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THERAPEUTIC HOTLINE: SHORT PAPERS

WILEY DERMATOLOGIC THERAPY

A novel topical agent in the treatment of seborrheic keratoses: A proof of concept study by clinical and dermoscopic evaluation

Francesco Lacarrubba | Maria Rita Nasca | Anna Elisa Verzì | Giuseppe Micali

Dermatology Clinic, University of Catania, Catania, Italy

Correspondence
Giuseppe Micali, MD, Dermatology Clinic, University of Catania, Via S. Sofia 78, 95123 Catania, Italy.
Email: cldermct@gmail.com

Abstract

In this proof of concept study, 50 lesions from 15 patients with multiple seborrheic keratoses (SKs) were treated with a novel aqueous solution containing nitric acid, zinc and copper salts, and organic acids (acetic, lactic, and oxalic acid). Treatment consisted in the application of an amount of the solution sufficient to obtain a whitening/yellowish reaction. Application of the nitric–zinc solution was performed every other week until clinical and dermoscopic clearance or crust formation, for a maximum of 4 applications. Efficacy evaluation was performed at 8 weeks (T1) and 6 months (T2). All subjects, who reported no or minimal discomfort during and after the application of the solution, completed the study. At T1, a complete clinical and dermoscopic resolution was observed in 37 lesions after an average of 3 applications/lesion (range 2–4). A partial response, with minimal persistent residual spots, was detected in the remaining 13 lesions. All patients with complete clearance showed no relapses at a 6-month follow-up (T2). The positive preliminary results indicate that this novel solution may represent a promising alternative option for SKs especially in patients not keen or eligible to undergo invasive tissue-destructive procedures.

KEYWORDS

dermoscopy, nitric–zinc complex, non-invasive treatment, seborrheic keratoses

1 | INTRODUCTION

Seborrheic keratoses (SKs) are common acquired benign pigmented and warty lesions that may develop in adults in any body area, except palmo-plantar areas, and are more often observed on the trunk of elderly patients. They may be of variable color, size, and thickness, and usually show sharp margins and a typical "stuck-on" appearance. Although devoid of malignant potential, they often tend to increase in size and number with advancing age, sometimes raising cosmetic concerns or becoming itchy, inflamed or bleeding following occasional mechanical traumas. For these reasons, their removal may be required. Common standard treatments for SKs include curettage, shaving, cryotherapy with carbon dioxide or liquid nitrogen, electric cautery, and laser therapy (Micali, Dall'Oglio, Nasca, & Tedeschi, 2004). These treatments may sometimes be performed in combination and are usually effective and well tolerated, with minimal risk of complications, such as permanent pigmentary changes or scarring. In the past, alternative treatments with topical chemicals, such as salicylic, glycolic, trichloroacetic, or pyruvic acid, have also been suggested, either alone or in combination with surgical methods (Caperton, Valencia, Romanelli, & Fulton, 2012; Chun, Lee, & Lee, 2004; Moy, Murad, & Moy, 1993; Swinehart, 1992). Recently, a multicenter phase I/II clinical trial using a novel topical formulation (BL-5010) has also been performed (Levy-Nissenbaum, Thio, Burstein, & Thaci, 2015).

We report our experience in the treatment of SKs with a novel nitric–zinc complex aqueous solution, a mixture of organic and inorganic acids that has shown to be effective and well tolerated in the topical treatment of common and genital warts in a previous prospective, multicenter, open study (Cusini et al., 2015).

2 | MATERIALS AND METHODS

In this proof of concept study performed between June 2015 and March 2017 at the Dermatology Clinic of the University of Catania, Italy, 50 SKs from 15 immunocompetent patients (9 M, 6 F, mean age 63 years) with multiple lesions (size ranging between 5 and 15 mm) located on the trunk and legs were selected and treated with a medical device containing nitric–zinc solution 30–50% w/w, organic acids (acetic, lactic, and oxalic acid) 5–15% w/w, copper salt 0.001–1% w/w,

water QS to 100% w/w, after patients had signed their informed consent.

