Evaluation of Efficacy and Safety of Modified Technique of Autowart Injection Therapy in the Treatment of Multiple, Recurrent and Recalcitrant Warts

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ABSTRACT
Background: Multiple recurrent warts affect patient’s quality of life by causing physical and psychological discomfort. Common treatment modalities are painful, cause scarring, have high recurrence rates and are impractical for treatment of multiple lesions. Immune stimulation by exposing the viral antigens to body’s immune system forms an ideal modality of treatment. Autowart injection works under this principle.
Aim: To evaluate the safety and efficacy of modified technique of auto wart injection in the treatment of multiple recurrent recalcitrant warts.
Methods: A total of 40 patients with multiple recurrent cutaneous warts were enrolled in this prospective open labelled study. The donor tissue was harvested by just paring the wart, instead of taking the whole of wart tissue. The harvested tissue was then crushed and injected in the gluteal region in suspension of 1 ml of distilled water. Patients were followed up once in 2 weeks for one month and then monthly for 3 months. Patients were evaluated with lesion count at each visit and the response to the treatment was assessed at the end of 12 weeks.
Results: All 40 patients with multiple warts (male: female = 29:11) were available for follow-up. At the end of 3 months, 28 patients (75%) showed complete clearance of warts, 9 patients (22.5%) had partial clearance and one patient showed no improvement. No apparent side effects were observed.
Conclusion: Modified autowart injection technique was found to be a safe and effective therapeutic modality with rapid resolution of warts in the treatment of multiple, recurrent, recalcitrant warts.

Key Words: Auto wart injection; Immune stimulation; Paring; Multiple, Recurrent, Recalcitrant warts

INTRODUCTION
Warts are benign proliferation of the skin and mucosa caused by various strains of double stranded-DNA containing human papilloma virus (HPV). They clinically manifest as common warts (verruca vulgaris), filiform warts (digitate wart), flat warts (verruca plana), plantar warts, genital warts (condyloma accuminata), oral and laryngeal papillomas and epidermodysplasia verruciformis.1

Multiple recurrent warts are associated with significant morbidity by causing physical and psychological discomfort.2 Common modalities of treatment (electro cauterity, radiofrequency, laser and cryotherapy) ablate the wart tissue but do not stimulate the immune system against the pathogen.3 These procedures are painful, cause scarring, having high recurrence rates, thereby are impractical for treatment of multiple lesions. Hence for effective treatment of warts, stimulation of the immune system by exposing the virus to immune mediators forms an ideal modality of treatment, causing spontaneous regression of wart with long lasting immunity. Autowart injection is one such novel, single visit procedure which treats the warts by stimulation of immune response against the virus.4

In our study, the donor tissue was harvested by paring the wart instead of removing substantial amount of wart tissue. This was adopted to reduce discomfort and risk of infection at donor site. The present study was taken up to evaluate the safety and efficacy of modified technique of autowart injection in the treatment of multiple recurrent recalcitrant warts.

MATERIALS AND METHODS
This study was carried out between September 2013 to September 2014 in the Dermatology out-patient department of a tertiary care rural hospital as a prospective open labelled study. Ethical clearance was obtained before starting the study. Forty patients with multiple (more than five warts), recurrent (warts which have recurred after any modality of treatment) and palmoplantar warts were enrolled in the study. Our exclusion criteria were patients less than 10 years, pregnancy and lactation, immunocompromised individuals (HIV) and patients on immunosuppressive drugs. Written informed consent was obtained from all the patients.
A detailed history was taken as per the pre-tested semi structured questionnaire. An elaborate general and systemic examination was done and recorded in the standard proforma.
Procedure of modified technique of autowart injection:
Under aseptic precautions, donor tissue for auto wart was harvested by paring a well-developed verrucous lesion or palmoplantar wart. The lesion to be pared was cleansed with spirit-povidone iodine-spirit followed by paring using a sterile surgical blade no.11 (Fig. 1). The pared tissue was transferred onto the sterile surgical gauze and crushed in a sterilized pastel and mortar with 1ml of distilled water. A fine suspension was prepared and with a sterile disposable 5ml syringe, it was injected into upper outer quadrant of gluteal region (half way between posterior iliac spine and trochanter) after making sure that the tip of the needle was not in a blood vessel by withdrawing the piston.
Patients were assessed every 4 weeks for 3 months. At each follow-up visit, lesion count and percentage reduction in number of warts were undertaken. Resolution of all the warts within three months was considered as complete clearance (Fig. 2 & 3).
Patients were followed up for one more month after clearance for any recurrence.

