions in 77 (35.64%) patients and >30 lesions in

Characteristic	Number	Percentage
Gender :		
Male	143	66.2
Female	73	33.8
Age Distribution (in years) :		
0-10	0	0
11-20	52	24.07
21-30	83	38.43
31-40	51	23.62
41-50	18	8.33
51-60	9	4.16
>61	3	1.38
Residence :		
Rural	157	72.68
Urban	59	27.32
Socioeconomic status :		
Upper	25	11.57
Upper-middle	24	11.11
Lower-middle	35	16.20
Upper-lower	55	25.46
Lower	77	35.64
Occupation :		
Farmer	88	40.74
Office Worker	42	19.44
Housewife	32	14.81
Unemployed	54	25.00
Educational status :		
Illiterate	79	36.57
Primary	51	23.61
Secondary	47	21.75
Graduate and above	39	18.05

Clinical Types of Warts	No of Cases	Percentage
Verrucae Plana	31	14.35
Verrucae Vulgaris	114	52.77
Palmo-Plantar Wart	51	23.61
Genital Wart	20	9.25

Sites	No of Cases	Percentage
Face	22	10.18
Upper extremities	81	37.5
Lower extremities	69	31.94
Trunk	5	2.31
Genitalia	20	9.25
Generalized	19	8.79

Duration of Lesion	No of Cases	Percentage
<1 month	7	3.24
1-3 month	50	23.14
3-6months	78	36.11
>6months	81	37.5

No of Lesions	No of Cases	Percentage
<10	106	49.07
10-30	77	33.64
>30	33	15.27

33(15.27%) patients. In the present study, 43(19.90%) patients had family contact history of wart.

Out of 216 patients immune-suppression was present in 19(8.79%) cases (Table 6&7).

Out of 216 patients treated with isotretinoin, Chelitis was the most common side effect seen in 170(78.70%) patients.

DISCUSSION

The prevalence of viral wart in our study was found to be 0.92% however Larsson and Liden and Belivea TL *et al* have found it to be 20.1% and 12.9% respectively^{6,7}. This wide variation in prevalence may be probably due to variation between samples and populations, variation in study design and age related effects.

In our study mean and median age were calculated to be 27.89 ±10.03 years and 24.5 years respectively which is comparable to the findings of study done by Gonul M *et al* where the mean age was found to be 24.7±13.5⁸. In our study out of 216 patients maximum no of patients 83(38.24%) belonged to third decade while 52(24.07%) belonged to second decade and 51(23.61%) patients belonged to fourth decade while in the study by Ghadgepatil SS *et al* 32% belonged to second decade and 30% patients belonged to third decade⁹. Similarly in the study of Bilgili ME *et al* the incidence of viral wart was found to be 32.52% and 20.8% in the second and third decade respectively¹⁰.

Most of the studies by various workers have reported a definite male preponderance which was in accordance with our study so far as gender distribution was concerned.

In our study out of 216 cases verrucae vulgaris was present in 114 (52.77%) patients followed by palmo-plantar wart 51 (23.61%) cases and verrucae plana 31 (14.77%) cases and conyroma acuminata 20 (9.25%) cases which is comparable to the findings of study by Ghadgepatil SS *et al* where cutaneous warts comprised of verrucae vulgaris (42%), palmo-plantar wart (20%), verrucae plana (18%), mosaic wart (6%), and filiform/digitate wart (4%) type and condyloma accuminata was present in 10% of cases⁹. Similar results were found in the study by Baysal *et al*¹¹ However in the study by Gönül M *et al* the most frequent

	Complete Response No of cases (%)	Partial Response No of cases (%)	No Response No of cases (%)
Verruca plana	27(87.09)	3(9.67)	1(3.24)
Verrucae Vulgaris	64(56.17)	33(28.94)	17(14.91)
Genital Wart	6(30)	9(45)	5(25)
Palmo-Plantar Wart	31(60.78)	11(21.56)	9(17.64)

type was verrucae vulgaris (77.6%) followed by ano-genital wart (23.7%), plantar (18.8%), verrucae plana (6.9%), filiform (4.7%) which may be due to the pattern of sexual life in that country⁸. Out of 216 cases in 81 patients warts

