Therapeutic targets in the management of striae distensae: A systematic review

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Title: Therapeutic targets in the management of striae distensae: A systematic review

Article Type: Review

Keywords: striae distensae; striae rubrae; striae albae; stretch marks; therapy; treatment; management; systematic review.

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Abstract: Background: Striae distensae are permanent dermal lesions that can cause significant psychosocial distress. A detailed understanding of the numerous treatment modalities available is essential to ensuring optimal patient outcomes.

Objective: To evaluate and summarize the different treatment methods for striae distensae, by linking their proposed modes of action with the histopathogenesis of the condition, in order to guide patient management.

Methods: A systematic review of the literature was performed with no limits placed on publication date. Relevant studies were assigned a level of evidence by the authors.

Results: 92 articles were identified, with 74 being eligible for quality assessment. The majority of treatments aim to increase collagen production. The use of vascular lasers can reduce erythema in striae rubrae by targeting hemoglobin, whilst increasing melanin, through methods such as UV light, is a major focus for treatment of striae albae. Despite some topical treatments being widely used, uncertainty regarding their mode of action remains. No treatment has proven to be completely efficacious.

Limitations: Low quality evidence, small sample sizes, and varying treatment protocols and outcome measures limit our findings, along with concerns regarding publication bias.

Conclusions: Further randomized controlled trials are needed before definitive conclusions and recommendations can be made.
Dear Editor,

Thank you for accepting our systematic review for publication in JAAD, as well as providing us with suggestions for improvement regarding our tables. Please find below our response to these comments, along with a description of the changes that have subsequently been made in the revised manuscript and highlighted.

We look forward to hearing from you.

Yours sincerely,

Dr. Ardeshir Bayat
Editors comments

1. “JAAD is on a strict page budget. Tables 1, 2, and 3 are far too long to run in the print JAAD and can run online only and will be referenced with a link in the print JAAD. The online version of JAAD (which will contain all the tables) is the official archived version of the journal which is accessed by anyone doing a literature search (PubMed, etc.).

Please rename Tables 1, 2 and 3 as Supplementary Tables 1, 2 and 3 and make the same changes to their citations in the text.

Table IV (which will run the print JAAD) should be renamed Table 1; please make the same change to its citation in the text.” – Thank you for informing us of this. Tables I, II and III have been renamed as Supplemental Table II, III and IV respectively (Supplemental Table I outlining our quality rating scheme remains the same). Table IV has now been renamed Table I. Changes to their citations in the text have also been made.

2. “Regarding current Table IV, it seems that tretinoin fits into both categories, which is a bit awkward. Please insert a footnote explaining that different studies came to opposite conclusions.” - Thank you for this suggestion. Table I (previously Table IV) has now been amended accordingly.
Therapeutic targets in the management of striae distensae:

A systematic review

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Capsule Summary

- Striae distensae are extremely common, permanent dermal lesions. There is great demand for an effective treatment option.
- The majority of treatments aim to increase collagen production, reduce erythema or increase pigmentation.
- Despite some positive outcomes, definitive recommendations cannot yet be made due to a lack of high quality evidence.
Abstract

Background: Striae distensae are permanent dermal lesions that can cause significant psychosocial distress. A detailed understanding of the numerous treatment modalities available is essential to ensuring optimal patient outcomes.

Objective: To evaluate and summarize the different treatment methods for striae distensae, by linking their proposed modes of action with the histopathogenesis of the condition, in order to guide patient management.

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Limitations: Low quality evidence, small sample sizes, and varying treatment protocols and outcome measures limit our findings, along with concerns regarding publication bias.

Conclusions: Further randomized controlled trials are needed before definitive conclusions and recommendations can be made.
Keywords: striae distensae, striae rubrae, striae albae, stretch marks, therapy, treatment, management, systematic review.
Introduction

Striae distensae (SD), also known as stretch marks, are common, permanent dermal lesions that can be symptomatic, and are considered aesthetically undesirable. Thus, they pose a significant psychosocial and therapeutic challenge. They arise in areas of dermal stretching and most commonly occur on the abdomen, breasts, buttocks and thighs.\(^1\)-\(^3\) Most literature has described SD during pregnancy (striae gravidarum) and puberty, with reported prevalences varying from 11\%-88\%.\(^1\),\(^2\),\(^4\)-\(^7\) Hormonal influences,\(^8\)-\(^12\) reduced genetic expression of fibronectin, collagen and elastin,\(^13\),\(^14\) along with mechanical stretching of the skin,\(^2\),\(^15\)-\(^17\) have all been postulated to contribute to SD formation. In the acute phase, SD present as red/violaceous lesions (striae rubrae; SR) that can be raised and symptomatic.\(^18\) The chronic form (striae albae; SA) exists as hypopigmented dermal depressions.\(^18\),\(^19\)

Because of their high prevalence and impact on patients’ quality of life,\(^20\) there is great demand for an effective treatment. A vast array of treatment modalities have been investigated, ranging from topicals\(^19\) and acid peel treatments,\(^21\) to more invasive methods such as laser therapy.\(^22\) Although completely eradicating SD is not attainable, improving appearance whilst reducing physical symptoms certainly is. It is therefore essential that clinicians managing SD have a detailed understanding of available treatment strategies in order to optimize patient outcomes and expectations.
We herein present a systematic review of SD focusing on the different treatments and their proposed modes of action with outcomes, in relation to the histopathogenesis of the condition.

Methods

Searches of both PubMed/Medline and Scopus were conducted using the keywords “stretch marks”, “striae distensae”, “striae rubra”, “striae alba”, “striae gravidarum”, AND “management”, OR “treatment”. No limits were placed on publication date, with the last literature search being conducted in November 2016. Citations of articles were also reviewed. Exclusion criteria consisted of animal/in vitro studies, non-English articles, unavailability of full text, book chapters, conference papers, letters, and reviews not specific to SD.

Data including treatment protocols, number of participants, and striae type were extracted. Relevant articles were assigned a level of evidence (LOE) independently by the authors based on a quality rating scheme modified from the Oxford Centre for Evidence-Based Medicine for ratings of individual studies (Supplemental Table I). The risk of bias was assessed for at both study and outcome level.

Results

92 articles of the 383 initially identified were included for analysis (Figure 1). 74 publications, representing 2328 patients, were relevant for quality
assessment and assigned a LOE, the results of which are as follows: level 1, 15 (20.3%); level 2, 31 (41.8%); level 4, 28 (37.8%).

**Histopathogenesis**
SD were first histologically described in 1889, with SR and SA being histologically distinct from one another (Figure 2). They exhibit abnormalities in three core components of skin which normally provide it with tensile strength and elasticity; collagen, elastin and fibrillin. Early changes associated with SR include accumulation of degranulating mast cells and macrophages around mid-dermal elastic fibers, resulting in elastolysis. These changes may be seen in macroscopically normal skin up to 3cm away from the lesion. As the striae progress to form SA, there is gradual epidermal atrophy with loss of rete ridges.

**Treatment**
Enhanced collagen production **(Supplemental Table II)**
The vast majority of treatments are targeted towards stimulating collagen production (Figure 3).

**Topical agents**
Tretinoin (retinoic acid) is believed to increase tissue collagen I levels through stimulation of fibroblasts, and has also inhibited activation of matrix-degrading enzymes following ultraviolet (UV) induced skin damage, implying it may also protect the skin from other mechanisms of injury. Numerous studies, have investigated its efficacy (LOE 1,2,4), with the majority...
suggesting that it can improve the appearance of early SD but not at lower
doses. However, study populations were small and common side effects
included transient erythema and scaling of the skin.

Centella asiatica is a plant used in Asian herbal medicine. It contains
asiaticoside which stimulates fibroblasts, with antagonistic effects on
glucocorticoids also described. Its use in the prevention of striae gravidarum
has been investigated, with reported reductions in the development and
severity of striae (LOE 1). No side effects were observed. The use of
Centella asiatica combined with boswellic acid, previously found to have anti-
inflammatory effects, has also been tested. Reductions in striae severity
were noted, however side effects included pruritus (LOE 4).

Hyaluronic acid is also thought to increase collagen production through
stimulation of fibroblasts. Two RCTs (LOE 1) have reported improvements in
the appearance of striae following its use, with a reported side effect being
pain following treatment. No follow up was conducted and both
incorporated subjective assessments into their outcome measures.

*Chemical peel treatments*

Chemical peel treatments involve the application of trichloroacetic acid (TCA)
or glycolic acid (GCA). They are thought to induce an initial inflammatory
response, with subsequent increased collagen production. A nonrandomized controlled trial investigating GCA reported decreases in striae
furrow width, however concluded it may yield better results when used in
combination with other products. GCA combined with tretinoin and L-ascorbic acid, and TCA combined with the use of sand abrasion or a postpeel cream are such examples, all of which produced improvements in the appearance of striae. No RCTs have been performed (GCA – LOE 2, TCA – LOE 4) and postinflammatory hyperpigmentation (PIH) remains a concern.