Fig. 1: Paring of wart tissue using 11 no. surgical blade

Fig. 2: Recurrent warts over the left palm

RESULTS
All 40 patients were available for follow-up. In the present study males outnumbered females (M:F = 29:11) with commonest age of presentation being 24-28 years. Out of 40 patients, 23 had verruca vulgaris and the remaining 17 had palmo-plantar warts. Majority of the patients (75%, 30 patients) had warts persisting for more than 6 months. At week 4 of post treatment evaluation, 60% (24 patients) had 50-75% clearance of warts and 10% (4 patients) had more than 75% clearance of warts. At week 12, total of 28 patients (75%) showed complete clearance of warts (Fig. 4 & 5), 9 patients (22.5%) had partial clearance and one patient showed no improvement. No apparent side effects were observed.

DISCUSSION
Warts are benign proliferation of the skin and mucosa caused by various strains of double stranded-DNA containing human papilloma virus (HPV). The common modalities of treatment namely electrocautery, cryotherapy, radiofrequency and laser are based on ablation of the viral growth but do not stimulate the immune system against the pathogen. Immunotherapy by exposing the virus to immune mediators forms an ideal modality of treatment for multiple, recurrent, recalcitrant warts. Autowart injection works under this principle. Intralesional antigen therapy was found to be associated with increase in production of Th1 cytokines wherein TNF-α and IL-1 down regulates the transcription of HPV genes; INF-γ and IL-2 stimulates the cytotoxic T cells and NK cells. In a study done by Srivastava et al. on the autowart injection technique substantial amount of wart tissue was harvested and injected. In our study we performed the procedure with some modification i.e., the donor tissue was harvested by just paring the wart since HPV is an epidermal infection. By this method, wound at donor site was avoided and in addition eliminating the unwanted deeper tissue.
In our study, males outnumbered the females with male to female ratio being 29:11 and common age of...
presentation being 24-28 years. A complete clearance of warts was observed in 75% of patients (Table 1), whereas in a study done by Srivastava et al, 66.03% of patients had complete resolution of warts. Nine patients (22.5%) had partial clearance and one patient (2.5%) showed no improvement at all. No apparent side effects were observed.

<table>
<thead>
<tr>
<th>Author</th>
<th>Technique Adopted</th>
<th>Complete Clearance (%)</th>
<th>Partial Clearance (%)</th>
<th>Non responders (%)</th>
<th>Reaction at the site of implantation or injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shivakumar et al.</td>
<td>Auto implantation using a subcutis deep wart tissue</td>
<td>73.3</td>
<td>NA</td>
<td>26.7</td>
<td>Some cases (exact number not known)</td>
</tr>
<tr>
<td>Nischal et al.</td>
<td>Auto implantation of the pared wart tissue (modified technique)</td>
<td>74.1</td>
<td>3.7</td>
<td>18.5</td>
<td>3 cases</td>
</tr>
<tr>
<td>Lal et al.</td>
<td>Autoinoculation of the full thickness wart tissue</td>
<td>62.5</td>
<td>NA</td>
<td>NA</td>
<td>11 cases</td>
</tr>
<tr>
<td>Srivastava et al.</td>
<td>Autowart injection of crushed wart tissue in distilled water suspension</td>
<td>66.03</td>
<td>22.64</td>
<td>11.32</td>
<td>Nil</td>
</tr>
<tr>
<td>Present Study</td>
<td>Autowart injection of the pared wart tissue (modified technique)</td>
<td>75</td>
<td>22.5</td>
<td>2.5</td>
<td>Nil</td>
</tr>
</tbody>
</table>

**CONCLUSION**

To conclude, modified autowart injection technique was found to be an effective therapeutic modality with rapid resolution of warts in the treatment of multiple, recurrent, recalcitrant warts.

Limitations of our study include small sample size, lack of HPV serotyping to measure type specific differences in therapeutic outcomes and lack of tests to check the levels of relevant Th1 cytokines to ascertain their role in resolution of warts.

**REFERENCES**