 ORIGINAL ARTICLE

Enhancing Outcomes in Seborrheic Keratosis: Using a Novel Treatment Solution

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ABSTRACT

Seborrheic keratosis (SK) is an extremely common benign cutaneous lesion that often appears on individuals older than the age of 50. SK lesions can appear in numerous clinical variations, but typically, SKs present with a well-demarcated, "stuck-on" appearance having a waxy or keratotic surface. Even though SK lesions are usually benign, many individuals elect for SK treatment or removal due to cosmetic concerns. One study regarding SK appearance reported that 61% of women tried to conceal the appearance of the SKs by using certain hairstyles, make-up, and clothes. Conventional treatment for SK lesions ranges from cryosurgery to curettage. Although these removal methods are effective for SK treatment, each method contains a potential for side effects such as pigmentation changes, scarring, and discomfort before and after the procedure. Due to many of these concerns, patients prefer topical treatments for SKs, which has led to a new emerging topical containing hydrogen peroxide topical solution 40% (HP40; Eskata™). Here, we report the methods and results from an HP40 treatment for two individuals, each over 70 years old. Application of the topical solution was performed on each target SK, up to four times, with a 20-second application and 1 minute between applications. The two participants reported moderate success of HP40 in the removal of their SKs with minimal adverse effects.

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INTRODUCTION

Seborrheic keratosis (SK) is one of the most common cutaneous lesions that a dermatologist will encounter daily.[1] SKs can develop anywhere on the body excluding the soles, palms, and mucous membranes.[1] SKs are benign epithelial tumors that present as "stuck-on", well-demarcated, waxy, or verrucous papules or plaques that consist of varying coloration from flesh-colored to heavily pigmented (brown, yellow, grey, or black).[2] SKs appear most commonly in middle-aged individuals, 31-50 years (42%), and the number and size of SKs increases with age.[3] One study conducted in Australia reported that the prevalence of SKs increased from 12% of individuals between 15-25 years old to 100% in individuals over the age of 50.[4] Within the same study, the average number of lesions increased from 6 lesions per individual in the age group of 15-25 years old to 69 lesions per individual in the group that was 75 years or older.[4] Even though studies indicate that the incidence of SKs increases with age, the etiopathology is still misunderstood.[5] Age, chronic ultra-violet (UV) exposure, and genetic inheritance are commonly proposed hypotheses that are associated with the occurrence of SKs. SKs can appear anywhere on the body, but one study of 406 total patients found the majority of SKs were found on the truncal region (chest, back, shoulders, abdomen) in approximately 85% of patients, and the face in approximately 68% of the patients.[6]

Typically, SKs present with dermoscopic findings such as fissures and ridges, hairpin vessels with white halo, comedo-like openings, and milia-like cysts.[7] Fissures and ridges are terms used to describe the linear grooves produced in the epidermis that present as thick, curved lines giving the lesion a "brain-like" appearance.[8] Hairpin vessels are characterized by linear vessels that form a U-shape with a bend at one end resembling a hairpin with a whitish halo surrounding the vessels.[7,8] Comedo-like openings are keratin-filled invaginations of the epidermis and appear as black or brown, roundish structures.[7,8] Finally, milia-like cysts are characterized by round white to yellowish globules.[7,8]

The presence of these dermoscopic findings correspond with the histopathologic changes within the epidermis and dermis. The thickened, papillomatous surface of the epidermis forms grooves and clefts that can be filled with keratin. The intralesional cysts of loose filled keratin cleft are called pseudohorn cysts and correlate to the appearance comedo-like openings of the SK.[7,9,10] The presence of intraepidermal cysts signify milia-like cysts, while the appearance of hairpin vessels are caused by enlarged capillaries within the dermis.[7,9,10]

The majority of SKs are typically asymptomatic and benign, therefore, do not require removal, but patients will often choose to have these lesions removed. The truncal regions are subject to frequent contact by clothing fabric, which may cause SKs to become symptomatic resulting in irritation, pain, bleeding, or itching.[11] Patients also elect for removal of SKs for cosmetic reasons, often stating a desire to improve their quality of life

and maintain a more youthful appearance since SKs are often termed "age-spots".[11] One study specifically reported that 61% of the female patients attempted to conceal or disguise the appearance of SKs by using specific clothing, hairstyles, and even make-up.[6] The majority of SKs are removed or treated for cosmetic purposes. Treatment methods include cryosurgery, electrodessication, shave excision, curettage, and emerging topical treatment, such as hydrogen peroxide topical solution (HP40) (Eskata™, Aclaris Therapeutics, Wayne, PA).

