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A Comparative study of effectiveness of measles–mumps–rubella vaccine versus salicylic acid–lactic paint in the treatment of Cutaneous warts in a tertiary care centre

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ABSTRACT
Background: Cutaneous warts (verrucae) are benign, epithelial tumors characterized by the formation of thick, hyperkeratotic lesions. Human papillomavirus (HPV) is a double-stranded DNA virus, and is responsible for the appearance of warts. The basis of immunotherapy is the manipulation of the immune system to achieve a human papilloma virus targeted immune reaction.This paper is intendedto compare the effectiveness of measles, mumps, and rubella (MMR) vaccine immunotherapy and Salicylic acid–lactic (SAL) pain in managing common warts.**Material and methods:**This study was conducted at Department of Skin and VD, Nalanda Medical College and Hospital, Patna,fortheperiod of 1 year from Mar 2019 to Feb 2020, on 100 patients with cutaneous wart dividedinto two groups A & B i.e. MMR and SAL of 50 each. **Results:**Studied 100 patients ofCutaneous warts in skin outpatients in a tertiary care centre and found that mean age of patients were 31.24 ± 14.97 years and maximum patient belonged the age group 21-30 years i.e. 42 (42.00%) Most of the patients in MMR vaccine Group A showed excellent result i.e.28 cases (56.00%) in comparison to SAL Group B i.e. 07cases (14.00%) respectively. Only 04 i.e. 08.00% in-group A but 14 i.e. 28.00% in-group B showed no response. Most common excellent response showed in 31 males and 04 females i.e. 88.57% & 11.43% respectively no response given by 04 males and 14 females i.e. 22.22% & 77.78% respectively. **Conclusion:**Despite the study's limitations, it was discovered that intra-lesional MMR vaccine as an immunotherapy is an emerging technique of treatment for multiple warts with lower recurrence rates.

Key words: Measles, Mumps, and Rubella (MMR) vaccine, Salicylic acid–Lactic (SAL) paint, Warts

I. INTRODUCTION:

Cutaneous warts (verrucae) are benign, epithelial tumors characterized by the formation of thick, hyperkeratotic lesions. Human papillomavirus (HPV) is a double-stranded DNA virus, and is responsible for the appearance of warts. Virus particles reside in the basal layer of epithelia, but replicate only in the well-differentiated, superficial layer. The ensuing cellular proliferation gives rise to the characteristic morphology of warts. Several types of cutaneous warts have been described: common warts (verrucae vulgaris), plantar warts (verrucae plantaris), and flat warts (verruca planus). Although verrucae are more frequently encountered in children and young adults, all ages may be affected. At particular risk are immunocompromised individuals. Human papillomavirus may be transmitted indirectly through contact with the skin of an infected individual or by transmission of virus that has survived in warm, moist environments. The virus may also be transferred from one site to another when autoinoculation occurs upon traumatizing warts by scratching or biting. The incubation period is unknown, but may be several months or years. Viral warts are common, benign, and usually self-limiting skin lesions that occur usually on the hands and feet [1].At least 90 different types of HPV have been determined using hybridization and polymerase chain reaction techniques. There is a definite association between HPV type and predilection for certain anatomic sites (Table 1). Types 1,2, and 4 are associated with common and plantar warts. Common warts are located preferentially on the hands, especially the periungual region, but may develop anywhere on the skin including the palmar and plantar surfaces, the face, neck, and lips. Plantar warts (vermcae plantaris) are more common in adolescents and young adults, perhaps because of inadequate

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maturity of the immune system, repetitive microtrauma to the foot occurring in sports, use of public showers or excessive perspiration. These warts exhibit a tendency to develop on weight-bearing areas of the foot such as the heel or metatarsal heads where abrasions and calluses occur. Human papillomavirus types 1,2, and 4 have been isolated from plantar warts. About one third of patients with warts have plantar warts or a variant (mosaic, myrmecia). The incidence of cutaneous warts is around 150 per 100000 population [2].The spontaneous resolution rate for warts is 65-78%. The associated cosmetic disfigurement, tendency to spread and the associated poor quality of life makes it necessary to intervene faster. Management of palmoplantar and periungual warts are usually painful, unsightly and prone for recurrences. There are various destructive and immunotherapeutic treatment modalities for cutaneous warts, but no single treatment has yet proven to be 100% effective [3].

