Research Article

INTERNATIONAL RESEARCH JOURNAL OF PHARMACY

www.irjponline.com

ISSN 2230-8407 [LINKING]

COMPARATIVE ASSESSMENT OF FOUR IMMUNOTHERAPEUTIC AGENTS IN THE TREATMENT OF MULTIPLE CUTANEOUS WARTS

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How to cite: Lahiri AK. Comparative assessment of four immunotherapeutic agents in the treatment of multiple cutaneous warts. International Research Journal of Pharmacy. 2017;8:3:33-37.
Doi:10.7897/2230-8407.080332

ABSTRACT

Background: Depending on the kind of cutaneous wart, several treatment approaches may be needed. Some patients may benefit from a combination of several therapy techniques. Immunotherapy has been quite popular recently, particularly for cases with resistant warts.

Aim: In order to cure numerous cutaneous warts, the current study compared the effectiveness of four immunotherapeutic agents: vitamin D3, candida extract, PPD (purified protein derivative), and MMR (measles, mumps, and rubella).

Methods: 200 individuals with more than five cutaneous warts were randomly assigned to four groups, and the subjects in Group I, II, III, and IV received treatments with MMR, PPD, Candida extract, and vitamin D, respectively.

The objective was a wart, and intralesional injections were administered to the group at 3-week intervals for a maximum of three treatments. Three months following the previous injection, both remote and target warts showed signs of response.

Result: MMR had the lowest efficacy in terms of clearing the target warts, whereas intralesional vitamin D3 had the most efficacy. Vitamin D3 showed the lowest efficacy in clearing the remote warts, whereas intralesional candida extract showed the maximum efficacy. Intralesional candida extract proved to be the most successful therapy for both local and distant warts. The side effects were mild and short-lived.

Conclusion: The current study comes to the conclusion that the most effective, reasonably priced, and secure method of treating cutaneous warts is intralesional immunotherapy.

Keywords: Candida extract, cutaneous warts, intralesional immunotherapy, intralesional vitamin D3

INTRODUCTION

Verrucae, also called warts, are clinical cutaneous diseases characterized by benign proliferations on the skin and mucosa that are brought on by an HPV (human papillomavirus) infection. Wart occurrence has risen recently in many countries, including India, placing a significant strain on the global healthcare system, particularly in emerging countries like India.[1]

There are several ways to cure warts, such as topical immunologic therapy, occlusotherapy, virucidal and antiproliferative drugs, surgery, local destructive treatments, and reassurance. Vitamin D3, Trichophyton antigens, tuberculin PPD (purified protein derivative), MMR (measles, mumps, and rubella) vaccine, intralesional immunotherapy with Candida extract, SADBE (squaric acid dibutyl ester), or DPC (diphencyprone) are among the immunotherapies that have recently become extensively popular for treating cutaneous warts.[2,3]

Cutaneous warts can also be treated with systemic therapies apart from local therapies. Several systemic treatments, such as zinc sulfate, zinc oxide, histamine receptor 2 antagonists, and isotretinoin, have been used to treat cutaneous warts. Previous

literature data suggests that the effectiveness of these therapy has been observed to differ.[4] With larger and more frequent reported frequencies of recurrences and failures, no one medication is consistently virucidal or successful across all known treatment methods for cutaneous warts. In certain cases, several existing treatment methods may need to be used in conjunction to treat warts, and different types of warts may require different therapies depending on their locations. Since many damaging methods are cumbersome and have a significant risk of recurrence, immunotherapy has become quite popular, especially for treating resistant warts.[5]

The present study aimed to comparatively assess the efficacy of four immunotherapeutic agents vitamin D3, candida extract, PPD (purified protein derivative), and MMR (measles, mumps, and rubella) in the treatment of multiple cutaneous warts.

MATERIALS AND METHODS

The goal of the current prospective, randomized, interventional trial was to compare the effectiveness of four immunotherapeutic agents—vitamin D3, candida extract, pure protein derivative, and MMR (measles, mumps, and rubella) in treating numerous cutaneous warts. Following approval from the relevant Institutional Ethical committee, the study was conducted at Department of Dermatology. Before beginning the study, all participants gave their written and verbal informed permission.

Two hundred participants with cutaneous warts of both sexes were enrolled in the research. The research required participants to have cutaneous warts, be willing to participate, and have never received therapy from another method before, and were in the age range of 18 years to 75 years. The study excluded participants who did not consent to participate, those who had facial or genital warts, immunocompromised individuals, nursing mothers, and pregnant women.

A thorough clinical examination was conducted after each participant's history was thoroughly documented following the research subjects' final inclusion. All of the individuals' demographic information, such as their age, gender, employment, and marital status, was documented in addition to their background. The warts' history was then documented, including the lesions' development, length, and any previous treatments received. Throughout the trial, data confidentiality was upheld for each participant.