Mechanical techniques
Aluminum oxide microdermabrasion mechanically ablates damaged skin. A study investigating its use in SD reported clinical improvements and increased type 1 procollagen formation (LOE 2). Reported side effects included PIH.

Radiofrequency (RF) devices
RF devices deliver RF current to the skin, which is converted to heat in the dermis due to its electrical resistance. Following initial collagen denaturation with its use, there is subsequent increased collagen production. The majority of trials investigating RF for the treatment of SD have reported clinical improvements (LOE 1,2,4). However, side effects include erythema and edema, and the majority of trials had small cohorts.

Fractional lasers
Fractional lasers deliver microscopic beams of coherent and monochromatic light energy to the skin, creating areas of thermal damage termed
microthermal zones, leading to increased dermal collagen production.\textsuperscript{53-56} Both ablative and non-ablative lasers are available, with ablative lasers targeting water and resulting in cell vaporization.\textsuperscript{53} Improvements in SD following treatment with a 1540-nm fractional non-ablative erbium glass (Er:glass) laser have been reported (LOE 1,2,4).\textsuperscript{55-60} Malekzad et al\textsuperscript{61} however, observed only a fair or poor improvement in 70\% of patients with its use (LOE 4), and although improvements in SR have been described (LOE 4),\textsuperscript{62-64} the literature suggests that non-ablative lasers are most effective on SA (LOE 4).\textsuperscript{57} Concerns surrounding PIH also remain.\textsuperscript{18,57,61,63} Fractional ablative CO\textsubscript{2} lasers have primarily been utilized in SA, with reported clinical improvements (LOE 2,4).\textsuperscript{65-69} Side effects include PIH. Gungor et al\textsuperscript{70} compared the efficacy of an ablative erbium-yttrium aluminum garnet (Er:YAG) laser with a non-ablative neodymium-doped yttrium aluminum garnet (Nd:YAG) laser and found poor clinical results with both (LOE 2). When compared to non-ablative lasers, the literature suggests ablative lasers are less well tolerated and produce inconsistent results.\textsuperscript{53} Diode laser The 1450-nm diode laser is a non-fractional laser, which has been shown to increase dermal collagen.\textsuperscript{71} However, a RCT investigating its use in Fitzpatrick skin types IV-VI reported no improvements in SD, but high rates of PIH (LOE 1).\textsuperscript{71}
*Intense pulsed light (IPL)*

IPL consists of a broad-spectrum (515-1200-nm) visible beam of high intensity light. Studies investigating its use in SD have demonstrated increased dermal collagen levels following treatment (LOE 4). However, a study comparing IPL against a fractional CO\(_2\) laser for the treatment of SD, concluded that the laser was more effective (LOE 2). No RCTs have yet been performed and PIH remains a cause for concern.

*Percutaneous collagen induction therapy (PCT)*

PCT, or needling therapy, involves the creation of micro-clefts extending to the papillary dermis, resulting in increased production of collagen and elastin. Aust et al reported improvements in skin texture and tightening following treatment (LOE 4). More recently, PCT compared favorably against microdermabrasion combined with sonophoresis, and a CO\(_2\) laser (LOE 2). However, there are no RCTs, and side effects include erythema.

*Platelet-rich plasma (PRP)*

PRP is a concentrated solution of autologous platelets containing growth factors and cytokines injected intradermally. Ibrahim et al investigated its use in SD with microdermabrasion, and despite increased collagen levels following PRP treatment alone, 13% developed worsening of their striae (LOE 2). They concluded it is best to use PRP in combination with microdermabrasion. Other studies have combined PRP with RF (LOE 4) and microneedling (LOE 2), all reporting varying degrees of clinical
improvement. However, small sample sizes and no RCTs make drawing definitive conclusions difficult. Side effects include bruising.\textsuperscript{45,80}

\textit{Infrared light}

Infrared light applied to skin causes heating of the dermis and collagen denaturation, with subsequent neocollagenesis.\textsuperscript{83} Trelles et al\textsuperscript{83} investigated its use in the treatment of SA. Despite positive histological findings, including more pronounced rete processes, detection of improvements clinically remained low (LOE 4). Side effects were limited to erythema of the skin.

\textit{Galvanopuncture}

Galvanopuncture is a needling therapy which applies a continuous microcurrent, inducing an inflammatory reaction with subsequent collagen production.\textsuperscript{84} Bitencourt et al\textsuperscript{84} investigated its use in SA. All patients demonstrated clinical improvements and erythema was the only side effect (LOE 4). Further trials, with histological analysis, are needed to further assess its efficacy.

\textbf{Reduced vascularity (Supplemental Table III)}

\textit{Vascular lasers}

The 585-nm pulsed dye laser (PDL) is a commonly used vascular laser. Due to its high affinity for hemoglobin, which is present in the microvasculature of SR, it can reduce the erythema of these lesions (LOE 2).\textsuperscript{85} Although improvements in both collagen\textsuperscript{85,86} and elastin\textsuperscript{87} been described following PDL treatment, these are probably subclinical and PDL is likely to have minimal
benefit in the treatment of SA (LOE 2,4). Care should be taken when using PDL with darker skin types (Fitzpatrick IV to VI), as melanin competes with hemoglobin for the light energy, which can result in PIH. Longo et al tested the 577-nm copper bromide laser, which has higher rates of absorption by hemoglobin than its PDL counterpart. 33% had complete resolution of their SD with the remainder showing a reduction in striae size (LOE 4). Crusting of the skin was a reported side effect. The Nd:YAG vascular laser has also produced clinical improvements in SR (LOE 2,4), however side effects include PIH.

Increased melanin (Supplemental Table IV)

UV light

A major aim for the treatment of SA is repigmentation of the lesion. Sadick et al investigated the combined use of UVB (296-315-nm) and UVA1 (360-370-nm) light in nine individuals. Despite all patients initially having >50% improvement in pigmentation, this was only temporary and side effects included transient hyperpigmentation (LOE 2).

Excimer laser

The xenon chloride (XeCl) excimer laser delivers narrow band (308-nm) UVB radiation. Its proposed advantages include being able to deliver the radiation quicker with increased precision when compared with standard UV therapy. Studies have reported improvements in striae pigmentation following its use (LOE 1,4). However, poor results were observed elsewhere (LOE 2) and
spaying of the pigment to involve surrounding skin is a reported side effect.\textsuperscript{93,95}

A study investigating UVB light therapy and the XeCl excimer laser found that both cause hypertrophy and increase of melanocytes, along with an increase in melanin, albeit not permanent.\textsuperscript{96}

Other (Supplemental Table IV)

Bio-Oil\textsuperscript{®} (Union Swiss Ltd, South Africa) consists of vitamins and plant extracts with an oil base.\textsuperscript{97} One study investigating its use in SD demonstrated visual improvements after two weeks (LOE 2).\textsuperscript{98} No side effects were reported.

Cocoa butter is a natural fat, and used as a topical formulation to rehydrate the skin.\textsuperscript{99} Two trials have investigated its use in preventing SD (LOE 1).\textsuperscript{100,101} Both failed to show any significant benefits with its use.

Soltanipoor et al\textsuperscript{102} and Taavoni et al\textsuperscript{103} hypothesized that, because of its high vitamin E content and moisturizing properties, olive oil could have a role in preventing striae gravidarum. However, no benefits with its use were reported (LOE 1).

Taşhan et al\textsuperscript{104} studied the use of almond oil alone and with massage in preventing striae gravidarum formation, and observed fewest striae in those applying almond oil with massage (LOE 2). However, a RCT comparing the
effects of an Iranian produced cream (Saj®, Seoidrood Co, Iran), containing almond oil, against olive oil, found neither were effective at reducing severity of striae gravidarum (LOE 1).\textsuperscript{105} No side effects were reported in either trial.

Silicone gel has previously been used to improve scars, with promoting skin hydration being one proposed mode of action\textsuperscript{106} Ud-din et al\textsuperscript{106} investigated the effect of silicone against a placebo on SD. They demonstrated increased melanin and decreases in hemoglobin and collagen with both gels. They concluded that the application of gels by topical massage can improve SD (LOE 1). No side effects were reported.

Discussion

SD are common yet undesirable permanent dermal lesions. Despite a basic understanding of the etiology and histopathological changes that occur, finding an effective treatment is proving challenging. The majority of treatment modalities are targeted towards increasing collagen production. Topical treatments in this category still lack consistent high quality evidence, with the effects of massage potentially influencing the findings. Tretinoin has had variable outcomes, with its efficacy mostly demonstrated for the treatment of SR, and despite both Centella asiatica and hyaluronic acid yielding promising results (Table I), uncertainty regarding the type of striae they are most effective against remains. Chemical peel treatments, microdermabrasion, PRP and PCT also lack high quality evidence, with no RCTs having yet been performed. Emerging techniques such as galvanopuncture look promising, however knowledge regarding its mode of action specific to SD is lacking,
along with evidenced-based trials. Lasers have been used in attempts to increase collagen production, reduce erythema in SR, and increase pigmentation in SA.Accurately interpreting these studies is difficult, owing to the small sample sizes used and short follow up periods. UV light has shown promise for the repigmentation of SA, although its lack of permanency means repeated sessions would be needed. Numerous other topicals, which mostly claim to hold moisturizing properties, are widely marketed despite lack of evidence regarding their mode of action or efficacy.