The basis of immunotherapy is the manipulation of the immune system to achieve a human papilloma virus targeted immune reaction. Injection of viral antigen results in peripheral blood mononuclear cell proliferation, promoting Th1 cytokine responses, particularly interferon gamma and interleukin 2,4. This causes activation of cytotoxic T cells and natural killer cells that eradicates the human papilloma viral infected cells. Immunotherapy also stimulates tumour necrosis factor α and interleukin 1 release, downregulating gene transcription of HPV virus. The various agents used in immunotherapy of warts include topical agents like imiquimod, sinecatechins, BCG and intralesional agents like Mw vaccine, BCG vaccine, PPD, MMR vaccine, candida extract, trichophyton antigen, tuberculin, vitamin D3 and interferon alpha 2B [4]. Salicylic acid–lactic paint is a keratolytic agent useful in the removal of warts with minimal discomfort and a low risk of scarring. Therapy with salicylic acid–lactic paint in its various forms requires persistence; the patient at home applies the daily treatment for a period of weeks to months. Cure rates for common hand warts and plantar verrucae have varied between 70% and 80% [5-8]. This paper is a pointer toward measles, mumps, and rubella (MMR) vaccine immunotherapy and salicylic acid–lactic paint effectiveness in managing cutaneous warts.

Table 1: Clinical presentation and HPV type

Clinical presentation	Common HPV types
Common warts	1,2,4,26-29
Plantar warts	1,2,4,63
Flat warts	3,10,26-29,41
Butcher's warts	7
Epidermodysplasia verruciformis	5,8,9,12,14,15,17,19-25,36-38,46

II. MATERIAL AND METHODS:

Place of study: Department of Dermatology, Nalanda Medical College & Hospital, Patna. **Type of study:** Non-Randomised Prospective Study. **Target population:** Patients with Cutaneous wart attending Dermatology outpatient department. **Study population:** Patients with cutaneous wart attending Dermatology outpatient department. **Duration:** A total 100 patients were included for the study over a period of 1 year from Mar 2019 to Feb 2020.

The patients were randomly divided into two groups with the help of random number table-Group A and B, each containing 50 patients each. Group A patients were given 0.3 mL of MMR vaccine intralesionally in the largest wart. Four injections were given every 2 weeks. Patients were followed up every 2 weeks and the last follow-up visit was scheduled 2 months after the last injection. Lesion count and reduction in the size of lesions were noted at each visit. The lesions were graded by percentage reduction in size of the largest lesion and also reduction in the lesion count. Group B patients were given SAL paint (composition: salicylic acid 16.7% and lactic acid 16.7% in flexible collodion base) for local application on the warts. Before application of SAL paint, lesions were pared down and/or soaked in warm water for at least 5 min. SAL paint was then applied to the warts twice a week for a maximum period of 2 months and stopped earlier if the lesions disappeared. Overall, the patients werecalled for four follow-up visits, first three visits 2 weeks apart and the last follow-up visit was scheduled 2 months after the third follow-up visit. For socio-economic status, modified BG Prasad classification 2020 was used.

Patients who presented to the outpatient department of dermatology with cutaneous warts anywhere on the body other than the anogenital area clearance from the ethical committee of the institution was obtained. Included patients were 15

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to 50 years of age with single or multiple extra-genital warts for duration of at least one month without using anti-wart treatments for the last one month. Exclusion criteria included prior hypersensitivity reaction to MMR antigen, pregnancy/lactation, presence of any active infections (e.g., herpes), tuberculosis, chronic diseases (e.g., diabetes mellitus), hypertension, immunosuppression (e.g., human immunodeficiency virus [HIV]) or if the patient was taking immunosuppressives, and patients who were non-adherent. All of the patients who fulfilled the inclusion criteria underwent clinical examination to confirm the diagnosis of wart. In suspicious cases, a biopsy for histopathological confirmation was done. Detailed history was taken to note the duration, number of warts, and the sites involved. Demographic details including age and sex were noted. Photographic documentation was done. Written consent was obtained from all of the patients.

Assessment: The response to treatment was evaluated as follows: Grade 1: no response, Grade 2: 1%–25% reduction in size – poor response, Grade 3: 26%–50% reduction in size – good response, Grade 4: 51%–75% reduction in size – fair response, and Grade 5: complete disappearance of lesion – excellent response. Size of the lesion was assessedby measuring tape [9].

