

Combination of 80% Trichloroacetic Acid Cross and Platelet-rich Fibrin Lysate for Improving Atrophic Acne Scar: A Case Series

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Abstract: Atrophy scar is a major complication of acne vulgaris. Therapy for atrophic acne scar is a challenge for dermatologists. The technique of chemical reconstruction of skin scar (CROSS) by applying focal high concentrations of trichloroacetic acid (TCA) on the basis of an atrophic scar can stimulate collagen production. Platelet-Rich Fibrin (PRF) lysate is an immune concentrate and platelets that accumulate in one fibrin membrane which may be useful for atrophic acne scar by stimulating collagen deposition. Trichloroacetic acid and Lysate PRF work synergistically to improve atrophic acne scar. The purpose of this case report was to determine the effectiveness of a combination of 80% TCA CROSS and PRF lysate for atrophic acne scar to 2 patients of grade 3 and 4 in Goodman classification. Eighty percent TCA was applied on the basis of the atrophy scar using a wooden toothpick with a pointed tip and then PRF lysate applied to basis of scar every night. Digital photography analysis was performed in the next visit and found a significant improvement from the basis of atrophy in both patients with only once TCA CROSS application. The combination of 80% TCA CROSS and PRF lysate are simple, easy to do, inexpensive procedures but provide excellent results for atrophic acne scar.

1 INTRODUCTION

Permanent scar is the main complication of acne vulgaris which can cause emotional and psychological disorders. Acne scars can be grouped into two types, that were hypertrophy and atrophy, where atrophy is more common after acne. Atrophic acne scars divided into types of ice pick, boxcar and rolling. Based on Goodman classification, there are 4 degrees of acne severity, namely macula, mild, moderate and severe grade. Various therapeutic modalities have been used to treat atrophic acne scars such as laser resurfacing, chemical peeling, subsidence, filler, dermabrasion, and excision punch. Until now there has been no definitive and simple therapy for atrophic acne scars. (Rajan et al., 2017; Nofal et al., 2014)

The application of focal high levels of trichloroacetic acid (TCA) on the basis of atrophy scar is known as Chemical Reconstruction of Skin Scar (CROSS). The therapeutic effect of TCA is thickening of the dermis and collagen production. Trichloroacetic acid CROSS is a promising therapy for various types of atrophy scar, because it results

in rapid healing and lower complication rates because the normal skin around it is not affected. This therapy is still developing, so there are no standard guidelines for its use.

Platelet lysate is a component of human blood that contains many growth factors that can be obtained from platelet-rich fibrin. Platelet-Rich Fibrin (PRF) is an immune concentrate and platelets that accumulate in one fibrin membrane. Beside that platelets and their products, the wound response naturally requires the fibrin matrix, which can increase growth factors and play a role in wound healing and the immune system. Therapy of PRF resembles a natural healing process, is said to be safe because of its autologous nature, and is a cost-effective choice in the treatment of chronic skin diseases that are not easily cured. (Acne et al., 2015; Risya et al., 2017). There has never been a reported topical use of PRF lysate for atrophic acne scars.

This paper reports two cases of atrophic acne scars that were treated with a combination of 80% TCA CROSS and PRF lysate. The discussion will emphasize the response of the combination therapy

of 80% TCACROSS and PRFlysate on the healing of atrophic acne scars so that it is expected to become a new innovation in the management of atrophic acne scars at a lower cost.

2 CASE

First case. A 20-year-old woman came for treatment at the DermatovenereologypoliclinicRSUP Dr. Sardjito with the chief complaint of acne scars on her forehead, cheeks and chin to the upper neck since 3 years ago. The patient has acne in face that has lost and arising since 6 years ago. The patient feels very disturbed and ashamed of his acne scars. Patients do not have a history of keloids.

Dermatological examination of the forehead, left and right cheeks, upper chin and neck are atrophic scar, multiple, varied forms (rolling scars, scar boxes, icepick scar), sizes varying from 1 mm to 3 mm. Based on the history and physical examination, the diagnosis of this case is the atrophic acne scars of grade 3 (moderate).

