Journal of Medicine, Physiology and Biophysics
ISSN 2422-8427 An International Peer-reviewed Journal
Vol.38, 2017

Efficacy of Intralesional MMR Vaccine Versus Cryotherapy in the Treatment of Viral Warts

DR. RABIA ALI, MBBS
NISHTAR HOSPITAL, MULTAN

DR. RAMSHA MEHAK, MBBS
NISHTAR HOSPITAL, MULTAN

DR. SAJIDA PERVEEN, MBBS
NISHTAR HOSPITAL, MULTAN

Abstract:
Background: Viral warts (verrucae) are extremely common. Although many will spontaneously disappear without treatment, treatment may be sought for a variety of reasons such as discomfort. There are a number of different treatments for cutaneous warts, with salicylic acid, immunotherapy and cryotherapy using liquid nitrogen being two of the most common forms of treatment. **Objective:**To determine the efficacy of intralesional MMR vaccine versus cryotherapy in the treatment of viral warts. **Material and Methods:** Patients were randomly allocated in to two groups by lottery method. Group A, having 32 patients, was injected with intralesional MMR vaccine (0.3ml) into the largest wart using an insulin syringe. The injection was given on alternate weeks for maximum of 5 sessions. Group B, also having 32 patients, was given cryotherapy by applying liquid nitrogen with a cotton tip applicator for 10 to 30 seconds until the ice ball formation spreads to involve 1mm margin of surrounding normal skin, at weekly interval for maximum of 8 sessions. Patients of both groups were followed up at 2nd, 4th, 6th, 8th, 10th and 12th week. Those who cleared their warts on follow up visits were not given further treatment. At the end of 12 weeks both groups were evaluated for treatment efficacy. **Results:** Of these 64 study cases, 26 (40.625%) were males and 38 (59.375%) were females. Mean age of our study cases was 27.59 ± 3.99 years (with minimum age was 20 years while maximum age was 35 years). Mean age of our study cases in patients treated with intraleisonal MMR was 28.19 ± 3.95 years while patients treated with cryotherapy was 27.00 ± 4.07 years. Mean weight of our study cases was 64.06 ± 6.16 kilograms (with minimum weight was 54 kilograms and maximum was 78 kilograms). Mean weight in group A was 65.19 ± 6.52 kilograms while in Group B was 62.94 ± 5.67 kilograms. Majority of our study cases i.e. 46 (71.875%) were having weight over 60 kilograms. Size of lesion was less than 1 cm in 36 (56.25%) of our study cases while in remaining 28 (43.75%) was in the range of 1 to 1.5 centimeters. In 40 (62.5%) of our study cases, number of lesions was 5-6. Mean no. of lesions was 2.48 ± 1.35. Mean no. of lesions in group A was 6 ± 0.88 while in group B was also 6 ± 0.88. Mean duration of disease was 1.844 ± 0.67 months (with minimum duration was 1 month while maximum duration was 3 months). Our study results have indicated that majority of our study cases i.e. 44 (68.75%) were having disease for more than 1.5 months. Mean duration of disease in group A was 1.94 ± 0.67 months while in group B was 1.75 ± 0.67 months. In group A efficacy was noted in 22 (68.75%) of our study cases, while in group B efficacy was seen in 20 (62.5%) of our study cases. Majority of our overall study cases were in middle socioeconomic group. While in Group A 50% were in high, 43.75% in middle and 6.25% in low socioeconomic group. In Group B 50% was in middle, 31.25% in low and 18.75 in high socioeconomic group.**Conclusion:** Efficacy of intraleisonal MMR injection is more than cryotherapy. It can be safely used for the treatment of viral warts, as no serious side effects were observed in our study. Being cost effective, it provides cheaper treatment option compared with cryotherapy which is quite expensive. Early treatment can help patients to maintain routine daily lives and physical activities such as sports without any pain and side effects.
Keywords: Intraleisonal MMR, Salicylic acid, Cryotherapy, warts.