The most common traditional technique for SK removal is with the use of cryosurgery.[12] Although the specific mechanism of cryosurgery is not fully understood, cryosurgery destroys the SK lesion by inducing intracellular ice crystal formation within the benign tissue, which leads to various inflammatory responses.[13-15] Cryosurgery can be effective for SK removal depending on characteristics of the lesions and patient, freezing technique, freezing time, and the number of freeze/thaw cycles.[11,12] Larger and thicker lesions will often require extended freezing durations or more treatment sessions compared to small flat SKs.[11] Another commonly employed technique used by dermatologists is electrosurgery, which uses an electrode held at a certain distance away from the skin that creates a local energy delivery specifically destroying the epidermal tissue.[11] Curettage is another technique that can be used in combination with both electrosurgery or cryosurgery to remove any remaining SK lesions.[11] A study done by Wood et al. reported that 64% of the patients who had their SK lesions treated by cryosurgery or curettage, preferred cryosurgery due to a decreased amount of postoperative wound care after cryosurgery.[16] Adverse effects such as erythema, slight bleeding, blister formation, and pain are typically found at the treatment site after both treatments. However, both treatments can cause potential long-term complications such as scarring, permanent pigmentation changes (hyper or hypopigmentation), infection, and lesion recurrence.[17] Patients with darker skin types have an increased likelihood of pigmentary changes, recurrence, and scarring compared to individuals with a lighter skin type.[11,15]

Due to many of these concerns of adverse effects and postoperative care, patients have expressed interest in a noninvasive, safe, cosmetically acceptable treatment for SK removal.[18] Patients indicated that they avoided the removal of SKs due to potential long-term side effects such as scarring, discomfort, pain, and post-treatment hypo or hyperpigmentation.[6] Recently, the US Food and Drug Administration approved a hydrogen peroxide topical solution 40% (HP40; Eskata) as the first and only topical treatment for raised SKs. The high concentration of hydrogen peroxide within the topical solution can produce reactive hydroxyl radicals and other oxygen species that cause oxidative damage to the SKs.[17-20] However, the exact mechanism of action for HP40 is unknown. Although a similar adverse effect profile as traditional therapies may be seen using HP40, a recent ex vivo study compared cryosurgery and HP40, concluding that HP40 caused less cytotoxicity and reduced melanocyte damage than cryosurgery.[21] The authors suggested that HP40 is a safer option for SK removal that features a decrease in posttreatment pigmentary alteration.[19,21] Two randomized, double-blind, placebo-controlled studies evaluated the safety and efficacy of hydrogen peroxide topical solution on patients with seborrheic keratosis. After day 106, lesions undergoing two treatments with hydrogen peroxide resulted in scarring, hypopigmentation, and hyperpigmentation in <1%, 3.0%, and 7.8% of lesions, respectively.[22] The authors also found that the percentage of subjects achieving clearance of all four target lesions at day 106 were 4% and 8% while the percentage of subjects in which 3 of 4 target lesions were "clear" was 13% and 23%.[22] Here, we report the methods and results from an HP40 treatment for two individuals.