Limitations
Exclusion criteria used may have resulted in relevant studies being missed, if for example they were not published in the English language. Of those included making direct comparisons is extremely difficult, even for those using the same treatment modality, due to widely varying treatment protocols and differences in study populations. This is compounded by the different outcome measures utilized, of which none are yet validated. A large proportion assessed for improvements through the use of clinical photographs, with differences in lighting potentially influencing results. Patient satisfaction scores were also widely used, however one may question whether scores would change if the treatments were not free/provided outside the trial setting. Small sample sizes and limited follow up periods are also major limitations in a large proportion of studies. Concerns surrounding publication bias also remain, as the vast majority of papers reported some positive results.
Conclusion

Further RCTs are needed before definitive conclusions and recommendations can be made. Future work should focus on creating standardized outcome measures and treatment protocols in order to enable accurate comparisons between treatments.

Acknowledgements

We would like to thank Helen Carruthers for producing the figure illustrations. No external funding was received and we have no conflicts of interest to disclose.
**Abbreviations used**

SD, striae distensae; SR, striae rubrae; SA, striae albae; LOE, level of evidence; UV, ultraviolet; RCT, randomized controlled trial; TCA, trichloroacetic acid; GCA, glycolic acid; PIH, postinflammatory hyperpigmentation; RF, radiofrequency; Er:glass, erbium glass; Er:YAG, erbium-yttrium aluminum garnet; Nd:YAG, neodymium-doped yttrium aluminum garnet; IPL, intense pulsed light; PCT, percutaneous collagen induction therapy; PRP, platelet-rich plasma; PDL, pulsed dye laser; XeCl, xenon chloride.
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**Figure 1:** Flow diagram outlining article selection.

**Figure 2:** Striae Distensae. Histological differences between normal skin (a), striae rubrae (b), and striae albae (c).

Haematoxylin and eosin stain. a) Small collagen bundles and elastin fibers gradually increase in thickness towards deeper areas of the dermis.\(^{32}\) b) Perivascular lymphocyte cuffing along with dermal edema and an increase in glycosaminoglycans may be observed.\(^{25,27,30,53}\) c) Collagen fibers are stretched, aligned parallel to the dermal-epidermal junction and a scanty lymphocytic infiltrate predominates.\(^{25-28,32,53}\)

**Figure 3:** Treatments for SD and the highest LOE available for their use.

The majority of treatments are targeted towards enhancing collagen production. A large proportion of the RCTs conducted have been with topical agents, producing varying results. (LOE – level of evidence, TCA – trichloroacetic acid, GCA – glycolic acid, RF – radiofrequency, IPL – intense pulsed light, PCT – percutaneous collagen induction therapy, PRP – platelet-rich plasma, PDL – pulsed dye laser, Nd:YAG - neodymium-doped yttrium aluminum garnet, UV – ultraviolet, XeCl – xenon chloride).
133 Records identified through PubMed/MEDLINE

250 Records identified through Scopus

53 Duplicate records removed

330 Records screened by title/abstract

246 Records excluded:
Animal studies/in vitro, non-English, full text not available, book chapters, letters, conference papers, irrelevant, reviews not specific to SD

84 Full-text articles assessed for eligibility

11 Articles identified by reference screening

3 Articles excluded:
Irrelevant, reviews not specific to SD

92 Articles included in synthesis
**Normal Skin**

- Visible downward epidermal projections (rete ridges)
- Thin, randomly arranged collagen and elastin fibers in the papillary dermis
- Thick collagen bundles predominate in the reticular dermis

**Striae Rubrae**

- Predominance of fine dermal elastic fibers with evidence of structural changes in collagen
- Dermal edema
- Increased microvasculature contributing to their erythematous color

**Striae Albae**

- Epidermal atrophy with loss of rete ridges
- Densely packed collagen fibers aligned parallel to dermal-epidermal junction
- Elastic fibers arranged in a similar pattern to those of collagen
- Reduced microvasculature resulting in their pale color
Treatment of striae distensae

Modes of action

Enhanced collagen production
- Topicals:
  - Retinoic acid (LOE 1)\(^{12,15,17}
  - Centella asiatica (LOE 1)\(^{16,18}
  - Hyaluronic acid (LOE 1)\(^{19,20}

- Chemical peels:
  - TCA (LOE 4)\(^^{13,14}
  - GCA (LOE 2)\(^^{21,22,23}

- Fractional lasers:
  - Ablative (LOE 2)\(^^{24,25,26}
  - Non-ablative (LOE 1)\(^{27}

- Mechanical techniques:
  - Microdermabrasion (LOE 2)\(^{28,29}

Reduced vascularity
- Vascular lasers:
  - PDL (LOE 2)\(^{30,31,32}
  - Copper bromide laser (LOE 4)\(^{33}
  - Nd:YAG laser (LOE 2)\(^{34,35}

- UV light:
  - UVB/UVAF (LOE 2)\(^{36}

- Laser light:
  - XeCl excimer laser (LOE 1)\(^{37}

Increased melanin
- UV light:
  - UVB/UVAF (LOE 2)\(^{38}

Other
- Topical agents:
  - Bio-oil (LOE 2)\(^{39}
  - Cocoa butter (LOE 1)\(^{40,41}
  - Olive oil (LOE 1)\(^{42,43,44}
  - Almond oil (LOE 1)\(^{45}
  - Silicone gel (LOE 1)\(^{46}

\(\text{References:}\)
1. [12,15,17]
2. [16,18]
3. [19,20]
4. [21,22,23]
5. [24,25,26]
6. [27]
7. [28,29]
8. [30,31,32]
9. [33]
10. [34,35]
11. [36]
12. [37]
13. [38]
14. [39]
15. [40,41]
16. [42,43,44]
17. [45]
18. [46]
**Table I:** Treatment modalities with level 1 evidence supporting their efficacy and/or ineffectiveness.

<table>
<thead>
<tr>
<th>Effective</th>
<th>Ineffective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tretinoin*¹⁹,³³</td>
<td>Tretinoin*³⁵</td>
</tr>
<tr>
<td>Centella asiatica¹⁸,⁴⁰</td>
<td>Non-fractional diode laser⁷¹</td>
</tr>
<tr>
<td>Hyaluronic acid⁴⁰,⁴¹</td>
<td>Cocoa butter¹⁰⁰,¹⁰¹</td>
</tr>
<tr>
<td>Radiofrequency⁴⁹</td>
<td>Olive oil¹⁰²,¹⁰³,¹⁰⁵</td>
</tr>
<tr>
<td>Fractional erbium glass laser⁵⁶</td>
<td>Almond oil¹⁰⁵</td>
</tr>
<tr>
<td>Xenon chloride excimer laser⁹⁴</td>
<td>Silicone gel¹⁰⁶</td>
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</tbody>
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*Separate studies came to opposite conclusions
**Supplemental Table I**: Quality rating scheme modified from the Oxford Centre for Evidence-Based Medicine for ratings of individual studies.

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Study design</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Randomized controlled trial</td>
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<td>Systematic review with meta-analysis</td>
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<td>2</td>
<td>Nonrandomized controlled trial</td>
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<td></td>
<td>Prospective comparative cohort trial</td>
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<td>3</td>
<td>Case-control study</td>
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<td>Retrospective cohort study</td>
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<td>4</td>
<td>Case series</td>
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<td>Cross sectional study</td>
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<td>5</td>
<td>Expert opinion</td>
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<td></td>
<td>Case reports</td>
</tr>
</tbody>
</table>
**Supplemental Table II**: Summary and LOE for treatments used to enhance collagen production in SD.

