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The role of antimetabolite medication compared with traditional technique (cryotherapy) for treatment of verrucae.

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A R T I C L E I N F O

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A B S T R A C T

Background: Human papillomavirus, or HPV, is the cause of warts, which are benign skin and mucosal proliferations that typically affect the hands and feet. Due to innate immunity, warts in immune-competent individuals are benign and typically go away on their own in a matter of months or years. Fluorouracil, also known as 5-fluorouracil or 5-FU, belongs to the class of chemotherapy drugs used to treat various neoplasms. In addition, topical fluorouracil (5%) is Food and Drug Administration -approved for managing dermatologic conditions such as multiple actinic or solar keratoses and superficial basal cell carcinomas in cases where alternative methods are not feasible.

Aim of the Study: Compare the effectiveness of intralesional injections of 5-fluorouracil (5-FU) and cryotherapy for the treatment of plantar warts.

Patients and Methods: 60 patients with many plantar warts (more than three warts) were involved in this randomized clinical research. Patients from dermatological clinic were recruited.

Results: When treating palmoplantar warts, intralesional injections of 5-fluorouracil were equally effective as cryotherapy (P-value<0.05).

Conclusion: A 5-FU intralesional injection proved to be effective in treating palmoplantar warts. For palmoplantar warts, cryotherapy is also a successful treatment.

Keywords: Cryotherapy, 5-fluorouracil, Wart.

Introduction

Human papilloma virus (HPV) infection of the skin or mucous membrane results in warts, which are tiny, benign growths. Direct contact, interpersonal interaction, or indirect contact through friends and family can all result in the spread of warts (1). One of the most frequent reasons people contact their primary care physician and dermatologist is still warts (2). There are several types of warts, including common warts, plantar warts, plane warts, and genital warts, and their clinical appearance varies depending on the HPV type and infection site (3). Warts may undergo spontaneous resolution in some patients whereas, in others, they may show persistence and progression with distant spread, despite of the conventional therapy, hence becoming recalcitrant (4).

The majority of treatments concentrated mainly on the destructions of the epidermal lesion or elimination of observable lesions or on the inductions of cytotoxicity against the infected cells (5). Different physical and medicinal managements have been evaluated for the treatment of extragenital cutaneous warts (ECWs), with varying rates of response and recurrence. Several antimetabolite medications, such as 5-fluorouracil and bleomycin, were tested for their effectiveness in treating ECWs (6). Due to their thick cornified layers and endophytic growth pattern, palmoplantar warts are difficult to cure since ablative techniques induce discomfort, temporary immobility, secondary infections, and scarring. To address limitations in the treatment of warts, the utilization of cytotoxic and immunotherapeutic approaches is growing (7).

In dermatology, intralesional medication therapy is a common treatment approach. This mode of drug delivery circumvents the skin barrier, results in a greater local concentration of the drug in the skin, and typically has minimal systemic drug absorption (8). An antimetabolite medication called 5-fluorouracil (5-FU) is used to treat a variety of skin conditions in dermatology, such as vitiligo, keloid scars, premalignant and malignant lesions, and inflammatory skin disorders. It also suppresses cell division and causes cell cycle arrest. According to a study by Searle et al. (9), intralesional injections of (5-FU) at greater medication concentrations are efficient in treating warts.

Use of 5-FU intralesionally combined with epinephrine allowed the medication to be released gradually into the lesion. The effectiveness of local drug use was enhanced by this kind of application. Together with lidocaine, combination reduced discomfort and increased patient comfort (10).

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A common wart treatment that can be performed in a doctor's office is cryotherapy. Using an extremely cold material (often liquid nitrogen), the wart is frozen during cryotherapy (11). Cryotherapy causes tissue damage through two different ways. The first mechanism is the development of tissue ischemia, which results in ischemic necrosis of the tissue by destroying the blood arteries and capillaries inside the target area. By creating ice crystals, causing osmotic cell damage, and disrupting cellular membranes, the second method causes more sophisticated cell damage. Additionally, freezing causes cell damage (12). In order to cure palmoplantar warts, this study compared the effectiveness of cryotherapy with intra-lessional injections of 5-FU.

Patients and Methods

Study design

Study design and setting

A prospective, double-blinded, randomized study with randomization. sixty patients with palmo-planter warts were among them. The patients came from dermatological outpatient clinic. After treatment, the number of warts in group 1 was 1.68 ± 0.97, the number of warts in group 2 was 1.89 ± 0.99. The size of warts in group 1 was 1.94 ± 0.81, the size of warts in group 2 was 2.31 ± 1.01, there was no statistically significant difference between the cases in the different study groups. Table 4.

The satisfaction degree in group 1 was 7 (23.3%) with slightly satisfied, 6 (20.0%) with satisfied and 8 (26.7%) with very satisfied, the satisfaction degree in group 2 was 7 (23.3%) with slightly satisfied, 9 (30.0%) with satisfied and 2 (6.7%) with very satisfied, there was no statistically significant difference between the cases in the different study groups. Table 5.

