

# Comparison of the Effectiveness of Onion Extract, Topical Steroid, and Petrolatum Emollient in Cosmetic Appearance of Upper Blepharoplasty Scar

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## Abstract

**Purpose:** To compare the effectiveness of onion extract, topical steroid, and petrolatum emollient in the prevention of scars in cases who underwent bilateral upper eyelid blepharoplasty.

**Methods:** A prospective, interventional, comparative, double-blinded case series was designed on cases who underwent upper lid blepharoplasty. After suture removal (1 week following the surgery), the eyelids of participants were randomly allocated into the three groups: The first group used onion extract on the right eyelids ( $n = 18$ ), and the second group used topical steroid on the right eyelids ( $n = 19$ ). In the third group, the control group, petrolatum emollient was used on the left eyelids ( $n = 37$ ) of the first and second group's cases. They used drugs for 2 months and were evaluated by the Manchester Scar Scale (MSS) objectively by two graders who were blinded to the type of medication. MSS evaluates five different characteristics of the scar in addition to the Visual Analog Scale (VAS). These characteristics include color, distortion, contour, texture, and transparency. VAS scores the overall scar appearance which ranged among 0–10. The sum of the scores for the five different parameters, and VAS was calculated, analyzed, and compared among the groups.

**Results:** A total of 37 cases (74 eyelids) who underwent bilateral upper blepharoplasty were included. The mean  $\pm$  standard deviation (SD) of age was  $51.94 \pm 9.26$  years,  $49.40 \pm 9.37$  years, and  $47.00 \pm 9.06$  years in the onion extract, topical steroid, and petrolatum emollient groups, respectively ( $P = 0.275$ ). There were no statistically significant differences in the mean  $\pm$  SD of the sum of the MSS scores among the three groups ( $P = 0.924$ ) or between the onion extract and topical steroid groups ( $P = 0.951$ ). Furthermore, the color, distortion, contour, texture, transparency, and VAS scores were not statistically significantly different among the three groups or between the onion extract and topical steroid groups ( $P > 0.05$ ).

**Conclusion:** There were no significant differences among these three groups of drugs regarding the appearance of the upper blepharoplasty scar.

**Keywords:** Blepharoplasty scar, Onion extract, Petrolatum emollient, Topical steroid

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## INTRODUCTION

Blepharoplasty is among the most common types of esthetic surgeries worldwide.<sup>1</sup> A significant problem following facial and eyelid cosmetic surgery is scar formation. It can be discolored, pigmented, elevated, erythematous, and also cosmetically unacceptable.<sup>2-4</sup> Since the scars at the incision

sites may produce functional and esthetic problems and cause psychological stress in the patients, scar prevention is of great concern for every surgeon.<sup>3-5</sup> There is an increasing trend in the use of herbal-extracted, silicon-based, and growth factor-containing products for post-surgical scar

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prevention.<sup>6-8</sup> Although corticosteroids are used worldwide for the postoperative management of periorbital and eyelid incisions, the standard treatment of surgical eyelid wounds is yet to be determined.<sup>5</sup> Investigations on the efficacy of topical drugs in the prevention and management of the upper blepharoplasty scars are scarce.<sup>5-7</sup> Andrew *et al.* performed a comparative study to compare the efficacy of petrolatum emollient with dexamethasone-tobramycin ointment in patients who had undergone skin cancer surgery. Their results demonstrated similar effects in both groups.<sup>5</sup> Murdock *et al.* in 2016 performed a study to evaluate the efficacy and safety of growth-factor and cytokine-containing topical cream for the upper blepharoplasty scar (cream on one eyelid for 12 weeks, and no treatment on the other eyelid).<sup>6</sup> Furthermore, Kalasho *et al.* performed a retrospective study to assess the effectiveness of silicon-based product on the post-blepharoplasty hypertrophic scar.<sup>7</sup> We aimed to compare the effectiveness of one of the best-selling products – onion extract - with one of the popular and frequently used medications – topical steroid - and petrolatum emollient for scar prevention.

