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ORIGINAL ARTICLE

Morphea patients treated with platelet rich plasma. A pilot study

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ABSTRACT

Background: There are multiple treatment options for morphea, but all have limited success or a wide range of side effects. Platelet-rich plasma is an innovative type of contour defect therapy, with long-lasting morphea, good cosmetic outcomes and limited side effects.

Aim: To assess clinically the effect of PRP in the treatment of patients with morphea.

Methods: A pilot study conducted on five morphea patients were recruited for this study. Intradermal platelet rich plasma was injected into morphea plaques once weekly for 12 sessions. The disease severity and damage were evaluated at the first visit and after the last session using the Localized Scleroderma Assessment Tool.

Results: After 12 sessions, one case showed significant improvement, three cases showed partial improvement and one showed no response. The modified Localized Skin Severity Index and Localized Scleroderma Damage Index were significantly reduced after treatment. Patients with short disease duration (< 1 year) showed better response.

Conclusion: Platelet rich plasma is a successful option for patients with localized types of morphea with good cosmetic outcome and minimal side effects.

Key words: morphea, platelet-rich plasma, cosmetic outcome.

INTRODUCTION

Morphea is an autoimmune, inflammatory, a skin disease of the connective tissue which leads to dermis and subcutaneous tissue sclerosis and may spread to the fascia, muscle and underlying bone [1]. Morphea affects adults as well as children, frequently contributing to severe cosmetic and functional comorbidities such as joint deformities and lost movement range [2]. Morphea is reported in different clinical presentations, including plaque, the commonest subtype overall that is generally seen among adults and present in 1 or 2 anatomical places, mostly on trunk or limbs as clearly defined, oval or round areas of white, indurated skin [3]. Linear morphea, usually seen in children and adolescents on the scalp, forehead, trunk, or extremities as a linear induration. It may be associated with atrophy of limb or joint immobilization [4]. Generalized morphea is characterized by four or more plaque lesions affecting two or more sites or by the subtle initiation of a slowly developing plaque on the trunk, involving the whole trunk eventually, leading to progressive dyspnoea due to mechanical restrictions in the expansion of chest cages [5]. There are different treatment options for morphea vary from topical steroids and derivatives of vitamin D to systemic treatments such as methotrexate, systemic steroids and UV therapy [6]. However, there is no effective global treatment; the management is always based on the severity and extent of the disease and is focussed in particular on the risk of deformity and restriction of movement [7]. For many years, the idea of using a patient's own blood or components for enhancing the physiological healing process was in place [8]. Autologous platelet rich plasma (PRP) has been used for soft tissue rejuvenation, wound healing, angiogenesis and tissue remodeling [8]. There are also trials for the evaluation of PRP in the treatment of contour defects as localized morphea; PRP is likely to be a successful and cost-effective therapeutic line with equal efficiency and even better longevity, compared with other treatment options [9]

SUBJECT & METHODS

This study was conducted between September 2017 and March 2018 in the Department of Dermatology, Venereology and Andrology, Faculty of Medicine, U. Z. Hospital. Approval was

obtained from the Z.U. Institutional Review Board (IRB#: 3399-14-2-2017). The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

2.1 Patients

Five patients with morphea (of both sexes and any age) were enrolled in this study. Patients with other dermatological disorders, chronic liver disease, essential thrombocytopenia, HIV and anti-coagulation treatment were excluded. Patients signed informed consent and were informed about the treatment's benefits and possible adverse effects.

2.2 Methods

Patients were subjected to the following complete history taking: personal history, including name, age, sex, family history of similar conditions or any other dermatological diseases; history of previous medication, minor trauma, psychological stress or surgery; and present history of the onset, course and duration of morphea. Patients were examined both generally to discover any associated autoimmune diseases or medical conditions and dermatologically to determine morphea lesion site, size, shape and type. Laboratory investigations were performed, including a complete blood picture, liver function test, kidney function test, prothrombin time, bleeding time, clotting time and random blood sugar. The study was photographically documented at every treatment session for evaluation of the results by a digital camera (Cyber shot DSC-WX7; Sony, Japan).

2.3 Clinical assessment by LoSCAT

The severity and damage caused by the disease was assessed by the LoSCAT (Localized Scleroderma Assessment Tool) before the first session and at each follow-up visit. LoSCAT includes the following LS domains: the modified Localized Skin Severity Index (mLoSSI), which is used for assessment of disease activity; and the Localized Scleroderma Damage Index (LoSDI), which is used for assessment of skin damage.The mLoSSI consists of the sum of the following three different activity scores: Skin thickness (ST): 0: skin is normal in thickness and freely mobile; 1: minimal increase in thickness and mobile; 2: moderate increase in thickness; impaired skin mobility and 3: major increase in thickness or absence of skin mobility. Erythema (ER): colour of rim of the lesion. 0: no erythema; 1: minimal erythema/pink; 2: red/clear erythema and 3: dark red or sever erythema/violaceous.

