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The Study on the Efficacy of Topical Vitamin K Versus 5% Urea on Laser-induced Purpura

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Abstract

Background: Purpura is a common adverse effect of dermatological procedures and can compromise the patients'appearance especially when they occur on the face. Topical vitamin K oxide has been known to be effective in treatment of purpura from vascular laser and minor surgical procedures. However its effectiveness on purpuric skin with minimal ablation produced by Q-switched Nd-YAG laser has not been studied

Methods: Twenty volunteers had two areas of skin lasered on the upper inner arm using Q-switched Nd:YAG 1064nm laser at slightly purpuric settings. Vitamin K and 5% urea cream were blindly applied to the purpura twice daily as randomly allocated for 10 days. Photographs were taken on days 0, 1,2,4,8, and 10. Improvement of purpura using VAS and adverse effects were recorded.

Results: Twenty volunteers with average age of 35.9 years completed the study. Evaluation by investigators showed no difference in reduction of purpura between the 2 regimens although vitamin K showed a faster onset. Interestingly subjects detected fading of the vitamin K-applied site significantly from the 2nd day after application. All lesions eventually lightened by the 6th day.

Conclusion: In this study topical vitamin K oxide induced lightening of purpura faster than 5% urea cream.

Keywords: Vitamin K oxide; Purpura; Lase

Introduction

Bruising and purpura is common after dermatological procedures associated with surgery, injections and laser procedures. Although the purpuric lesions that are left are temporary, they may take weeks to resolve and can be cosmetically discouraging when they occur on the face or exposed areas. As a result, some regimens were introduced to minimise post-procedural bruising such as various non-prescriptional topical and oral agents.

Topical vitamin K alone or combined with retinol, can reduce bruising intensity and accelerate resolution of Purpura [1-2]. Topical vitamin K is considered safe since vitamin K is a cofactor in the biosynthesis of clotting factors (II, VII, IX and X), and therefore when given topically it is unlikely to affect the systemic levels of vitamin K and the clotting cascade [1,3,4]. The active metabolite of vitamin K is vitamin K oxide, which includes the addition of oxygen to the unstable double bond in the naphthoquinone ring, generating higher stability, less sensitivity to UV light and less allergenicity [1]. Moreover a preliminary study suggests that topical vitamin K oxide preparations are more active for dermal indications than are non-oxide vitamin K creams [1]. Karavani et al. demonstrated that topical vitamin K oxide was safe and non-irritating even after applying since the second day post blepharoplasty [2]. It accelerates the clearing of purpura by unknown mechanism.

Several studies support the efficacy of topical vitamin K in reducing purpura after pulsed dye laser procedures [1, 3, 5]. The pulse-dye laser produces superficial purpura and has penetration of about 2 mm deep [6]. However the Q-switched Nd:YAG 1064nm can produce striking purpura, which could be deeper owing to the Q-switched laser penetration depth of 4-6 mm[6]. Therefore in this study, we compare the efficacy of topical vitamin K oxide to placebo in reducing purpura produced by the Q-swtiched Nd:YAG 1064 nm laser.

Methodology

Twenty-one healthy volunteers age range 21-65 years, skin types II-IV, not currently using oral anticoagulation therapy , e.g., warfarin, heparin, aspirin, clopidogrel and herbals, and without a history of bleeding disorders, were invited to participate. Elemental data: sex, age, skin type, underlying medical conditions and medications were recorded. Exclusion criteria include pregnancy, history of keloidal scar, allergy to cosmetic ingredients, allergy to adhesive dressing and underlying blistering diseases. Informed consent for entering trial was signed by volunteers.

Local application of EMLA, a eutectic mixture of 2.5% lidocaine and 2.5% prilocaine cream (AstraZeneca LP, Wilmington, Delaware) was used as a local anesthetic to the area to be tested 1 hour prior to procedure. Two areas (1cm^2) of normal skin aligned vertically on the upper inner arm of each volunteer was allocated as test areas produced by Q-switched Nd:YAG 1064 nm at slightly purpuric setting (3mm spot size, energy 2.5 J/cm^2, 2 Hz) to minimize ablating the skin. A pair of topical vitamin K

oxide cream (Auriderm XO cream, Auriga International, Belgium) and 5% urea in butyrospermum parkii base cream in identical containers randomly marked as A and B, were assigned to be applied to each purpuric area wherein "A" is for the purpura above and "B" is for the purpura below without the knowledge of both the investigators and patients of which ones contains the active ingredient. The medications were applied twice daily for 10 days. The formula will be disclosed only after the study was complete.