Blood tests were performed under rigorous aseptic and sterile circumstances at baseline following inclusion to evaluate the Mantoux test, HIV (human immunodeficiency virus), and HbsAg (hepatitis B surface antigen) in addition to a chest X-ray.

Using basic random sampling, all cutaneous wart patients were split up into four treatment groups and placed in computer-generated, sealed envelopes. Groups I, II, III, and IV were randomly assigned to four equal-number groups (n = 50) and treated with MMR, PPD, Candida extract, and vitamin D, respectively.

According to the group assigned, the target wart was the biggest wart in which the immunogen was to be injected. when there was a noticeable decrease in the wart's size between sessions. The session's target wart was chosen from among the other lesions because it was the biggest. The wart that wasn't injected and was located far from the target wart was arbitrarily designated as the remote site.[6,7]

Every participant was evaluated for side effects, recurrence, and treatment effectiveness. When the size of the target lesion and the number of lesions at a remote site decreased by more than 75%, the therapy was considered effective. The target lesion size and number of remote site lesions decreased by 25–49% in a mild response, and by 50–74% in a moderate response.

No response was considered to be a <25% decrease in the target lesion size and number of lesions at distant sites. In all the participants, follow-up was done after three months after the last injectable dose.

RESULTS

In this prospective, randomized, interventional trial, the effectiveness of four immunotherapeutic agents—vitamin D3, candida extract, pure protein derivative, and MMR (measles, mumps, and rubella)—in treating numerous cutaneous warts was to be similarly evaluated. There were 200 participants with cutaneous warts of both sexes in the research. Four groups were randomly selected from among the individuals, and MMR, PPD, Candida extract, and vitamin D were administered to Group I, II, III, and IV, respectively. Of the 200 research participants, 42% (n=84) were female and 58% (n=116) were male. Acral wasn't the most prevalent place for warts. In 53% (n=106) of the participants, the disease lasted shorter than six months. Four participants, or 2% of the total, reported having a positive family history. 8.8% (n=196) of the individuals had warts smaller than 30 mm2.

It was observed that at the 21st day, mild, moderate, severe, and no response were observed in 56% (n=28), 8% (n=4), 0, and 36% (n=18) of the subjects from Group I; in 88% (n=44), 0, 0, and 12% (n=6) of the subjects from Group II; in 88% (n=44), 4% (n=2), 0, and 8% (n=4) of the subjects from Group III; and in 100% (n=50), 0, 0, and 0 from Group IV. Upon completion of the third session (on the sixty-third day), 24% (n=12), 12% (n=6), 56% (n=28), and 8% (n=4) of Group I individuals, 4% (n=2), 8% (n=4), 76$ (n=38), and 12% (n=6) of Group II subjects, 2% (n=1), 0, 84% (n=42), and no reaction were seen in 12% (n=6) subjects from Group III, and 100% (n=50), 0, 0, and 0 subjects from Group IV respectively as shown in Table 1.

Three months following the final therapy session, 68% (n=34) and 60% (n=30) of the individuals showed full clearance at local and distant locations, respectively. Group II showed that 84% (n=42) and 72% (n=36) of the individuals had full clearance at both local and distant locations. Eighty-four percent (n=42) and eighty percent (n=20) of the individuals in Group III had full clearance at both local and distant locations. According to Table 2, Group IV showed 100% (n=50) and no subjects, respectively, having full clearance at local and distant locations.

Regarding intergroup comparison, the p-value was 0.9315 for Group I vs Group II and 0.9909 for Group II versus Group III and Group I versus Group III, the p-value was 0.8513, and for Group I versus Group IV, the p-value was 0.001. For Group II versus Group IV, the p-value was 0.001, and for Group III versus Group IV, the p-value was 0.001. According to the study's findings, vitamin D3 and other immunotherapeutic drugs significantly differed in how well patients responded to therapy overall for warts. Eight patients in Group I were treated using other modalities as they did not respond to the treatment. According to the study's findings, all of the 100% (n=50) patients in Group I, 92% (n=46) subjects in Group II, 96% (n=48) subjects in Group III, and no subjects in Group IV had any negative side effects following wart treatment. Two individuals from Group II had ulcers, four individuals from Group IV had discomfort and edema, and ninety-two percent (n=46) of the Group IV participants reported having pain, only swelling in 2 subjects from Group III, and mild swelling and erythema in 2 subjects from Group II as depicted in Table 3.

DISCUSSION

200 participants with cutaneous warts of both sexes were evaluated in this research. MMR, PPD, Candida extract, and vitamin D were administered to Group I, II, III, and IV of the individuals, who were split into four groups at random. Males made up 58% (n=116) of the 200 research participants, while females made up 42% (n=84). Acral was where warts were most frequently found. Of the 106 individuals, 53% had a disease duration of less than six months. Of the individuals, 2% (n=4) reported having a positive family history. Out of 196 individuals, 88% had warts smaller than 30 mm2. Similar demographic data to the current study and assessments of people with warts were made by Angeletti PC et al. (2008) and Salah E et al.