## METHODS

We designed a prospective, interventional, comparative, double-blinded case series on patients who underwent bilateral upper blepharoplasty. This study was performed on middle-aged Caucasians with Fitzpatrick skin classification type 3. The exclusion criteria were: (1) diseases that impair wound healing, such as diabetes mellitus and connective tissue disorders, (2) previous upper eyelid surgery or trauma, (3) history of dermatology disorders, (4) significant postoperative hematoma, and (5) patients who used retinoid within 3 months of the surgery. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki, as reflected in the approval by the Ethics Committee of Shiraz University of Medical Sciences (ethics committee approval number #92-01-01-5783). We aimed to compare the difference between two main ingredients in over-the-counter (OTC) products. Two topical OTC products were selected: corticosteroid (hydrocortisone 1% eye ointment, Sina Darou, Karaj, Iran) and onion extract base gel (Contractubex, Merz Pharmaceuticals, Frankfurt, Germany). These two OTC products were compared to the petrolatum emollient as the control group. The sample size was at least 18 in each group ( $r = 3$ ) by considering error type 1 = 0.05, power = 0.90, and  $Effect\ Size\ \mu_1 = \frac{\Delta}{\sigma} = 1.25$

We divided our eyelids into the three groups. The first group used onion extract on the right eyelids ( $n = 18$ ), and the second group used topical steroid on the right eyelids ( $n = 19$ ). In the third group, the control group, petrolatum emollient was used on the left eyelids ( $n = 37$ ) of the first and second groups' cases. The upper blepharoplasty was done under standby anesthesia with intravenous sedation by an oculoplastic surgeon (N.O.). Preoperative skin marking was performed while the patient was sitting upright. Furthermore, the location of fat was marked preoperatively. Then, superficial

subcutaneous injection of local anesthetic agent (lidocaine 2% with 1/100,000 epinephrine) was done using a 27 G needle. Skin incision was made with a No. 15 blade. The medial and central fat components through small incisions in the septum were resected using the radiofrequency monopolar tip (only the fats that came easily into the incision were excised). Skin incisions were closed with continuous 6/0 nylon sutures. Sutures were removed on the 7<sup>th</sup> postoperative day. Patients were instructed to apply cold compress for 48 h, and topical erythromycin eye ointment twice daily till suture removal. After removal of the suture, each participant was given one opaque drug canister for the right eye and another one for the left eye, and instructed to apply on the eyelid two times a day for 2 months, concurrently with wound line massage. Both of the observers (B.Kh. and M.R.Kh.) were blinded to the type of medication. Topical medications were given to the patients in opaque canisters by a third ophthalmologist (M.Sh.). The patients and the observers were blinded to the types of drugs given. All patients were evaluated 1 week postoperatively and then in the 4<sup>th</sup> postoperative week for assessing the side effects and for refilling the drugs, if required. All patients were evaluated objectively in the 2<sup>nd</sup> postoperative month. For objective assessment of the scar, all patients were evaluated by the two observers using the Manchester Scar Scale (MSS).<sup>9</sup> MSS evaluates five different characteristics of the scar, in addition to the Visual Analog Scale (VAS). These characteristics include color (score 1–4), distortion (score 1–4), contour (score 1–4), texture (score 1–4), and transparency (score 1–2). In each parameter, higher scores indicated the worst scar. VAS scores the overall scar appearance ranging from 0 to 10, with the highest number showing the worst appearance. The sum of the scores for the five different parameters and VAS were calculated and compared.

The results were statistically described as mean  $\pm$  standard deviation (SD) in continuous variables. Furthermore, frequency and percentage of categorical variables were reported. The normality of continuous variables was checked using the Shapiro-Wilk test, and parametric tests were used to perform the statistical analysis. The inter-rater agreement was calculated by computing the intraclass correlation coefficient (ICC). ICC values higher than 0.75 were considered good, and those above 0.90 were regarded as excellent.<sup>10</sup> In addition, the analysis of variance was carried out to compare the scores (according to the means of the scores of two observers) among the three groups. The level of significance for statistical tests was 0.05. SPSS software version 24 (IBM Corp., Armonk, NY, USA) was used for the statistical analysis.