III. DATA ANALYSIS:

The collected data were analysed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis was used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference between the bivariate samples in Independent groups the unpaired sample t-test was used. To find the significance in categorical data Chi-Square test was used. In all the above statistical tools the probability value 0.05 is considered as significant level.

IV. RESULTS:

A prospective study was conducted in the Department of Dermatology, Nalanda Medical College & Hospital, Patna, from Mar 2019 to Feb 2020. A total of 100 patients who were clinically diagnosedwith cutaneous warts were included in the study.

Table 1: Demographic profile of studied cases

Variables	**MMR Vaccine Group A (N=50)**	**SAL Group B (N=50)**	**Total**
Age in years			
<20 years	12(24.00%)	09 (18.00%)	21 (21.00%)
21-30 years	19 (38.00%)	23 (46.00%)	42 (42.00%)
31-40 years	09 (18.00%)	11 (22.00%)	20 (20.00%)
41-50 years	07 (14.00%)	03 (06.00%)	10 (10.00%)
51-60 years	03 (06.00%)	04 (08.00%)	07 (07.00%)
Mean ± S.D	31.24 ± 14.97 years		
P-value	The chi-square statistic is 2.7524. The p-value is 0.60008. The result is not significant at p <0.05.		
Total	50	50	100
Gender			
Male	31 (62.00%)	34 (68.00%)	65 (65.00%)
Female	19 (38.00%)	16 (32.00%)	35 (35.00%)
Total	50	50	100
Socio-economic status (According to modified BG Prasad classification)			
I	02 (04.00%)	01 (02.00%)	03 (03.00%)
II	07 (14.00%)	05 (10.00%)	12 (12.00%)
III	23 (46.00%)	21 (42.00%)	44 (44.00%)
IV	11 (22.00%)	17 (34.00%)	28 (28.00%)
V	07 (14.00%)	06 (12.00%)	13 (13.00%)

MMR: Measles–mumps–rubella vaccine**,** SAL**:** Salicylic acid–lactic paint, SD: Standard deviation

Studied 100 patients ofcutaneous wartsin skin outpatients in a tertiary care centre and found that mean age of patients were 31.24 ± 14.97 years

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and maximum patient belong to age group 21-30 years i.e. 42 (42.00%) [19 i.e. 38.00% in-group A and 23 i.e. 46.00% in-group B] and minimum from 51-60 years i.e. 07 (07.00%) [03 i.e. 06.00% in-group A and 04 i.e. 08.00% in-group B] respectively. Most of the cases were males i.e. 65 (65.00%) [31 i.e. 62.00% in-group A and 34 i.e. 68.00% in-group B] and mostly patient belong to Socio-economic statusIII i.e. 44 (44.00%) %) [23 i.e. 46.00% in-group A and 21 i.e. 42.00% in-group B].

Table 2: Response to treatment

Response	**MMR Vaccine Group A (N=50)**	**SAL Group B (N=50)**	**Overall response**
Grade 5: Excellent	28 (56.00%)	07 (14.00%)	35 (35.00%)
Grade 4: Fair	10 (20.00%)	08 (16.00%)	18 (18.00%)
Grade 3: Good	03 (06.00%)	05 (10.00%)	08 (08.00%)
Grade 2: Poor	05 (10.00%)	16 (32.00%)	21 (21.00%)
Grade 1: No Response	04 (08.00%)	14 (28.00%)	18 (18.00%)
P-value	The chi-square statistic is 24.6397. The p-value is 0.000059. The result is significant at $p < 0.05$.		

Most of the patients in MMR vaccine Group A showed excellent result i.e.28 (56.00%) cases in comparison to SAL Group B i.e. 07 (14.00%) respectively.

Only 04 i.e. 08.00% in-group A but 14 i.e. 28.00% in-group B showed no response.

Table 3: Response to treatment with respect to gender.