<table>
<thead>
<tr>
<th>Author</th>
<th>Intervention</th>
<th>Dosage/Regimen</th>
<th>Striae type</th>
<th>Sample size</th>
<th>Outcome measures</th>
<th>Results</th>
<th>Side effects</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kang et al.</td>
<td>Tretinoin cream vs. placebo</td>
<td>0.1% Daily for 6 months</td>
<td>SR</td>
<td>22 (10 treatment, 12 placebo)</td>
<td>Severity assessment scale: none, mild, moderate, severe Patient self assessment Striae length and width Histological analysis</td>
<td>47% reduction in mean severity score of treatment group vs. 2% increase in control 80% of treatment group had marked or definite improvement vs. 8% in control Reduction in length and width (14% and 8% respectively) in treatment group vs. increase (10% and 24% respectively) in control group No significant changes in dermal elastic or collagen fibers</td>
<td>Erythema Scaling Pruritus/burning sensation More common in first 2 months</td>
<td>1</td>
</tr>
<tr>
<td>Pribanich et al</td>
<td>Tretinoin cream vs. placebo</td>
<td>0.025% Daily for 7 months</td>
<td>SR and SA</td>
<td>11 (6 treatment, 5 placebo)</td>
<td>Severity assessment scale: none, mild, moderate, moderate-severe, severe</td>
<td>No significant differences between treatment and control group</td>
<td>Pruritus</td>
<td>1</td>
</tr>
<tr>
<td>Rangel</td>
<td>Tretinoin</td>
<td>0.1%</td>
<td>Not</td>
<td>20</td>
<td>Overall response to</td>
<td>80% had marked to</td>
<td>Erythema and</td>
<td>2</td>
</tr>
<tr>
<td>Reference</td>
<td>Treatment</td>
<td>Duration</td>
<td>Method</td>
<td>Global Improvement</td>
<td>Treatment Duration</td>
<td>Global Improvement</td>
<td>Treatment Side Effects</td>
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<tr>
<td>Elson et al.</td>
<td>Tretinoin cream</td>
<td>3 months</td>
<td>Not stated</td>
<td>16</td>
<td></td>
<td></td>
<td>Erythema</td>
<td></td>
</tr>
<tr>
<td>Hexsel et al.</td>
<td>Tretinoin cream vs. superficial dermabrasion</td>
<td></td>
<td>SR</td>
<td>Global Aesthetic Improvement Scale: worse, no change, improved, much improved, very much improved Patient satisfaction: very unsatisfied, unsatisfied, neither satisfied nor unsatisfied, satisfied, very satisfied Length and width of striae Histological analysis</td>
<td></td>
<td></td>
<td>Pruritus, Erythema Burning sensation, Scaling/crusting Pain Swelling Papules</td>
<td></td>
</tr>
</tbody>
</table>

Note: The table above summarizes information from different studies on the treatment of striae. The duration of treatment, method, and observed outcomes are listed for each reference. The side effects associated with each treatment are also noted.
<table>
<thead>
<tr>
<th>Mallol et al\textsuperscript{38}</th>
<th>Trofolastin (Centella asiatica, α-tocopherol, collagen-elastin hydrolysates) vs. placebo</th>
<th>Daily 12\textsuperscript{th} week of pregnancy to labor</th>
<th>Not stated</th>
<th>80 (41 trofolastin, 39 placebo)</th>
<th>Presence of new striae and severity: 0 = no striae, 1 = few and thin, 2 = many thin or few thick, 3 = many thick</th>
<th>34% of treatment vs. 56% of placebo group developed striae. Severity score was 1.42 in treatment vs. 2.13 in placebo group</th>
<th>None stated</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sparavi-gna et al\textsuperscript{39}</td>
<td>Boswellic acid based cream with Centella asiatica, soia phospholipids and polyunsaturated fatty acids</td>
<td>Twice daily for 3 months to striae and forearm</td>
<td>Not stated</td>
<td>113</td>
<td>Severity score: Grade 1 = &lt; 10 lesions, &lt; 3 cm long and &lt; 5 mm thick, Grade 2 = &gt; 10 lesions, &lt; 3 cm long, and &lt; 5 mm thick, Grade 3 = &gt; 10 lesions, &gt; 3 cm long and &lt; 5 mm thick, Grade 4 = &gt; 10 lesions, &gt; 3 cm long and &gt; 5 mm thick</td>
<td>Mean global severity score reduced by 10% Significant mean improvements in erythema (46.1%), edema (35.3%) and atrophy (29.6%) Mean increase in skin extensibility at 90 days by 3%</td>
<td>Pruritus Erythema Burning</td>
<td>4</td>
</tr>
<tr>
<td>Study</td>
<td>Treatment Description</td>
<td>Application Schedule</td>
<td>SR</td>
<td>Clinical Assessment</td>
<td>Skin elasticity</td>
<td>Notes</td>
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<tr>
<td>Draelos et al⁴⁰</td>
<td>Onion extract cream with Centella asiatica and hyaluronic acid</td>
<td>Twice daily for 12 weeks to thigh Opposite thigh acted as control</td>
<td>52</td>
<td>Clinical assessment by patient and investigator of softness, texture, color and appearance: 0 = no improvement, 1 = minimal improvement, 2 = mild improvement, 3 = moderate improvement, 4 = marked improvement</td>
<td>None stated</td>
<td>Significant mean improvements in appearance, texture, color and softness in patient and investigator evaluations vs. untreated side No significant improvements in skin elasticity</td>
<td></td>
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<tr>
<td>Morganti et al⁴¹</td>
<td>Injectable + topical hyaluronic acid, betaglucan, vit C vs. topical application</td>
<td>Twice weekly dermal injections with twice daily application of topical agents for 16 weeks</td>
<td>Not stated</td>
<td>Prophilometry and reduction in color/overall appearance: 0 = normal color and dermatoglyphic pattern, 0.5 = white/pinky color</td>
<td>None stated</td>
<td>Use of treatment injection and topical provided superior results in all areas when compared to both other groups Topical treatment alone had significant</td>
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</tbody>
</table>