## RESULTS

In total, 74 eyelids from 37 age- and gender-matched cases (19 females and 18 males) were enrolled in this study, met the inclusion criteria, and completed the study. The mean  $\pm$  SD of age was  $51.94 \pm 9.26$  years (range, 35–69) in the onion extract group,  $49.40 \pm 9.37$  years (range, 28–69)

in the steroid group, and  $47.00 \pm 9.06$  years (range, 28–69) in the petrolatum emollient group [Table 1]. There was no significant difference among the three groups regarding age ( $P = 0.275$ ).

The measurement of inter-rater agreement showed good value ( $ICC > 0.75$ ). It was  $0.852$  (95% confidence interval of  $0.78$ , and  $0.91$ ). We used the mean of the scores of the two observers for analysis of data. Each group scar appearance was scored according to the MSS values plus VAS. The mean  $\pm$  SD of sum of MSS scores (according to the mean of the scores of the two observers) was  $9.08 \pm 3.23$ ,  $9.08 \pm 3.45$ , and  $9.26 \pm 3.37$  in the onion extract, steroid, and petrolatum emollient groups, respectively, which were not statistically different among the three groups or between the onion extract and steroid groups ( $P = 0.924$  and  $0.951$ , respectively). The mean  $\pm$  SD of color score was  $1.54 \pm 0.43$ ,  $1.62 \pm 0.61$ , and  $1.69 \pm 0.53$  in the onion extract, steroid, and petrolatum emollient groups, respectively ( $P = 0.71$ ). The mean  $\pm$  SD of distortion score was  $1.66 \pm 0.33$ ,  $1.63 \pm 0.41$ , and  $1.57 \pm 0.59$  in the onion extract, steroid, and petrolatum emollient groups, respectively ( $P = 0.61$ ). The mean  $\pm$  SD of contour score was  $1.25 \pm 0.39$ ,  $1.13 \pm 0.66$ , and  $1.19 \pm 0.57$  in the onion extract, steroid, and petrolatum emollient groups, respectively ( $P = 0.22$ ). The mean  $\pm$  SD of texture score was  $1.51 \pm 0.40$ ,  $1.60 \pm 0.68$ , and  $1.72 \pm 0.29$  in the onion extract, steroid, and petrolatum emollient groups, respectively ( $P = 0.13$ ). The mean  $\pm$  SD of transparency score was  $0.91 \pm 0.21$ ,  $0.96 \pm 0.35$ , and  $0.90 \pm 0.28$  in the onion extract, steroid, and petrolatum emollient groups, respectively, ( $P = 0.84$ ). The details of the results are summarized in Table 2.

## DISCUSSION

Scar formation can cause esthetic problems and loss of function and have a detrimental impact on a patient's quality of life. Scar formation has a significant association with anxiety, social avoidance, and depression.<sup>11</sup> Physical appearance of a surgical scar following elective surgery has a great impact on the patients' satisfaction.<sup>12</sup> Surgical planning is the main area of focus in the prevention of scar formation after blepharoplasty, as evidenced by many studies that have compared different surgical planning,<sup>13-15</sup> suturing technique, and materials.<sup>16,17</sup> Wound healing is a harmonious process which consists of different phases that overlap with each other. These include hemostasis, inflammation, proliferation, maturation, and remodeling.<sup>18</sup> Type III Collagen, the main synthesized collagen in the early stage of healing, is gradually replaced by type I collagen. Remodeling and cross-linking of collagen occur in later stages.<sup>19</sup> Transformation of collagen III to collagen I in the wound healing process has a pivotal role in scar formation and appearance. The main players in the chemical arm of remodeling include transforming growth factor beta (TGF- $\beta$ ), matrix metalloproteinase (MMP), and tissue inhibitor of metalloproteinase, as well as hyaluronic acid-stimulating activity.<sup>20</sup>

Active ingredients of OTC products fall in nine main categories. These groups include onion extract, silicon and its derivatives, Vitamin E, Vitamin C, hyaluronic acid, hydrocortisone, hydroquinone, copper peptide, and methylparaben. Among these, the best-selling products contain any or a combination of onion extract, silicon, and Vitamin E.<sup>4</sup>

The exact mechanism of onion extract in the wound-healing process is unknown. Its role probably occurs through its anti-bacterial, anti-inflammatory, anti-proliferative, and