Treatment consisted in the application on each SK, right after cleaning with 70% ethanol, of an amount of nitric–zinc solution sufficient to obtain a whitening/yellowish reaction using a dedicated applicator brush. After each treatment, patients were instructed to clean the treated area twice daily with ethanol. Application of the nitric–zinc solution was performed every other week until clinical and dermoscopic (Dermlite hybrid®, 3 Gen, San Juan Capistrano, CA) clearance or crust formation, for a maximum of four applications. Efficacy evaluation was performed at 8 weeks (T1) and 6 months (T2) using a 5-point score: complete response (clearance), good response (size reduction >70%), partial response (size reduction 50–70%), poor response (size reduction <50%), no response.

3 | RESULTS

All subjects, who reported no or minimal discomfort during and after the application of the nitric–zinc complex solution, completed the study and responded to treatment. At T1, a complete response was observed in 74% of lesions (37 out of 50) after an average of 3 applications/lesion (range 2–4) (Figures 1 and 2). A good response, with

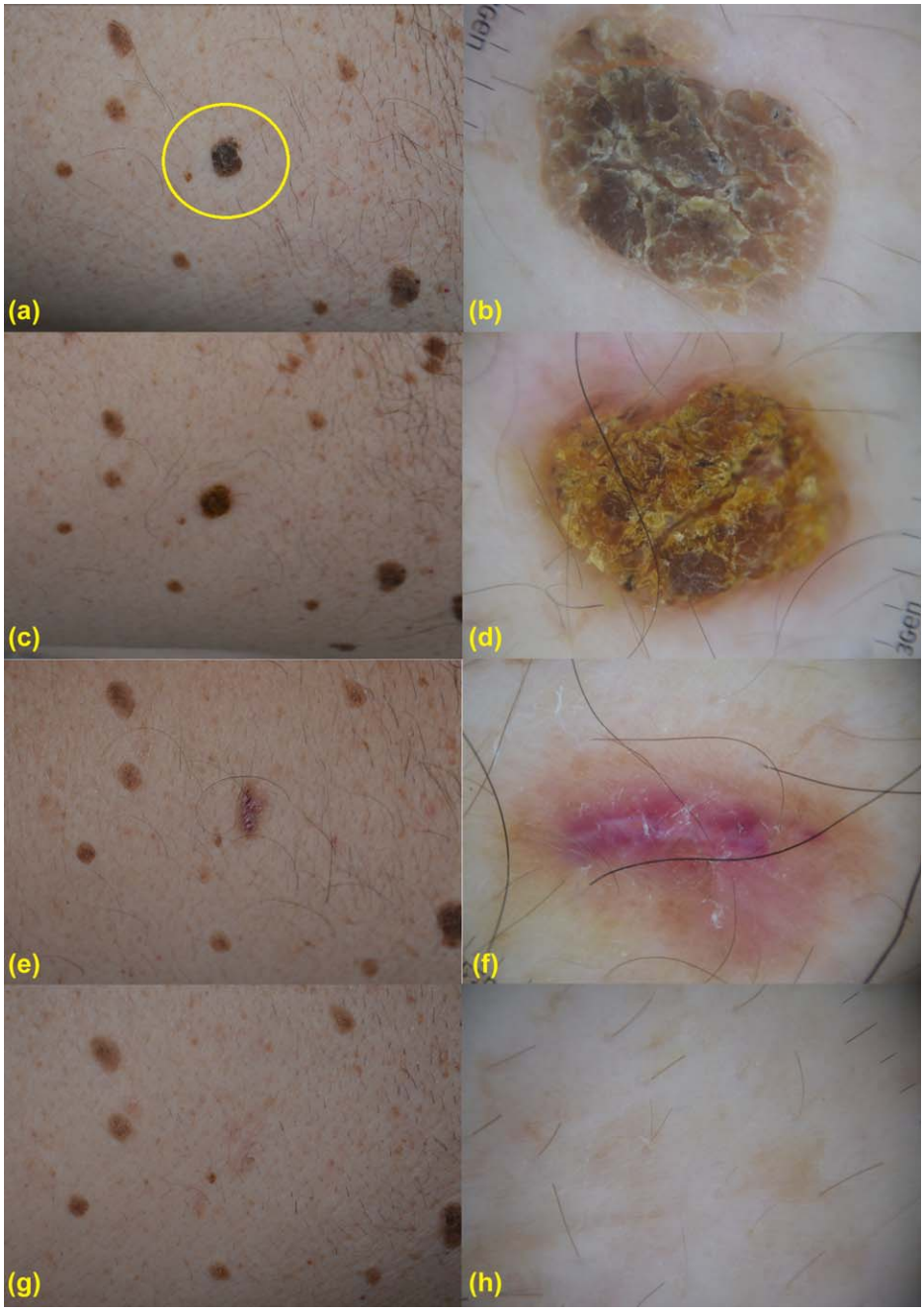

FIGURE 1 Patient 1. Clinical and dermoscopy features of a seborrheic keratosis (size: 8 mm) of the chest at baseline (a,b) after 2 weeks (c,d), after 8 weeks (e,f) and after a follow-up of 6 months (g,h): complete resolution with two applications of the solution