<p>| | | | | | | Pain on injection | 1 |</p>
<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Methodology</th>
<th>Results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>only vs. topical placebo</td>
<td>and dermatoglyphic pattern less evident, 1 = pink, moderately flat, 2 = intense pink, flat, 3 = violaceous, flat skin</td>
<td>improvements on the dermatoglyphic pattern and collagen bundle organization when compared with placebo</td>
<td></td>
</tr>
<tr>
<td>Adatto and deprez</td>
<td>Sand abrasion + TCA + post-peel cream (fatty acids, vit C,E,H, tretinoin precursors, algues and oligo-elements)</td>
<td>TCA – 15% 0.5 g post-peel cream per 10 x 10 cm area 1-8 treatments &gt;1 month apart</td>
<td>Clinical appearance: 1 = fresh, inflammatory, 2a = white, superficial without laddering and palpable depressions, 2b = white, without laddering but with palpable depressions, 3a = white, with laddering &lt;1cm width without deep pearliness, 3b = white, with laddering &lt;1cm width with deep pearliness, 4 = white with laddering &gt;1cm width +/- deep pearliness</td>
</tr>
<tr>
<td>Mazzare-</td>
<td>GCA lotion</td>
<td>70%</td>
<td>SR</td>
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<tr>
<td>Study</td>
<td>Treatment</td>
<td>Duration</td>
<td>Comparison</td>
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<tr>
<td>Ilo et al&lt;sup&gt;21&lt;/sup&gt;</td>
<td>vs. placebo</td>
<td>6 times over 6 months</td>
<td>furrow width and number, hemoglobin and melanin content</td>
</tr>
<tr>
<td>Ash et al&lt;sup&gt;43&lt;/sup&gt;</td>
<td>GCA + L-ascorbic acid, zinc sulfate, tyrosine vs. GCA + Tretinoin</td>
<td>GCA – 20% Tretinoin – 0.05% Daily for 12 weeks to opposite sides of abdomen or thigh</td>
<td>Clinical evaluation based on length, width and overall appearance Profilometry Histological analysis</td>
</tr>
<tr>
<td>Deprez&lt;sup&gt;44&lt;/sup&gt;</td>
<td>TCA based easy peel solution + post-peel cream</td>
<td>TCA – 50% Up to 8 treatments monthly</td>
<td>Clinical appearance Depth of striae</td>
</tr>
<tr>
<td>Ibrahim et al&lt;sup&gt;45&lt;/sup&gt;</td>
<td>Intradermal PRP (group</td>
<td>4-6 sessions at 2-week</td>
<td>SR and 68 (23 group 1, Clinical assessment of improvement:</td>
</tr>
<tr>
<td>Study</td>
<td>Treatment Details</td>
<td>Outcomes</td>
<td>Adverse Effects</td>
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<tr>
<td>1) vs. microdermabrasion (group 2) vs. intradermal PRP + microdermabrasion (group 3)</td>
<td>intervals 34 group 2, 11 group 3) worsening, no improvement, mild (&lt;25%), moderate (25-50%), marked (50-75%), excellent (≥75%) Patient satisfaction: not satisfied (&lt;25%), slightly satisfied (25-50%), satisfied 50-75%, very satisfied (≥75%) Histological analysis</td>
<td>higher patient satisfaction in groups 1 and 3 when compared to group 2. Increased dermal collagen deposition in all groups Increased epidermal thickness and rete ridges formation especially after PRP injection</td>
<td>ecchymosis, worsening of striae Group 2 – worsening of striae Group 3 – pain on injection, ecchymosis</td>
</tr>
<tr>
<td>Abdel-Latif and Elbenda-ry46</td>
<td>Microdermabrasion 5 sessions at weekly intervals Other half of body acted as control</td>
<td>SA 20 Clinical assessment of improvement: mild (&lt;25%), moderate (25-50%), good (50-75%), excellent (≥75%) Analysis of type 1 procollagen α1 mRNA levels</td>
<td>Good to excellent improvement in 50% and mild to moderate improvement in the rest Greater improvement in SR Increased type 1 procollagen α1 mRNA levels in treated striae PIH Erythema</td>
</tr>
<tr>
<td>Manuskiatti et al47</td>
<td>TriPollar RF device 40-50 W 6 sessions with weekly intervals</td>
<td>SA 17 Clinical assessment of improvement: &lt;25%, 25-50%, 51-75%, &gt;75% Patient satisfaction: not satisfied, slightly 25-50% and 51-75% improvement in 38.2% and 11.8% of patients respectively 12%, 23% and 65% of patients were slightly Occasional pinching sensation during treatment</td>
<td>Occasional pinching sensation during treatment</td>
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<tr>
<td>Authors</td>
<td>Treatments</td>
<td>Protocol Details</td>
<td>Scale</td>
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<tr>
<td>Suh et al 48</td>
<td>RF + PDL</td>
<td>3 sessions 4 weeks apart RF - 53-97 J/cm² PDL – 585-nm First session both PDL + RF were used Weeks 4+8 PDL alone was used</td>
<td>SR and SA</td>
</tr>
<tr>
<td>Harmelin et al 49</td>
<td>Bipolar RF + IR light vs. fractional bipolar RF vs. fractional bipolar RF + IR light</td>
<td>Bipolar RF + IR light - 100 J/cm² Fractional bipolar RF - 50-65 mJ/pin Monthly sessions for 3 months Abdomen</td>
<td>Not stated</td>
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<tr>
<td>Study</td>
<td>Treatment</td>
<td>Sessions</td>
<td>Length and Width of Striae</td>
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<tr>
<td>Dover et al(^{50})</td>
<td>Multipolar RF + pulsed magnetic fields</td>
<td>6 sessions (No further information given)</td>
<td>Not stated</td>
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<tr>
<td>Issa et al(^{51})</td>
<td>Ablative fractional RF + Tretinoin cream + acoustic pressure</td>
<td>4 sessions every 4 weeks RF - 45 W Tretinoin - 0.05%</td>
<td>SA</td>
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<tr>
<td>Study</td>
<td>Treatment 1</td>
<td>Treatment 2</td>
<td>Outcome 1</td>
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<tr>
<td>Mishra et al(^{52})</td>
<td>Ablative fractional micro-plasma RF</td>
<td>US - 50 Hertz + 80% intensity</td>
<td>Clinical assessment of severity on a scale of 1-4 (4 = most severe) Patient assessment of improvement on a scale of 0-4 (4 = marked improvement)</td>
</tr>
<tr>
<td>Shin et al(^{54})</td>
<td>Succinylated atelocollagen or placebo vs. succinylated atelocollagen or placebo + ablative fractional CO(_2) laser</td>
<td>4 sessions every 2 weeks</td>
<td>Clinical improvement: 0 = no improvement, 1 = 1-25%, 2 = 26-50%, 3 = 51-75%, 4 = 76-100% Erythema and melanin index Histological analysis (6 patients)</td>
</tr>
<tr>
<td>Study</td>
<td>Laser Type</td>
<td>Parameters</td>
<td>Clinical Improvement</td>
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<tr>
<td>de Angelis et al&lt;sup&gt;55&lt;/sup&gt;</td>
<td>Fractional non-ablative Er:glass laser</td>
<td>1450-nm at 12-55 mJ/mb 2-4 sessions with 4-6 week intervals</td>
<td>SR and SA 51</td>
</tr>
<tr>
<td>Stotland et al&lt;sup&gt;56&lt;/sup&gt;</td>
<td>Fractional non-ablative Er:glass laser</td>
<td>1550-nm at 12-18 J/cm&lt;sup&gt;2&lt;/sup&gt; 6 sessions with 2-3 week intervals Untreated site matched striae acted as controls</td>
<td>SR and SA 20</td>
</tr>
<tr>
<td>Bak et al&lt;sup&gt;57&lt;/sup&gt;</td>
<td>Fractional non-ablative Er:glass laser</td>
<td>1550-nm at 30 mJ 2 sessions with a 4 week interval</td>
<td>SR and SA 22</td>
</tr>
<tr>
<td>Study</td>
<td>Treatment Details</td>
<td>Number of Sessions</td>
<td>Intervals</td>
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<tr>
<td>Clementoni and Lavagno</td>
<td>1565-nm Er:glass laser (50-55 J/cm²)</td>
<td>3</td>
<td>4-5 week</td>
</tr>
<tr>
<td>Wang et al.</td>
<td>Fractional non-ablative Er:glass laser</td>
<td>6</td>
<td>3-6 week</td>
</tr>
<tr>
<td>Study Authors</td>
<td>Laser Type</td>
<td>Parameters</td>
<td>Treatment Duration</td>
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<tr>
<td>Malekzadeh et al 61</td>
<td>Fractional non-ablative Er:glass laser</td>
<td>1540-nm at 50-70 J/cm² 4 sessions at 4 week intervals</td>
<td>SA</td>
</tr>
<tr>
<td>Kim et al 18</td>
<td>Fractional non-ablative Er:glass laser</td>
<td>1550-nm at 15 mJ/MTZ 1 session Normal adjacent skin and untreated striae used as controls</td>
<td>SA</td>
</tr>
<tr>
<td>Alves et al 62</td>
<td>Fractional non-ablative Er:glass laser</td>
<td>1540-nm at 70 mJ/MTZ 3-6 sessions</td>
<td>SR</td>
</tr>
</tbody>
</table>
Clinical improvement was noted in the remaining 2 patients after 4 and 6 sessions respectively.

