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Clinical Assessment of AK following Levulan and BLU-U Photodynamic Therapy after Pre-treatment with a Sterile, Plastic Microneedle Device (MSS™)

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ABSTRACT SUMMARY

A small-scale clinical study was conducted wherein the use of a sterile, plastic microneedle device (Microchannel Skin System – MSS™) was investigated for pretreatment prior to photodynamic therapy for the treatment of actinic keratosis (AK) lesions. Over the 30 day study, lesions that were pretreated with the MSS were cleared at a significantly higher rate than those that were not pretreated with the MSS. MSS pretreatment of AK lesion may enhance photodynamic therapy by increasing the absorption of the photosensitizing agent prior to blue light treatment.

INTRODUCTION

AK is a skin condition resulting from years of sun exposure. AK is manifested as rough or scaly lesions that typically occur on the face, neck, ears and lips, where sun exposure is maximized. AK lesions will grow overtime and are considered by some to be precancerous with the potential to develop into squamous cell carcinoma, a serious form of skin cancer. There are several treatment options for AK including cryotherapy, curettage, chemical peeling and photodynamic therapy. Each of these options has advantages and draw backs (1).

In photodynamic therapy, a photosensitizing agent, such as Levulan (or 5-aminolevulinic acid) is applied to the skin prior to blue light treatment to destroy the, now

sensitized, cells. One of the most significant barriers to patient treatment with photodynamic therapy is the need for multiple treatments in order to achieve desired endpoints. Both the number of office visits required and the length of time required for full penetration of the Levulan (typically > 6 hours) prior to blue light treatment make the treatment regime somewhat cumbersome for patients and dermatologists (2).

Research has demonstrated that, when the stratum corneum is disrupted in a controlled fashion, drugs that normally either cannot, or are slow to penetrate into the skin, may be delivered rapidly. Controlled disruption of the stratum corneum offers the opportunity for precise, targeted drug delivery to enhance therapeutic end points for conditions such as AK (3, 4).

EXPERIMENTAL METHODS

Three subjects with at least 10 AK lesions distributed such that there were at least 5 lesions on each side of the face, were presented for photodynamic therapy with Levulan. Study subjects were men and women, over the age of 18 and in good health. On Day 1 of the study, the investigator conducted an AK count and a photoaging assessment and the subject's faces were photographed (full face, left & right 45 degree). Also on Day 1, the left side of each subject's face was pretreated with the MSS device in a designated pattern from hairline to chin

(including the left half of the nose) immediately prior to application of Levulan. The right side of the face was not pretreated with the MSS prior to Levulan application. After 1 hour, the subject's faces were cleansed with witch hazel and then placed in a Blue Light Photodynamic Therapy Illuminator (BLU-U) which was used in the prescribed manner. The BLU-U is designed to deliver a uniform dose of energy at a stable wavelength throughout the entire treatment period (5-10 minutes). Subjects returned for reassessment 2-4 days following treatment and again at 23-37 days following treatment. At each return visit, the subjects were photographed and during the third visit the investigator repeated the AK count and photoaging assessment.

RESULTS AND DISCUSSION

Results of the AK count for the described subjects are shown in Table 1, below.

Table 1. AK Count (initial and 1 month) for subjects treated with photodynamic therapy with and without MSS pre-treatment

Number of Lesions		Initial	Day 30	% clearance
Subject 1	Left (with MSS)	7	1	86%
	Right	6	5	17%
Subject 2	Left (with MSS)	5	1	80%
	Right	7	4	43%
Subject 3	Left (with MSS)	10	0	100%
	Right	10	6	40%
Total	Left (with MSS)	22	2	91%
	Right	23	15	35%

The AK count data were analyzed using two-way Analysis of Variance (ANOVA) with subject and treatment as factors ($\alpha=0.05$). The clearance rate for each subject was used as the response. Treatment was statistically significant ($p=0.028$), with the MSS pre-treatment helping to clear 55% more lesions. If the initial number of lesions is added to the ANOVA as a covariate, treatment remains statistically significant ($p=0.009$).

Previous studies have characterized the depth of penetration associated with the MSS to be approximately 85-140 μ m (4). The devices are designed to be used multiple times within a single treatment session. AK resides within the epidermis, right with the target penetration range for MSS pretreatment. The disruption the MSS provides through the stratum corneum opens access to the epidermis and, perhaps more importantly, replaces the hydrophobic outer layer of the skin with hydrophilic channels to enhance the transport of water soluble compounds such as 5-aminolevulinic acid. It is likely that the success of the MSS pre-treatment regime in this study can be attributed to this phenomenon: the very water soluble photosensitizer was more effectively transported through the upper layers of skin where the AK resides (5), making these cells more sensitive to the effects of the BLU-U.

It should be noted that 1 hour is a very short treatment period for the Levulan; a more typical treatment period is 6-8 hours. This truncated treatment period may be why the untreated portion of the face showed such a low clearance rate. This study evaluated a small population treated with photodynamic therapy. Future directions should be focused at the potential to improve transdermal delivery of other therapeutic and cosmetic products.

CONCLUSION

Although a small study, these results indicate the potential for pretreatment of the skin with the MSS to enhance the therapeutic effects of photodynamic therapy for the treatment of AK. MSS pretreatment creates hydrophilic channels in the skin that are the likely means by which the Levulan is more effectively absorbed by the target cells, making those cells more sensitive to the subsequent blue light treatment. The MSS is a sterile, single use device that can be used for precise and repeated application within a single treatment session.

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