minimal persistent residual spots, was detected in the remaining 13 lesions. Patients reported no adverse events, with a slight, transient post-treatment erythema. The clinical results were supported by dermoscopy, which confirmed the complete resolution of those lesions clinically cleared, and minimal signs of residual lesions in the remaining cases. Patients were satisfied with the treatment outcome and expressed a preference for this non-invasive method. All patients with complete clearance showed no relapses at a 6-month follow-up (T2) with minimal residual hypopigmentation in some cases.

4 | DISCUSSION

In current clinical practice, SKs are usually removed by standard destructive methods. However, in case of extensive and/or multiple lesions, invasive procedures are often painful and may be troublesome, sometimes requiring several sessions. In addition, they may be not advisable in patients with bleeding disorders or under treatment with anticoagulants. Local injection of anesthetic drugs is often necessary to minimize pain from these procedures, and this may represent an issue in subjects with known or supposed drug allergy. Finally, the cost of disposable materials and the potential risk of accidental blood-transmissible infections when using such surgical techniques should also be taken into account.

The solution used in our study acts by enhancing acid hydrolysis of peptide bonds through the formation of nitrates and nitrites, facilitated by the presence of organic acids contained in the solution. This process induces a rapid and controlled protein denaturation/coagulation and a consequent caustic effect on the target lesions. In the 1980s

