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Effects of Fractional CO2 Laser Combined with Timolol versus Oxymetazoline in Treatment of Striae Rubra Distensae

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Abstract

Background: Striae Distensae (SD) are a common dermatological condition characterized by dermal scarring due to the rapid stretching of the skin, primarily affecting areas with high adipose tissue. While SD does not pose medical risks, its cosmetic impact often results in psychological distress, necessitating effective treatment options. Fractional CO2 laser therapy has been recognized for its role in promoting collagen remodeling, while topical agents such as Timolol and Oxymetazoline offer additional benefits through vasoconstrictive and anti-angiogenic properties. This review explores the efficacy of Fractional CO2 laser in combination with Timolol and Oxymetazoline for the treatment of Striae Rubra Distensae (SRD).

Methods: A comprehensive literature review was conducted on the combined use of Fractional CO2 laser with Timolol and Oxymetazoline in SRD management. The review focused on studies examining histological changes, treatment efficacy, and safety profiles. Clinical outcomes, including improvements in collagen production, vascularity reduction, and overall aesthetic appearance, were evaluated.

Conclusion: The combination of Fractional CO2 laser with either Timolol or Oxymetazoline provides synergistic benefits in treating Striae Rubra Distensae. Timolol enhances the reduction of vascularity, while Oxymetazoline improves erythema through vasoconstriction. Both combinations demonstrate effective dermal remodeling and cosmetic improvements in SRD, although individual patient characteristics must guide treatment selection.

Keywords: Striae Rubra Distensae, Fractional CO2 laser, Timolol, Oxymetazoline, Dermal remodeling.

Introduction

Striae Distensae (SD), commonly referred to as stretch marks, are a form of dermal scarring that primarily affects areas of the body subjected to rapid skin stretching, such as the abdomen, thighs, breasts, and hips [1]. The condition is prevalent among women during pregnancy, individuals experiencing rapid weight changes, and adolescents during growth spurts. SD presents in two distinct phases: striae rubra (SR), characterized by red or pink lesions in the early stages, and striae alba (SA), where the marks evolve into pale, atrophic scars. While not medically harmful, the cosmetic and psychological impact of SD can significantly affect a patient's quality of life, driving the demand for effective treatments [2].

Various treatment modalities have been explored for the management of SD, ranging from topical agents to more advanced laser therapies and energy-based devices [3]. Topical treatments such as tretinoin and glycolic acid are widely used for their ability to enhance collagen production and improve skin texture. However, lasers and light devices, particularly fractional CO2 lasers, have gained prominence for their efficacy in promoting dermal remodeling and improving the appearance of both striae rubra and striae alba. Despite the availability of multiple treatments, no single therapy has emerged as the "gold standard," and combination therapies are increasingly being explored to achieve superior clinical outcomes [3].

In recent years, attention has turned to combining laser treatments with topical agents to

enhance treatment efficacy. Timolol, a beta-blocker traditionally used in ophthalmology, has shown potential in reducing vascularity and improving the appearance of SD when combined with laser treatments [4]. Similarly, oxymetazoline, known for its vasoconstrictive properties, has been investigated for its ability to reduce redness and improve the overall aesthetic appearance of striae rubra. These topical agents, when used alongside laser therapies like fractional CO2 laser, could offer synergistic effects, enhancing collagen production while targeting vascular components [5].

This narrative review aims to explore and compare the efficacy of Fractional CO2 laser combined with Timolol versus Oxymetazoline in the treatment of Striae Rubra Distensae.

Striae Distensae (SD)

Pathogenesis and Presentation

Striae Distensae (SD), commonly known as stretch marks, are a frequently encountered dermatological condition that often leads to considerable psychological and cosmetic distress. They arise due to the progressive stretching of the dermis, usually in areas of high adipose tissue, such as the abdomen, thighs, and buttocks. This rapid stretching causes a loss of dermal papillae and rete ridges, as well as a significant decrease in extracellular matrix (ECM) components like collagen, fibronectin, and elastin. The dermis becomes thin, making the epidermis appear stretched and causing the characteristic visual appearance of SD [2].