**Table 1: Demographic data of patients**

	Onion extract (n=18)	Steroid (n=19)	Petrolatum emollient (n=37)
Age (year), maximum-minimum	51.94 $\pm$ 9.26 (35-69)	49.40 $\pm$ 9.37 (28-69)	47.00 $\pm$ 9.06 (28-69)
Gender (%)			
Male	9 (50)	9 (47.3)	18 (48.6)
Female	9 (50)	10 (56.7)	19 (51.4)

**Table 2: Comparison of the mean  $\pm$  standard deviation of Manchester Scar Scale scores plus Visual Analog Scale among the three groups**

	Onion extract (n=18)	Steroid (n=19)	Petrolatum emollient (n=37)	P <sup>a</sup>	P <sup>b</sup>
Color <sup>c</sup> (1-4)	1.54 $\pm$ 0.43	1.62 $\pm$ 0.61	1.69 $\pm$ 0.53	0.32	0.71
Distortion <sup>c</sup> (1-4)	1.66 $\pm$ 0.33	1.63 $\pm$ 0.41	1.57 $\pm$ 0.59	0.78	0.61
Contour <sup>c</sup> (1-4)	1.25 $\pm$ 0.39	1.13 $\pm$ 0.66	1.19 $\pm$ 0.57	0.14	0.22
Texture <sup>c</sup> (1-4)	1.51 $\pm$ 0.40	1.60 $\pm$ 0.68	1.72 $\pm$ 0.29	0.29	0.13
Transparency <sup>c</sup> (1-2)	0.91 $\pm$ 0.21	0.96 $\pm$ 0.35	0.90 $\pm$ 0.28	0.76	0.84
VAS <sup>c</sup> (0-10)	2.21 $\pm$ 1.23	2.14 $\pm$ 1.36	2.19 $\pm$ 1.45	0.46	0.15
Sum of MSS plus VAS <sup>c</sup>	9.08 $\pm$ 3.23	9.08 $\pm$ 3.45	9.26 $\pm$ 3.37	0.951	0.924

<sup>a</sup>The comparison between the onion extract and steroid groups, <sup>b</sup>The comparison among the three groups, <sup>c</sup>Higher scores indicate worse scar. MSS: Manchester Scar Scale, VAS: Visual Analog Scale

fibrinolytic properties.<sup>18,21</sup> Quercetin, the active ingredient of onion extract, has been shown to reduce fibroblast proliferation and matrix metalloproteinase-1 expression, both of which play a role in extracellular matrix remodeling.<sup>22</sup> Contractubex® (Merz Pharma, Frankfurt, Germany) contains *Allium cepae* (onion extract) as the active ingredient, with 50U sodium heparin and 1% allantoin. Topical Mederma®, the American formulation of onion gel (Merz North America, Raleigh, North Carolina) lacks heparin. Heparin strengthens the anti-inflammatory effect of onion extract and can enhance the pain relief and collagen restoration.<sup>4,18,21,22</sup>

Steroids by several mechanisms such as decreasing inflammation, inhibition of fibroblast proliferation and collagen synthesis, vasoconstriction and tissue oxygen deprivation, and modulation of TGF- $\beta$ 1 and  $\beta$ 2 ultimately lead to decreased scar tissue formation.<sup>5,18,21,23-26</sup>

Optimal healing after surgery incorporates rapid scar formation with high tensile strength and minimal disfiguring appearance.<sup>18</sup> The standard post-surgical treatment of wounds after dermatologic procedures is yet to be fully understood.

Based on our results, no significant difference was observed in scar appearance when onion extract gel was compared to topical steroid and petrolatum emollient by means of MSS score. In line with our results, a study on the effects of onion extract and petrolatum emollient on scar formation in patients with Mohs surgery, no significant effect of onion extract on color and itching of the scar was observed, but a significant reduction of redness was seen in the petrolatum group.<sup>27</sup> Hosnuter *et al.* demonstrated no significant influence of onion extract gel on the height, itching, and color of scar.<sup>28</sup> Saulis *et al.* also showed that onion extract gel is ineffective in the prevention of redness and scar hypertrophy in an induced rabbit ear wound.<sup>29</sup>

