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Platelet-Rich Plasma Injection Versus Combined Fractional Carbon Dioxide Laser with Platelet-Rich Plasma in Treatment of Vitiligo: A Comparative Study

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Abstract

Vitiligo is an acquired skin disorder characterized by depigmented macules and patches due to the loss of functioning melanocytes in the skin, with a global prevalence around 1%. Vitiligo does not produce direct physical impairment; however, it has a negative social and psychological impact on the afflicted patients when the depigmented lesions occur in exposed areas, such as face, neck, and extremities.

Keywords: laser with platelet-rich plasma; melanocytes; skin; melanocytorrhagy

Introduction

Vitiligo is an acquired skin disorder characterized by depigmented macules and patches due to the loss of functioning melanocytes in the skin, with a global prevalence around 1% [1]. Vitiligo does not produce direct physical impairment; however, it has a negative social and psychological impact on the afflicted patients when the depigmented lesions occur in exposed areas, such as face, neck, and extremities [2]. The patho-physiologic theory remains unclear. Various patho-genetic concepts have been proposed and supported by many studies. Autoimmunity, oxidative stress, accumulation of toxic compounds, infections, mutations, alter cellular environment, melano-cytorrhagy, and impaired melanocyte migration and survival can all contribute to the patho-physiologic processes of vitiligo [3].

Vitiligo is classified into segmental vitiligo (SV), nonsegmental vitiligo (NSV) and mixed vitiligo. In non-segmental vitiligo (NSV) there is usually some form of symmetry in the location of the patches of depigmentation. New patches also appear over time and can be generalized over large portions of the body or localized to a particular area. It is classified further into generalized vitiligo (the most common pattern, wide and randomly distributed areas of depig-mentation), universal vitiligo, focal vitiligo, acro-facial vitiligo and mucosal vitiligo [4]. Multiple treatment modalities are established but the response is variable [5]. This problem is exaggerated by the multifactorial and polygenic nature of the pathomechanism of the disease [6]. Platelet-rich plasma (PRP) is composed of high concentration of platelets with high concentration of growth factors (GFs) [7]. This may help in stimulation of the proliferation of melanocytes and re-pigmentation within vitiliginous patches [8]. Fractional CO2 laser has been introduced as an add-on treatment of vitiligo [9].

The beneficial effect of fractional CO2 laser on vitiligo is postulated to come from the release of cytokines and growth factors that act as mitogens for melanogenesis [10], also alters the skin barrier which results in increased penetration of topical drugs and ultraviolet (UV) radiation [11]. These facts pave the way to combination therapy that showed better repig-mentation response than monotherapy [12]. Several combination therapies have been introduced to obtain better results and to reduce risks [13]. The prolonged duration of therapy is the main reason for patient noncompliance [12].

Patients & methods

Study design: A prospective, randomized, comparative, controlled study.

Location of recruitment: patient will be recuited from the outpatient clinic of Dermatology, Andrology and STDs Department, Mansoura university Hospitals

Consent: A written and informed consent will be obtained from all patients before study enrollment for both participation and publication of images.

Inclusion criteria

20 patients presenting with stable, non-progressive non segmental vitiligo (NSV) having bilateral distributed lesions (Stability was defined over the prior 6 months as lack of; development of new lesions, enlargement of existent lesions, Koebner's phenomenon, trichrome or confetti lesions, and lesions with ill-defined for the past 6 months) [14].

Exclusion criteria

- Pregnant and lactating women.
- Patients on local medications or laser therapy one month prior to their enrollment.
- Patients with bleeding and coagulations disorders.
- History of keloid formation.
- Patients with chronic liver diseases.
- Patients with autoimmune diseases.
- Patients with debilitating diseases.
- history of koebnerization, photosensitivity and seizure disorders.

Methods

For each patient one side of the body will be treated with PRP, while the other side will be treated with Fractional CO2 laser and PRP. Patients will receive 6 treatment sessions with 2- week interval for 2.5 months and will be followed up 3 months after last session. Dermoscope will be used to assess disease activity as well as response to treatment.

All the participants will be subjected to the following

1. Complete history taking: including
   - Personal history: name, age, sex, occupation, marital status, address, pregnancy and lactation to be excluded, special habits.
   - History of present illness: onset, duaration and course
   - History of precipitating and aggravating factors.
   - Medical history of systemic diseases.
   - Family history of similar condition
2. General examination.
3. Dermatological examination.
4. Investigations: CBC, bleeding and coagulation time, liver and renal function tests.

PRP therapy

Patients will receive 6 sessions of autologous Intradermal PRP injection with 2- week interval.

PRP preparation method

Ten milliliters of venous blood will be aspirated from the anticubital vein under complete aseptic conditions. The whole blood sample will be collected in tubes containing sodium citrate as an anticoagulant (sodium citrate 9NC, VACO MED, containing sodium citrate 3.2% as anticoagulant). Then, the citrated blood will be centrifuged in a standard laboratory centrifuge for 7 min at 3,000 rpm. Subsequently, the yellow plasma (containing buffy coat with platelets and leukocytes) taken up using a micropipette. A second round of centrifugation will be performed for 5 min at 4,000 rpm. The pellet containing platelets will be accumulated at the bottom and the platelet-poor plasma will be surfaced to the top. The plasma supernatant will be used as PPP and the thrombocyte pellet in 1.0 ml of plasma used as PRP. A 30-G needle will be used for superficial intradermal (ID) microinjections (0.1mL per injection and will space about 1 cm apart [15].

