

# Autoinoculation Therapy for the Treatment of Widespread Cutaneous Warts

**BACKGROUND** Cutaneous warts are common lesions that are often unresponsive to various therapeutic modalities.

**OBJECTIVE** To assess the role of autoinoculation therapy in the treatment of widespread cutaneous warts.

**MATERIALS AND METHODS** This interventional study included patients with widespread skin warts who did not respond to conventional treatments. Two methods were used to perform the autoinoculation therapy. The first procedure was performed by obtaining a small piece of the wart and inoculating it into a subcutaneous pocket. The second method was developed by the investigator and was performed by inserting a needle into the center of the wart toward the nearby subcutaneous tissue, with multiple forward and backward movements in several directions around the lesion.

**RESULTS** The prospective study included 23 patients. The illness duration ranged from 3 months to 5 years. Autoinoculation interventions revealed full recovery of all warts in 20 cases (87%) within 20 to 90 days (mean: 40.7 days).

**CONCLUSION** Autoinoculation procedures demonstrated effectiveness, less cost, lesser pain, less invasiveness, without leaving skin scars in comparison with other conventional therapies.

Warts are skin growths that appear on areas of the skin and mucous membrane that are infected with a virus belonging to the human papillomavirus (HPV) family of viruses. Human papillomavirus is a nonenveloped double-stranded DNA virus that invades the epithelial cells of mucus membranes and skin. There are more than 200 different HPV types that have been identified and fully sequenced.<sup>1</sup> Verruca is the medical term for warts. The main symptom of HPV infection is triggering excessive growth of skin cells. This makes the affected areas appear thickened, hard, and rough. Some types of warts are flat and smooth. Humoral and cell-mediated immune responses are activated to control the disease in most patients with active warts, but many patients with warts have no demonstrable immune reactions.<sup>2,3</sup>

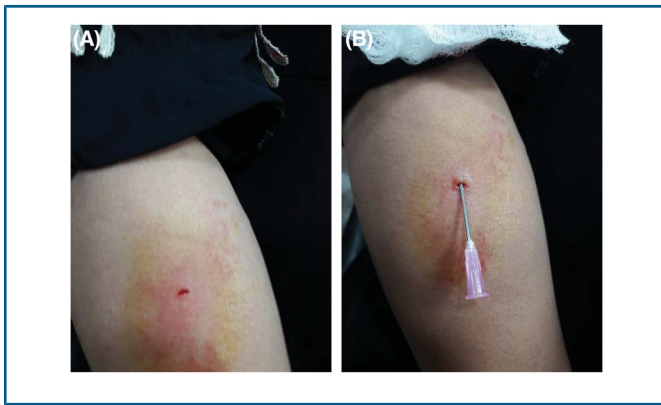
There are many modalities for the treatment of cutaneous warts. Topical keratolytics applications are usually of little effect and painful. Electrocautery removal most commonly leaves scars, which should be avoided for removal of facial warts. Other methods of wart treatment are cryotherapy,

surgical excision, CO<sub>2</sub> laser, and curettage. Various immunotherapeutic agents were used because of their nondestructive effect, easiness of use, and favorable outcomes. These include intralesional injection of mumps and rubella vaccines, measles, candida antigen, trichophyton skin test antigens, imiquimod, bacillus Calmette–Guérin vaccine, cimetidine, HPV vaccine, zinc, levamisole, and autoimplantation therapy.<sup>4,5</sup> Cidofovir intralesional infiltration of stubborn common warts revealed a reliable and dramatic response with little complications.<sup>6</sup> Dall’oglio and colleagues,<sup>7</sup> outlined 3 stages for the treatment of cutaneous warts depending on evidence-based medical studies. First-line treatment is by medical treatments (salicylic acid, glutaraldehyde, silver nitrate) for a single or a few and/or small warts of <1 year duration. Second-line treatment is by cryotherapy when the first line is failed or contraindicated. Third-line treatment is by physical destruction, topical, intralesional, and systemic therapeutic options, which are used for difficult-to-treat or recurrent warts.

The current study has used the wart causative virus as a source of immunity enhancement as a replacement for an unavailable vaccine. Therefore, the aim of this study is to investigate the role of autoinoculation therapy for the healing of widespread cutaneous warts.