CASE REVIEWS

Patient one, a 73-year-old female with Fitzpatrick skin type III, stated that she has an extensive history of sun exposure throughout her youth and adulthood. The individual reported that she began to notice the appearance of her SKs approximately 30 years ago on her chest and back region, and she had seen that the number and size of the SKs slowly began to increase over the years. Patient one stated that she has been continuously bothered by the appearance of the SKs indicating that they appear "ugly and unappealing," and made her skin seem "aged," which affected how she perceived her image. She expressed dislike in the color and texture of the SKs, and due to the appearance, she believes that when people saw her, they thought she was older than her actual age. She also noted that the SKs are sometimes irritating, producing discomfort. Patient one explained that she previously had traditional treatments, including cryosurgery, and excision, for the cosmetic removal of her SKs, after which she experienced moderate to severe adverse effects. Adverse effects included erythema, blistering, tenderness, and hypopigmentation that mostly resolved after 1 week to 2 months. She indicated that she had noticed some residual post-treatment hypopigmentation in the areas treated with traditional therapies. The patient explained that she scheduled an appointment to talk about the removal of her SKs, and during the appointment, she was introduced to the hydrogen peroxide topical solution called Eskata. The patient stated that she became very interested in Eskata due to it being an alternative, non-invasive treatment compared to the traditional treatment. The patient revealed that she tolerated the initial treatment well with a slight amount of irritation. The patient expressed after the treatment there were very mild adverse effects such as, blistering, redness, and tenderness, for approximately 1 week with no evidence of post-treatment hypopigmentation. In comparing HP40 with her previous treatments, the patient stated the side effects with the HP40 were less overall, but she noted the areas targeted were smaller compared to her other

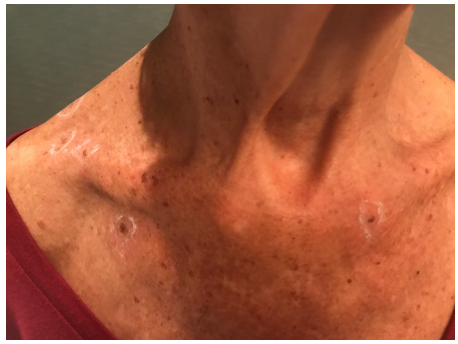
treatments. The patient indicated that she had no trouble caring for the areas treated and that she believes that the HP40 was effective in the removal of her SKs. She observed that a majority of the treated SKs completely disappeared, and the ones that did remain after treatment had a reduction in size. The patient expressed that she was delighted with the outcome and that the treatment has improved her lifestyle. The patient proclaimed that she expresses more confidence and rejuvenation as her skin appears "more youthful and feels younger" since the treatment.

Patient two, a 75-year-old male with Fitzpatrick skin type III, expressed that he had an extensive history of sun exposure throughout his youth and adulthood. Patient two reported that he first noticed his SKs approximately 7 to 10 years previously on his back and chest region. The patient stated that he had never been embarrassed by the appearance of SKs; however, he did express that they were "aesthetically, very unpleasant" and made him feel much "older." The patient stated that he had never previously tried any treatments for the cosmetic removal of his SKs but became very interested in the treatment of HP40 after hearing about the potential of this non-invasive treatment. Specifically, the patient expressed that the reduction of potential adverse effects of HP40 compared to other traditional therapies was appealing. He stated that he never tried any conventional treatment due to his concerns with potential scarring and post-treatment pigmentation changes. The patient stated that he tolerated the initial treatment of HP40 well with no sign of discomfort or irritation, and that he does not recall any pain of adverse side effects after the procedure. The patient stated that within approximately 3 days, two of the treated lesions were completely gone. Altogether, the patient indicated that two of the target lesions were clear, two were partially destroyed, and two were left unaffected. Even with this result, the patient stated that he was thrilled with the outcome, and that the targeted treatment sites appear more youthful and appealing to the eye.

The two patients, both adults over the age of 60, presented with multiple (ranging from 5-6) benign, clinically typical SKs on the neck and chest region as seen in Figure 1.

Lesions ranged from 1 to 1.5 mm in thickness and 5-15 mm in length and width. The SKs were free from any hair that could interfere with the application and diminish the effect of the topical solution. Prior to the application of the topical solution, each targeted SK was disinfected and degreased with alcohol. The treatment was applied by a physician using the single-use, disposable applicator provided with Eskata. Topical solution was applied onto the targeted SKs, and each SK was rubbed, using the angled soft tip of the disposable applicator, with moderate pressure in a circular motion for approximately 20 seconds. The application process was designed to saturate the lesion with the HP40 solution including under any lesion edges using the tapered applicator tip. Treatment cycles were repeated up to 4 times per targeted SK and, according to the instructions for use for Eskata, each targeted lesion requires 60 seconds between each application. Only one treatment session was given for each patient. In some cases, two or more may be required for best results.

