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CLINICAL REPORT

Split-face study to evaluate efficacy of global cryomodulation for reduction of pain and inflammation after nonablative fractional resurfacing

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Abstract

Objectives: Cryomodulation, or the delivery of controlled cooling to down-regulate inflammatory processes in the skin, has been proposed to mitigate acute side effects following various dermatologic treatments. A new controlled cooling device has been developed to deliver cryomodulation for a range of different indications. In this clinical study, we evaluate the device for the reduction of pain, erythema, and edema following nonablative fractional resurfacing (NAFR).

Methods: A single-blind, prospective, randomized, split-face study was conducted to assess the efficacy of the controlled dermal cooling device for the reduction of pain, edema, and erythema following nonablative fractional resurfacing with the dual 1550 nm erbium-doped fiber and 1927 nm thulium fiber laser. Subjects were randomized to receive a 10-min controlled cooling treatment to either the left or right side of the face immediately following full face NAFR. Pain ratings were recorded immediately postlaser treatment and immediately postcryomodulation treatment. At follow-up, subjects were surveyed for reduction of side effects and treatment satisfaction. Blinded review of photographs by two physicians was conducted to assess efficacy.

Results: The average pain score for subjects immediately post-NAFR was 5.15. Following cryomodulation, the average pain score on the treatment side was reduced by 69%, to an average of 1.6. The untreated side of the face was reduced by 19%, to an average of 4.2. Overall, 90% of subjects endorsed reduced discomfort. At follow-up, 70% of subjects reported a noticeable improvement in edema and 50% reported a noticeable improvement in erythema between the treatment and control sides. The average subject satisfaction score for the cryomodulation treatment was 4.2. All subjects (100%) indicated that they would elect to undergo the cryomodulation treatment again. Both blinded physician reviewers were successful in identifying the cryomodulation-treated side of the face in 70% of subjects' posttreatment photographs.

Conclusions: The results of this split-face study support the efficacy of a global cryomodulation device for the reduction of pain, edema, and erythema following NAFR treatment. Cryomodulation was delivered in a simple 10 min procedure and yielded high patient satisfaction.

KEYWORDS

cryomodulation, fractional laser, laser resurfacing, nonablative fractional resurfacing, postlaser cooling

INTRODUCTION

Nonablative fractional lasers, a common treatment modality for rejuvenation of photoaged skin, are associated with acute posttreatment side effects including pain, erythema, and edema. Most laser systems have cooling incorporated into them. Contact cooling and noncontact cooling methods have been employed, with specific terminology known as precooling, parallel cooling, and postcooling. The goal of this technology is to protect the epidermis, decrease pain and erythema, and improve laser efficacy. It is well established that cooling has led to improved safety, better patient tolerance and satisfaction, and reduced downtime without affecting laser efficacy.[1–4] Yet, despite these measures, there is often still significant erythema, edema, and discomfort following nonablative fractional resurfacing (NAFR).

The analgesic and anti-inflammatory properties of cold have been understood for centuries, with cold medical applications documented as early as 3500 BC in ancient Egyptian medical treatises, and later by Hippocrates in the fourth century BC. Research advancing our understanding of the physiological responses to cold accelerated rapidly in the 20th century, spawning the development of diverse cryomedical applications including pain management, treatment of inflammatory diseases, musculoskeletal injury recovery therapies, and cryosurgical destruction of benign and malignant tumors.[5–7] Researchers determined that cold analgesia involves several mechanisms including reduced nerve conduction velocity and inhibition of nociceptors.[8] The ability of cold to blunt inflammatory reactions is believed to be associated with vascular response, cellular hypometabolism, and changes in the production of inflammatory mediators. Cold-induced vasoconstriction acts as a protective mechanism to reduce edema and infiltration of immune cells. Slowing of metabolic cellular activity inhibits inflammatory signaling and diminishes the production of proteases. Furthermore, research has demonstrated lower production and release of proinflammatory cytokines as well as higher production and release of anti-inflammatory cytokines following therapeutic cooling.[9,10]

A new contact cooling device (Glacial Rx®; R2 Technologies) has been developed to deliver cryomodulation, or precision-controlled cooling. We propose global cryomodulation as an additional postcooling method to mitigate acute side effects following nonablative fractional laser treatment by downregulating inflammatory processes in the skin. A study was conducted at our center to test the hypothesis that postlaser cryomodulation treatment can mitigate the acute side effects of laser treatment by reducing pain and inflammation, improving patient experience, and accelerating recovery.