<table>
<thead>
<tr>
<th>Study</th>
<th>Laser Type</th>
<th>Parameters</th>
<th>Sessions</th>
<th>Clinical Improvement</th>
<th>Patient Satisfaction</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guimarães et al&lt;sup&gt;63&lt;/sup&gt;</td>
<td>Fractional non-ablative Er:glass laser</td>
<td>1550-nm at 80-100 mJ/MTZ 4-8 sessions at 4 week intervals</td>
<td>SR 10</td>
<td>Clinical improvement and patient satisfaction score: 0 (no improvement) – 10 (total improvement)</td>
<td>Mean clinical improvement of 8.4 after an average of 6.5 sessions Mean patient satisfaction score of 8.2</td>
<td>PIH 4</td>
</tr>
<tr>
<td>Katz et al&lt;sup&gt;64&lt;/sup&gt;</td>
<td>Fractional non-ablative Er:glass laser</td>
<td>1550-nm at 20-70 mJ/MTZ 3-5 sessions at 4 week intervals</td>
<td>SR 2</td>
<td>Clinical appearance Patient satisfaction</td>
<td>&gt;75% improvement in both patients Both patients highly satisfied with results</td>
<td>Erythema Edema 4</td>
</tr>
<tr>
<td>Lee et al&lt;sup&gt;65&lt;/sup&gt;</td>
<td>Fractional ablative CO&lt;sub&gt;2&lt;/sub&gt; laser</td>
<td>10,600-nm at 10 mJ/MTZ 1 session Retrospectively reviewed</td>
<td>SA 27</td>
<td>Clinical improvement: 0 = worsened, 1 = 0-25%, 2 = 26-50%, 3 = 51-75%, 4 = &gt;75% Patient satisfaction: unsatisfied, slightly satisfied, satisfied, very satisfied</td>
<td>7.4% had grade 4 improvement, 51.9% had grade 3 improvement, 33.3% had grade 2 improvement and 7.4% had grade 1 improvement 22.2% of patients were very satisfied, 51.9% were satisfied, 18.1% were slightly satisfied,</td>
<td>PIH Pruritus Crusting Oozing Erythema 4</td>
</tr>
<tr>
<td>Authors</td>
<td>Treatment Details</td>
<td>Sessions</td>
<td>Outcomes</td>
<td>Comments</td>
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<tr>
<td>Naeini and Soghrati</td>
<td>Fractional ablative CO$_2$ laser (group 1) vs. GCA + Tretinoin (group 2)</td>
<td>SA 6</td>
<td>Clinical improvement: weak = 0-25%, moderate = 25-50%, good = 50-75%, excellent = &gt;75%</td>
<td>Patient satisfaction: 0 (no improvement) to 10 (complete improvement) Surface area of striae significantly higher in group 1 (27%) vs. group 2 (5.2%) Mean difference in striae surface area significantly lower in group 1 (-37.1 cm) vs. group 2 (-7.9 cm) Mean patient satisfaction scores significantly higher in group 1 (3.05) vs. group 2 (0.63)</td>
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<tr>
<td>Yang and Lee</td>
<td>Fractional non-ablative Er:glass laser vs. Fractional ablative CO$_2$ laser</td>
<td>SA 22</td>
<td>Clinical improvement: 0 = no improvement, 1 = &lt;25%, 2 = 26-50%, 3 = 51-75%, 4 = &gt;76%</td>
<td>Clinical improvements observed in 90.9% of striae in both treatment groups Increased skin elasticity and reduced width of striae with both treatments from baseline 81.8% of patients judged their striae as</td>
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<td>Patient satisfaction: 0 = not satisfied, 1 = slightly satisfied, 2 = satisfied, 3 = very satisfied, 4 =</td>
<td>Pain during treatment, PIH and crusting were seen with both lasers but noted to be worse with the CO$_2$ laser</td>
<td></td>
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<tr>
<td>Study</td>
<td>Treatment Details</td>
<td>Outcome Measures</td>
<td>Results</td>
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</tbody>
</table>
| Naeini et al\(^68\) | Fractional ablative \(\text{CO}_2\) laser + fractionated microneedle RF vs. fractionated microneedle RF | Clinical improvement: 0-25\%, 25-50\%, 50-75\%, >75\%  
Patient satisfaction: 0 (lack of improvement) to 10 (complete improvement)  
Surface area of striae | Significantly higher clinical improvement and patient satisfaction scores in \(\text{CO}_2\) laser + RF group vs. RF alone  
Greater reductions in mean surface area of striae with \(\text{CO}_2\) laser + RF vs. RF alone |  
Erythema in both groups  
PIH in \(\text{CO}_2\) laser + RF group |
<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment Details</th>
<th>Clinical Improvement</th>
<th>Histological Analysis</th>
<th>PIH</th>
<th>Pain</th>
<th>Pruritus</th>
</tr>
</thead>
</table>
| Ryu et al.69                   | Fractional ablative CO<sub>2</sub> laser vs. fractionated microneedle RF vs. combination | CO<sub>2</sub> laser – 700 to 1000 mJ RF – 4-7 intensity 3 treatment sessions with 1 month intervals | Not stated | 30 (10 per group) | Clinical improvement: 1 = 0-30%, 2 = 30-50%, 3 = 51-80%, 4 = ≥81%  
Histological analysis (2 patients) | Mean clinical improvement was 2.2 in CO<sub>2</sub> laser only group, 1.8 in RF only group and 3.4 in combination group  
Thickened epidermis and increased collagen in combination group | PIH Pain Pruritus |
| Gungor et al.70                | Ablative Er:YAG laser vs. non-ablative Nd:YAG laser                               | Er:YAG laser - 2940-nm at 3.2 J + 1 J Nd:YAG laser - 1064-nm at 50 J/cm<sup>2</sup> 3 sessions at monthly intervals Treatments randomized to either side of abdomen  
SR and SA | 20 | Clinical improvement: <33% = poor, 33-66% = moderate, >66% = good  
Histological analysis (6 patients) | Those with SA had a poor response to both lasers (17 patients)  
Those with SR had a moderate response to both lasers (3 patients)  
No change in epidermal or dermal thickness  
Collagen fibers following Nd:YAG treatment showed decrease parallelism compared to Er:YAG treated side | Erythema and PIH with Er:YAG laser |
| Tay et al.71                   | Non-ablative diode laser                                                         | 1450-nm at 4,8 and 12 J/cm<sup>2</sup> 3 sessions with 6 week intervals Opposite side SR and SA | 11 | Clinical improvement: 1 = ≤25%, 2 = 26-50%, 3 = 51-75%, 4 = >75%  
Patient satisfaction: A = not satisfied, B | No noticeable improvements when compared with control  
No patients were satisfied with treatment | Erythema PIH |
<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Wavelength</th>
<th>Intensity</th>
<th>Sessions</th>
<th>Scale</th>
<th>Improvement Description</th>
<th>Length and number of striae</th>
<th>Histological Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hernández-Perez et al. 72</td>
<td>IPL</td>
<td>515-1200-nm</td>
<td></td>
<td>5 sessions with 2 week intervals</td>
<td>SA</td>
<td>Clinical improvement: scale by crosses – 0 = no improvement, + = mild, ++ = moderate, +++ = good, ++++ = very good Length and number of striae Histological analysis</td>
<td>Clinical improvement was moderate in 40%, good in 20% and very good in 40% Reduced total length and number of striae Improved collagen fiber quality Increased dermal thickness (2.03 mm pre treatment vs. 3.31 mm post treatment)</td>
<td>PIH</td>
</tr>
<tr>
<td>Bedewi and Khalafawy 73</td>
<td>IPL</td>
<td>535, 550 + 580 nm</td>
<td>25-35 J/cm²</td>
<td>5 sessions with 3-4 week intervals</td>
<td>SR and SA</td>
<td>Synchrotron IR microspectroscopic study of dermal fibroblasts Histological analysis</td>
<td>Increased collagen, amide1 and beta sheet expression following IPL treatment</td>
<td>Stinging sensation</td>
</tr>
<tr>
<td>El Taieb and Ibrahim 74</td>
<td>Fractional ablative CO₂ laser vs. IPL</td>
<td>CO₂ laser - 10,600-nm at 40 mJ</td>
<td>5 sessions with 1 month intervals</td>
<td>IPL - 590-nm at 20-30</td>
<td>Not stated</td>
<td>Clinical improvement: 1 = ≤50%, 2 = &gt;50% Width and length of striae Patient satisfaction: none or less satisfied = 0, 80% and 32% were deemed to have ≥50% improvement in the laser and IPL groups respectively Significant improvements in striae width in both groups but Erythema Burning Pruritus PIH (Occurrence rates within each treatment group not stated)</td>
<td></td>
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<tr>
<td>Author</td>
<td>Treatment</td>
<td>Duration</td>
<td>Intervals</td>
<td>Objective</td>
<td>Efficacy</td>
<td>Side Effects</td>
<td>Results</td>
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<tr>
<td>Al-Dhalimi \ Abo Nasyria\textsuperscript{75}</td>
<td>IPL</td>
<td>J/cm(^2) 10 sessions twice weekly for 5 months</td>
<td>No intervals stated</td>
<td>Sum of length and width of striae</td>
<td>Satisfied = 1</td>
<td>No significant changes in striae length</td>
<td>80% of patients were satisfied in laser group vs. 20% in IPL group</td>
<td></td>
</tr>
<tr>
<td>Aust et al\textsuperscript{76}</td>
<td>PCT</td>
<td>1 session</td>
<td>No intervals stated</td>
<td>Skin texture, tightening and dermal neovascularization</td>
<td>Improved skin texture, no change in pigmentation</td>
<td>None stated</td>
<td></td>
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<tr>
<td>Park et al\textsuperscript{77}</td>
<td>PCT</td>
<td>3 sessions with 4 week intervals</td>
<td>No intervals stated</td>
<td>Clinical improvement: no change (0%)</td>
<td>Marked to excellent improvement in 43.8% with minimal to mild erythema</td>
<td>Pain Spotty</td>
<td></td>
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</tr>
<tr>
<td>Study</td>
<td>Comparison</td>
<td>Treatment Details</td>
<td>Patient Satisfaction</td>
<td>Histological Analysis</td>
<td>Clinical Improvement</td>
<td>Erythema</td>
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<tr>
<td>Nassar et al.⁷⁸</td>
<td>PCT vs. microdermabrasion + sonophoresis</td>
<td>PCT - 3 sessions with 4 week intervals; Microdermabrasion - 10 sessions over 5 months</td>
<td>SR and SA 40 (20 PCT, 20 microdermabrasion)</td>
<td>Clinical improvement: no improvement, mild (≤25%), moderate (26-50%), good (51-75%), excellent (≥76%) Patient satisfaction: not satisfied, slightly satisfied, satisfied, very satisfied, extremely satisfied Histological analysis</td>
<td>Clinical improvements in 90% of PCT treated group vs. 50% in microdermabrasion + sonophoresis treated group Significantly higher satisfaction scores with PCT Epidermal thickness, number of fibroblasts and collagen levels were increased in 90% and 50% of the PCT and microdermabrasion + sonophoresis treated groups respectively</td>
<td>Erythema PIH (more common in microdermabrasion + sonophoresis group) 2</td>
<td></td>
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<tr>
<td>Khater et al.⁷⁹</td>
<td>PCT vs. fractional ablative CO₂</td>
<td>PCT – 3 sessions with 4 week</td>
<td>SR and SA 20 (10 PCT, 10 laser)</td>
<td>Clinical improvement: none, mild (≤25%),</td>
<td>Clinical improvements in 90% of PCT treated group vs. 50% in laser</td>
<td>Erythema PIH (more common in)</td>
<td></td>
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</tr>
<tr>
<td>Study</td>
<td>Treatment</td>
<td>Sessions and Intervals</td>
<td>RF Power</td>
<td>Clinical Improvement</td>
<td>Patient Satisfaction</td>
<td>Histological Analysis</td>
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<tr>
<td>Kim et al(^{80})</td>
<td>Intradermal RF + PRP</td>
<td>3 sessions with 4 week intervals RF - 12 W</td>
<td>Not stated</td>
<td>Clinical improvement: no change, mild (0-25%), moderate (25-50%), marked (50-75%), excellent (75-100%)</td>
<td>Patient satisfaction: unsatisfied, slightly satisfied, satisfied, very satisfied</td>
<td>Excellent improvement in 5.3%, 36.8% marked improvement, 31.6% moderate improvement, 26.3% mild improvement 63.2% of patients satisfied or very satisfied with improvement</td>
<td></td>
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<tr>
<td>Suh et al(^{81})</td>
<td>Plasma fractional RF + PRP + US</td>
<td>RF - 40-45 W 3 sessions with 3 week intervals</td>
<td>SA</td>
<td>Clinical improvement: no improvement, mild (&lt;25%), moderate (25-49%), good (50-74%), excellent (&gt;75%)</td>
<td></td>
<td>Excellent improvement in 33%, 38.9% very good, 22.4% good, 5.6% mild Average reduction in width of striae from 0.75 mm to 0.27 mm</td>
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<tr>
<td>Source</td>
<td>Treatment</td>
<td>Sessions/Intervals</td>
<td>Side</td>
<td>Clinical Improvement</td>
<td>Histological Improvement</td>
<td>Striae Depth Improvement</td>
<td>Erythema</td>
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<tr>
<td>Agamia et al.²²</td>
<td>PCT vs. PCT + PRP</td>
<td>4 sessions with 2 week intervals</td>
<td>PCT alone on right side of body with left side receiving PCT + PRP</td>
<td>None, minimal, moderate, marked</td>
<td>PCT alone - 20% showed marked improvement, 40% moderate improvement, 40% minimal improvement PCT + PRP - 50% marked improvement, 35% moderate improvement, 15% minimal improvement</td>
<td>Significant increase in collagen in PCT + PRP group</td>
<td>None stated</td>
<td></td>
</tr>
<tr>
<td>Trelles et al.²³</td>
<td>Infrared light</td>
<td>800-1800-nm at 31 J/cm²</td>
<td>4 sessions with 15 day intervals</td>
<td>Worse, same, fair, good, very good</td>
<td>4 patients reported improvement as fair, 4 as same and 2 as good</td>
<td>25-50% improvement in striae depth</td>
<td>Erythema</td>
<td></td>
</tr>
<tr>
<td>LOE – level of evidence, SR – striae rubrae, SA – striae albae, TCA – trichloroacetic acid, GCA – glycolic acid, PRP – platelet-rich plasma, RF – radiofrequency, US – ultrasound, Er – erbium, Er:YAG – erbium-yttrium aluminum garnet, IPL – intense pulsed light, Nd:YAG – neodymium-doped yttrium aluminum garnet, PCT – percutaneous collagen induction therapy, PIH – postinflammatory hyperpigmentation</td>
<td>Histological analysis (2 patients)</td>
<td>More pronounced rete processes with tightening of dermis</td>
<td>Bitencourt et al (^8^4) Galvanopuncture</td>
<td>10 sessions once a week at 200 μA</td>
<td>SA 32</td>
<td>Clinical improvement: no improvement, slight (1-25%), moderate (26-50%), good (51-75%), very good (76-100%)</td>
<td>Plasma inflammatory marker levels Cholesterol levels Antioxidant activity</td>
<td>Very good and good improvement in 53% and 47% respectively No significant increase in inflammatory markers No significant changes in cholesterol levels No change in antioxidant activity however overall decrease in oxidative injury</td>
</tr>
</tbody>
</table>
Supplemental Table III: Summary and LOE for treatments used to reduce vascularity in SD.