Furosemide, a loop diuretic, works with the cell membrane ion co-transporters Na+/K+-ATPase and Na+-K+-2Cl − co-transporter-1 to block the K + influx. Thus, it is posited that might be useful in the management of warts caused by HPV. Van Der Kolk et al. (18) refer to this novel strategy as ionic contra-viral therapy. This is the first study attempting to compare the effectiveness of cryotherapy against intra-lessional injections of 5-fluorouracil in the treatment of palmoplantar warts.

Inhibiting DNA and RNA production, 5-FU is an antimetabolite medication that may also have immunomodulatory properties. 5-FU causes cell cycle arrest and decreases cell division. 5-FU is a fluorinated pyrimidine antimetabolite that inhibits the synthesis of DNA and RNA processing, resulting in cell cycle arrest and a decrease in epidermal proliferation, all of which contribute to the reduction of wart tissue proliferation. It inhibits the synthesis of nucleic acids. It works by inhibiting thymidylate synthetase, an enzyme that synthesizes nucleotides, preventing the formation of pyrimidine thymidine, a nucleoside needed for DNA replication. Because of this mode of action, intralesional 5-FU can be used to treat viral warts brought on by the HPV virus. Higher drug concentrations are possible throughout the lesion when 5-FU is injected intralesionally (19).

In a study conducted by Yazdanfar et al. (20), the use of intralesional 5-FU to treat warts was examined; only 34 out of 40 participants finished the study, and 22 patients, or 64.7% of the total, showed complete resolution of their warts after four weeks of therapy and follow-up at one month and six months. Six patients (17.6%) had a partial resolution of their warts, and six patients (17.6%) had no resolution at all by the end of the trial. After six intralesional 5-FU doses, 30 (75%) patients

Table (4). Comparison of the number of warts (After treatment) within the study groups.

Variable	Group 1	Group 2	Test of sig.
Number of warts (After treatment)			
Mean ± SD	1.68 ± 0.97	1.89 ± 0.99	P=0.298
Range	(0 -4)	(0-4)	
Size of warts (After treatment) (mm)			
Mean ± SD	1.94 ± 0.81	2.31 ± 1.01	P=0.214
Range	(1 -4)	(2 -5)	

Table (5). Patients' degree of satisfaction among the studied group.

Variable	Group 1	Group 2	Test of sig.
Satisfaction degree			
Not satisfied	9 (30.0%)	12 (40.0%)	c2 = 4.6286
Slightly satisfied	7 (23.3%)	7 (23.3%)	
Satisfied	6 (20.0%)	9 (30.0%)	P = 0.201
Very satisfied	8 (26.7%)	2 (6.7%)	

Discussion

Human papilloma virus (HPV) infection of the skin or mucous membrane results in warts, which are tiny, benign growths (15). According to Vakharia et al. (16), warts can spread directly between individuals or indirectly through bites. Since basal keratinocytes are the main targets of HPV infection, maceration of the epithelia may be the path via which HPV enters these cells (17). DNA viruses like HPV require an inflow of K+ to replicate.

showed complete remission of their warts, according to Kamal et al.'s (21) 2-week therapy regimen. After the third injection, three patients had total resolution of their warts; ten patients (or 25%) had complete clearance of their warts following the fourth injection; and five patients (or 12.5%) had complete resolution following the fifth injection.

We picked endophytic palmoplantar warts, which have a greater viral load and a thicker stratum corneum, making it more

difficult for 5-FU to penetrate and be delivered. This could account for some of the heterogeneity in our study. Additionally, certain virus subtypes can react differentially to immunotherapy or cytotoxic treatments.

When 5-FU was examined intralesionally for the treatment of warts, Srivastava et al. (22) found that 95.38% of the patients exhibited a complete response, suggesting that 5-FU is a safe and effective treatment for palmoplantar warts. In treating palmoplantar warts, they observed that intralesional 5-FU (50 mg/mL) combined with lidocaine (20 mg/mL) and epinephrine (0.0125 mg/mL) solution produced full responses in 95.38% of the patients, according to the study. Similar to this, Ghonemy et al.'s (23) study compared intralesional 5-FU with microneedling alone versus microneedling combined with 5-FU solution in the treatment of planter warts. In this study, intralesional injection of a mixture (1 mL of 5-FU + 0.25 mL of local anesthesia) into the wart base resulted in a complete clearance in 76.7% of patients in this group.

Among the disadvantages of our study include a brief follow-up time, a small sample size, and no independent assessments of each treatment strategy. We suggest carrying out additional extensive investigations that include histological assessments.

Conclusion

It would be one of the foundational research to learn more about 5-fluorouracil. This study reveals the use of 5-fluorouracil in the treatment of warts, which were notably low in adverse effects and reliable in therapy.

Conflict of interest

None.

Data sharing plans

Data will be provided upon request.

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