At the 21st day, it was observed that 56% (n=28), 8% (n=4), 0, and 36% (n=18) of the subjects in Group I had mild, moderate, severe, and no response, respectively; 88% (n=44), 0, 0, and 12% (n=6) of the subjects in Group II; 88% (n=44), 4% (n=2), 0, and 8% (n=4) of the subjects in Group III; and 100% (n=50), 0, 0, and 0 in Group IV. Upon completion of the third session (on the sixty-third day), 24% (n=12), 12% (n=6), 56% (n=28), and 8% (n=4) of Group I individuals, 4% (n=2), 8% (n=4), 76$ (n=38), and 12% (n=6) of Group II subjects, 2% (n=1), 0, 84% (n=42), and no reaction were seen and 12% (n=6) subjects from Group III, and 100% (n=50), 0, 0, and 0 subjects from Group IV respectively. These outcomes were in line with research by Shivkumar V et al. (2009) and Kwok CS et al. (2012), whose authors found comparable findings on the effectiveness of treatment to those of the current study.

According to research findings, 68% (n=34) and 60% (n=30) of the participants had full clearance at local and distant locations three months following their last therapy session. Group II showed that 84% (n=42) and 72% (n=36) of the individuals had full clearance at both local and distant locations. Eighty-four percent (n=42) and eighty percent (n=20) of the individuals in Group III had full clearance at both local and distant locations. Group IV showed 100% (n=50) and no subjects, respectively, having full clearance at nearby and distant locations. These results were consistent with those of Abdel Razik LH et al12 in 2021 and Thappa DM et al13 in 2016, where the authors reported findings like those of the current investigation for local and distant clearance.

The results of the intergroup comparison showed that the p-values for Group I vs Group II were 0.9315, Group II versus Group III were 0.9909, Group I versus Group III was 0.8513, and Group I versus Group IV was 0.001. The p-value was 0.001 for Group II against Group IV and 0.001 for Group III versus Group IV.

According to the study's findings, vitamin D3 and other immunotherapeutic drugs significantly altered the overall response to therapy for warts. Eight participants in Group I were treated using alternative modalities as they did not respond to treatment. These outcomes were consistent with research by Shaheen MA et al. (2015) and Abdel-Azim ES et al. (2014), who

also noted a noteworthy variation in the overall response to treatment of cutaneous warts with vitamin D3 and other immunotherapeutic drugs. The study's findings also demonstrated that, in terms of negative side effects experienced by research participants following wart treatment, all 100% (n=50) of Group I subjects, 92% (n=46) of Group II subjects, 96% (n=48) of Group III subjects, and no patients from Group IV had any side effects.

Two participants from Group II had ulcers, four from Group IV had pain and swelling, ninety-two percent (n=46) of Group IV subjects reported discomfort, two from Group III had just swelling, and two from Group II had minor swelling and erythema. Similar side effects following immunotherapy for common warts were described by Agarwal C et al. in 2018 and Ahmed R et al. in 2020, according to the current study.

CONCLUSIONS

The current study shows that intralesional immunotherapy is the most effective, economical, and secure treatment option for cutaneous warts, taking into account its limitations. To arrive to a conclusive conclusion, further longitudinal research with bigger sample numbers and longer observation times is required.

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Group	After 1st session (21st day)				After 3rd session (63rd day)			
	Mild n (%)	Moderate n (%)	Severe n (%)	No n (%)	Mild n (%)	Moderate n (%)	Severe n (%)	No n (%)
I	28 (56)	4 (8)	0	18 (36)	12 (24)	6 (12)	28 (56)	4 (8)
II	44 (88)	0	0	6 (12)	2 (4)	4 (8)	38 (76)	6 (12)
III	44 (88)	2 (4)	0	4 (8)	1 (2)	0	42 (84)	6 (12)
IV	50 (100)	0	0	0	50 (100)	0	0	0

Table 1: Observation of efficacy in study subjects after 1st and 3rd sessions

Groups	Complete clearance				Total
	Local site		Distant site		
	n	%	n	%	
I	34	68	30	60	50
II	42	84	36	72	50
III	42	84	20	80	50
IV	50	100	0	0	50

Table 2: Results after three months of the last therapy session

Group	Side effects						Total
	None	Ulcers	Pain and swelling	Pain	Swelling	Mild swelling and erythema	
I	50	0	0	0	0	0	50
II	46	2	0	0	0	2	50
III	48	0	0	0	2	0	50
IV	0	0	4	46	0	0	50
Total	144	2	4	46	2	2	200

Table 3: Adverse effects seen in study subjects after therapy for warts