FIGURE 1. Clinically typical SK on the neck and chest.

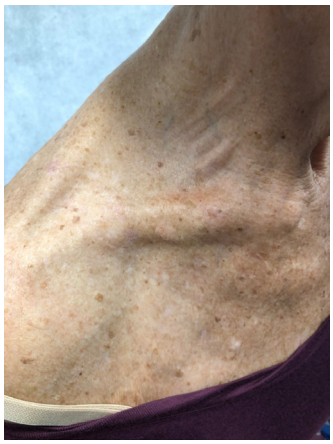


DISCUSSION

Seborrheic keratosis can impose a substantial burden on individuals due to their unappealing appearance, potentially accompanied by medical or cosmetic concerns as well. Many individuals express dissatisfaction with the presence of SKs and seek removal of these benign lesions. From a survey of 406 patients who sought treatment for their SKs, 53% stated they did not like how SKs looked, 33% reported that they were embarrassed by the appearance of SKs, and 31% indicated they believed the presence of SKs resulted in an older appearance.[6] Furthermore, 61% of surveyed female patients stated they have actively tried to disguise the presence of SKs with clothing, make-up, and jewelry.[6]

Similarly, both participants described here indicated they were bothered with the appearance of their skin and uncomfortable with how people perceived them. The patients stated that the presence of SKs hindered their confidence and negatively affected the quality of their life. The individuals became interested in HP40 treatment after learning about the potential benefits and reduced risks compared to traditional therapies for SKs including pigmentary changes, erythema, edema, crusting, and blister formation.[19,21,22] While one individual stated that he had no side effects during and after treatment, the other said that she felt no pain during the initial treatment and after, only mild erythema, tenderness, and minor pain that lasted approximately 1 week. Each expressed no evidence of post-treatment permanent pigment alterations, and many of the targeted lesions were clear or partially clear within 1 to 2 weeks after treatment (Figure 2). Ultimately, both individuals expressed satisfaction with the pro-

FIGURE 2. Partially clear within 1 to 2 weeks after one treatment session with HP40.



cedure. It is important to note that in this application process, only one treatment session was administered per patient. The package insert for Eskata suggests that another treatment may be administered after approximately 3 weeks, if the first treatment did not completely clear the lesions.

In these cases, HP40 produced sufficient and satisfactory results for destruction of SKs while yielding minimal adverse effects. However, HP40 contains a high concentration of hydrogen peroxide, potentially leading to oxidative damage to areas of the skin with increased irritation, pain, and erythema, if treated improperly. To maximize successful clearance of SK and minimize adverse effects, physicians and other practitioners can consider the following techniques.

The first key to treatment success comes with thorough saturation of the lesion during each application. The provider applying the topical solution must treat the lesion with the recommended number application (four) sessions to achieve the optimal clinical endpoint, which is a thorough whitening of the lesion and surrounding skin (approximately 1 millimeter). The affected area should display no evidence of bleeding, erosion, or blister formation. If one of these adverse effects occurs, the lesion has been saturated with too much topical solution, and the provider should move on to a different lesion. The lesion surface should be uniformly wet without any excessive running or dripping onto the surrounding area of the skin. If any residual solution drips onto the surrounding unaffected skin, the provider should remove the excess solution with a clean absorptive wipe. It is important to use a paper towel or tissue because residual solution may still reside on the unaffected skin, which may increase the risk of adverse effects. For best results, allow the lesion to completely dry before another application. The provider should wait the recommended 1 minute between applications and ensure that the topical solution is applied only to targeted lesions.

After treatment with HP40, it is important to leave each lesion dry without applying a dressing or ointment for 4 hours so the hydrogen peroxide solution will have maximum effect. After 4 hours, the patient should apply an occlusive dressing to the treated areas. The targeted areas should remain covered with a bandage and lubricated as needed until the SKs slough off naturally. HP40 is a novel FDA approved treatment for seborrheic keratosis. With careful patient selection and attention to best-practice treatment technique, patients can benefit from removal of unsightly lesions with minimized adverse effects.

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