

Treatment of Recalcitrant Warts With Occlusive Warming Patches

Georgia Schuller-Levis MD,^a William Levis MD,^b and Israel Dvoretzky^c

^aLaboratory of Cellular Immunology, Department of Developmental Neurobiology, New York State Institute for Basic Research in Developmental Disabilities, Staten Island, NY

^bNYU Langone Medical Center, New York, NY

^cYale University, New Haven, CT

ABSTRACT

Prior studies have identified local heat therapy as a treatment for recalcitrant warts. We have employed a thermal pad that raises local temperature to 42-43°C for at least 2 hours in a proof of concept study of three patients with recalcitrant warts. The recalcitrant warts cleared in all three patients beginning in the fourth and fifth weeks after daily treatment with the pads. There were no adverse events. We conclude that the timing of clearance following use of these thermal pads is likely via direct viral killing and immunologic mechanisms. Further controlled trials are underway.

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INTRODUCTION

Local hyperthermia has been shown to promote migration and maturation of HPV infected skin.¹ HPV is a virus that causes verrucae on the hands, feet, and lesions of the mucous membranes of the oral, anal, and genital cavities. Treatments such as cryotherapy, acid preparations, laser therapy, ultrasound, and tape occlusion have been used in the management of verrucae with limited success.² Prior experience has identified local heat therapy as a treatment for recalcitrant warts.^{2,3,4} Hands and feet have temperatures below core body^{2,5} that are favored by certain strains of HPV.

A novel method of treating warts with heat is the use of an occlusive patch that contains a mixture of chemicals (ferric chloride), which in the presence of oxygen reacts to generate reproducible thermochemical warming of the skin to a temperature of 42-43°C for at least 2 hours. Prior to use, the patch is sealed in a pouch. Once the pouch is opened, atmospheric oxygen reacts with the chemicals to generate heat that is believed to kill the HPV virus in the wart tissue. We have tested a unique special design heating patch that raises the local temperature to 42°C without side effects in 3 patients with recalcitrant warts. This heat patch may induce transcutaneous immunization and deliver antigenic proteins to antigen presenting cells in the epidermis and dermis.^{6,7}

MATERIALS AND METHODS

The test product is a unique self-adhesive "patch-type" delivery system containing a mixture of chemicals, which react exothermically in the presence of oxygen.² It was developed to simultaneously secure the exothermic patch to the skin, regulate the flow of the oxygen to the exothermic chemicals inside the patch, and insulate it in order to optimally maintain the desired temperature at the wart site and surrounding skin.

These exothermic patches used in our study were specifically designed to provide long-lasting and reproducible heat on the surface of the skin. The temperature rises fast to the target level of 42-43°C and remains at the same temperature for at least 2 hours continuously.

Prior to the use, the patch is sealed in a pouch containing an inert gas. Once the pouch is opened, the chemicals react with atmospheric oxygen to reach the desired therapeutic temperature without burning or injuring the skin (Figure 1).

Subjects with two clinically diagnosed target verrucae were provided with the occlusive patches to apply daily for a minimum of 2 hours to the first target verruca. No patch was applied to the second target verruca that served as a control.

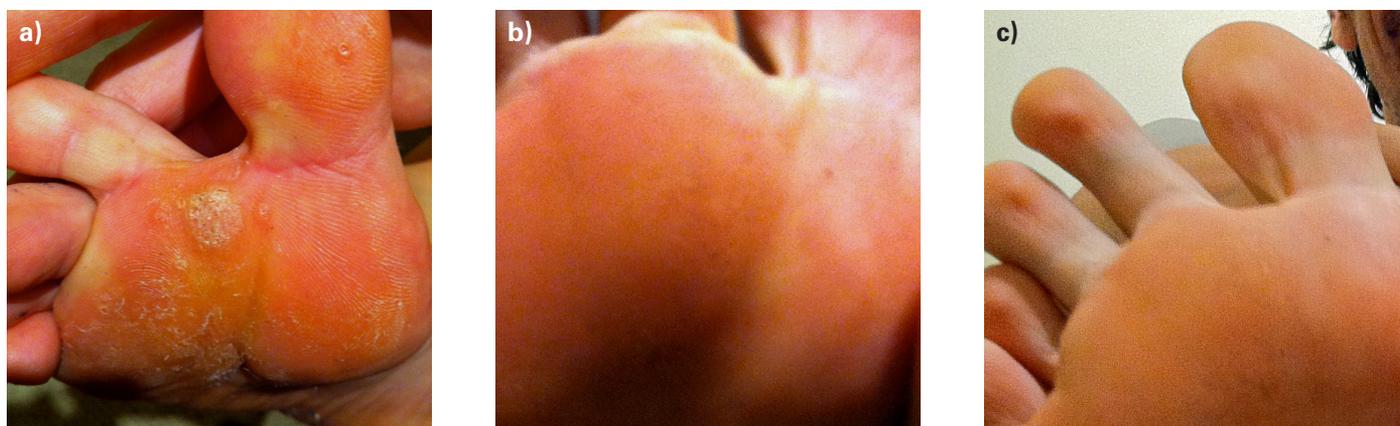
Efficacy was assessed by the percent reduction in verrucae surface area (Lesion Measurement) as well as the Investigator Global Improvement Score (IGIS) over the treatment period, at week 12, and during the post-treatment period.

