



Original Research Article

Efficacy of Intralesional 5- Fluorouracil in Recalcitrant Warts a study at Tertiary Care Centre

Authors

Kannambal K¹, Kaviarasan PK², Prasad PVS³, Poorana B⁴, Balajiganesh J^{5*}

¹Associate Professor, Department of Dermatology Venereology and Leprosy, Rajah Muthiah Medical College & Hospital, Annamalai University, Chidambaram, India – 608002

²Head of the Department, Department of Dermatology Venereology and Leprosy, Rajah Muthiah Medical College & Hospital, Annamalai University, Chidambaram, India – 608002

³Professor, Department of Dermatology Venereology and Leprosy, Rajah Muthiah Medical College & Hospital, Annamalai University, Chidambaram, India – 608002.

⁴Assistant Professor department of Dermatology Venereology and Leprosy, Rajah Muthiah Medical College & Hospital, Annamalai University, Chidambaram, India – 608002

⁵Post Graduate, Department of Dermatology Venereology and Leprosy, Rajah Muthiah Medical College & Hospital, Annamalai University, Chidambaram, India – 608002

*Corresponding Author

Balajiganesh J

Post Graduate, Department of Dermatology Venereology and Leprosy, Rajah Muthiah Medical College & Hospital, Annamalai University, Chidambaram, India – 608002

Abstract

Background: Warts are rough verrucous spiny papules that can be found on cutaneous surface. In most patients warts spontaneously regress, whereas others show persistence and progression leading to physical and emotional stress. Several therapeutic approaches like electrosurgery, cryotherapy, keratolytics, vaccines have been used in treating warts, but resistance and recurrences to these therapies have been reported. 5-Fluorouracil (5-FU) is a fluorinated pyrimidine antimetabolite, an anti neoplastic agent that acts by blocking DNA synthesis. It has gained increasing popularity in the recent past for treatment of warts particularly in recalcitrant common and palmoplantar warts as other modalities are not very effective.

Aim: To evaluate the role of intralesional 5- Fluorouracil in recalcitrant warts.

Materials and Methods: The study group comprised of 20 cases of multiple recalcitrant cutaneous warts. We administered 4 ml of 5-FU which was mixed with 1ml of 2% lignocaine and epinephrine which was then injected intralesionally into the warts until blanching occurred at an interval of every 3 weeks till the clearance in about 20 patients who has attended DVL outpatient department at Rajah muthiah medical college and hospital. Ethical clearance was sought and informed consent was obtained from all patients.

Results: After completion of 3 sittings at an interval of 3 weeks we observed the complete response in common warts, palmar warts and plantar warts was 60%, 63% and 60% respectively.

Conclusion: Our study showed that intralesional 5-FU injection was safe and efficacious in the treatment of multiple recalcitrant cutaneous warts.

Keywords: 5- Fluorouracil, intralesional injection, palmoplantar warts.

Introduction

Warts are benign cutaneous and mucosal epithelial proliferations caused by Human papilloma viruses (HPV). More than 100 HPV types have been recognised.¹ The common warts are caused by HPV types 1, 2, 4, 27 and 57. HPV infection occurs through inoculation of virus into the viable epidermis through defects in the epithelium. They infect different areas of skin and mucous membranes. Warts can appear at any age. In few patients, warts may spontaneously regress, whereas others show persistence and progression with spread to other body sites, leading to physical and emotional stress. Several therapeutic approaches like electrosurgery, cryotherapy, keratolytics, vaccines have been used in treating warts, but resistance and recurrences to these therapies has been reported. 5-Fluorouracil is an antimetabolite that suppresses cell division and causes cell cycle arrest.² Topical 5-fluorouracil is used in the treatment of warts but is not very effective.³ Intralesional injection of 5-fluorouracil permits higher drug concentrations throughout the lesion and previous study has shown its effectiveness in treatment of warts.⁴ In the recent times it has been showing promising efficacy in the management of recalcitrant warts.