## Patients and Methods

A prospective interventional study included 23 patients with extensive cutaneous warts. Selection criteria: patients with extensive widespread cutaneous warts (>10 warts or large mass warts) who were not responding to previous conventional therapies (2 years mean duration) such as electrocautery or keratolytic agents. Exclusion criteria: small number of warts (<10 warts), patients consulting for warts treatment for the first time, patients previously



**Figure 1.** Imaging data of forearm. (A) Making a small incision as preparation for insertion small pieces of wart into the subcutaneous tissue. (B) Placing a tissue piece of a wart on the tip of an 18 G needle and then introduced into the subcutaneous tissue.

received any immunotherapy method, immunocompromised patients, and those receiving immunosuppressive drugs. The diagnosis of warts was concluded from clinical

features and from histopathologic examination in cases that were not confirmed by clinical examination. The study was registered and approved in the College of Medicine, University of Basrah, Iraq. The study was performed during the period of March 2017 to April 2022 at Basrah Province.

A consent to perform the autoinoculation procedure was obtained from all patients or their guardians. After autoinoculation of the wart into the skin, the patient was followed-up to see the response. The methods of autoinoculation were conducted by 2 different technical procedures. The first method was performed by excision of a wart piece and inserted into a pocket of subcutaneous tissue as described previously<sup>8</sup> (Figure 1). The author of this study has developed the second procedure, which was performed as the following: 1 wart was chosen for autoinoculation therapy. Local antiseptic was applied to the wart and to the nearby skin. Lidocaine local anesthetic was infiltrated beneath and around the wart for about 2 cm distance in a circular manner. Then, an 18-gauge needle was inserted into the center of the wart toward the normal subcutaneous tissue around the wart. This was performed

**TABLE 1. The Outcome of 23 Patients With Cutaneous Warts**

No.	Age	Sex	Warts Type	Illness Duration	Autoinoculation Method	Period for Healing
1	14	F	Common	3 yrs	First method	21 d
2	26	M	Common	2 yrs	First method	90 d
3	13	M	Common	1 yr	Second method	28 d
4	29	F	Common	2 yrs	Second method	30 d
5	10	M	Plane	3 yrs	Second method	42 d
6	40	M	Common	1 yr	First method	No healing
7	25	F	Common	1 yr	Second method	30 d
8	18	M	Common	1 yr	Second method	28 d
9	25	F	Common	2 yrs	Second method (twice)	60 d
10	10	F	Common	1 yr	Second method (twice)	70 d
11	11	F	Common	3 mo	Second method	21 d
12	21	M	Common	1 yr	Second method	20 d
13	27	F	Common	4 yrs	First method	28 d
14	31	M	Genital	1 yr	First method	No healing
15	25	M	Common	5 yrs	First method	30 d
16	19	M	Plane	4 mo	First method (twice)	60 d
17	27	F	Common	2 yrs	First method	No healing
18	18	M	Common	3 yrs	First method	55 d
19	56	M	Common	5 yrs	First method	30 d
20	13	F	Common	1 yr	First method	21 d
21	42	F	Common	2 yrs	First method	60 d
22	25	F	Common	1 yr	First method	60 d
23	24	M	Common	5 yrs	First method	30 d
Mean	23.9 yrs			2 yrs		40.7 d

by about 8 to 10 times inward and backward needle movements that help in the dissemination of wart particles into the normal subcutaneous tissue in vicinity of the wart.

The patients were reexamined after 1 month and took full history about the warts changes during the period after the autoinoculation procedure. If there were signs of warts shrinkage, no second autoinoculation was performed, and the patient would be seen after 1 month for evaluation. In patients who were not responding to the first autoinoculation procedure, a second 1 was conducted and looking for the result that checked after 1 further month. The follow-up period was up to 3 months after the last autoinoculation therapy.