<table>
<thead>
<tr>
<th>Author</th>
<th>Intervention</th>
<th>Wavelength/ Regimen</th>
<th>Striae type</th>
<th>Sample size</th>
<th>Outcome measures</th>
<th>Results</th>
<th>Side effects</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goldman et al(^{25})</td>
<td>Long-pulsed Nd:YAG laser</td>
<td>1064-nm at 80-100 J/cm(^2)</td>
<td>SR</td>
<td>20</td>
<td>Clinical improvement: poor = ≤30%, good = 30-70%, excellent = &gt;70%</td>
<td>Improvement rated as excellent by 55% of patients and 40% of doctors</td>
<td>Edema Erythema</td>
<td>4</td>
</tr>
<tr>
<td>Elsaie et al(^{60})</td>
<td>Long-pulsed Nd:YAG laser</td>
<td>Striae divided into 3 sections and treated with 1064-nm at 75 J/cm(^2) vs. 100 J/cm(^2) vs. control</td>
<td>SR and SA</td>
<td>45</td>
<td>Global Aesthetic improvement scale: 1 (much improved) to 5 (no change)</td>
<td>Clinical improvements in SA and SR with both fluencies</td>
<td>Pain PIH (Occurrence rates for each fluence not stated)</td>
<td>2</td>
</tr>
<tr>
<td>Reference</td>
<td>Laser Type</td>
<td>Laser Parameters</td>
<td>Treatment Protocol</td>
<td>Outcome Measures</td>
<td>Results</td>
<td></td>
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<tr>
<td>Jimeén-ez et al&lt;sup&gt;85&lt;/sup&gt;</td>
<td>PDL</td>
<td>585-nm at 3 J/cm², 2 treatments 6 weeks apart</td>
<td>Untreated striae acted as controls</td>
<td>Striae area and color Histological analysis</td>
<td>No significant differences in striae area in treatment vs. control striae Improvement in color in SR No improvement in SA Increased collagen in treated striae</td>
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<tr>
<td>Shokeir et al&lt;sup&gt;86&lt;/sup&gt;</td>
<td>PDL vs. IPL</td>
<td>PDL - 595-nm at 2.5 J/cm², IPL - 565-nm at 17.5 J/cm², 5 sessions with 4 week intervals Body area split into two with each side receiving one of the treatments</td>
<td>SR and SA</td>
<td>Clinical improvement: 0-5 Striae width Skin texture Histological analysis</td>
<td>Striae width decreased and skin texture improved with both treatments SR showed greater clinical improvements vs. SA PDL induced higher levels of collagen I expression Erythema, pain, itching and PIH recorded with both treatments</td>
<td></td>
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</tr>
<tr>
<td>McDaniel et al&lt;sup&gt;87&lt;/sup&gt;</td>
<td>PDL</td>
<td>585-nm 4 treatment protocols (spot diameter, fluence): 1 =</td>
<td>SR and SA</td>
<td>Percentage return to normal visual skin patterns Skin shadowing using shadow profilometry</td>
<td>Best results observed with 10 mm spot size + 3 J/cm² fluence All protocols reduced skin shadowing Elastin appeared normal Purpura Erythema Hyperpigmentation Hypopigmentation</td>
<td></td>
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</tr>
<tr>
<td>Study</td>
<td>Platform</td>
<td>Wavelength</td>
<td>Energy Density</td>
<td>Treatment Schedule</td>
<td>Evaluation Parameters</td>
<td>Outcome</td>
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<tr>
<td>Nehal et al(^{88})</td>
<td>PDL</td>
<td>585-nm at 4.25 J/cm(^2)</td>
<td>Sessions at 2-month intervals for 1-2 years</td>
<td>SA</td>
<td>Clinical appearance Striae texture Histological analysis</td>
<td>All 5 patients reported mild improvements in appearance Independent investigators reported minimal to no improvements Improved surface texture in 3 patients No significant histological changes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gauglitz et al(^{89})</td>
<td>PDL vs. fractional ablative Er:YAG laser</td>
<td>PDL - 585-nm at 7 J/cm(^2) Er:YAG laser – 2940-nm at 72 J/cm(^2)</td>
<td>5 sessions with 4-5 intervals Each axilla</td>
<td>SR</td>
<td>Clinical appearance Patient satisfaction Skin texture</td>
<td>Greater improvements with Er:YAG laser reported in first patient Similar improvements with both treatments reported in second patient Both patients favored Er:YAG laser</td>
<td>PIH Erythema Pruritus Crusting</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Laser/Technique</td>
<td>Treatment Details</td>
<td>Clinical Improvement</td>
<td>Results</td>
<td>Complications</td>
<td>LOE</td>
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<tr>
<td>Nouri et al.</td>
<td>PDL vs. short pulsed CO₂ laser</td>
<td>PDL – 585 nm at 3 J/cm² CO₂ laser – 350 mJ and 400 mJ 1 session Striae split into 3 areas and treated with both + control area</td>
<td>Clinical improvement: “did the treated areas look more like normal skin than the untreated control?”</td>
<td>No improvement with either treatment</td>
<td>PIH with both Erythema with CO₂ laser</td>
<td>2</td>
<td></td>
<td></td>
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<tr>
<td>Longo et al.</td>
<td>Copper bromide laser</td>
<td>577 nm at 4-8 J/cm² 1-5 sessions with 1 month intervals</td>
<td>Clinical improvement: Poor, less, good, excellent Striae width, depth and color</td>
<td>5 patients had total disappearance of striae 8 patients had good improvement 2 patients improvements were categorized as less Results maintained at 2 years in 13 patients</td>
<td>Burning Crusting</td>
<td>4</td>
<td></td>
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</tr>
</tbody>
</table>

