Section A-Research paper

Post-acne erythema; Pathogenesis, presentation, and Treatment

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Abstract

Background: Post-acne erythema (PAE), also referred to as Post-inflammatory erythema (PIE), is defined as lesions consisting of telangiectatic and erythematous macules, which occur as a result of skin inflammation. The occurrence of post acne erythema follows wound healing-related microvascular dilatory changes in microcapillary plexus in the very superficial dermis which are detectable by the naked eye as general redness. In addition, thinner epidermis is still in the process of maturation after repair, allowing more incident light to be reflected off the dilated microvasculature, which adds to the perceived "redness." This is more evident in patients receiving isotretinoin. Many patients suffering from acne not only have the after effects of scarring, but also have post inflammatory dyspigmentation. In darker skin phototypes, this dyspigmentation often presents as hyperpigmentation. However, in patients with lighter skin types (I-III), it presents instead as discrete erythematous macules. Acne may not be the only cause of post inflammatory erythema, as any resolving cutaneous inflammatory process may also cause a residual erythema. Different treatment modalities including topical and interventional treatments have been used for PAE.

Keywords: Post-acne erythema

Introduction

Acne is a common skin disease that affects individuals of all skin types. It is a disease of the pilosebaceous unit, that causes noninflammatory lesions (open and closed comedones), inflammatory lesions (papules, pustules, and nodules), and varying degrees of scarring **(1).** The concept of acne pathogenesis focused on inflammatory processes which occurs in both early and late stages. Acne is primarily an inflammatory disease from beginning to resolution. Thus, the aim of acne treatments should emphasize on suppression of inflammation. **(2).**

Acne vulgaris is one of the most common dermatological disorders seen in adolescents**.** It is an extremely common condition with a prevalence of approximately 85% occuring mostly during teenage period. **(3).**

Acne vulgaris can persist into adulthood, with a 50.9% prevalence rate of acne in women ages 20 to 29 years versus 26.3% in women ages 40 to 49 years**.** Female patients account for two thirds of visits made to dermatologists for acne, and one third of all dermatology office visits for acne by women who are older than 25 years **(4).**

Acne is more common in Urban than rural populations. About 20% of the affected individuals develop severe acne, which results in scarring. Some races appear to be more affected than others. Asians and Africans tend to develop severe acne, while mild acne is more common in white populations. Acne can also develop in neonates but in most cases, resolves spontaneously **(5).**

Acne vulgaris (AV) is presented by pleomorphic lesions in the form of non-inflammatory lesions (open and closed comedones) and inflammatory lesions (papules, pustules, and nodules) with various extent and severity. **(1)**

A closed comedone is a whitehead and an open comedone is a blackhead. A whitehead is an acne lesion that forms when oil and skin cells block the opening of hair follicle, this usually appears as small, whitish bumps under the surface of the skin. A blackhead is an acne lesion that is also filled with excess oil and dead skin cells, but with a dark appearance such as black or brown color on the skin surface. **(2)**

A spanish consensus in 2016 agreed to classify inflammatory acne into mild or moderate papulopustular acne, severe papulopustular acne, moderate nodular acne, and nodulo-cystic acne (or acne tending to leave scars). **(3)**

Post-inflammatory erythema (PIE) is a common sequalae of acne inflammation. Some acne erythema lesions may improve with time However, persistent red marks after clearing of inflammation following acne treatment are cosmetically unacceptable and remains a therapeutic challenge. In some cases, complete clearance of PIE cannot be achieved **(6).**

Pathogenesis

The occurrence of PAE follows wound healing-related microvascular dilatory changes in microcapillary plexus in the very superficial dermis which are detectable by the naked eye as general redness. In addition, thinner epidermis is still in the process of maturation after repair, allowing more incident light to be reflected off the dilated microvasculature, which adds to the perceived "redness." This is more evident in patients receiving isotretinoin. **(6).**

Dilatation of microcapillaries in papillary dermis secondary to healing process and intracapillary aggregations of erythrocytes have essential roles in the development of post acne erythema **(7).**

Furthermore, P. acnes induces IL-8 and IL-12 release from TLR2 positive monocytes which stimulate the infra-infundibular inflammatory process, follicular rupture, and perifollicular abscess formation, which stimulate the wound healing process. The wound healing process progresses through 3 stages inflammation, granulation tissue formation, and matrix remodeling. **(8).**

Blanching occurs secondary to vasoconstriction for hemostasis. After the blood flow stops, vasodilatation and resultant erythema replace vasoconstriction. Melanogenesis may also be stimulated. This step plays an important role in the development of PAE and hyperpigmentation. A variety of blood cells, including granulocytes, macrophages, neutrophils lymphocytes, fibroblasts, and platelets are activated and release inflammatory mediators which prepare the site for granulation tissue formation **(8).**