Adverse Effects	No of Cases	Percentage
Chelitis	170	78.70
Xerosis	79	36.57
Hairloss	8	3.70
Epistaxis	2	0.92
Hypertriglyceridemia	7	3.24
Hypertransaminases	3	1.38
None	13	6.01

were present on upper extremities followed by 69 patients on lower extremities followed by 22 cases over face and 19 cases involving more than one site. Trunk

was the least common site involved only in 5 cases. The findings are comparable to findings of the study done by Theng TSC *et al* where hands were involved in 39.1% cases and feet were involved in 38.4% cases followed by face involved in 23% of cases while trunk was involved in only 3.3% of cases¹² while in the study by Al-Mutairi N *et al* hands were the most common sites (40.19%) followed by feet (37.59%)¹³. Similarly in the study done by Ghadgepatil SS *et al* extremities (66.7%) were most favored sites of warts followed by the face (23%)⁹. Frequent involvement of extremities in warts is due to their increased exposure to trauma. Involvement of face is probably attributable to the increased cosmetic procedures like waxing, threading, facials etc. The trunk is the least common site involved as it is less exposed and less prone to trauma involved only in 5 (2.31%) cases comparable to findings of Ghadgepatil SS *et al* (3%)⁹ and Theng TSC *et al* (3.3%) cases¹². In our study out of 216 patients 88 (40.74%) cases were farmers followed by unemployed 54 (25%) cases followed by office workers 42 (19.44%) cases and housewives in 32 (14.81%) cases while in the study by Ghadgepatil SS *et al* 32% cases were students, 28% cases were labourer, 16% cases were housewives and 14% cases were office workers⁹. In our study higher cases of warts in farmers may be due to lower level of literacy and high amount of physical activities in them.

In our study out of 216 patients a positive family history was present in 43 patients which was comparable to study of Theng TSC *et al* (30%)¹² and Al-mutairi and Alkhalf (19.8%)¹³.

In our study the mean duration of lesion before treatment was 6.25±4.39 month. The mean no. of lesions per patient was 9.2±3.9 comparable to findings of Al-Mutairi N *et al* (5.6)¹³ and Theng TSC *et al* (7.03±8.08)¹².

In our study out of 216 patients 31(14.35) cases were verrucae plana. On treatment with oral Isotretinoin 0.5 mg/kg/day for 3 months 27(87.09%) patients showed complete clearance of warts and 3(9.67%) patients showed partial clearance while 1(3.24%) patient showed no re-

sponse. The results are comparable to finding of the study by Al-Hamamy HR *et al* in which 73.07% patients showed complete clearance while 7.92% patients showed partial clearance of plane warts present on face¹⁴. In the study conducted by Olguin Garcia MG *et al* 100% patients showed complete clearance of recalcitrant plane warts present over face¹⁵.

In our study out of 216 patients 20 (9.25%) had condyloma acuminata. After 3 months of treatment with oral Isotretinoin at the dose of 0.5mg/kg/day for 3 months 6 (30%) patients showed complete clearance, 9 (45%) patients showed partial clearance while 5 (25%) patients showed no response to therapy. The results were comparable to the findings of a double-blind placebo controlled clinical trial conducted by Georgala S *et al* in which 32.1% cases responded completely to treatment, 39.1% showed partial response while 28.5% showed no response¹⁶. In another study Tsambaos D *et al* treated 56 male patients with recalcitrant genital warts using Isotretinoin 1 mg/kg for 3 months. Of these, 39.6% responded completely and 13.2% responded partially¹⁷.

In a study by Olsen EA *et al* patients with condyloma acuminata showed no response to therapy with Isotretinoin 1mg/kg/day for 6 weeks which may probably be due to a shorter duration of therapy used in the study¹⁸. In our study out of 216 patients 114 patients had verrucae vulgaris. On treatment with oral Isotretinoin 64(56.14%) patients showed complete response 33(28.94%) patients showed partial response while 17(14.91%) patients did not show any response to therapy. The lesions on the upper extremities were more responsive in comparison to the lesions over the lower extremities.

Viral warts are very common entities in dermatological practices. The response to therapy in different patients depends on their immunity status as well as number, size of the lesions and duration of the disease. However there is no definite therapy in the literature which is 100% effective in the treatment of warts. Hence newer modalities of treatment like oral Isotretinoin which would be efficient in the treatment of warts with minimal side-effects as well as cost-effective should be tried out.