The management given to patients was a combination of 80% TCACROSS and PRFlysate which was applied at night to a CROSS spot location. Taking blood for PRF is done on the 14th day after the first day of menstruation. Before the treatment, patients were informed about the risk of transient or permanent hyperpigmentation. Patients were asked to come in 2 weeks to do the second TCACROSS. The patient is planned to do TCACROSS up to 3-4 times at intervals of 2 weeks. At the time of application of TCA, the patient feels like a mild burning sensation and lost within a few minutes later. The scars then turn to erythem and in a few days a crust appears on top of it and releases itself within 6-7 days. When patient control in 2 weeks later, the base of the scar

is very up and parallel to the healthy skin around it but the base of the scar becomes reddish. Patients were not treated with TCA CROSS anymore and only plateletlysate were given at night, and were asked to avoid sunlight. At 4 weeks later, the redness in the area on CROSS has been greatly reduced. The severity of acne decreases to grade 2 (mild).

Second case. A 21-year-old man came to the DermatovenereologypoliclinicRSUP Dr. Sardjito with the chief complaint of acne scars on his forehead, cheeks and chin since 1,5 years ago. The patient has acne that has lost and arising since 5 years ago. The patient feels very disturbed and ashamed of his acne scars. Patients do not have a history of keloids

Dermatological examination of the forehead, left and right cheeks, and chin is obtained erythematous atrophic scar, multiple, varied forms (rolling scar, scar box, icepick scar), size varies from 1-5 mm. Based on the history and physical examination, the diagnosis of this case is the atrophic acne scars of grade 4 (severe).

The management given to patients was a combination of 80% TCACROSS and PRFlysate which was applied at night to a CROSS spot location. Before the treatment, patients were informed about the risk of transient or permanent hyperpigmentation. Patients were asked to come in 2 weeks to do the second TCACROSS. At the time of application of TCA, the patient feels like a mild burning sensation and lost within a few minutes later. The scars then turn to erythem and in a few days a crust appears on top of it and releases itself within 10 days. Because of the full activity, the patients were only able to get control in the third month, and the results of the scar test showed significant improvement. The degree of severity of acne decreases to degree 2 (mild).



Figure 1. Female patient with atrophic acne scar grade 3. A) Before therapy B) Good treatment response after 1 month from the first therapy



Figure 2. Male patient with atrophic acne scargrade 4. A) Before therapy B) Excellent treatment response after 3 months from the first therapy

In the CROSS technique, the face is cleaned first with the cleanser face and eye were closed, then the TCA is applied to the base of the scar using a wooden toothpick which is pointed for several seconds until the "white frost" appears on the scar. After that, the patient is given gentamicin cream twice a day until crusts are formed and the patient is asked to avoid sun exposure.

Platelet-rich fibrinlysate was isolated from about 20 ml of healthy subjects venous blood, then 20 ml of venous blood was put in 2 sterile test tubes 10 ml. Blood is taken on day 14 after the first day of menstruation in female patients. Centrifugation of 2000 RPM for 10 minutes. The fibrin matrix formed is separated from erythrocyte deposits using sterile scissors or tweezers. The fibrin matrix is then incubated for 24 hours at 4°C until a supernatant is formed which is the PRF lysate. After ensuring that the remaining fibrin is attached to the bottom of the tube, the supernatant is sucked and transferred into 2 ml ependorf tube and stored at -20°C until used.

3 DISCUSSION

Acne is an inflammatory disease that can form an atrophic scar, if the response to repair and healing is poor. The occurrence of atrophic acne scars is associated with loss of collagen which causes the formation of atrophy. Atrophic acne scars has a significant psychosocial impact especially for adolescents. Various therapeutic modalities are available to treat atrophic acne scars such as surgical revision, chemical resurfacing, laser resurfacing, with mixed results and quite expensive costs.(Abbrocini et al., 2008; Zaleski-larsen et al., 2016)

Trichloroacetic acid has long been used and safe for superficial chemical peel or deep chemical peel in the atrophic acne scars. The therapeutic effect of