Standardized photographs at right angles to the skin of the lesions were taken on days 0 (baseline), 1, 2, 4, 6, 8 and 10. Immediately post laser, or baseline, patients apply a pea-sized amount (approximately 1/4 tester creams corresponding to the number or code sampled by the patient earlier, and then cover each bruise with an semi-occlusive, commercially available (3M™Tegaderm™Transparent Film) twice daily morning and evening until the end of the trial in order to lessen soreness and prevent accidental removal of the material by rubbing on clothing, and prevent spreading of the creams to an adjacent purpura. If irritation occurs or if rash develops either from sensitivity to the dressing or cream, the subject will be asked to discontinue the treatment. Clinical follow up were appointed on the same days as photograph taking (days 1, 2, 4, 6 and 8) to evaluate efficacy of treatment and adverse effects.

Purpura was assessed using visual analogue scale (VAS) on a 0-10 scale (0=no purpura to 10=intense purpura) by 2 blinded investigators and the subjects. The change in intensity of the purpura on each day compared to baseline was evaluated by the differences of the VAS between baseline compared to 1st 2nd 4th 6th and 8th day after treatment. Irritation was graded by the subjects on a 0-3 scale (0=no irritation to 3=severe irritation). The statistical analysis using in this study was paired t-test.

Results

All 21 volunteers completed the study. There were 19 women and 2 men. The average age was 35.9 years. Evaluation by 2 blinded investigators using VAS comparing efficacy of vitamin K oxide versus 5% urea cream on purpura reduction showed no differences in the rate of lightening of purpura between the 2 tested sites.

The changes in purpura which was evaluated by the differences of VAS score on the 2nd 4th, 6th and 8th day of purpura compared to VAS immediately after (baseline) the purpura was induced by laser. The fading of purpura between

urea cream and vitamin K oxide showed no statistical significance according to the investigators' observations. However all sites showed distinct fading of purpura on the 6th day of application. Although topical vitamin K oxide cream initiated lightening of purpura at an earlier onset than 5% urea , the difference in the timing was not remarkable.(Figure 1 and Table 1 respectively) Volunteers detected more lightening of the lesions treated with vitamin K oxide cream as opposed to 5% urea cream, significantly since the 2nd day post laser. However all lesions faded by the 6th day, which was consistent with the investigators' evaluations (Images 1,2). In terms of side effects, irritation was anticipated in the areas applied by the vitamin K oxide cream more than the area applied by placebo. Mild to moderate irritation was evident on the 1st to 6th day of purpura but none of our volunteers withdrew from the study. Other treatment-related adverse events were not reported.

	Day2	Day4	Day6	Day8
5% urea cream	-0.23800 (p=0.489)	-0.90500 (p=0.125)	-2.57100 (p= 0.000)	-3.905 (p=0.000)
Vitamin K cream	-0.85700 (p= 0.018)	-1.04800 (p= 0.036)	-2.52300 (p= 0.000)	-3.85700 (p= 0.000)

