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RELATIVE EFFICACY AND SAFETY OF HOMOLOGOUS AUTOIMPLANTATION AND INTRALESIONAL MMR IN MULTIPLE AND RECALCITRANT VERRUCAE VULGARIS

Dermatology

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ABSTRACT

INTRODUCTION: Verrucae are the viral infection of skin and mucosae caused by Human Papilloma Virus (HPV). Destructive modalities, mainstay of treatment have their own shortcomings like pain, infection, scarring and recurrence. To overcome these, immunotherapy is the emerging modality.

MATERIALS AND METHODS: 40 patients with multiple (>5) and recalcitrant warts were enrolled and divided randomly into two groups (Group A and Group B): In Group A, autoimplantation was done in 20 patients whereas in Group B, 20 patients were injected 0.3ml MMR vaccine into the largest wart at 2 weeks interval until complete clearance or for maximum of 3 injections whichever was earlier. Patients were followed up at 4 week intervals for 12 weeks.

RESULTS: In Group A, 13 (65%) patients showed Grade 4, 1 (5%) patients had Grade 3 , 5 (25%) patients had Grade2 and only 1 (5%) patient had Grade 1 improvement. In Group B on the other hand, 15 (75%) patients showed Grade 4, 3 (15%) patients had G3, 2 (10%) patients had Grade 2 and 0 (8%) patients had Grade 1 improvement.

CONCLUSION: Both the immunotherapeutic treatments are safe, economic and less traumatic to the patients as compared to the destructive procedures for the treatment of warts.

KEYWORDS

Warts, Verrucae, Injection MMR, Autoinoculation

INTRODUCTION

Warts are benign hyperkeratotic protrusions caused by a virus, Human Papilloma Virus (HPV). They affect adolescent and adult age group frequently. Different treatment modalities are available and choice is made based on the type and site affected. There are chances of spontaneous regression of warts but due to unpredictability, cosmetic impairment and its psychosocial effects, treatment is necessary.[1] Destructive procedures like chemical cauterisation with TCA, salicylic acid and lactic acid; cryotherapy, radiofrequency ablation etc are currently most often used modalities. They have a number of disadvantages like scarring, pain, secondary infection, recurrence to name a few. Hence, treatment with immunotherapeutic agents which stimulate T cells and NK cells against the causative virus is a better option. In this study, we evaluated the clinical efficacy and safety of two such modalities i.e. autoimplantation therapy and MMR vaccine.

MATERIAL AND METHODS

For the present study, 40 patients of verruca vulgaris of 15-50 years with multiple >5 verruca of 3 or mire than 3 months were selected. Patients were divided into two groups of 20 patients each. After obtaining a written informed consent and investigations, procedure was done.

In Group A, autoimplantation was done. Tissue was pared with surgical blade no. 11 and transferred to glass slide and then minced. The recipient site i.e. anteromedial thigh was cleaned and anaesthetized, a incision was made in subcutis and minced tissue was inserted. Hemostasis achieved and wound closed with micropore tape. Oral antibiotics and analgesics given for five days. In Group B, the largest wart was injected with 0.3 ml MMR vaccine using insulin syringe. The procedure was repeated every 2 weeks till complete clearance or maximum of 3 treatment.In both the groups, follow up was done four weekly for a total of 12 weeks.

Assessment was done and grading done as follows:

Grade 0 = development of any new lesion or no response
Grade 1= <25% response in size and number of old lesions
Grade 2= 25-50% response in size and number of old lesions
Grade 3= 51-75% response in size and number of old lesions
Grade 4=>75% response in size and number of old lesions

RESULTS

In this study, mean age group of patients was 23.2±4.6yrm Males were involved more frequently than females in ratio of 3.4:1. The mean duration in Group A was 14.65±9.93 months and in Group B was 16.7±8.46 months. The mean number of warts in Group A was 14.65+8.43 and in Group B was 15.6+11.95. The mean size of the largest wart in Group A was 0.95± 0.31cm and in Group B was 1.02±0.41cm.

In Group A, at 12 weeks, 13 (65%) patients had grade 4 improvement (Figure 1), 1 (5%) had grade 3, 5(25%) had grade 2 and 1 (5%) patient had grade 1 improvement (Table 1). 1 (5%) patient developed infection whereas 4 (20%) patient developed post inflammatory hypopigmentation (Table 2). In Group B, at 12 weeks, 15 (75%) patients had grade 4 improvement (Figure 2), 3 (15%) had grade 3, 2 (10%) had grade 2 and none had grade 1 improvement (Table 1). 20 (100%) patients had developed pain during injection (Table 2). On analysis of therapeutic improvement at 12 weeks post treatment, there was no statistically significant difference between two groups (p value= 0.330).

TABLE 1 GRADING OF IMPROVEMENT AT THIRD VISIT (AT 12 WEEKS)

Grading of improvement	Group A		Group B		Total	
	No.	%	No.	%	No.	%
0	0	0.00	0	0.00	0	0.00
1	1	5.00	0	0.00	1	2.50
2	5	25.00	2	10.00	7	17.50
3	1	5.00	3	15.00	4	10.00
4	13	65.00	15	75.00	28	70.00
Total	20	100.00	20	100.00	40	100.00

TABLE 2 COMPLICATIONS IN GROUPS

Complications	No. of patients in Group A	No. of patients in Group B
Infection at site of implantation	1	0
Post inflammatory hypopigmentation at the site of lesions	4	3
Pain during injection	0	20
Flu like symptoms	0	1
Nil	15	0

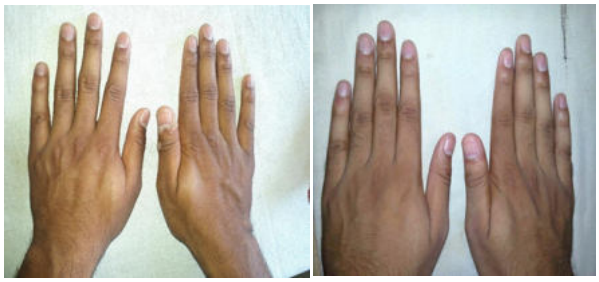

Figure 1: Showing Grade 4 improvement in Group A patients from (a) baseline (b) at 12 week follow up.