Response	**Male**	**Female**	**Overall response**
Grade 5: Excellent	31 (47.69%)	04 (11.42%)	35 (35.00%)
Grade 4: Fair	17 (26.15%)	01 (02.86%)	18 (18.00%)
Grade 3: Good	06 (09.23%)	02 (05.72%)	08 (08.00%)
Grade 2: Poor	07 (10.76%)	14 (40.00%)	21 (21.00%)
Grade 1: No Response	04 (06.15%)	14 (40.00%)	18 (18.00%)
Total	65 (100.00%)	35 (100.00%)	100 (100.00%)
P-value	The chi-square statistic is 39.4942. The p-value is < 0.00001. The result is significant at $p < 0.05$.		

Most common excellent response showed in 31 males and 04 females i.e. 88.57% & 11.43% respectively no response given by 04 males and 14 females i.e. 22.22% & 77.78% respectively.

Fig 1: Therapeutic effect of intra-lesional MMR vaccine – before and after

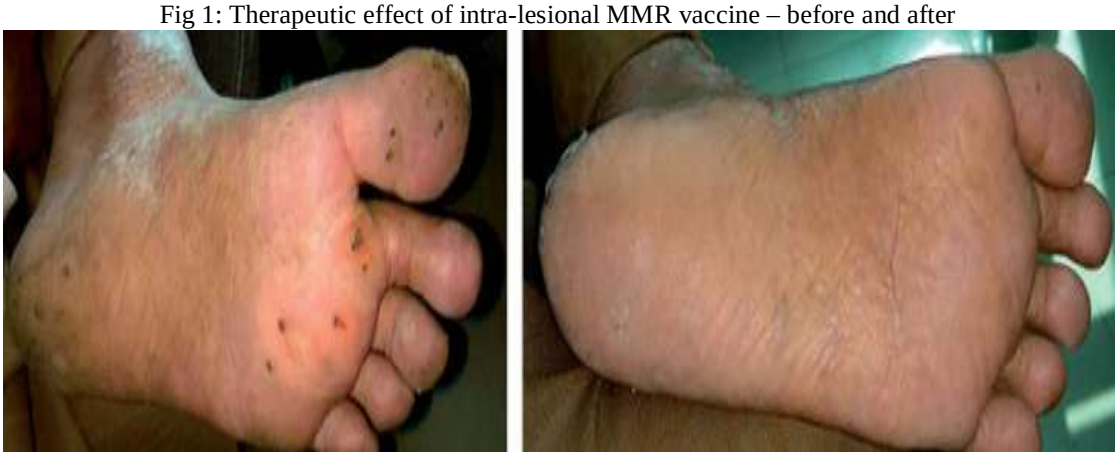

Fig 2: Therapeutic effect of intra-lesional MMR vaccine – before and after

V. DISCUSSION:

Hence, receiving MMR vaccine rather than SAL paint. The findings of this study also showed that there was relapse seen in patients applying SAL paint. No important adverse effects were reported in any of the patients in both therapeutic groups, except pain at the time of injections. Warts with shorter duration (<6 months) responded better when compared with the ones present for a longer duration (>6 months).

In another study, With the MMR vaccine, Gamil et al. reported an 87 percent complete cure, 4.3 percent relative cure, and 8.7% no cure. According to the authors of this study, MMR vaccine may have a beneficial therapeutic effect in the treatment of warts, and comparable findings were found in our study [10]. Saini et al. observed 46.5 percent full clearance in 40 of 86 patients, with individuals with shorter disease duration responding better, which is similar to our findings [11].Studied 100 patients ofcutaneous warts in skin outpatients in a tertiary care centre and found that mean age of patients were 31.24 ± 14.97 years and maximum patient belong to age group 21-30 years i.e. 42 (42.00%). Similarly Deshmukh AR et al [9] found most of the patients belonged to the age group of 18–25 years, of which 28 (46.6%) were males and 14 (23.3%) were females.

AlsoDeshmukh AR et al [9] found that 21 (35%) patients showed excellent response, that is Grade 5 [17 (56.6%) were due to MMR vaccine and 4 (13.3%) were due to SAL paint], which indicates that there is a significant difference in both the groups (P = 0.001) and out of the 21 patients who showed excellent clearance of warts (comprising both due to MMR vaccine and SAL paint), 13 (61.9%) patients were males and 8 (38%) patients were females. These all results are very much comparable to our study.

VI. CONCLUSION:

Despite the study's limitations, it was discovered that intra-lesional MMR vaccine as an immunotherapy is an emerging technique of treatment for multiple warts with lower recurrence rates and the added benefit of clearing warts at distant sites.

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