## Results

An interventional study included 23 cases with extensive cutaneous warts. Autoinoculation was conducted by 2 different means. The procedure was performed by implantation of a wart piece into a subcutaneous tissue pocket in 14 patients, whereas the other 9 patients were treated by inserting an 18 G gauge needle into the center of the wart toward the peripheral subcutaneous tissue with forward and backward movement. The age of the patients ranged from 10 to 56 years (mean: 23.9 years, SD:  $\pm 11.1$ , median: 25 years, Table 1). The illness duration was between 3 months and 5 years (mean: 2 years, SD:  $\pm 1.5$ , median: 2 years). Full recovery was achieved in 20 (87%) patients (Figures 2, 3). Seventeen cases were improved after 1 session of the autoinoculation procedure, whereas the other 3 cases required 2 sessions within 1 month apart to obtain full recovery (Table 1). After 1 month of the first autoinoculation session, 3 cases did not respond to therapy. One case had genital warts, 1 case had face and neck warts, and the third had body warts. All 3 cases were treated by



**Figure 3.** (A) Showing multiple warts on the leg before performing the autoinoculation procedure. (B) Showing the result of the same leg on (A) image after 64 days of performing the autoinoculation procedure.

subcutaneous insertion of wart particles into a pocket. They preferred to take keratolytic agents instead of a second autoinoculation procedure. The period for full recovery after autoinoculation therapy ranged from 20 to 90 days (mean: 40.7 days, SD:  $\pm 20$ , median: 30 days). Two cases with extensive plane warts were also improved after autoinoculation therapy. One patient was treated with the first procedure and the other was treated with the second method. One patient (No. 4 in Table 1) revealed pus discharge around all cutaneous warts after 15 days from the time of autoinoculation followed by full healing after 30 days from the time of the procedure. This may indicate an activation of cell-mediated immune response. Infection side effects at the subcutaneous pocket were noticed in 9 patients (64%) who were treated by the first method. However, no infection side effects were observed in patients who were treated by the second method (wart needle insertion). No other side effects were reported. No recurrence was recorded in patients who acquired complete warts clearance.

## Discussion

This study revealed that autoinoculation therapy is effective in 87% of cases for curing extensive cutaneous warts that were unresponsive to other therapeutic measures. The full resolution rate in this study (87%) was higher than that reported by Lal and colleagues,<sup>8</sup> (62.5%), and Shivakumar and colleagues,<sup>9</sup> (73.3%). Das and colleagues,<sup>10</sup> found that homologous autoimplantation therapy cured 40% completely, whereas 13.3% revealed moderate clearance and 17.3% showed mild clearance. Another study including 27 patients with recurrent and multiple palmoplantar warts revealed complete clearance in 74.1% of patients within 3 months after autoimplantation therapy.<sup>11</sup> Complete clearance was also established in 60% of patients with multiple warts after autoimplantation therapy every 2 weeks for



**Figure 2.** (A) Showing multiple warts on the finger before performing the autoinoculation procedure. (B) Showing the result of the same finger on (A) image after 55 days of performing the autoinoculation procedure.

a maximum intervention of 4 times.<sup>12</sup> Fifteen patients were recruited in the study for evaluation of 3 successive autoinoculation techniques for the treatment of multiple or recurrent viral warts. The study showed average improvement in 65% of patients after 12 weeks and complete resolution in 67% of patients at the end of the follow-up.<sup>13</sup> Abdelmonaem and colleagues,<sup>14</sup> studied the safety and efficacy of homologous autoinoculation therapy in the treatment of multiple stubborn warts. They concluded that after 12 weeks of the autoinoculation procedure, 66% of cases revealed complete resolution, 26% revealed moderate resolution, and 4% revealed mild resolution, whereas only 1.5% of cases revealed treatment failure, with trivial side effects and without recurrence.

The procedure, which was developed in this study by multiple needle penetration from the wart center toward the subcutaneous tissue, was as effective as that previously used by insertion of a wart piece into a subcutaneous pocket. However, the advantages of the newly developed procedure in this study are less invasive, less time-consuming, easier to perform, and without the side effect of pocket infections. The autoinoculation procedures by either method are intended to expose viral antigens to the immune system, because the intact warts are mostly bloodless and may be hidden from the immune cells. Therefore, autoinoculation therapy is recommended for widespread refractory cases and even for less severe cases, because it causes natural healing without scars. It will lead to an avoidance of painful cautery removal or keratolytic applications for all warts. Furthermore, it required less time for full recovery and less cost. The treatment by cryosurgery, electrocautery, or topical keratolytic therapies could remove some part of wart bulk and leave other remnants. This will lead to recurrence of viral growth from viable pieces of the warts without eradication of the disease and without enhancement of the immune system. These conventional treatment methods are intended to destroy the viruses with high failure rates, whereas the autoinoculation therapy uses live viruses for warts healing with a high success rate.

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