The Role of 5-fluorouracil in recalcitrant warts

5-Fluorouracil (5-FU) is a fluorinated pyrimidine antimetabolite, an antineoplastic agent that acts by blocking DNA synthesis. 5-FU is a nucleic acid synthesis inhibitor. It inhibits the nucleotide synthetic enzyme, thymidylate synthetase thereby blocking the synthesis of pyrimidine thymidine, which is a nucleoside required for DNA replication. It is an antineoplastic and antimetabolite that inhibits DNA and RNA synthesis in cells, thereby preventing cell replication and proliferation. This mechanism of action may allow 5-FU to be utilized in the treatment of HPV infection⁵.

Materials and Methods

The present clinical study was conducted between October 2016 and February 2017 in the Department of Dermatology. A written informed consent was obtained from all the patients and ethical clearance was sought from the Institutional Ethics Committee. The study group comprised of 20 patients with multiple common warts, palmar and plantar warts of more than 3 month duration, age ranging from 18 to 65 years were included in the present study. Pregnant women, children and immunosuppressed patients were excluded from the study. Diagnosis was made on the basis of history and clinical examination. Patients were categorized into two groups (groups A and B) of 20 each. Alternate patients were included in groups A and B which were treated with intralesional 5-FU and normal saline (control), respectively. Inj 5 FU is available in 5 ml ampule as 250 mg/5ml. 4 ml of 50 mg/mL 5FU + 1 ml mixture of 20 mg/mL (2%) lidocaine and 0.0125 mg/mL epinephrine was mixed in a 5ml syringe. The freshly prepared solution was injected intralesionally in multiple warts until blanching of the lesion occurred with insulin syringe. A black, ecchymosed eschar developed after 3 weeks which was then pared. Residual warts if present were injected a second time. Follow up visit was done every 3 weeks till the resolution of warts.

In the control group, normal saline was injected intralesionally in a similar manner as the 5-FU solution. Antibiotics and anti-inflammatory agents were prescribed to prevent secondary infection and pain after injection. The patients were followed fortnightly up to 3 months and then quarterly up to 1 year. Results were evaluated on the basis of clinical improvement. Patients were considered as cured if there was complete absence of clinically apparent wart. A chi-square test was applied for statistical analysis. Statistical analysis was done using software version. Routine hemogram, liver function tests, renal function tests and X-ray of the chest were done before and after 3 months of treatment.

Results

A total of two hundred and forty warts (240) were present in 40 patients which were included in the present study. There were 26 males and 14 females whose mean age was 27.35 years and 29.05 years, respectively. Group A and group B patients were having 130 and 110 warts, respectively [Table 1]. The baseline parameters (age, sex, distribution of warts) between the two groups were statistically comparable, and no significant statistical difference was observed. A total of 130 warts were treated with intralesional 5-FU. The response in common warts was 60%, while the response in palmar warts was 63% and plantar warts was 60 % at visit 3. Reduction in number of warts at each visit is shown in Table 2. Warts regressed with a slight hyperpigmentation that gradually faded during the follow-up of 1 year. Of the 110 warts treated with normal saline (group B), only 10% showed disappearance of the lesion within 9 weeks. The difference in the resolution rate at the end of 12 weeks was statistically significant ($P = 0.001$) between groups A and B. Most patients in group A experienced moderate pain during injection that was of short duration and was overcome by mixing with xylocaine with adrenaline. None of the patients experienced any systemic toxicity.