New lesion/lesion extension (N/E): development of new lesion and/or expansion of an existing lesion during the last month (score of 3).

Three cutaneous damage domains were summed up to achieve the LoSDI as follows.

Dermal atrophy (DAT): 0: normal skin; 1: minimal skin atrophy, i.e., glossy skin; 2: moderate atrophy, i.e., obvious blood vessels or minimal ‘cliffdrop’ sign and 3: marked skin atrophy, i.e., apparent ‘cliffdrop’ sign. Dyspigmentation (DP): evaluation of either hyper-or hypopigmentation, the most prominent of which is as follows: 0: normal skin pigment, 1: minimal, 2: moderate and 3: marked dyspigmentation. Subcutaneous atrophy (SAT): 0: normal subcutaneous thickness, 1: flattening or 1/3 loss of fat, 2: apparent concave surface or 1/3–2/3 loss of fat and 3: severe loss of subcutaneous fat (>2/3 loss) [10].

2.4 PRP preparation

PRP preparation was performed as follows: 10 millilitres of venous blood were aspired from the patients by using a 21 G butterfly needle to venepuncture the median cubital forearm vein. The blood was obtained in specific sterile tubes with an anticoagulant, Na citrate 3.8%, which centrifugally separates red blood cells from plasma that containing the 'buffy coat' (white blood cells and platelets). For 7 min at room temperature, each test tube was centrifugated at 800 rpm. The plasma was softly aspired from every test tube into a syringe and transferred to a 2nd tube and then centrifuged again at 1200 rpm for 12 minutes at room temperature, PRP was thus aspired from every test tube and prepared for activation by calcium chloride in the ratio of 0.1 ml of $CaCl_2$ per 0.9 ml of PRP and thus obtaining a concentration of activated PRP [9].

2.5 Injection technique

The target surface of the skin was thoroughly cleaned with alcohol pads before injection. One hour prior to injection, topical EMLA cream was added. Around 3 ml of PRP per tube was produced; this activated PRP was then injected intradermally with a 30 G needle with a point-to point distance of approximately 1 cm and a ' serial puncture ' was used at each position to inject the PRP solution intradermally. Compression of bleeding points was done for a few seconds and an ice pack was placed on the area for few minutes when the injection was over. The treated area was gently covered with a topical antibiotic cream (2% fusidic acid). Every patient was injected with PRP once a week (12 sessions total).

1.Statistical analysis

Data obtained from the history, basic clinical examination and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then transmitted to analytical software (SPSS version 22.0). Depending on the type of data, quantitative data is represented as the mean ± SD

and qualitative data is represented as the percentage and number. The following tests were used to test for significance differences; ANOVA (F test) compared parametric quantitative independent variables and Chi-square test compared differences between frequencies (qualitative variables) and percentages in groups. For significant results, the P-value was set at < 0.05 and for highly significant results at < 0.001.

2. Results

The present study was carried out on 5 female morphea patients. The age of the patient ranged from 7-15 years with 10.6 ± 3.65 mean ± SD. According to the type of morphea, 3 patients had plaque morphea, 2 patients had linear morphea.

Patient disease duration varying from 6 months to 4 years with a mean ± SD of 15.6±18.14. The duration was less than 24 months in 4 patients and more than 24 months in 1 patient. Regarding previous treatment, 3 patients had previous treatment options with no response and 2 patients did not try any treatment previously. (Table 1)

After treatment with PRP, there was a high significant reduction in the severity of morphea assessed by LoSCAT, which was derived from the addition of mLoSSI and LoSDI. The mean of mLoSSI was reduced from 3.6±1.14 before treatment to 1.4±1.67 after treatment and the LoSDI mean was reduced from5.4±0.89 before treatment to 3.2±0.83after treatment (Fig 1a, b, Table 2).

Table (1): Demographic and clinical data of morphea patients in the study

n = 5		
Age (years)		
Mean ± SD	10.6 ± 3.65	
Median	9 years	
< 10	3	60%
> 10	2	40%
Sex		
Male	0	0%
Female	5	100%
Duration (months)		
Mean ± SD	15.6±18.14	
Range	6 months – 4 years	
Median	8 months	
≤ 24 months	4	80.0%
> 24 months	1	20.0%
Previous treatment		
No	2	40%
Yes	3	60%

Table (2): Changes in the severity of morphea assessed by mLoSSI, LoSDI and LoSCAT before and after treatment.