Introduction:

Warts are firm papules with a rough surface, caused by human papillomavirus (HPV) infection. They range in size from less than 1mm to over 1 cm and by confluence can form large masses[1]. Different clinical forms of warts include common warts, palmoplantar warts, flat warts, filiform warts and anogenital warts[2]. HPV is a small DNA virus that infects squamous epithelium and causes cell proliferation[1]. It has 29 genera formed by 189 genotypes of which 120 types are isolated from humans[3]. Viral warts and common warts are caused by types 1,2,4,27,29[2,4]. The incidence of viral warts is found to be 12.94%.[4]

Different methods of treatment for warts include occlusion, topical salicylic acid, cryotherapy, electrocautery, laser, topical chemotherapeutic agents, topical retinoic acid, oral cimetidine and immunotherapy[2]. But no single therapy has been proven effective at achieving complete remission in every patient.

Cryotherapy is one of the most commonly used methods for treating warts. It involves freezing a wart with

the use of a very cold substance, usually liquid nitrogen. The studies done previously on cryotherapy showed variable cure rates ranging from 39%[5] to 76.5%[6]. One study showed 41.7%[7] cure rate with cryotherapy.

Topical salicylic acid is another very common treatment for warts. Salicylic acid has keratolytic effect [8,9]. It reduces the thickness of the warts[1] by causing mechanical removal of epidermal cells infected with virus. In one study the results of 6 trials were combined and it showed that topical salicylic acid had 75% cure rate[8]. Another study showed 69%[9] cure rate. Cryotherapy is considered a standard treatment for most warts[2]. Many studies show that it is superior in efficacy when compared to other treatment option for warts. But a study combining the results of 6 trials[8] showed that topical salicylic acid therapy is safe and effective and there is no clear evidence that other therapies are better than this. Salicylic acid, for topical use, is available over the counter and is very cheap. But cryotherapy is not available in all hospitals, in our country and is a lot more costly[10]. On an average 3 to 4 visits to a doctor's office are required for cryotherapy[10]. But topical salicylic acid can be applied at home. Also, cryotherapy is more painful than topical salicylic acid application[10, 11].

Immunotherapy using intralesional MMR vaccine is a new therapeutic modality in the treatment of viral warts. Immunotherapy appears to enhance the recognition of the virus by the immune system; this allows clearance of treated as well as distant warts and helps to prevent future clinical infection through induction of a long-term immunity to HPV [12-15]. This study was conducted to compare two treatment modalities; the immunotherapy and cryotherapy in the treatment of warts.

Material and methods:

Patients with warts attending the dermatology out-patient department were included in the study. Approval from ethical committee of the hospital was taken. Disease was diagnosed on the basis of clinical features while Pregnant ladies, lactating mothers and patients not willing to participate. Written informed consent was taken from every patient. Patients were randomly allocated in to two groups by lottery method. Group A, having 32 patients, was injected with intralesional MMR vaccine (0.3ml) into the largest wart using an insulin syringe. The injection was given on alternate weeks for maximum of 5 sessions. Group B, also having 32 patients, was given cryotherapy by applying liquid nitrogen with a cotton tip applicator for 10 to 30 seconds until the ice ball formation spreads to involve 1mm margin of surrounding normal skin, at weekly interval for maximum of 8 sessions. Patients of both groups were followed up at 2nd, 4th, 6th, 8th, 10th and 12th week. Those who cleared their warts on follow up visits were not given further treatment. At the end of 12 weeks both groups were evaluated for treatment efficacy. All data was entered and processed using software SPSS version 18. Mean and standard deviation were calculated for age, weight, gender, size of warts, number of lesions and duration of disease of patients. Frequencies and percentages were calculated for gender and efficacy of drugs in both groups.

Results:

Our study included a total of 64 cases of viral warts from OPD of Dermatology department of Nishtar Hospital Multan. Our study included 26 (40.625%) males and 38 (59.375%) were females. Mean age of our study cases was 27.59 ± 3.99 years (with minimum age was 20 years while maximum age was 35 years). Mean age of our study cases in patients treated with intraleisonal MMR was 28.19 ± 3.95 years while patients treated with cryotherapy was 27.00 ± 4.07 years. Mean weight of our study cases was 64.06 ± 6.16 kilograms (with minimum weight was 54 kilograms and maximum was 78 kilograms). Mean weight in group A was 65.19 ± 6.52 kilograms while in Group B was 62.94 ± 5.67 kilograms. Majority of our study cases i.e. 46 (71.875%) were having weight over 60 kilograms. Size of lesion was less than 1 cm in 36 (56.25%) of our study cases while in remaining 28 (43.75%) was in the range of 1 to 1.5 centimeters. In 40 (62.5%) of our study cases, number of lesions was 5-6. Mean no. of lesions was 2.48 ± 1.35. Mean no. of lesions in group A was 6 ± 0.88 while in group B was also 6 ± 0.88. Mean duration of disease was 1.844 ± 0.67 months (with minimum duration was 1 month while maximum duration was 3 months). Our study results have indicated that majority of our study cases i.e. 44 (68.75%) were having disease for more than 1.5 months. Mean duration of disease in group A was 1.94 ± 0.67 months while in group B was 1.75 ± 0.67 months. In group A efficacy was noted in 22 (68.75%) of our study cases, while in group B efficacy was seen in 20 (62.5%) of our study cases. Majority of our overall study cases were in middle socioeconomic group. While in Group A 50% were in high, 43.75% in middle and 6.25% in low socioeconomic group. In Group B 50% was in middle, 31.25% in low and 18.75 in high socioeconomic group.

Table No. 1
Distribution of study cases by Efficacy.
(n = 64)

Efficacy (n=64)	Group A		Group B	
	Frequency	**%**	**Frequency**	**%**
Yes n=42 (65.625%)	22	68.75	20	62.5
No n=22 (34.375%)	10	31.25	12	37.5
P – value	**0.001**			

Discussion:
Our study included 26 (40.625%) males and 38 (59.375%) were females. Cockayne et al [16] reported 59 % female patients in their study and 41 % male patients, these findings are similar to our study results. Bruggink et al [5] reported 56% female patients, in our study female gender was also predominated over males. Mean age of our study cases was 27.59 ± 3.99 years (with minimum age was 20 years while maximum age was 35 years). Mean age of our study cases in patients treated with intraleisonal MMR was 28.19 ± 3.95 years while patients treated with cryotherapy was 27.00 ± 4.07 years. Cockayne et al [16] reported 24.3 years and 23.2 years, these findings are close to that of our study results. Mean weight of our study cases was 64.06 ± 6.16 kilograms (with minimum weight was 54 kilograms and maximum was 78 kilograms). Mean weight in group A was 65.19 ± 6.52 kilograms while in Group B was 62.94 ± 5.67 kilograms. Majority of our study cases i.e. 46 (71.875%) were having weight over 60 kilograms. Size of lesion was less than 1 cm in 36 (56.25%) of our study cases while in remaining 28 (43.75%) was in the range of 1 to 1.5 centimeters.

In 40 (62.5%) of our study cases, number of lesions was 5-6. Mean no. of lesions was 2.48 ± 1.35. Mean no. of lesions in group A was 6 ± 0.88 while in group B was also 6 ± 0.88. Cockayne et al [16] reported mean value to be 3.4 ± 3.6 in those treated with cryotherapy. This finding is bit lower than our study results, the reason for this difference can be explained in the fact that we included only those with maximum no. of 7 lesions while Cockayne et al included as many as 55 lesions (maximum value). Bruggink et al [5] reported median no. of lesions as 2 lesions in both groups which is also lower than our findings. Mean duration of disease was 1.844 ± 0.67 months (with minimum duration was 1 month while maximum duration was 3 months). Our study results have indicated that majority of our study cases i.e. 44 (68.75%) were having disease for more than 1.5 months. Mean duration of disease in group A was 1.94 ± 0.67 months while in group B was 1.75 ± 0.67 months. Cockayne et al [16] reported very high duration of disease, this difference is also due to our inclusion criteria as we only included with 3 months maximum disease duration cases. Majority of our overall study cases were in middle socioeconomic group. While in Group A 50% were in high, 43.75% in middle and 6.25% in low socioeconomic group. In Group B 50% was in middle, 31.25% in low and 18.75 in high socioeconomic group. In group A efficacy was noted in 22 (68.75%) of our study cases, while in group B efficacy was seen in 20 (62.5%) of our study cases. Similar results have been reported by Cockayne et al [16]. Bruggink et al [5] reported 39 % cure rate with cryotherapy. Dhar et al[6] reported 76.5 % cure rate with Cryotherapy. Our findings are in middle of these range values as reported by Bruggink et al[5] and Dhar et al[6]. Nofal et al [17] reorted 74.5% cure rate with intraleisonal MMR, while Gamil et al [18] reported 87 % cure rate with that of intraleisonal MMR. These findings of Gibbs et al and Bart et al are close to our study results.