MATERIALS AND METHODS

A single-blind, prospective, randomized, split-face study was conducted to assess the efficacy of the controlled dermal cooling device for the reduction of pain, edema, and erythema following fractional laser treatment with the 1550 nm erbium-doped fiber laser or a combination of the 1550 nm erbium-doped fiber laser and the 1927 nm thulium fiber laser. Subjects received full-face NAFR treatment and were randomized to receive a 10-min controlled cooling treatment to either the left or right side of the face immediately following the laser treatment.

Subject pain ratings were recorded immediately postlaser treatment and immediately postcryomodulation treatment on an 11-point scale ranging from 0 = no pain to 10 = very severe pain. Photos were taken immediately postcryomodulation treatment and at a 2-day follow-up. At the 2-day follow-up, subjects were surveyed on whether they appreciated a noticeable difference in erythema, edema, and healing time between the cryomodulation-treated side and the control side of the face. Subjects were also surveyed on patient satisfaction at a 2-day follow-up using a 5-point scale as follows: 1 = not satisfied, 2 = slightly satisfied, 3 = somewhat satisfied, 4 = satisfied, 5 = very satisfied. Blinded review of photographs by two physicians was conducted to assess efficacy based on the correct identification of the cryomodulation-treated side of the face.

RESULTS

Ten female subjects were enrolled at one investigational site. Eight subjects were treated using a dual 1550-nm erbium-doped fiber laser and 1927-nm thulium fiber laser, and two subjects were treated using a 1550-nm erbium-doped fiber laser. Subject ages ranged from 35 to 66 with Fitzpatrick skin types I–V represented. The average pain score for subjects immediately postlaser was 5.15 on a scale of 0–10 (0 = no discomfort and 10 = very severe discomfort). Immediately following cryomodulation, the average pain score on the side of the face treated with the cooling device was reduced by 69%, to an average of 1.6 (Figure 1). The untreated side of the face was reduced by 19%, to an average of 4.2. Overall, 90% of subjects reported reduced pain on the treatment side immediately following cryomodulation.

At the 2-day follow-up, subjects were surveyed on whether they appreciated a noticeable difference in erythema, edema, and healing time between the cryomodulation-treated side and the control side of the face. Seventy percent of subjects reported a noticeable difference in edema, 50% reported a noticeable difference in erythema and 40%

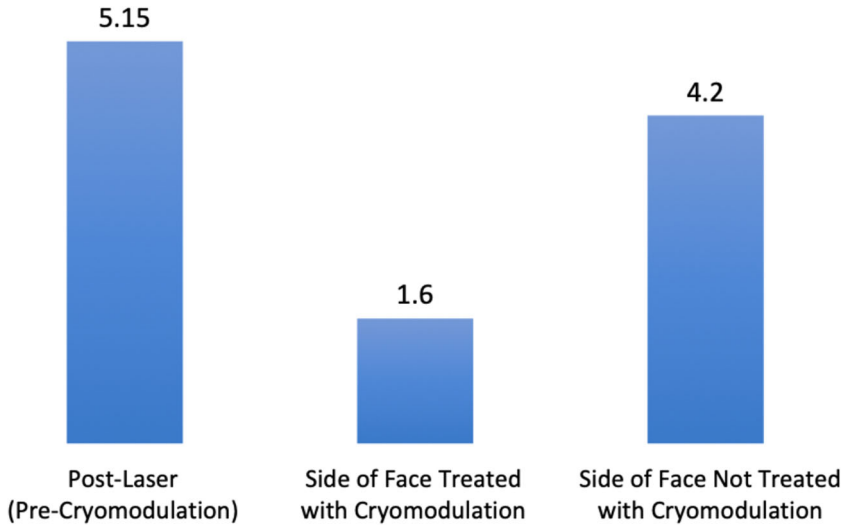

FIGURE 1 Average subject pain rating pre-cryomodulation and postcryomodulation for treatment and control side. Based on an 11-point scale from 0 (no discomfort) to 10 (very severe discomfort).

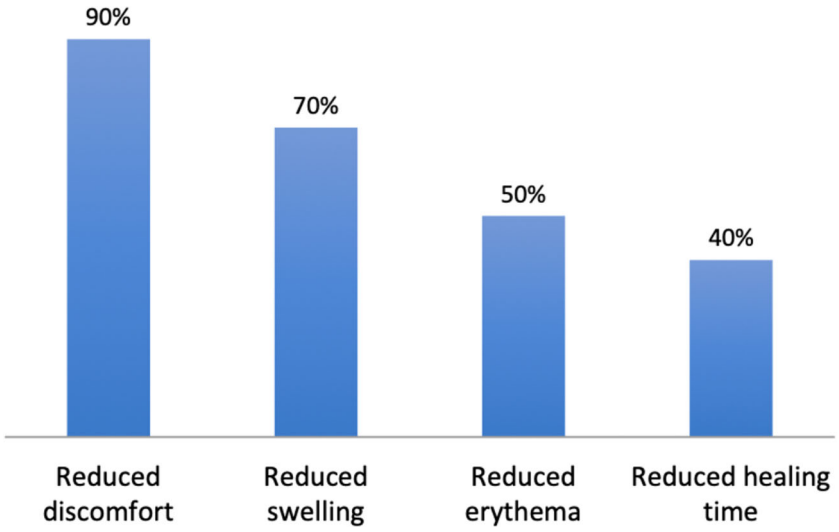

FIGURE 2 Subjective impact of cryomodulation on reduction of postlaser side effects at 2-day follow-up. Defined as a noticeable improvement between treatment and control sides of the face.