	Mean±SD	**Range**	**Paired "t"**	**P**
mLoSSI				
Before	3.6±1.14	2-5	3.77	0.019*
After	1.4±1.67	0-4		
LoSDI				
Before	5.4±0.89	5-7	3.8	0.019*
After	3.2±0.83	2-4		
LoSCAT				
Before	9±1.225	7-10	3.91	0.011*
After	4.6±2.4	2-8		

Fig (1): plaque morphea under right eye **(**a)before treatment shows hypo pigmentation, hyperpigmentation and induration of skin. (b) After 12 sessions platelet-rich plasma injection showing marked improvement of hypopigmentation and induration of skin.

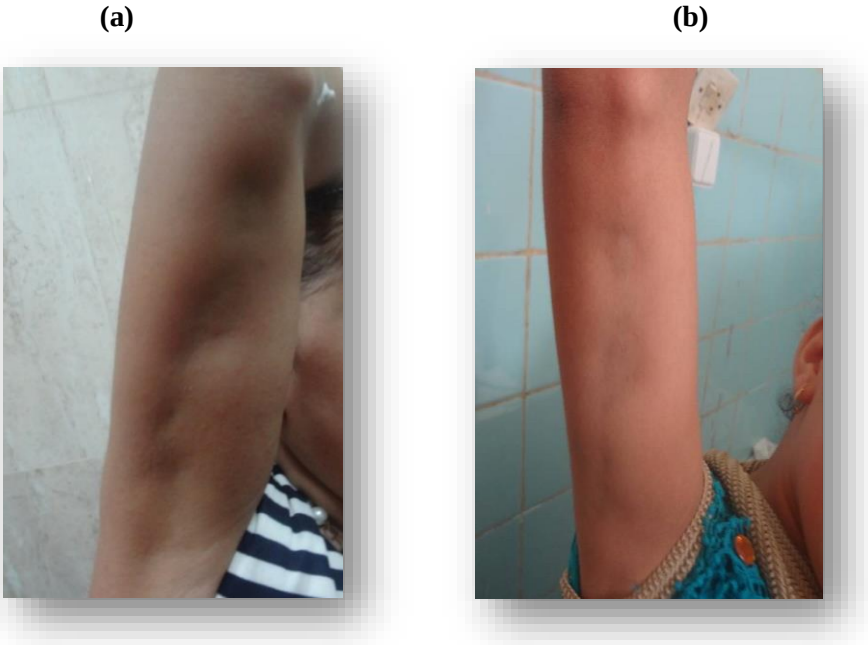

Fig 2 (a, b): linear morphea on right arm (a) shows linear contour defects with hyperpigmentation of skin. (b) After 12 sessions platelet-rich plasma injection showing partial filling up of contour defects and reduction in hyperpigmentation

4. DISCUSSION

Morphea aetiology is still unknown, but autoimmune, genetic, infectious, and ecologic factors were involved. To date, no effective morphea therapy has been confirmed. Many medications have been reported in the treatment of morphea in various degrees of success, such as methotrexate, corticosteroids, antimalarial drugs, calcitriol, retinoids, cyclosporine, and interferon gamma. [11].PRP is an autologous concentration of human platelets in a small volume of plasma. This concentrate includes the trophic growth factors released after platelets are activated with either calcium, thrombin or fibrinogen. In several surgical and medical fields PRP represents a long-standing effective treatment. [12].The present study is a pilot study carried out on 5 female morphea patients. Two with linear morphea, three with plaque type. After 12 sessions of PRP injection, 1 patient showed no improvement, 3

patients showed partial improvement and 1 patient showed nearly normal skin. Belgaumkar et al [9] conducted a case report using PRP as a monotherapy in a female who had a non-progressive linear hyperpigmented atrophic lesion over the left supraorbital region. An excellent cosmetic outcome was noted for a remarkable reduction in hyperpigmentation of the overlying skin.In the present study, PRP injections demonstrated a high rate of success with variable improvement levels. In the treatment of morphea PRP operates through multiple possible mechanisms. PRP contains several growth factors, such as transforming growth factor (TGF), platelet-derived growth factor (PDGF), insulin-like growth factor (IGF) and vascular endothelial growth factor (VEGF), which are released from concentrated platelets by α-granules and activated via the aggregation inducers. These factors organize processes such as cell migration, attachment, proliferation and differentiation and encourage extracellular matrix (ECM) accumulation through attaching to specific cell surface receptors [13].