Clinical presentation

Many patients suffering from acne not only have the after effects of scarring, but also have post inflammatory dyspigmentation. In darker skin phototypes, this dyspigmentation often presents as hyperpigmentation. However, in patients with lighter skin types (I-III), it presents instead as discrete erythematous macules. Acne may not be the only cause of post inflammatory erythema, as any resolving cutaneous inflammatory process may also cause a residual erythema **(9).**

Treatments

Different treatment modalities including topical and interventional treatments have been used for PAE. **(7).**

1- Topical treatment

Some PAE lesions can spontaneously resolve over time, but persistent lesions are quite common. **(10-13).**

The treatment of PAE and scars is as important as treating acne lesions. Several topical agents including 0.025% retinoic acid, 12% glycolic acid, 0.2% brimonidine tartrate, 5% tranexamic acid solution and

vitamin C preparations have been used **(6).** but the efficacy and safety of these modalities have not yet been supported by large-scale or long-term trials **(13).**

1.1 Oxymetazoline (OXZ)

Topical OXZ 1.5% twice daily in the liposomal base was significantly effective in reducing PAE. Adverse effects related to topical OXZ included dryness, pruritus, pallor, paradoxical, and rebound erythema with gradual improvement **(6).**

1.2 Topical 5% tranexamic acid

Topical 5% tranexamic acid applied for 6–8 weeks showed great efficacy. Aside from its ease of use and affordability, it was reported to have no prominent side effects making it a good option in treating PAE **(7).**

1.3 Vitamin C gel

Topical vitamin C was reported to show significant reduction in PAE with no reported adverse effects. **(13).**

1.4 Brimonidine tartrate 0.2% solution

Genedy (14) revealed that applying topical brimonidine tartrate 0.2% solution caused a significant reduction in erythema after 4 weeks of treatment. Adverse effects included pallor, contact dermatitis, burning sensation, rebound, and paradoxical erythema.

2- Lasers and energy-based modalities

Treatment of PAE with lasers and energy-based modalities has likewise been challenging. Various vascular lasers have been utilized to treat PAE; however, most publications report the effects only in active inflammatory acne. Laser treatments, including the 585 and 595-nm pulsed dye laser (PDL), the low-fluence 585-nm Q-switched Nd:YAG laser, and the 1550-nm fractional Erbium-glass laser, can be used to target dilated blood vessels and decrease the appearance of redness **(15).**

2.1. Non-ablative lasers

The main chromophore for facial erythema is oxyhemoglobin which has three peak points—one at 418-nm, 542-nm and at 577-nm in visible light. Because of its ability to specifically target oxyhemoglobin, the 577-nm pro-yellow laser has been deemed ideal for vascular lesions. **(15).**

The 577-nm yellow laser was introduced more than 20 years ago for the treatment of diabetic retinopathy, but has only been utilized in the field of dermatology in the past 2 years**.** This laser emits 100% yellow light, which allows it to specifically target oxyhemoglobin in vascular lesions, but with less absorption in melanin and a slightly deeper penetration into the dermis, thereby minimizing the risk of hyperpigmentation especially in patients with darker skin types. **(16).**

The 585 and 595-nm lasers target oxyhemoglobin in blood vessels, while the 1550-nm wavelength targets water causing heat production and as a result, photothermal destruction of dermal vasculature **(17).**

2.2. Intense pulsed light (IPL) therapy

Intense pulsed light (IPL) provides a noncoherent polychromatic source of intense light ranging from 400 to 1200-nm. The vascular mode of IPL operates at 560-nm, which allows for more selective destruction of superficial vessels by allowing peak absorption of oxyhemoglobin at 577-nm **(16).**

There was an observed significant reduction in the mean erythema score following IPL therapy. In addition, IPL was used to treat both acne and erythema in patients with persistent acne erythema with having additional benefits such as reducing oil production, improving skin tone, and improving texture. Moreover, all adverse effects including erythema, hyperpigmentation, and hypopigmentation were transient **(16).**

3- Radiofrequency

There are different types of Radiofrequency (RF) including monopolar, bipolar, fractional, and multipolar energy modes. The idea behind RF is achieving skin tightening by thermal heating of the reticular dermis,

which triggers a healing cascade leading to new collagen and elastin formation, as skin surface temperatures reach 40° to 45°C. Histological findings also suggest that fractional micro-needling radiofrequency (FMR) has anti- angiogeneic and anti-inflammatory features **(17).**

The newest method to deliver Fractional RF is through an array of microneedles. the Microneedle RF applicators introduce into the skin extra sharp microneedles while heating the dermis up to a depth of 3.5 mm. There are multiple types of microneedle RF delivery systems available in the market with significant differences in needle length (2.5 mm, 3.5 mm), needle sharpness, needle coating (stainless steel, gold), and methods of needle insertion (manual, spring, or electronically control stepper motor). **(18)**

Treatment with invasive short pulsed-type bipolar radiofrequency device (IPBRF) caused an improvement in IGA scores for erythema and mean erythema index (EI).Trans-epidermal water loss and Melanin Index (MI) showed mild improvement. In addition, no severe adverse effects were reported **(19).**

Conflicts of Interest: The authors declare no conflict of interest.

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