reported a noticeable difference in healing time (Figure 2). Overall, 80% of subjects reported a noticeable difference in either erythema or edema while 40% saw improvement in both erythema and edema. The average subject satisfaction score for the cryomodulation treatment was 4.2 on a scale of 1–5 (1 = not satisfied, 2 = slightly satisfied, 3 = somewhat satisfied, 4 = satisfied, 5 = very satisfied). All subjects (100%) indicated that they would elect to undergo the cryomodulation treatment again and that they would recommend the treatment to others. Two blinded physician reviewers were successful in identifying which side of the face had received treatment with the cryomodulation device in 70% of subjects posttreatment photographs (Figures 3–5 comparative images).

DISCUSSION

Historically, therapeutic cooling for pain and inflammation has been administered using ice packs, cold water immersion, or cold air application. These methods produce poorly controlled thermal conditions, limiting their predictability and efficacy. Cryomodulation is based upon scientific recognition that cold can selectively and differentially impact biological cells and processes depending on specific thermal conditions. It has been hypothesized that precisely controlled cooling could be used to purposefully modulate processes in the skin, including neurological and inflammatory processes activated by injury or by pathological conditions.

FIGURE 3 (A, B) Reduced erythema on the left side of the face was seen immediately postcryomodulation (A) compared to control (B).

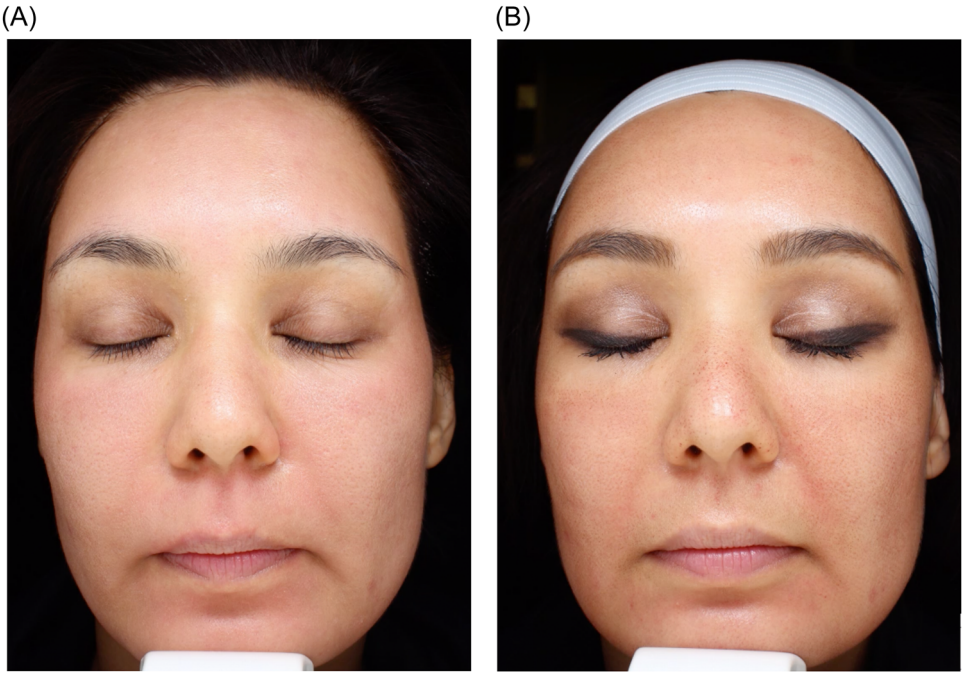

FIGURE 4 (A, B) Reduced edema on the right side of the face was seen immediately postcryomodulation (A) and at 2-day follow-up (B). Accelerated exfoliation seen on the right side of the face at 2-day follow-up (B).

The cooling device was developed to deliver cryomodulation through precise feedback-controlled contact cooling for dermatologic applications. It provides preset thermal algorithms over a broad temperature range which enable a variety of treatment modalities including controlled epidermal freezing as well as precision cooling without ice nucleation. By providing cryomodulation across wide operating ranges and with different target indications, treatments with the device can be tailored to address individual patient needs including treatment of benign lesions, hyperpigmentation, inflammatory skin disorders, and reduction of pain and thermal injury in conjunction with dermatologic procedures.