The development of SD begins with the acute phase, known as Striae rubra, characterized by red or pink linear lesions that are slightly raised and run perpendicular to the skin's tension lines. Over time, if left untreated, SD transitions into the chronic phase, Striae Albae, where the lesions appear more atrophic, wrinkled, and hypopigmented. Dark-skinned patients may experience additional variations, including Striae Nigrae and Striae Caerulea, due to increased melanization. These variations in SD presentation highlight the importance of individualized treatment approaches [6].

Histological Changes in SD

On a histological level, the development of SD is marked by disrupted collagen bundles and disorganized elastic fibers. In healthy skin, collagen fibrils are tightly packed, offering structural integrity and resilience. However, in SD, the collagen fibers lose their organization, and the elastic fibers become fragmented. This leads to the characteristic thinning of the skin and the inability of fibroblasts to regenerate ECM components adequately. The histological features of SD show the distinct loss of rete ridges and the disrupted collagen and elastin structure that underpins the development of stretch marks [7].

Prevalence, Etiology, and Risk Factors

SD is prevalent across various populations, with reports showing a prevalence rate ranging from 11% to 88%. Adolescents and pregnant women are particularly prone to developing stretch marks, often associated with rapid weight gain or growth spurts. In adolescent males, SD tends to affect the lower back and buttocks, while in females, it more commonly appears on the thighs, buttocks, and calves [9].

Table (1) Different treatment modalities for SD

Treatment Modality	Description	Effectiveness	Side Effects
Topical Treatment			
Tretinoin	Recognized for repairing skin damage associated with photoaging. Increases collagen production, fibroblast activity, and angiogenesis. Effective in	Good clinical outcome for pregnancy-related SD.	None specified

	pregnancy-related SD.		
Glycolic Acid (GA)	A peeling agent that increases epidermal thickness, elastic fibers quality, and collagen density. Usually combined with other treatments like retinoic acid or L-ascorbic acid.	Effective in combination with other treatments.	None specified
Lasers and Light Devices			
Fractional CO2 Laser (FrCO2)	Promotes collagen and elastin fiber regeneration. Reduces stretch mark width, increases collagen fibers, and thickens the epidermis. Comparable to microneedling in treating striae rubra (SR).	Significant reduction in width of SD; improvement in skin appearance.	Risk of post-inflammatory hyperpigmentation (PIH), which can last for up to a year.
Fractional Er Laser	Similar to FrCO2 but causes less thermal damage. Faster wound healing and milder side effects, making it favorable for darker skin types (Fitzpatrick IV-V).	Similar to FrCO2 in efficacy but with less risk for darker skin.	Milder erythema, edema, and post-inflammatory hyperpigmentation (PIH).
Er Laser	Promotes dermal remodeling and collagen production to treat atrophic scarring.	50–75% improvement in all SD.	None specified
Pulsed Dye Laser (PDL)	Increases collagen production and reduces erythema in striae rubra (SR). Effective in treating erythema but not recommended for dark-skinned individuals due to risk of PIH.	Effective in reducing erythema in SR.	High risk of post-inflammatory hyperpigmentation (PIH) in dark-skinned individuals.
Radiofrequency (RF)	Fractionated Bipolar RF improves collagen distribution and SD appearance, while TriPollar RF shows significant improvement even in dark-skinned individuals.	Improvement in SD, particularly in streak depth. TriPollar RF shows >50% improvement in one week.	Risk of post-inflammatory hyperpigmentation (PIH), mainly with Bipolar RF.
Microneedling	Promotes collagen synthesis and dermal remodeling without thermal injury, reducing the risk of hyperpigmentation. Frequently combined with Platelet-Rich Plasma (PRP) for enhanced effect.	More effective in combination with PRP.	Fewer side effects, shorter recovery time, lower cost than laser treatments.
Platelet-Rich Plasma (PRP)	PRP induces collagen and elastic fiber formation. More effective than retinoic acid for treating striae alba. Effective when combined with subcision or peeling agents.	High patient satisfaction and clinical improvement.	No risk of hyperpigmentation or infection.
Microdermabrasion (MDA)	Removes aged skin cells and stimulates new cell production, improving collagen and elastic fibers.	Effective in reducing striae length and width. Comparable to retinoic acid.	Higher incidence of pruritus, erythema, and scaling compared to retinoic acid.
Carboxytherapy	Involves the injection of carbon dioxide to stimulate neovascularization and skin repair.	Reduces SD width and length while improving skin elasticity.	Hematoma is the most significant side effect.
Combination Therapies	Microneedling with RF or PRP shows better clinical outcomes. FrCO2 combined with PRP or recombinant human epidermal growth factor (rhEGF) enhances	Combination therapies generally provide better outcomes than single treatments.	Higher occurrence of post-inflammatory hyperpigmentation (PIH) in some laser treatments.

