

Successful treatment of plantar warts using topical Zijinding, a traditional Chinese medicine preparation: A case series

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Abstract

Introduction: Plantar warts are associated with high transmissibility and morbidity. Among the available therapeutic options, none is uniformly effective or virucidal. Salicylic acid is the first-line therapy but approximately one-third of lesions could not resolve and become recalcitrant despite repeated treatment. Cryotherapy is widely accessible with low cost but may be complicated by pain, blister formation, hemorrhage, infection, excessive granulation tissue formation, and hyper-/hypo-pigmentation. Hence, alternative treatment modalities are essential.

Methods: Three patients with debilitating plantar warts refractory or intolerant to cryotherapy were treated with a course of Zijinding (a traditional Chinese medicine preparation) paste prepared with white vinegar.

Results: All three patients showed excellent clinical response with Zijinding application with evolution of lesions to scabs and subsequently healthy skin within 1.5 to 5 months of treatment. Treatment was well tolerated and had no significant side effects with excellent compliance recorded for all three patients. There was no relapse for at least 10 months after stopping the treatment.

Conclusion: Topical Zijinding could be a promising alternative modality for the treatment of plantar warts. Further clinical trials on the comparison of Zijinding and other treatment modalities of plantar warts are warranted. Further studies are required to investigate the mechanism of action of Zijinding and to isolate the active ingredient.

KEYWORDS

plantar warts, traditional Chinese medicine, Zijinding

1 | INTRODUCTION

Plantar warts are common superficial skin lesions caused by human papilloma virus (HPV) infection. Plantar warts are hyperkeratotic papules that often form on pressure points such as the heel, but they may occur anywhere on the sole of the foot. Lesions are often asymptomatic, but a callus overlying the wart on pressure points may lead to pain with pressure or walking. They are frequently

transmitted from person-to-person through exposure to the virus on locker room floors, public showers, and pool areas. They are slightly more common in females, young children, and immunocompromised patients.¹⁻³ Treatment is aimed at relieving the patient's physical and psychological discomfort and at preventing the spread of infection by autoinoculation. Among the available medical and physical ablative therapeutic options for plantar warts, including salicylic acid, and cryotherapy, none are uniformly effective or virucidal.¹⁻⁸ Salicylic

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FIGURE 1 Serial photographs of Case 1 at baseline (A), after cryotherapy (B), while on topical Zijinding, the red-brown color on the foot due to the compound (C), after 4 weeks (D) and 6 weeks (E) of topical Zijinding, and at last follow-up (F)

acid is the first-line therapy but approximately one-third of lesions do not resolve and become recalcitrant despite repeated treatment which cause the patients psychological distress.⁹ Cryotherapy is a widely accessible therapeutic modality with low cost but may be complicated by pain, blister formation, hemorrhage, infection, excessive granulation tissue formation, and hyper-/hypo-pigmentation over the treated areas. Hence, alternative treatment modalities are essential.

Recently, we encountered three patients with refractory plantar warts that did not respond to repeated courses of cryotherapy. A search in the Chinese medical literature revealed that a traditional

Chinese herbal medicine called Zijinding combined with white vinegar could be useful. In this article, we report the successful treatment of these three patients with plantar warts using this topical treatment modality.

2 | CASE REPORTS

2.1 | Case 1

A 34-year-old previously healthy Chinese woman presented with more than 30 plantar warts on her right foot for 2 years. There were multiple



FIGURE 2 Photographs of Case 2 at baseline (A), black scab formation during Zijinding treatment (B), and at treatment endpoint (C). Photograph of Case 3 at baseline (D), black scab formation during treatment (E), and after treatment completion (F)

lesions on the big toe causing her considerable discomfort (Figure 1A). She had received monthly sessions of cryotherapy for nine months between June 19, 2015, and March 25, 2016. This treatment was complicated by blistering and scab formation. The lesions appeared to improve, but satellite lesions developed around the original lesions (Figure 1B). From May 4, 2016, she began to receive the treatment of the traditional Chinese herbal medicine preparation (Topical Zijinding, Lot No. Y10014, Guangzhou Baiyunshan Jingxiutang Pharmaceutical Co., Ltd.) and white vinegar. Pills of Zijinding were crushed to powder and mixed with white vinegar to make a paste; the paste was then applied to the lesions and 5 mm of normal skin surrounding the lesions (Figure 1C). Natural drying of the paste was allowed, and the paste was applied twice daily (in the morning and before bedtime).

After one month, the lesions had shrunken (Figure 1D). About one and a half months later, black scabs were formed with shedding two months later (Figure 1E) and exposing new healthy skin (Figure 1F). Topical Zijinding was applied for a total of three months. There was no relapse at the time of writing, 12 months after cessation of treatment.

2.2 | Case 2

A 27-year-old previously healthy Chinese man presented with one plantar wart on the big toe of his left foot for 1 month (Figure 2A).

Cryotherapy for the plantar wart was complicated by pain. From May 4, 2016, he began to receive the treatment of topical Zijinding (Lot No. Y10014; Guangzhou Baiyunshan Jingxiutang Pharmaceutical Co., Ltd.) with white vinegar as described for patient 1. A black scab formed after four weeks and was shed after six weeks (Figure 2B) exposing new healthy skin (Figure 2C). Topical Zijinding was applied for a total of 1.5 months. There was no relapse at the time of writing, 13 months after cessation of treatment.