In contrast to the above-mentioned studies, two studies when comparing the effects of onion extract with those of vehicle-based gel and no treatment on incision site of cesarean section found beneficial effects of onion extract in scar reduction.<sup>30,31</sup> This discrepancy between the studies may be due to diversity in the study population, different causes of scar formation, and use of various scales for scoring and assessing scars. The risk of abnormal scar tissue formation is higher in some parts of the body following the surgical wound, such as the shoulder, scapula, anterior chest, lower abdomen, earlobe, and all cutaneous tissues on bony prominences.<sup>32</sup> The discrepancies between the results of our study and other research might be due to the differences in the sites of surgical wounds. The use of onion extract on the areas of cesarean section and thoracic surgery reduces the chance of scar formation because these sites have a higher potential for abnormal scar formation, in comparison with the eyelids, which have a lower risk for scar formation.

From the pathological point of view, fibroblast proliferation, and collagen synthesis occur more vigorously during wound

healing in regions with thick dermis.<sup>33</sup> These processes occur in the eyelids with a lesser intensity due to a very thin dermis. Therefore, onion extract gel could be effective for anatomical regions with thickened dermis that are considered high risk for scar formation. As our results indicated, onion extract gel is not superior to petrolatum emollient for reducing scar formation in the eyelids, as a low-risk anatomical region for scar formation.

Steroids act on inflammation through different pathways, and the effectiveness of intra-lesional steroid injection in preventing scar formation has been reported between 50% and 100%.<sup>23,34,35</sup> Although the effectiveness of intra-lesional steroid on the scar has been proven, the preventive and therapeutic roles of topical forms in recent investigations are disappointing.<sup>19,36</sup> In line with our results, it has been demonstrated that the combination of tobramycin and dexamethasone ointment does not promote wound healing in comparison with petrolatum.<sup>5</sup> Jenkins *et al.* showed that topical steroid did not have any beneficial effect on thickness and final appearance of the scar in patients who had undergone facial reconstructive surgeries.<sup>37</sup> A few other studies have also emphasized that the topical form of steroid was neither effective in the treatment of hypertrophic and keloid scar nor in the prevention of scar formation.<sup>38,39</sup> Many cosmetically unacceptable side effects are reported for topical steroids.<sup>40</sup> Skin atrophy is the most common adverse effect of topical steroids,<sup>41</sup> which makes the appearance of the skin more transparent and shiny, which is cosmetically unacceptable. Contact hypersensitivity with topical corticosteroids is another side effect which increases with prolonged exposure. Non-fluorinated steroids, such as hydrocortisone, leads to even greater scar redness and a less desirable appearance.<sup>42,43</sup> The rate of absorption of topical steroids through the eyelids is significantly higher when compared with the other sites of the body.<sup>44</sup> Investigations about ocular side effects of periorbital steroids are scarce. However, several studies have reported glaucoma and cataract as side effects of topical steroids when used around the eyes,<sup>45-47</sup> which may lead to visual loss if used for prolonged periods.<sup>48</sup> These side effects need to be considered when analyzing the cost and benefits of using topical corticosteroids. When side effects and financial burden are taken into account, petrolatum emollient is considerably cheaper and has limited localized irritation compared to onion extract gel and topical steroids.<sup>49,50</sup>

This study was performed in middle-aged Caucasians with Fitzpatrick skin classification type 3. The risks of hypertrophic scar or keloid development are relatively lower than younger patients with darker skin. Although in the present study, a statistically significant difference was not detected among the treatment groups, a benefit might exist in a higher risk population.

Our study was limited due to the small sample size. Future studies that include a larger number of patients are needed to support our findings.

In conclusion, our study was a comparative investigation that compared the effects of topical steroids, which are used

abundantly after eyelid skin surgery, with one of the best-selling OTC products, onion extract, and petrolatum emollient. The result of this study revealed no significant difference among these three topical medications in the cosmetic appearance of upper blepharoplasty scar. Due to its lower cost and fewer side effects, petrolatum emollient might be suggested as a proper choice for post-blepharoplasty wound care. There is clearly a demand for further research to confirm the results of this study.

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### Conflicts of interest

There are no conflicts of interest.

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