Conclusion:
Efficacy of intraleisonal MMR injection is more than cryotherapy. It can be safely used for the treatment of viral warts, as no serious side effects were observed in our study. Being cost effective, it provides cheaper treatment option compared with cryotherapy which is quite expensive. Early treatment can help patients to maintain routine daily lives and physical activities such as sports without any pain and side effects.

References:
1. Sterling J; Virus infections. In: Burns T, Breathnach S, Cox N, Griffiths C. editors. Rook's textbook of dermatology. 8th ed. UK: Wiley- Blackwell. 2010;33.37-59.
2. Androphy EJ, Kirnbauer R; Human papillomavirus infections. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Wolff K. editors. Fitzpatrick's dermatology in general medicine. 8th ed. New york: Mc Graw-Hill. 2012;2421-33.

3. Bernard H, Burk RD, Chen Z, Doorslaer KV, Hausen HZ, de Villiers EM. Classification of papillomaviruses based on 189 PV types and proposal of taxonomic amendments. J Virol. 2010;401(1):70-9.
4. Gaston A, Garry RF. Topical vitamin A treatment of recalcitrant common warts. J Virol. 2012;9:21.
5. Bruqqink SC, Gussekloo J, Berger MY, Zaaijer K, Assendelft WJ, de Waal MW et al. Cryotherapy with liquid nitrogen versus topical salicylic acid application for cutaneous warts in primary care: randomized controlled trial. J Can Med Assoc. 2010;182(15):1624-30.
6. Dhar SB, Rashid MM, Islam A, Bhuiyan M. Intralesional bleomycin in the treatment of cutaneous warts: a randomized clinical trial comparing it with cryotherapy. Indian J Dermatol Venerol Leprol. 2009;75(3):262-7.
7. Kacar N, Tasli L, Ergin S, Erdogan BS. Cantharidin-podophylotoxin-salicylic acid versus cryotherapy in the treatment of plantar warts: a randomized prospective study. J Eur Acad Dermatol Venerol. 2012;26(7):889-93.
8. Gibbs S, Harvey I, Stark R. Local treatments for cutaneous warts: systematic review. Br Med J. 2002;325(7362):461.
9. Bart BJ, Biglow J, Vance JC, Neveaux JL. Salicylic acid in karaya gum patch as a treatment for verruca vulgaris. J Am Acad Dermatol. 1989;20(1):74-6.
10. Bagelieri R, Johnson SM. Cutaneous warts: an evidence based approach to therapy. Am Fam Physician. 2005;72(4):647-52.
11. Lipke MM, An armamentarium of wart treatments. Clin Med Res. 2006;4(4):273-93.
12. Bacelieri R, Johnson SM. Cutaneous warts: an evidence based approach to therapy. Am Fam Physician. 2005;72(4):647-52.
13. Loo SK, Tang WY. Warts (Non-genital). Am Fam Physician. 2010;81(8):1008-1009.
14. Patel H, Wagner M, Singhal P, Kothari S. Systematic review of the incidence and prevalence of genital warts. BMC infectious dis. 2013;13:39. doi:10.1186/1471-2334-13-39.
15. Bruggink SC, Gussekloo J, Zaaijer K, Assendelft WJJ, Berger MY, Koes BW, et al. Warts: cryotherapy, salicylic acid or expectantly awaiting? A randomised controlled trial. J Invest Dermatol 2008;128:8.
16. Cockayne S, Hewitt C, Hicks K, , , , et al. Cryotherapy versus salicylic acid for the treatment of plantar warts (verrucae): a randomised controlled trial. BMJ 2011;342:d3271.
17. Nofal A, Nofal E, Yosef A, Nofal H. Treatment of recalcitrant warts with intralesional measles,mumps, and rubella: a promising approach. Int J Dermatol. 2014 Jul 29. doi: 10.1111/ijd.12480.
18. Gamil H, Elgharib I, Nofal A, Abd-Elaziz T. Intralesional immunotherapy of plantar warts: report of a new antigen combination. J Am Acad Dermatol. 2010 Jul;63(1):40-3.