Combined Fr: CO2 laser and PRP therapy

Patients will receive 6 sessions of fractional CO2 laser (DEKA, Smart-Xide DOT, Italy), with 2-week interval. Topical aesthetic cream will be applied under occlusion 30 minutes before the session. Fractional CO2 laser will be performed over the vitiligo lesion and over the perilesional apparently healthy skin of about 5 cm around the lesion. The treatment settings powered 6-Watt, dot mode with spacing 550 mm, dwell time 400 ms, scanning mode, smart track, single stack. Square shape, ratio 10/10, and size 100%. Theses parameters are equivalent to fluence 0.3 J/cm, density 11.9%, and energy/dot 2.4 mJ. After each laser session, patient will receive intradermal injection of autologous PRP using the same previous injection protocol [16].

Follow up

Assessment of the efficacy of therapeutic procedure:

- Photographs with a digital camera will be obtained at baseline, before each treatment session, and 3 months after the final treatment for follow up.
- The patients will be evaluated using a dermoscope DermLite DL4 (San Juan Capistrano, CA) with a universal adaptor. As

perifollicular hyperpigmentation, reticulate hyperpigmentation, and marginal pigmentation were the dermoscopic markers of stable vitiligo and repigmenting vitiligo. Perilesional erythema and telangiectasias were seen in patients of vitiligo on treatment. Leukotrichia was seen in patients of stable vitiligo, majority being treatment refractory [17].

- Objective clinical assessments of repigmentation will be performed by 3 dermatologists 2 of them blinded, one non blinded using quartile grading scale (MISP) Mean improvement score will be calculated by comparing the photographs of patients (grade 0:no improvement; grade 1: <25%, minimal improvement; grade 2: 25%–49%, moderate; grade 3: 50%–74%, marked; grade 4: >75%–99%, excellent; and grade 5: 100%, complete) [18].
- Each patient will be asked at final visit about his / her satisfaction (unsatisfied, slightly satisfied, satisfied or very satisfied) using a 10-point visual analog scale (VAS,0_10; the 0 level will define as "Not satisfied at all," while a level of 10 will define as "completely satisfied"). Evaluation will be done at baseline (VAS0) and 3 months after the final session (VAS3m) [19].
- Each patient will be questioned before and after treatment. Using 10-point questionnaire scale dermatology life quality index (DLQssI) by [20]. consists of 10 questions, which show a connection with various aspects of the patient's life The purpose of this questionnaire is to determine the degree of influence of the disease on the patient's lifestyle. For each question, 4 variants of the answer are offered, each of which is rated from 0 to 3 points. The maximum number of points can be equal to 30, with this quality of life of the patient is inversely proportional to the total of points.

Table 1: 10-point questionnaire scale dermatology life quality index (DLQI) [21].

1	Over the past year, how much did you experience itching, tenderness, soreness, or tingling in your skin?	Very much, A lot A little, not at all
2	Over the past year, how embarrassing and uncomfortable have you felt about your skin condition?	Very much, A lot A little, not at all
3	Over the past year, how badly did your skin condition interfere with your shopping, housekeeping or gardening?	Very much, A lot A little, not at all
4	Over the past year, how much has your skin condition influenced the choice of clothing you wear?	Very much, A lot A little, not at all
5	Over the past year, how A lotly has your skin condition affected your social, activity or leisure time?	Very much, A lot A little, not at all
6	Over the past year, how much has your skin condition spun your sports activities?	Very much, A lot A little, not at all
7	Has your skin condition interfered with your presence at work or education over the past year? Yes Not If no, to what extent has your skin condition been a problem for your work or training?	Very much, A lot A little, not at all
8	Over the past year, how badly has your skin condition caused problems with your partner or your close friends or relatives?	Very much, A lot A little, not at all
9	Over the past year, how badly has your skin condition been at the root of your sexual problems?	Very much, A lot, A little, not at all
10	Over the past year, how much has the treatment of your skin condition created difficulties for you, for example, created a mess in the house or is it the right time?	Very much, A lot A little, not at all

Interpretation of DLQI values: 0-1 point - no influence on the patient's life; 2-5 points - illness has an unacceptable effect on the patient's life; 6-10 points - the disease has a moderate effect on the patient's life. 11-20 points - illness has a very strong influence on the patient's life; 21-30 points - the disease has an extremely strong influence on the life of the patient. Patients will be asked about any side effects as pain, inflammation and burning.

Ethical consideration

- The Mansoura Faculty of Medicine's Institutional Review Board (IRB) accepted this report

- Informed written consents will be taken from all patients.
- Confidentiality assured.

Data analysis

- Collected data will be analyzed using SPSS program.
- Description of quantitative data will be expressed as mean standard deviation using independent t-test if data were parametric.
- Qualitative data will be expressed as number and percentage.
- Level of significance is set to be significant at 0.05.

Aim of the Work

Asses the efficacy of platelet-rich plasma vs combined fractional carbon dioxide laser with platelet-rich plasma in the treatment of stable non segmental vitiligo lesions

Results

The results of this study will be tabulated and satistically analyzed by relevant tests.

Discussion

The results will be discussed.

Conclusions

The conclusions will be stated and emphasized at the end of the study.

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