2.3 | Case 3

A 32-year-old previously healthy Chinese woman presented with more than 10 plantar warts on the right foot for 2 years (Figure 2D). She had been treated with cryotherapy four times but the outcome was not satisfactory. From June 2, 2016, she also began to receive topical Zijinding (Lot No. Y10014, Guangzhou Baiyunshan Jingxiutang Pharmaceutical Co., Ltd.) in white vinegar. Three weeks later, black scabs formed (Figure 2E), and seven weeks later, the skin lesion area was reduced and the depth of the lesion became shallow. Four months later, the skin lesions became much shallower. Topical Zijinding was applied for a total of 5 months. Scabs were shed with healthy skin exposed at the end of treatment (Figure 2F). There was no relapse at the time of writing, 10 months after cessation of treatment.

3 | DISCUSSION

In this study, we have shown and documented that plantar warts of different severity can be cured by topical application of Zijinding. The duration of plantar warts in the three patients varied from one month to two years. All three patients have received cryotherapy treatment for their plantar warts but the outcome was not satisfactory. After treatment with topical Zijinding for 1.5 to 5 months, the plantar warts in all three patients were in remission and there was no relapse for at least 10 months after stopping the treatment. Moreover, the topical treatment is easy to apply and none of the patients reported any significant side effects. For the cost of this modality, one bottle of topical Zijinding costs 15RMB (about 2.5US\$). And the needing amount of drugs depends on the size of skin lesion and the severity of the infection. For these three cases, topical Zijinding consumption was 3–10 bottles. To our best knowledge, this is the first report documenting the success of using Zijinding for the treatment of plantar warts. Further clinical trials on the comparison of Zijinding and other treatment modalities of plantar warts are warranted.

The mechanism of action of Zijinding is probably a combination of antiviral and immunological effects. The ingredients of Zijinding include *Pseudobulbus Cremastrae seu Pleiones*, Cinnabar, Chinese Gallnut, Realgar, Red Euphorbia, *Andrographis paniculata*, moleplant seed, pseudo-ginseng, borneol, and basil oil. Among these ingredients, Chinese gallnut, realgar, *Andrographis paniculata*, moleplant seed and pseudo-ginseng may have direct antiviral effect or induce interferon production, according to *Pen Ts'ao Kang Mu (Compendium of Materia Medica)*, the most comprehensive herbal medicine book written in the history of traditional Chinese medicine, compiled by Li Shi-zhen in the 16th century. For example, the main ingredients of realgar are arsenic disulfide (As_2S_2) mixed with a small amount of arsenic and other heavy metal salt. Arsenic, or arsenic trioxide (As_2O_3), is a widely used ingredient in traditional Chinese medicine. In 1999, Zheng et al. found that As_2O_3 was able to increase apoptosis of HPV 16 DNA-immortalized human cervical epithelial cells (HCE16/3 cell line) at a low concentration, which might have a connection with viral oncogene suppression.¹⁰ As for *A. paniculata*, it is a traditional medicinal plant in the family *Acanthaceae* that has been used for centuries in Asia to treat upper respiratory infections, fever, and herpes. Moreover, many reports have found that various compounds isolated from *A. paniculata* possess antiviral activities. Panraksa et al. from Thailand observed that andrographolide had significant anti-dengue virus activity¹¹ and Tang et al. from Malaysia also found that the methanol extracts of *A. paniculata* possessed the ability of inhibiting the activity of dengue virus serotype 1 in in vitro assays.¹² Kongyingyoes et al. from Thailand found that 3,19-isopropylideneandrographolide, a diterpenoid lactone compound isolated from *A. paniculata*, is active against herpes simplex virus 1 and herpes simplex virus 2, but has a different molecular target from acyclovir; hence, it might be an alternative antiviral agent for both wild type and acyclovir resistant herpes simplex virus strains.¹³ Chen et al.

found that dehydroandrographolide and andrographolide, two natural diterpenoids isolated from *A. paniculata*, possessed activity against hepatitis B virus DNA replication.¹⁴ Luo et al. found that some components of *A. paniculata* exerted potent anti-influenza A virus activity in vitro.¹⁵

3.1 | Patient perspective

All the three patients were satisfied with their treatment results. Although their plantar warts were not extremely serious, but they all got psychological burden that the cryotherapy treatment was painful and the results were not ideal, they were worried about the spread of the plantar warts or the situation may get worse and it may be transmitted to their family members especially the children. This easy-apply modality has got the three patients' plantar warts cured with no pain and no other side effect; therefore, they all thought this method is quite worth sharing with other patients and the case reports will give other patients the confidence that this disease can be healed. On the other hand, one of the main disadvantage of this modality is that patients need to insist on applying the medicine twice a day for at least several months.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS

YZ carried out experiments and wrote the manuscript; LNG involved in the acquisition and analysis of data; SS, SKPL, and PCYW revised the manuscript critically for important intellectual content; YCX supervised the whole research group and has given the final approval of the version to be published.

Additional contributions: We thank the three patients for granting permission to publish these images and information.

ETHICAL APPROVAL

The study protocol was approved by the Institutional Review Board of Peking Union Medical College Hospital.

Consent to participate: Written informed consent was obtained from the patient.

Consent to publish: All patients provided written consent for their case details to be published. All the copies of the written consent are available for review by the Editor of this journal.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author (YCX) upon reasonable request.

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