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NONSURGICAL ASSESSMENT OF INTRALESIONAL THERAPIES IN CUTANEOUS WARTS – RETROSPECTIVE CLINICAL STUDY

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ABSTRACT

Background: Treatment options for different kinds of cutaneous warts may vary depending on the place. Immunotherapy has been quite popular lately, particularly for cases with resistant warts.

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

Methods: The study included 200 people with numerous (>5) cutaneous warts. The subjects were randomly assigned to four groups, Group I, II, III, and IV, and received treatment with MMR, PPD, Candida extract, and Vitamin D, in that order. The intralesional injections were administered at three-week intervals for a maximum of three doses, with the wart chosen as the target based on the group. The response was seen in distant and target warts three months after the last injection.

Results: When it came to the removal of the target warts, intralesional vitamin D3 showed the most efficacy whereas MMR showed the lowest efficacy. Intralesional candida extract demonstrated the best efficacy in clearing remote warts, whereas vitamin D3 demonstrated the lowest efficacy. Intralesional candida extract was the most successful therapy for both distant and localised warts. The side effects were mild and only temporary.

Conclusion: The current study comes to the conclusion that the most effective, economical, and secure way to treat cutaneous warts is using intralesional immunotherapy.

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

INTRODUCTION

Verrucae or warts are defined as clinical cutaneous conditions that have benign proliferations on the mucosa and skin caused by the infection from HPV (Human papillomavirus). The prevalence of warts has increased in the recent past in various countries including India posing a high burden on the healthcare sector globally, especially in developing nations including India.[1]

Different therapeutic options for warts are available, such as occlusotherapy, topical immunologic therapy, virucidal medications, antiproliferative agents, surgery, local destructive therapy, and reassurance. Immunotherapy, which includes vitamin D3, Trichophyton antigens, tuberculin PPD (purified protein derivative), the MMR (measles, mumps, and rubella) vaccine, intralesional immunotherapy using Candida extract, and SADBE (squaric acid dibutyl ester) or DPC (diphencyprone), has become increasingly popular in the management of cutaneous warts in recent times.2,3

In addition to local therapy, systemic therapies can also be used to treat cutaneous warts. Skin warts have been treated with a variety of systemic medications, such as zinc sulphate, zinc oxide, histamine receptor 2 antagonists, and isotretinoin. The evidence from earlier studies in the literature suggests that the effectiveness of these treatments has been documented to vary.4

There is no one therapy that is consistently virucidal or successful in treating cutaneous warts; failures and recurrences are more frequent and greater among the existing treatment options. Depending on where the warts are located, various forms of warts may need different treatments, and occasionally, warts may require the use of multiple currently available treatment methods in combination. Immunotherapy has become quite popular, especially in the treatment of resistant warts, because of the cumbersome nature of the numerous destructive techniques and the high risk of recurrence that goes along with it.5

The current study set out to evaluate four immunotherapeutic agents—Vitamin D3, candida extract, PPD (purified protein derivative), and MMR (measles, mumps, and rubella)—in comparison for their effectiveness in treating multiple cutaneous warts.

MATERIALS AND METHODS

In order to compare the effectiveness 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, this prospective, randomised, interventional trial was conducted. The study's participants were from the Institute's Department of General Surgery. Prior to their involvement in the study, all research participants provided their informed permission, both in writing and verbally.

Two hundred individuals with cutaneous warts of both sexes participated in the research. The study's inclusion criteria were patients with cutaneous warts who were between the ages of 18 and 75, willing to engage in the research, and who had not previously received any other kind of therapy. Subjects without informed agreement to participate in the study, individuals having warts on their faces or genitalia, immunocompromised individuals, nursing mothers, and expectant mothers were among the exclusion criteria.

Following the ultimate enrolment of the research subjects, each participant had a thorough clinical examination and a history that was recorded in detail. In addition to the history, all subjects' demographic information was also documented, including their age, gender, marital status, and kind of employment. After that, a history of the warts was recorded, including any previous treatments received, how long they had existed, and when the lesions first appeared. Throughout the whole study, the data's anonymity was protected for each participant.

Blood investigations were conducted under rigorous aseptic and sterile settings at the baseline following inclusion to evaluate the results of the Mantoux test, the chest X-ray, and HbsAg (hepatitis B surface antigen) and HIV. Using a computer-generated, sealed envelope with simple random selection, all of the cutaneous wart participants were split into four treatment groups. Subjects were split into four equal groups (n = 50) at random and given the names Groups I, II, III, and IV. These groups received treatments with MMR, PPD, Candida extract, and vitamin D, in that order.