We have treated 3 patients with patches. Two females (age 19-26) and one male (age 26) have completed the study. The three patients that completed the study were compliant with regard to doctor visits and using the patch daily. The male patient had been previously unsuccessfully treated with liquid nitrogen 6 months prior to this study. All patients have returned the used patches confirming their compliance. No complaints have been noted regarding either the heat generated by the patch or the daily application. Two completed patients (one female and one male) had plantar warts of the foot and one female had one wart on each hand.

FIGURE 1. An envelope and patch.**RESULTS****Patient 1**

A 26-year-old male was seen for extensive plantar warts on the left foot that were unsuccessfully treated 6 months earlier with liquid nitrogen. On the left first metatarsal (MT) head, the patient had a 30x30 mm mosaic plantar wart. On the left 4th MT, the patient had another mosaic plantar wart measuring 20x5 mm. On the right foot on the second MT head, he had a 5x4 mm plantar wart.

We began treating the 5x4 mm lesion on the right foot. After consulting with the study leader, we also treated the larger wart on the left foot and left the 20x5 mm lesion (left foot) untreated. By week 8, all warts were completely clear including the untreated wart. This patient was also compliant and returned unused patch packages at each visit. This patient came into the office a year post study for another dermatologic problem and his extensive mosaic plantar warts were still clear (Figures 2A, B, C).

FIGURE 2. a) Patient 1 at week 1; b) week 8; and c) 1 year.**Patient 2**

A 19-year-old female was seen for plantar warts on the right foot that were resistant to over the counter medications. The largest wart measured 9x9 mm and was treated daily with the study patch. A 2x2 satellite wart was untreated and served as a control. The treated wart showed some regression by the 4th week and was completely clear by week 8. The untreated satellite lesion remained unchanged. This patient was totally compliant and returned used packages at each visit. There were no observable changes in the untreated control.

Patient 3

A 26-year-old female was seen for warts on the dorsal surface of both hands that were resistant to over the counter medications. On visit 1, the left hand wart measured 7x7 mm and was treated with the study patch. The right hand had a wart of 2x2 mm and was left untreated as a control. At week 2, some regression was noted on the treated hand but the untreated hand was unchanged. At week 8, continued regression was noted on the left hand. The left hand wart showed marked improvement with a measurement of 3x3mm. The right hand was still unchanged. At week 10, the left hand was clear and with only slight post inflammatory hyperpigmentation. The control wart on the right hand was unchanged (2x2 mm). This patient was totally compliant and returned used packages at each visit.

DISCUSSION

The patients treated have had excellent results. Regression begins at 4-5 weeks and continues to improve in the subsequent weeks. This has been the case in all 3 patients who completed the study.

Particularly impressive was the complete and sustained regression of the large plantar mosaic warts that are among the most recalcitrant of all warts. This individual was still clear of warts at one-year post study.

Heat shock protein 70 will be produced from these thermochemical patches and has been shown to induce an autophagic pathway that leads to cross-presentation and activation of MHC class I cytotoxic CD-8 killer cells.⁸ Future controlled trials are indicated and should investigate the role of the immune system including measuring neutralizing antibodies and MHC class I restricted CD-8T cell killers. Recent evidence has shown that HPV- laden dendritic cells migrate to the T cell-dependent areas of regional nodes following local heat on the skin.¹ Mechanisms of action by heat may include direct killing of the HPV virion with additional immunologic mechanisms that would include dendritic cell antigen presentation of HPV immunogens like E7 to the T cell receptor in the regional node.^{9,10}

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AUTHOR CORRESPONDENCE

William Levis MD

E-mail:..... William_levis@yahoo.com

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CONCLUSION

In three patients, we used a thermochemical pad to raise the local temperature for treatment of recalcitrant warts. The warts cleared in all three patients beginning at 4-5 weeks of daily application for at least 2 hours. The warts completely cleared by the completion of this study. A larger study is underway that is expanding on these pilot data.

DISCLOSURES

The authors have no conflicts of interest to disclose.

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