TCA is thickening of the dermis and collagen production. This effect is more visible on deep chemical peel, but deep peel with higher concentrations of TCA is very risky and definitely not recommended. To maximize the effect of TCA therapy and reduce complications, such as scarring, hyperpigmentation, and hypopigmentation, a technique was found, namely the application of high focal TCA concentrations on the basis of the atrophic acne scars using sharp wood applicators, known as CROSS, popularized by Lee et al. This technique results in faster healing and fewer complications than full face chemical peels because normal tissue and adjacent adnexal structures are not exposed.(Acne A et al., 2015)

Several studies have examined the effects of TCA concentrations on CROSS. The application of TCA to the skin can cause cellular necrosis in the epidermis and necrosis of collagen in the papilla and reticular dermis.(Abbrocini et al., 2008). Therapy for atrophic acne scars with a very high 65% TCA CROSS concentration of has shown high efficacy with minimal side effects after 3-6 times therapy. Seventy percent of TCA CROSS is effective for all types, especially boxes scar after fourth therapies. CROSS TCA 100% is a cost-effective modality for icepick scar in individuals with darker skin but there is a hypopigmentation transient effect.(Bhargava S et al., 2018; Lee JB et al., 2002)

Platelets have a major role in hemostasis, but their function in regulating immune response, wound healing, osteogenesis, and angiogenesis has recently become a broad research topic. Some proteins released from platelets activated by platelets are specifically involved in the occurrence of wound healing, including tumor growth factor β (TGF- β), platelet-derived growth factor (PDGF), insulinlike growth factor-1 (IGF-1), basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF), and connective tissue growth factor

(CTGF). Platelets also release coagulation factors, serotonin, histamine, endostatin, and hydrolytic enzymes. If platelets meet with fibroblasts, interactions will occur between cells. Platelet lysates isolated from blood have been shown to stimulate fibroblasts, this is because platelet-generated PDGF can stimulate resting fibroblasts to migrate fibroblasts and proliferate through activation of PCNA and synthesis of TGF- β through the JAK-STAT signaling pathway. In addition to platelets and their products, the wound response naturally requires the fibrin matrix, which can increase growth factors. (Sclafani, 2009; Wirohadidjojo YW et al., 2016)

Platelet lysate can be obtained from PRF. Platelet-Rich Fibrin (PRF) is an immune concentrate and platelets that accumulate in one fibrin membrane, which contains all blood-forming components and plays a role in wound healing and the immune system. (Chirag B Desai et al., 2013) Platelet-rich fibrin (PRF) is referred to as platelet-rich plasma (PRP) second generation with a simpler manufacturing process without requiring additional anticoagulants. Platelet-rich Fibrin (PRF) has a natural fibrin structure that can protect growth factors from proteolysis. Platelet-rich Fibrin (PRF) releases periodically and maintains its activity for a long time. This happens because platelets on PRF are trapped in the matrix. TGF- β 1 and PDGF AB levels reached the highest number on day 14. Platelet-rich fibrin lysate until day 14 can still optimally trigger osteoblast proliferation and differentiation while PRP lysate does not. The growth factor level in the PRF lysate is higher than that in the PRP lysate. Growth factor can increase the repair time of damaged skin and accelerate tissue remodeling with increased collagen synthesis. (Rajan et al., 2017; Wirohadidjojo YW et al., 2016).

Both patients in this case had an icepick, rolling, boxcar atrophic acne type and were given 80% TCA CROSS therapy and PRF lysate. Significant results were obtained in the form of a base increase from the atrophy scar with only 1 time the TCA CROSS application. In the first case, the base of the scar is parallel to the normal skin around it, but the base of the scar becomes reddish. After 4 weeks of follow-up, the redness of the scar was reduced. In the second case, the base of the scar has risen and most of it has aligned with the normal skin around after the third month's follow-up. Permanent side effects were not found in the second case. Longer follow-up is still needed for the first case to find out the permanent side effects of this combination therapy.

4 CONCLUSION

This case report shows that a combination of 80% TCA CROSS and PRF lysate is a simple, easy-to-do, inexpensive procedure but provides excellent results for atrophic acne scar. Larger studies and longer follow-up time are still needed to assess the effectiveness of this combination therapy.

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