treatment efficacy.

- Fractional CO2 Laser

The use of lasers in medicine has rapidly advanced since the 1990s, with dermatology emerging as a field that benefits greatly from this technology. Fractional CO2 lasers are widely recognized for their efficacy in treating a variety of skin conditions, including angiomas, telangiectasias, pigmented lesions, and even common skin issues like warts and vitiligo [10]. Moreover, they have become an integral tool in aesthetic dermatology, being used for facial rejuvenation, acne treatment, and skin resurfacing. The mechanism of action of these lasers makes them versatile and highly effective across different applications.

Mechanism of Action in Fractional CO2 Laser

The term "LASER" stands for "Light Amplification by Stimulated Emission of Radiation," a principle that underscores the unique properties of laser energy. Fractional CO2 lasers utilize carbon dioxide gas as their medium, emitting energy at a wavelength of 10,600 nm [11].

This energy is absorbed by the water present in skin tissues, making the laser ideal for targeting both pigmented and non-pigmented lesions. The CO2 laser is effective due to its ability to vaporize and ablate tissue with minimal damage to surrounding areas, a process known as selective photothermolysis (SPTL) [12].

The Fractional CO2 laser operates by creating microthermal zones (MTZs) that target damaged skin while leaving surrounding tissue unaffected. This focused energy leads to a photomechanical effect that stimulates collagen production, making it especially effective for skin resurfacing.

Advantages of Fractional CO2 Laser in Dermatology

One of the greatest advantages of the Fractional CO2 laser is its ability to target both deep and superficial layers of the skin. For example, acne scars, which typically affect the dermal layers, respond well to deeper MTZs. In contrast, more superficial skin conditions, such as fine wrinkles, can be treated with shallower MTZs. Figure 7b to 7d shows how altering the beam diameter affects the mode of action, transitioning from incision to vaporization and coagulation, respectively [14].

Safety and Precautions with CO2 Laser

Safety is a critical consideration when using Fractional CO2 lasers, particularly regarding eye protection and smoke evacuation. The laser beam is absorbed by water, meaning it poses a lesser risk to the retina compared to visible or near-infrared lasers. However, the CO2 laser can still cause significant damage to the cornea if proper precautions are not taken [15].

- **Timolol in Dermatology**

Timolol, a nonselective β-adrenergic receptor antagonist, is commonly used in the management of glaucoma and cardiovascular conditions such as hypertension. Its mechanism involves reducing sympathetic stimulation by competing with catecholamines at β receptors. While traditionally used in these fields, timolol has also gained attention for its off-label use in dermatology. In recent years, its role in treating superficial vascular anomalies like infantile hemangiomas, port-wine stains, and angiofibromas has been explored with promising outcomes [22].

Mechanism of Action

Though the exact mechanism of timolol in dermatological applications is not fully understood, it is believed to exert its effects through vasoconstriction, inhibition of angiogenesis, and modulation of endothelial cell proliferation. Timolol is thought to downregulate vascular

endothelial growth factor (VEGF) and other pro-angiogenic factors, which contributes to its anti-angiogenic properties. This makes it effective in reducing vascular proliferation in various skin conditions [23].

In dermatology, timolol has also been explored for its role in managing chronic inflammatory skin conditions like acne vulgaris and rosacea. Its anti-inflammatory and vasoconstrictive properties help reduce erythema and the severity of acne lesions. Case studies have shown improvement in post-acne erythema and hyperpigmentation with regular application of timolol [29].