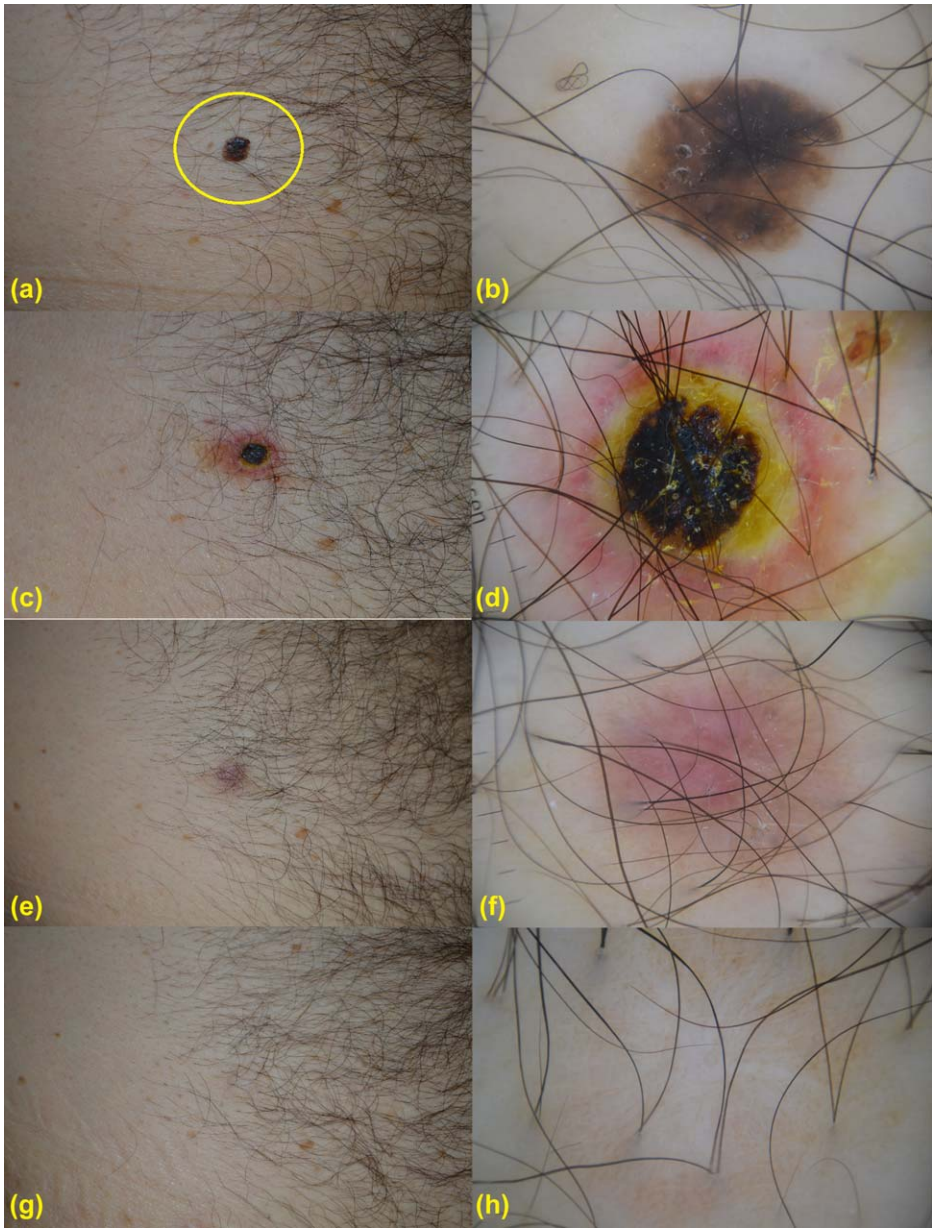

FIGURE 2 Patient 3. Clinical and dermoscopy features of a seborrheic keratosis (size: 5 mm) of the abdomen at baseline (a,b) after 4 weeks (c,d), after 8 weeks (e,f) and after a follow-up of 6 months (f,h): complete resolution with two applications of the solution

a topical solution containing acetic acid, copper, lactic acid, nitric acid, and oxalic acid was used for the treatment of SKs with promising results (Feuerman, Katzenelson, & Halevy, 1984). Compared with that solution, the one we used differs for the presence of zinc that may allow a faster and more effective action as it additionally contributes to protein denaturation (Shivaraja Shankara, Ganesh, & Hemavathi, 2008). With this simple method, which results in devitalization and mummification, lesions are gradually peeled off with no discomfort in the weeks following the application of the solution as the normal epidermal turnover progresses, minimizing any risk of scarring and pain.

In our preliminary study, a complete clinical and dermoscopic clearance was obtained in 74% of lesions, with no or minimal discomfort during and after the application of the solution. The results persisted at a 6-month follow-up, with only minimal post-treatment hypopigmentation observed in a few cases. It is however known that residual discoloration is common to all destructive procedures.

In conclusion, our results indicate that this approach may have a role in the management of SKs, representing a promising alternative nonsurgical option especially in patients not keen or eligible to undergo invasive tissue-destructive procedures. The dose and duration of treatment required to achieve complete clinical response warrant assessment by controlled trials on large series of patients.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

ORCID

Giuseppe Micali http://orcid.org/0000-0002-5157-3939

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