REFERENCES

- 1 Williams HC, Pottier A, Strachan D — The descriptive epidemiology of warts in British schoolchildren. *Br J Dermatol* 1993; **128**: 504-11.
- 2 Sterling JC, Handfield-Jones S, Hudson PM — British Association of Dermatologists. Guidelines for the management of cutaneous warts. *Br J Dermatol* 2001; **144**: 4-11.
- 3 Clifton MM, Johnson SM, Roberson PK, Kincannon J, Horn TD — Immunotherapy for recalcitrant warts in children using intra lesional mumps or Candida antigens. *Pediatr Dermatol* 2003; **20**: 268-71.
- 4 Lutzner MA, Blanchet-Bardon C, Puissant A — Oral aromatic retinoid (RO 10- 9359) treatment of two patients suffering with the severe form of epidermodysplasia verruciformis. In: Orfanos

- CE, Braun-Falco O, Farber EM, eds. Retinoids: advances in basic research and therapy. New York: Springer- Verlag, 1981: 407-10.
- 5 Katz RA — Isotretinoin treatment of recalcitrant warts in an immunosuppressed man. *Arch Dermatol* 1986; **122**: 19-20.
- 6 Larsson PA, Liden S — Prevalence of skin diseases among adolescents 12-16 years of age. *ActaDerm. Venereol (Stockh)* 1980; **60**: 415-23.
- 7 Beliaeva TL — The population incidence of warts. *Vestnik Dermatologii Venereologii* 1990; **2**: 55-8.
- 8 Gonul M, Unal E, Iyidal A, Cakmak S, Kilic A, Gul U, Doner P — Mucocutaneous warts in Middle Anatolia, Turkey: clinical presentations and therapeutic approaches. *Postep Derm Alergol* 2015; **XXXII (3)**: 179-83.
- 9 Ghadgepatil SS, Gupta S, Sharma YK — Clinicoepidemiological Study of Different Types of Warts. *Dermatology Research and Practice* Volume 2016; Article ID 7989817, 4 pages.
- 10 Bilgili ME, Yildiz H, Sarici G — Prevalance of skin diseases in a dermatology outpatient clinic in Turkey. A cross-sectional retrospective study. *J Dermatol Case Rep* 2013; **7**: 108-12.
- 11 Baysal V, Yildirim M, Alan H — Skin diseases most frequently encountered in the Goller region. *T Klin J Dermatol* 1997; **7**: 19-22
- 12 Theng TS, Goh BK, Chong WS — Viral warts in children seen at a tertiary referral centre. *Ann Acad Med Singapore* 2004; **33**: 53-6.
- 13 Al-Mutairi N, Alkhalaf M — Mucocutaneous warts in children: clinical presentations, risk factors, and response to treatment. *Acta Dermatovenerol Alp Pannonica Adriat* 2012; **21**: 69-72.
- 14 Al-Hamamy HR, Salman HA, and Abdulsattar NA— Treatment of Plane Warts with a Low-Dose Oral Isotretinoin. *International Scholarly Research Network ISRN Dermatology* Volume 2012, Article ID 163929, 3 pages.
- 15 Olguin-Gracia MG, Juado-Santa Cruz, Perlata- Pedrero ML, Morales Sanchez MA— A double blind, randomized, placebo controlled trial of oral isotretinoin in the treatment of recalcitrant facial warts. *J Dermatolog Treat* 2015; **26**: 78-82.
- 16 Georgala S, Katoulis AC, Georgala C, Bozi E, Mortakis A — Oral isotretinoin in the treatment of recalcitrant condylomata acuminata of the cervix: a randomised placebo controlled trial. *Sex Transm Infect* 2004; **80**: 216-8.
- 17 Tsambaos D, Georgiou S, Monastirli A, Sakkis T, Sagriotis A, Goerz G — Treatment of condylomataacuminata with oral isotretinoin. *J Urol* 1997; **158**: 1810-2.
- 18 Olsen EA, Kelly FF, Vollmer RT — Comparative study of systemic interferon alfa-n1 and isotretinoin in the treatment of resistant condylomataacuminata. *J Am Acad Dermatol* 1989; **20**: 1023-30.

If you want to send your queries and receive the response on any subject from JIMA, please use the E-mail facility.

Know Your JIMA

Website	: www.ejima.in
For Editorial	: jima1930@rediffmail.com
For Circulation	: jimacir@gmail.com
For Marketing	: jimamkt@gmail.com
For Accounts	: journalacct@gmail.com
General	: j_ima@vsnl.net