Figure 2: Showing Grade 4 improvement in Group B patients from (a) baseline (b) at 12 week follow up.

DISCUSSION

Treatment of the warts is frustrating for both patients and treating physicians. Immunotherapy is the current area of ongoing search. It act by stimulating immune system to work against the virus. It has added advantage of providing long term immunity from infection.[2]

Autoimplantation of wart is a novel, one time procedure which treats warts by stimulation of immune response against the virus.[3]

Shivkumar et al in 2009 enrolled 60 patients (40 having verruca vulgaris and 20 having palmo-plantar warts), clinical resolution was seen in 28 patients of verruca vulgaris (70%) and 16 of palmo-plantar warts (80%) within 3 months, accounting for a total clearance rate of 73.3%.[4]

Srivastava et al in 2010 enrolled 53 patients and 35 patients (66.03%) had complete disappearance of warts.[5] Similar results were found by Nischal et al in 2012 who reported complete remission in 74.1% patients.[3] In contrast to above results, a study by Kellapatha et al and Gugle et al in 2015 showed complete remission only in 36.7% patients and 49% patients respectively.[6,7]

Swaroop et al. in 2016 enrolled 40 patients of multiple recurrent cutaneous warts and modified homologous autoimplantation was used. 75% (28) patients showed complete clearance, while 22.5% (9) patients had partial clearance.[8]

V Suganthy in 2019 studied 100 patients with multiple warts. They were randomised into two groups,one was given cryotherapy and other received autoimplantation. The latter group had higher cure rate i.e 78% than cryotherapy group (56%). Complications were more frequently reported in cryotherapy group.[9]

In Group A, 1 (5%) patient developed infection at the site of implantation which had developed due to unhygienic practice which resolved with oral antibiotics therapy given for five days. 4 (20%) patients developed post inflammatory hypopigmentation which was also noted by Shivkumar et al and Lal et al in their studies.[4,10]

MMR is another form of immunotherapy where injection of these viral antigen lead to stimulation of cellular immunity and hence clearance of infection.

Gamil et al in 2010 studied 40 patients with plantar warts and injected MMR vaccine in the largest wart. Injections were repeated every 3 weeks. The results revealed complete clearance of the warts in 20 patients (87%), partial response in one patient (4.3%) and no response in two patients (8.7%).[11]

Mohamad et al in 2013 studied 100 patients complaining of plantar warts, distributed into two groups. One group was injected with MMR vaccine and other with normal saline. MMR-treated group showed significantly higher rate of complete clearance compared with the control group (82% versus 0% respectively).[12]

Contrasting results were reported by Na et al and Nofal et al in 2014 in their studies with complete clearance in 51.5% and 63% patients respectively.[13,14]

However, in later studies like study done by Shaheen et al in 2015, better results were seen with MMR vaccine. He compared MMR with PPD and found MMR to be better than PPD, with 60% response in the PPD group and 80% in the MMR group.[15]

Pushpendra Singh et al in 2019 conducted study on patients with common warts, 110 in total. They were injected with 0.25 ml MMR vaccine intralesionally into the largest wart. This procedure was repeated fortnightly until clearance was observed completely or for a maximum of five doses. Out of 51 patients who completed the study, complete results were found in 42 (82.4%) patients whereas 9 (17.6%) patients showed good or unsatisfactory results.[16]

In Group B, all patients experienced pain during injection, 1 (5%) patient had flu like symptoms which resolved in 1 to 2 days with anti inflammatory drugs, 3 (15%) patients had developed post inflammatory hypopigmentation. Nofal also noted pain during injection and flu like symptoms.[14] Gamil et al also noted pain during injection in 82.5% of cases and flu like symptoms in 4.3% of cases.[10]

Both the immunotherapeutic treatments are safe, economic and less traumatic to the patients as compared to the destructive procedures. Fewer sittings are required in both the therapies as compared to destructive procedures with good results. However, there is scarcity of data on comparison of both the therapies.

ElGhareeb in 2019 studied 80 patients and divided them into two groups, each containing 40 patients. Group A patients were treated by autoimplantation technique every 2weeks for a maximum of our treatments. Similarly, Group B patients received MMR intralesional injection at a dose of 0.5ml every 2 weeks for a maximum of four treatments. Complete clearance of the donor wart was observed in 60% patients in Group A, whereas complete clearance in the Group B was 72.5%.[17] Our findings are consistent with this study.

To conclude, both the techniques were found to be safe and effective with comparable efficacy for achieving the improvement in multiple and recalcitrant verruca vulgaris with minimal side effects. But as the clinical response was marginally more in case of intralesional MMR vaccine injection than the homologous autoimplantation and ease with which the injection can be given in a busy outpatient department it can be suggested that the intralesional injection of measles, mumps and rubella vaccine is the method of choice between the two treatment modalities though it was not statistically significant.

The limitations of our study were that the sample size was small. The control group with placebo to assess spontaneous resolution was not taken. The patients with complete response were not graded separately. Due to time constraints the follow up period was of 12 weeks but resolution or improvement in grading can occur even after 12 weeks.

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