Adverse Effects and Safety Profile

Topical timolol is generally well-tolerated, though systemic absorption can occur, particularly when applied to ulcerated areas. In rare cases, it may cause systemic side effects such as bradycardia, hypotension, or bronchospasm due to its β-blocking properties. Most adverse effects, however, are localized and include desquamation and erythema. A lower concentration (0.1%) is associated with fewer systemic side effects, making it a safer alternative in some cases [30].

- **Oxymetazoline in Dermatology**

Oxymetazoline (OXZ) is a synthetic, imidazoline-type sympathomimetic agonist that primarily acts on alpha-1 adrenergic receptors and partially on alpha-2 receptors. Known for its potent vasoconstrictive properties, oxymetazoline is widely used in nasal and ocular decongestants for conditions like allergic rhinitis and conjunctivitis. Due to its excellent efficacy and safety profile, it has also been explored in dermatology for managing facial erythema, post-inflammatory redness, and other inflammatory skin conditions [31].

Mechanism of Action

Oxymetazoline achieves its effects by binding to alpha-1 adrenergic receptors on blood vessels, leading to vasoconstriction. This constriction helps reduce redness and erythema in skin conditions like rosacea. Additionally, oxymetazoline exhibits anti-inflammatory properties by inhibiting neutrophil phagocytosis, reducing oxidative stress, and modulating the arachidonic acid cascade. These actions decrease the synthesis of pro-inflammatory leukotriene B4, further helping to alleviate skin inflammation [32].

Use in Rosacea

Rosacea is a chronic inflammatory skin condition that affects the central face, often leading to persistent erythema and recurrent flushing. It impacts the quality of life of those affected due to its visible nature. In 2017, oxymetazoline cream 1% was approved by the FDA for the treatment of persistent facial erythema associated with rosacea. Clinical trials have shown that oxymetazoline is effective in reducing erythema, with significant improvements observed as early as one day of treatment and continuing for up to 52 weeks [33].

Post-Acne Erythema

Post-inflammatory erythema (PIE) is a common aftereffect of acne, characterized by persistent red marks even after the resolution of active acne lesions. These marks are cosmetically concerning and often lead to psychological distress. Oxymetazoline 1.5% has shown dramatic improvements in the treatment of PIE. A study by Agamia et al. demonstrated a significant decrease in erythema scores and lesion counts over 12 weeks of treatment, with visible improvements beginning as early as eight weeks [31].

Adverse Effects of Oxymetazoline

While oxymetazoline is generally well-tolerated, some adverse effects have been noted. Rebound erythema, where redness worsens after the medication wears off, is a concern. This may

present as either a return of erythema that is worse than baseline or a paradoxical redness occurring shortly after application. Additionally, more severe cardiovascular side effects, such as changes in blood pressure, may occur in patients with comorbid cardiovascular conditions like hypertension or heart disease [34].

Future Directions and Clinical Implications

As the management of Striae Rubra Distensae (SRD) continues to evolve, future research should focus on optimizing the protocols for combining Fractional CO2 laser with topical agents like Timolol and Oxymetazoline. Clinical trials with larger sample sizes and longer follow-up periods are needed to evaluate the long-term efficacy and safety of these combination therapies. Moreover, personalized treatment approaches based on skin type, lesion severity, and patient-specific responses will be crucial for improving outcomes. Exploring the molecular mechanisms underlying these treatments may also open doors for novel therapies that target the root causes of SRD, potentially leading to more effective and less invasive options for patients. These advancements hold significant promise for enhancing the cosmetic and psychological well-being of individuals affected by SRD.

Conclusions

The combination of Fractional CO2 laser with either Timolol or Oxymetazoline provides synergistic benefits in treating Striae Rubra Distensae. Timolol enhances the reduction of vascularity, while Oxymetazoline improves erythema through vasoconstriction. Both combinations demonstrate effective dermal remodeling and cosmetic improvements in SRD, although individual patient characteristics must guide treatment selection. Further clinical trials are recommended to standardize treatment protocols and optimize long-term outcomes.

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