According to the group assigned, the target wart was the biggest wart in which immunogen was to be injected. in

situations where the wart's size significantly decreased in between sessions. The target wart for the session was selected among the remaining lesions based on its size. The wart that was not injected and was located apart from the target wart was arbitrarily designated as the remote location for the wart.6, 7

Every patient had their adverse effects, recurrence, and therapeutic effectiveness evaluated. The good response, which demonstrated a reduction of the target lesion's size and the number of lesions at a distant site by more than 75%, was considered indicative of the treatment's effectiveness. A 25–49% drop in the target lesion's size and the number of remote site lesions was considered a mild response, but a 50–74% decrease in both variables was considered a moderate response. A reduction of less than 25% in the size of the target lesion and the total number of lesions at distant locations was deemed to indicate a response. Three months following the final injectable dosage, follow-up was conducted with each subject.

RESULTS

In order to compare the effectiveness 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, a prospective, randomised, interventional trial was conducted. 200 participants with cutaneous warts of both sexes were included in the research. Participants were split into four groups at random, and the treatments given to Groups I, II, III, and IV were MMR, PPD, Candida extract, and vitamin D, in that order. Of the 200 participants in the research, 116 (58%), were men, and 84 (42%), were women.

Acral was the most often reported wart site. 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. Of the 196 individuals, 88% had warts less than 30 mm in size.

The first and third sessions were used to assess the effectiveness of the therapy in the study subjects. After 21 days, the results showed that at 56% (n=28), 8% (n=4), 0 and 36% (n=18) subjects from Group I, 88% (n=44), 0 and 12% (n=6) subjects from Group II, 88% (n=44), 4% (n=2), 0, and 8% (n=4) subjects from Group III, and 100% (n=50), 0, 0, and 0 from Group IV, respectively. On day sixty-three of the third session, mild, moderate, severe, and Table 1 displays the subjects for which no response was observed: 24% (n=12), 12% (n=6), 56% (n=28), and 8% (n=4) from Group I; 4% (n=2), 8% (n=4), 76$ (n=38), and 12% (n=6) from Group II; 2% (n=1), 0, 84% (n=42), and 12% (n=6) from Group III; and 100% (n=50), 0, 0, and 0 subjects from Group IV.

Following three months from the last therapeutic session, 68% (n = 34) and 60% (n = 30) of the individuals showed full clearance at distant locations. In Group II, 84% (n = 42) and 72% (n = 36) of the individuals showed full clearance at nearby and remote locations, respectively. Group III showed full clearance in 84% (n = 42) of the participants at nearby locations and 80% (n = 20) of the subjects at distant sites. As shown in Table 2, Group IV subjects saw complete clearance at local and distant locations in 100% (n=50) and no subjects, respectively.

Regarding intergroup comparability, The p-value for Group I vs Group II was 0.9315; the p-value for Group II versus Group III was 0.9909; the p-value for Group I versus Group III was 0.8513; and the p-value for 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. The findings of the study indicated a statistically significant difference between the overall response to therapy for warts with vitamin D3 and other immunotherapeutic drugs. Eight patients in Group I did not respond to the treatment and were treated using alternate techniques.

The study's findings indicated that, in terms of side effects observed by research participants following wart treatment, 100% (n=50) of individuals from Group I, 92% (n=46) of subjects from Group II, 96% (n=48) of subjects from Group III, and no patients from Group IV had any. Table 3 shows that only two participants from Group II had ulcers, four subjects from Group IV had pain and swelling, ninety-two percent (n=46) of the subjects from Group IV reported discomfort, two subjects from Group III only reported swelling, and two subjects from Group II had moderate swelling and erythema.

DISCUSSION

The 200 participants in this research, who had cutaneous warts, were of both genders. The participants were split into four groups at random, and the treatments given to Groups I, II, III, and IV were MMR, PPD, Candida extract, and vitamin D, in that order. Of the 200 participants in the research, 116 (58%), were men, and 84 (42%), were women. Acral was the most often reported wart site. Of the 106 individuals, 53% had disease duration of less than six months.