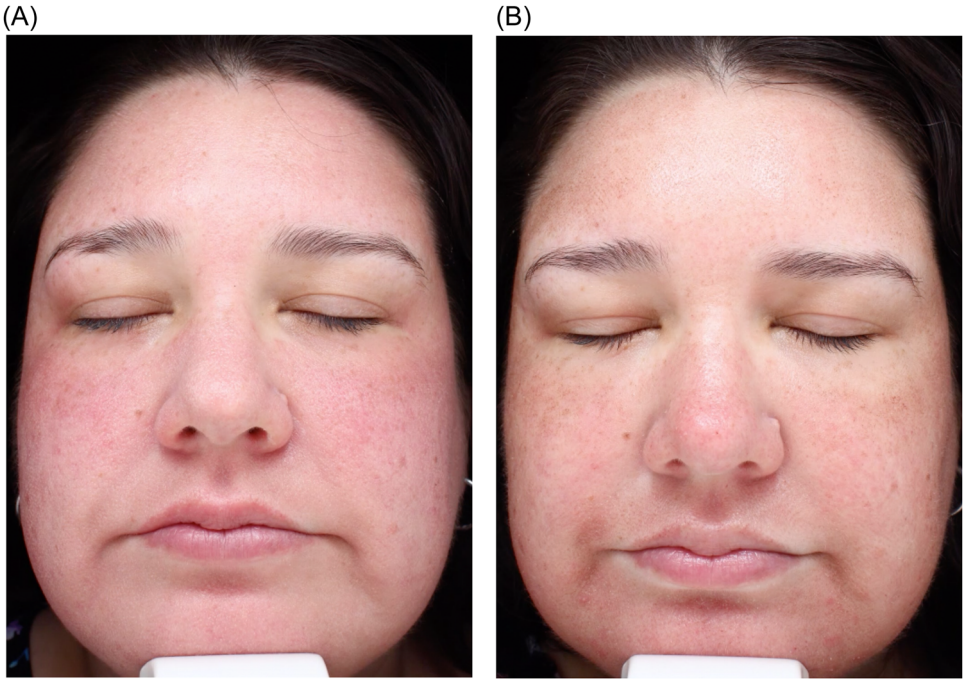

FIGURE 5 (A, B) Reduced edema seen on the right side of the face both immediately postcryomodulation (A) and at 2-day follow-up (B).

Nonablative fractional lasers have emerged as a mainstay of cosmetic dermatologic treatments to reduce the signs of photoaging. The creation of microscopic thermal injury zones in the dermis yield desired cosmetic improvements in the skin; however, treatment is commonly associated with acute side effects including pain, redness, and edema and longer-term complications associated with excess thermal injury and inflammation may occur in inexperienced hands. The importance of the role of cooling with laser treatments is well established.[1,2,11] Cooling is essential to spare the epidermis while high fluence laser energy is delivered to the skin.[1,2] Early cooling studies showed reduced pain, erythema, and healing time, which has also led to improved patient satisfaction and comfort.[1,12,13] Cooling has also been shown to enhance laser efficacy and improve aesthetic outcomes.[14,15]

Presently, most laser systems have cooling incorporated into them either as precooling, parallel cooling, or postcooling. Despite these measures, there is often still significant discomfort following nonablative fractional laser resurfacing that can persist anywhere from a few minutes to several hours. Commonly employed postlaser resurfacing cooling mechanisms include refrigerated cold air, cooling face masks, ice packs, and other various cold packs, which offer modest relief from discomfort and may have little to no impact on other acute postlaser side effects and healing. The cryomodulation device delivers cooling with a feedback-controlled low-temperature tip that is applied to the skin with active pressure and manual guidance enabling deeper cooling and uniform delivery across the treatment area for more predictable effects. Our results demonstrate that cryomodulation not only significantly improves discomfort following NAFR, but also improves erythema, edema, and overall healing time to varying degrees. These results, in addition to very high patient satisfaction, suggest that this cryomodulation system is superior to current commonly used cooling methods following nonablative fractional laser resurfacing.

CONCLUSION

The results of this split-face study support the efficacy of a global cryomodulation device for the reduction of pain, edema, and erythema following nonablative fractional laser resurfacing. Cryomodulation was delivered in a simple 10 min procedure and yielded high patient satisfaction. Additional clinical studies are currently underway at our center to evaluate cryomodulation as an adjunct to other common dermatologic laser procedures and to assess longer term impact on procedure outcomes.

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