**Supplemental Table IV**: Summary and LOE for treatments used to increase melanin in SD and various other topicals.

<table>
<thead>
<tr>
<th>Author</th>
<th>Intervention</th>
<th>Dosage/Regimen</th>
<th>Striae type</th>
<th>Sample size</th>
<th>Outcome measures</th>
<th>Results</th>
<th>Side effects</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sadick et al&lt;sup&gt;92&lt;/sup&gt;</td>
<td>UVB/UVA1 light therapy</td>
<td>UVB - 296-315 nm + UVA – 360-370 nm at 45-400 mJ/cm² Twice weekly treatments for a maximum of 10 treatments Adjacent area acted as control</td>
<td>SA</td>
<td>9</td>
<td>Repigmentation: 0-25%, 26-50%, 51-75%, 76-100%, &gt;100% Histological analysis (2 patients)</td>
<td>After final treatment 5 patients had &gt;100% pigmented striae (hyperpigmented), 3 had 76-100% and 1 had 51-75% improvement After 12 weeks 2 patients had 51-75% improvement, 3 had 26-50% improvement, and 4 had 0-25% improvement Increase in elastic fiber to collagen ratio in 1 patient</td>
<td>Erythema PIH</td>
<td>2</td>
</tr>
<tr>
<td>Goldberg et al&lt;sup&gt;93&lt;/sup&gt;</td>
<td>XeCl excimer laser</td>
<td>308 nm at 150-900 J/cm² Up to 15 sessions</td>
<td>SA</td>
<td>75</td>
<td>Repigmentation: none (0%), mild (1-25%), moderate (26-75%), substantial (76-100%) Patient evaluations: worsened, no change, improved Erythema: none,</td>
<td>All subjects achieved ≥76% darkening of their striae 80% noted improvement in appearance of striae Mild to moderate erythema in all patients</td>
<td>Splaying of pigment</td>
<td>4</td>
</tr>
<tr>
<td>Study</td>
<td>Treatment</td>
<td>Dose</td>
<td>Number of Treatments</td>
<td>Repigmentation</td>
<td>Mean Pigmentation Correction</td>
<td>Erythema</td>
<td>Comments</td>
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<tr>
<td>Alexiad-es-Armenakas et al\textsuperscript{94}</td>
<td>XeCl excimer laser</td>
<td>308 nm at minimal erythema dose minus 50 mJ/cm\textsuperscript{2} Up to 10 sessions with 2 week intervals Site matched controls used</td>
<td>SA</td>
<td>9</td>
<td>Repigmentation: 0-100% by visual and colorimetric assessment</td>
<td>Mean pigmentation correction after 9 treatments by visual and colorimetric assessment of 68% and 102% respectively vs. control Both values declined over 6-months</td>
<td>Erythema 1</td>
<td></td>
</tr>
<tr>
<td>Ostovari et al\textsuperscript{95}</td>
<td>XeCl excimer laser</td>
<td>308 nm Up to 10 sessions with weekly intervals</td>
<td>SA</td>
<td>10</td>
<td>Repigmentation and patient satisfaction: poor (0-25%), moderate (26-50%), good (51-75%), very good (76-100%) Colorimetric analysis</td>
<td>80% of patients had poor or moderate results 70% of patients rated their results as poor or moderate Poor effect on repigmentation</td>
<td>Splaying of pigment 2</td>
<td></td>
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<tr>
<td>Goldberg et al\textsuperscript{96}</td>
<td>XeCl excimer laser vs. UVB light</td>
<td>XeCl – 308 nm UVB – 290-320 nm Up to 10 treatments</td>
<td>SA</td>
<td>10 (5 XeCl laser, 5 UVB light)</td>
<td>Histological analysis of melanocytes</td>
<td>Increase in melanin Hypertrophy and increase of melanocytes with both treatments</td>
<td>None stated 2</td>
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<tr>
<td>Summe-</td>
<td>Bio-oil\textsuperscript{\textregistered}</td>
<td>Twice daily</td>
<td>Not</td>
<td>20</td>
<td>Patient and</td>
<td>Significant</td>
<td>None stated 2</td>
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</tr>
<tr>
<td>Study</td>
<td>Treatment</td>
<td>Duration</td>
<td>Methodology</td>
<td>Observer Scar Assessment Scale: 5 parameters (vascularization, pigmentation, thickness, relief, pliability) graded 1 (best) to 10 (worst) Subjective clinical evaluation</td>
<td>Improvements in treated striae vs. untreated striae</td>
<td>Side Effects</td>
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<tr>
<td>Buchan- et al.</td>
<td>Cocoa butter vs. placebo</td>
<td>Daily 12-15 weeks gestation until delivery</td>
<td>Not stated</td>
<td>300 (150 treatment, 150 placebo)</td>
<td>Development of striae: 0 (no striae) to 4 (severe striae)</td>
<td>No significant differences in the development of new striae between treatment vs. placebo group</td>
<td>Mild self-limiting allergic reaction 1</td>
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<tr>
<td>Osman et al.</td>
<td>Cocoa butter vs. placebo</td>
<td>Daily 12-18 weeks gestation until delivery</td>
<td>Not stated</td>
<td>175 (91 treatment, 84 placebo)</td>
<td>Development of new striae and severity: 1 = mild, 2 = moderate, 3 = severe</td>
<td>No significant differences in the development or severity of striae between treatment vs. placebo group</td>
<td>None stated 1</td>
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<tr>
<td>Soltanipoor et al.</td>
<td>Olive oil</td>
<td>Twice daily 18-20 weeks gestation for</td>
<td>Not stated</td>
<td>100 (50 treatment, 50 control)</td>
<td>Development of new striae and severity: 0 = none, 1 = few, 2 = numerous</td>
<td>No significant differences in the development or severity of striae between treatment vs. control</td>
<td>None stated 1</td>
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<tr>
<td>Taavoni et al.</td>
<td>Olive oil</td>
<td>Twice daily 18-20 weeks gestation for</td>
<td>Not stated</td>
<td>70 (35 treatment, 35)</td>
<td>Development of new striae</td>
<td>No significant differences in the development of striae</td>
<td>None stated 1</td>
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<tr>
<td>Study Authors</td>
<td>Treatment Group 1</td>
<td>Treatment Group 2</td>
<td>Outcome Measurements</td>
<td>Significance</td>
<td>Tissue Changes</td>
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<tr>
<td>Taşhan and Kafkasli (2004)</td>
<td>Almond oil vs. almond oil + massage</td>
<td>Every other day from 19 to 32 weeks gestation Daily from 32 weeks gestation until delivery</td>
<td>Development of new striae: Significant differences observed between all 3 groups Almond oil + massage group developed fewest striae</td>
<td>None stated</td>
<td>None stated</td>
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<td>Soltanipour et al (2005)</td>
<td>Olive oil vs. Saj® cream (lanolin, stearin, triethanolamine, almond oil and bizovax glycerin amidine)</td>
<td>Twice daily from 18-20 weeks until 38-40 weeks gestation Untreated subjects acted as controls</td>
<td>Development of new striae: abdomen divided into 4 quadrants – 0 = no striae, 1 = striae which do not affect a quadrant completely, 2 = striae which affect a quadrant completely 1-3 = mild, 4-6 = moderate, 7-8 = severe</td>
<td>None stated</td>
<td>None stated</td>
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<td>Ud-din et al (2006)</td>
<td>Topical silicone gel vs. placebo</td>
<td>Daily for 6 weeks Placebo applied to opposite side of abdomen</td>
<td>Severity, self conscious and impact scores Histological analysis Decreased hemoglobin and collagen with</td>
<td>None stated</td>
<td>None stated</td>
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increased melanin in both silicone and placebo treated sides. Collagen levels significantly higher with lower melanin levels in treatment group vs. placebo.

| LOE – level of evidence, SR – striae rubrae, SA – striae albae, XeCl – xenon chloride, PIH – postinflammatory hyperpigmentation | increased melanin in both silicone and placebo treated sides. Collagen levels significantly higher with lower melanin levels in treatment group vs. placebo. |
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I, Ardishir Bayat, attest that I have submitted for consideration for possible publication in the Journal of the American Academy of Dermatology (JAAD) a manuscript entitled: Therapeutic targets in the management of striae distensae: A systematic review.

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