Of the individuals, 2% (n=4) reported having a positive family history. Of the 196 individuals, 88% had warts less than 30 mm in size. This result was similar to those of analyses conducted by Salah E et al. (2018) and Angeletti PC et al. (2008) on participants with warts using demographic information similar to that of the current investigation.

When it came to the study subjects' response to the first and third sessions, the results showed that at day 21, there was no response, mild, moderate, severe, and 8% (n=4), respectively, in 56% (n=28), 8% (n=4), 0, and 36% (n=18) subjects from Group I, 88% (n=44), 0, 0, and 12% (n=6) subjects from Group II, 88% (n=44), 4% (n=2), 0, and 8% (n=4) subjects from Group III, and 100% (n=50), 0, 0, and 0 from Group IV. Mild, moderate, severe, and no reaction were seen in 24% (n=12), 12% (n=6), 56% (n=28), and 8% (n=4) of the individuals from Group I, 4% (n=2), 8% (n=4), 76$ (n=38), and 12% (n=6) of the patients from Group II, 2% (n=1), 0, 84% (n=42), after the third session (on the sixty-third day) and Subjects from Group IV comprised 100% (n=50), 0, 0, and 0 subjects, whereas Group III had 12% (n=6) people.

The findings aligned with the research conducted by Shivkumar V et al. (2009) and Kwok CS et al. (2012), whose findings on the effectiveness of the therapy were in line with the findings of the current study.

According to research findings, 68% (n=34) and 60% (n=30) of individuals had full clearance at distant sites and local sites, respectively, three months following the last treatment session. In Group II, 84% (n = 42) and 72% (n = 36) of the participants had full clearance at nearby and remote locations, respectively. Group III showed full clearance in 84% (n = 42) of the participants at nearby locations and 80% (n = 20) of the subjects at distant sites.

In Group IV, 100% of the subjects (n = 50) and none of the subjects saw total clearing at nearby and remote locations, respectively. These results were consistent with those of investigations by Abdel Razik LH et al. (12 in 2021) and Thappa DM et al. (13 in 2016), the authors of which reported findings pertaining to local and distant clearance that were comparable to those of the current research.

The results of the intergroup comparison showed that the p-values for Group I vs Group II, Group II versus Group III, Group I versus Group IV, and Group I versus Group III were 0.9315, 0.9909, and 0.001, respectively. Group II vs Group IV had a p-value of 0.001, while Group III versus Group IV had a p-value of 0.001.

The total treatment response to vitamin D3 and other immunotherapeutic drugs in the treatment of warts differed statistically significantly, according to the study's findings. Eight patients in Group I did not respond to the treatment and were treated using alternate techniques. These outcomes were consistent with studies by Shaheen MA et al. (2015) and Abdel-Azim ES et al. (2020) that also found a considerable variation in the overall treatment response to vitamin D3 and other immunotherapeutic drugs when treating cutaneous warts.

The study results also showed that for the negative consequences seen in research participants following wart treatment, 100% (n=50) of individuals from Group I, 92% (n=46) of subjects from Group II, 96% (n=48) of subjects from Group III, and no subject from Group IV had any side effects. Only two patients from Group II had ulcers; four subjects from Group IV had pain and swelling; ninety-six percent of subjects from Group IV expressed pain; two subjects from Group III reported only swelling; and two subjects from Group II experienced minor swelling and erythema.

Similar side effects following immunotherapy for treating common warts were described by Agarwal C et al in 2018 and Ahmed R et al in 2020, according to the authors of these studies.

CONCLUSIONS

The current study shows that intralesional immunotherapy is the most effective, cost-effective, and secures therapeutic option for cutaneous warts, taking into account its limitations. To get a firm conclusion, further long-term research with bigger sample numbers and longer observation times is required in the future.

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TABLES

S. No	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 (%)
1.	I	28 (56)	4 (8)	0	18 (36)	12 (24)	6 (12)	28 (56)	4 (8)
2.	II	44 (88)	0	0	6 (12)	2 (4)	4 (8)	38 (76)	6 (12)
3.	III	44 (88)	2 (4)	0	4 (8)	1 (2)	0	42 (84)	6 (12)
4.	IV	50 (100)	0	0	0	50 (100)	0	0	0

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

S. No	Groups	Complete clearance				Total
		Local site		Distant site		
		n	%	n	%	
1.	I	34	68	30	60	50
2.	II	42	84	36	72	50
3.	III	42	84	20	80	50
4.	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