Bendinelli et al [14] reported the anti-inflammatory effect of PRP by reducing the level of expression of COX 2 and CXCR4 genes. This mechanism explains the effectiveness of PRP in inflammatory component indications such as acne, recent scars and morphea. In addition, PRP has mitogenic effect on the endothelium and other mesenchymal stem cells, such as adipocytes and dermal fibroblasts. This stimulatory effect of platelets on the remodelling of collagen and fibroblasts ensures their use to correct small contour defects. Besides the good success rate, PRP has minor adverse effects, such as discomfort or pain in the injection site, redness and swelling.Thus, PRP monotherapy is a cost-effective alternative to other materials used in contour defects as fillers and fat grafts and for patients who are not affordable to dermal fillers or surgical costs of fat or dermal grafts, particularly, in a restricted-resource setting or in those with limited affordability. The benefits of using PRP alone against its combination with fat/dermal grafts are its simplicity, low cost and minimal-risk potential of the procedure.

Conflict of interest: no

Financial Disclosures: no

REFERENCES

1. **Laxer R. M. and Zulian F**. "Localized scleroderma," Current Opinion in Rheumatology, 2006; 186, 606–613.
2. **Leitenberger JJ, Cayce RL, Haley RW, Adams-Huet B, Bergstresser PR and Jacobe HT**. Distinct autoimmune syndromes in morphea: a review of 245 adults and paediatric cases. Arch Dermatol, 2009; 145(5): 545–50.
3. **Peterson L.S., Nelson A.M. and Su W.P.D**. Classification of morphea (localized scleroderma) May Clin Proc, 1995; 70, 1068-1076.
4. **Sartori-Valinotti JC, Tollefson MM and Reed AM**. Updates on Morphea: Role of Vascular Injury and Advances in Treatment. Autoimmune Dis, 2013; 2013:467808.
5. **Kreuter A, Wischnewski J, Terras S, Altmeyer P, Stücker M and Gambichler T.** Coexistence of lichen sclerosus and morphea: a retrospective analysis of 472 patients with localized scleroderma from a German tertiary referral centre. J Am Acad Dermatol, 2012; 67(6):1157–62.
6. **Morita A, Kobayashi K, Isomura I, Tsuji T and Krutmann J.** Ultraviolet A1 (340- 400 nm) phototherapy for scleroderma in systemic sclerosis. J Am Acad Dermatol, 2000; 43: 670-4.
7. **KreuterA, Altmeyer P and Gambichler T**. Treatment of localized scleroderma depends on the clinical subtype. Br J Dermatol, 2007; 156:1363-5.
8. **Valeri CR, Saleem B and Ragno G.** Release of platelet- derived growth factors and proliferation of fibroblasts in the releasates from platelets stored in the liquid state at 22 degrees C after stimulation with agonists. Transfusion, 2006; 46(2): 225-229.
9. **Belgaumkar VA, Deshmukh NS, Doshi BR and Mhaske CB.** En coup de sabre treated with platelet rich plasma. Indian J Drugs Dermatol, 2015; 1(1):27-9.
10. **Arkachaisri T, Vilaiyuk S, Torok K and Medsger TA Jr.** Development and initial validation of the localized scleroderma skin damage index and physician global assessment of disease damage: a proof- of- concept study. Rheumatology, 2010; 49: 373-381.
11. **Mariana FC and Ricardo R.** Localized scleroderma: clinical spectrum and therapeutic updates. An Bras Dermatol, 2015; 90 (1): 62-73.
12. **Mikhael NW and El-Esawy FM.** Skin rejuvenation with autologous concentrated platelet rich plasma. Egyptian Journal of Dermatology and Venereology, 2014; 34:5–9.
13. **Kim DH, Je YJ, Kim CD, Lee YH, Seo YJ, Lee JH, et al.** Can Platelet-rich Plasma Be Used for Skin Rejuvenation? Evaluation of effects of Platelet-rich Plasma on human dermal fibroblast. Annals of dermatology, 2011; 23(4), 424-431.
14. **Bendinelli P, Matteucci E, Dogliotti G, Corsi MM, Banfi G, Maroni P, et al.** Molecular basis of anti-inflammatory action of platelet-rich plasma on human chondrocytes: Mechanisms of NF-κB inhibition via HGF. J Cell Physiol, 2010; 225:757-66.

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