Figure 1



Initial Visit



After 9 Weeks

Figure 2



Table 1: Distribution of Warts in Study Group and Control Group

Groups	Common wart	Palmar	Plantar	Total
Group A IL 5-FU				
No of pts	12	5	3	20
No of lesions	77	40	13	130
Group B Control				
No of pts	10	5	4	20
No of lesions	52	34	16	110

Table 2: Reduction in Number of Warts at Each Visit

Type of wart	Group A IL 5-FU						Group B CONTROL					
	Visit 1		Visit 2		Visit 3		Visit 1		Visit 2		Visit 3	
	N	%	N	%	N	%	N	%	N	%	N	%
Common	77	59.2	54	62.8	34	61.8	52	47.3	52	47.3	45	40.9
Palmar	40	30.8	24	27.9	15	27.3	34	30.9	34	30.9	33	30.0
Plantar	13	10.0	8	9.3	6	10.9	16	21.8	16	21.8	16	21.8
Total	130	100.0	86	100.0	55	100.0	110	100.0	110	100.0	103	100.0

Table 3: Mean and Standard Deviation

Groups	Mean	SD	P Value
Group A	30.11	23.74	0.0001(P<0.01)
Group B	26.67	18.59	

P<0.01 Significant at 0.01 level

Discussion

Warts can extremely affect patient's quality of life. It causes embarrassment and frustration. It is known for its persistence and recurrence. Most of them are resistant even after repeated treatment with various physical modalities.⁵ The mean administered dose of intralesional 5-fluorouracil for the treatment of warts is usually in the range of 2 to 6 mg, that is, less than 1/150th of the amount of systemic chemotherapy. Therefore, the systemic adverse effects of 5-fluorouracil are eliminated.

This study was undertaken with the aim to evaluate efficacy of intralesional 5-FU in the management of recalcitrant warts.

We determined the efficacy of intralesional 5-FU in the treatment of common, palmar and plantar warts which were difficult to treat with other modalities.

Iscimen et al⁴ studied seventy-six patients with 315 warts after administering IL 5-FU. Their study was limited to only common warts and did not include any other type. They used the mixture of 5-FU with lignocaine and epinephrine and injected it into the base of the wart. The patients were injected once in a week for a maximum of four weeks. Complete response was noted in an average of 70%. In our

study we injected IL 5-FU every three weeks for a maximum of nine weeks. The mixture of 5 -FU along with lignocaine and epinephrine provided sustained release of drug into the warts in their study which was also followed in our study. Our study showed a complete response of 60% in 20 patients with 124 warts which included recalcitrant common, palmar and plantar warts.

Yazdanfar et al⁵ compared the efficacy of IL 5 -FU with placebo in 34 patients with 68 verrucae. In their study they used 5- FU with a mixture of epinephrine and lignocaine. The patients received four injections at weekly intervals till the resolution of warts occurred. Hence in the above mentioned study Yazdanfar used 5-FU along with epinephrine and lignocaine. In addition, the lignocaine present in the mixture makes the injection less painful. He showed 64.7% complete response in 34 patients with IL 5-FU. In our study we followed the same procedure of mixing 4ml of 5-FU injection and 1ml of lignocaine with epinephrine and injected intralesionally into the wart tissue. Our study showed 60% complete response in 20 patients with 124 verrucae which was consistent with the above mentioned study.

Potential side effects includes pain, burning immediately after injection, onycholysis when it is used for warts near the nails, blistering, erythema, edema, hyperpigmentation, hypopigmentation, ulceration, necrosis and scarring which were observed in few studies. But they were not observed in our study.

Our results have shown 5-FU to be highly effective in the treatment of common, palmo-plantar warts. The 5-FU was diluted with lignocaine and arenaline which reduced localized pain during and after injection. This method had advantage of maintaining high local drug concentrations for longer periods.

Limitations of the Study

A smaller study population and periungual warts were excluded from our study.

Conclusion

This study is being presented to highlight the efficacy of intralesional 5-FU in recalcitrant warts. 5-FU therapy requires less equipment and lesser expertise. Easy pain management and shorter pain period is an advantage of 5-FU compared to other modalities. We conclude that intralesional 5-FU injection is safe and efficacious in multiple recalcitrant cutaneous warts.

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