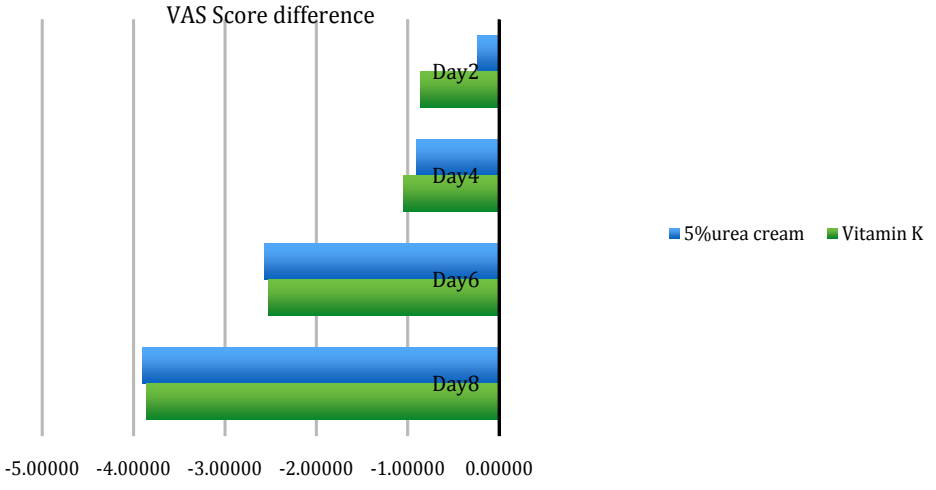

Figure 1 and Table1 show the VAS score difference, evaluated by 21 subjects on lightening of lesions using topical vitamin K cream versus placebo (% 5urea cream) on days 2, 4, 6 and 8 as compared to day1. Results have negative value because the scores on others days are lesser than day1 (paired-T-test).

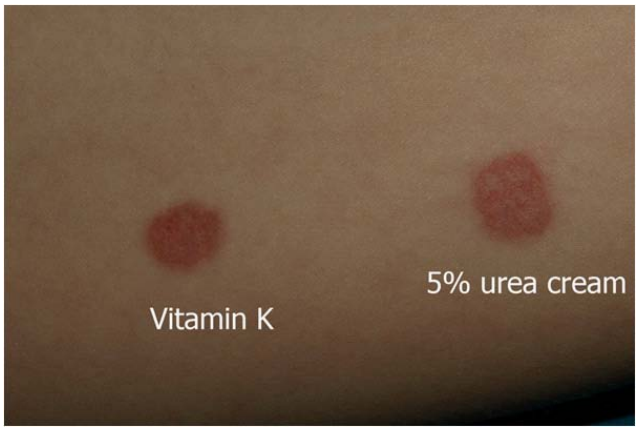

Image 1: The purpuric lesions in one subject on day 1.

Image 2: The purpuric lesions in the same subject on day 6.

Discussion

Cosmetic procedures is well-accepted in Asians as well as other parts of the world, but pigment lightening therapies are particularly popular. Q-switched laser is a common procedure performed to treat pigmented lesions such as freckles, Hori's nevi, tattoo and melasma and often inevitably causes Purpura [6]. Moreover the widespread use of whitening products results in telangiectasias on exposed skin, making it more vulnerable to bruising. Considering the ethnic skin types, post-inflammatory hyperpigmentation and purpura are concerned downtime of laser. Therefore in this study we are determined to discover if topical vitamin K oxide would be more effective than a bland moisturiser, which in this study is 5% urea cream for treating purpura produced by Q-switched Nd-YAG 1064 laser.

Although volunteers started out with a higher VAS compared with investigators'evaluation, the detection of the significant improvement of purpura as early as the second day was reported after vitamin K oxide application by the subjects, but not by the physicians. This can be explained by the fact that patients meticulously observe based on a 3-dimensional and close-up view of their lesions, over the curved contour of the arm, while photographs portray inferior hues and depths. The results of this study correlated with the previous reports which showed the improvement of purpura in the vitamin K used areas but were not statisctically significant[1,3,5,7]

The side effect in this study is irritation which is significantly from the topical vitamin K, and markedly felt on the 1st to 6th day of treatment. However the same vitamin K oxide preparation reported no side effect in a previous study on intact skin post PDL treatment and post blepharoplasty in 2 studies [3, 5, 7]. All of the subjects in our study experienced the irritation symptom which is attributable to the epidermal ablation from Q-switched Nd:YAG.

Conclusion

Topical vitamin K oxide has been known to be effective in treatment of purpura from vascular laser, minor surgical procedures and bruises. Nevertheless it has not be tried on pin point bleeding and purpura produced by Q-switched Nd-YAG 1064nm. In this study although topical vitamin K oxide seems to be superior than 5% urea cream in lightening purpura, the lightening effects is not significantly noticeable to others, and therefore might not be cost beneficial to apply on self-limited purpuric lesion in hopes it will resolve more rapidly. Moreover, due to its irritative formula, it might not be suitable to apply on non-intact skin.

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