ORIGINAL ARTICLE

Injections of Autologous Platelet-Rich Plasma into the Facial Skin: Assessing Safety and Influence on the Immune System According to the Routine Laboratory Tests

Alina R. Koshkinbayeva[1], Alina V. Ogizbayeva[2], Olga Anatolyevna Ponamareva[3], Bauyrzhan K. Omarkulov[1]

Departments of [1]Family Medicine, [2]Emergency Medical Care, Anesthesiology and Resuscitation and [3]Biomedicine, NJSC "Karaganda Medical University", Karagandy, Kazakhstan

Address for correspondence:
Dr. Alina R. Koshkinbayeva, Department of Family medicine, NJSC "Karaganda Medical University", 40 Gogol St., Karaganda, Kazakhstan.
E-mail: shar_surgeon89@mai.ru

Abstract

Aims: The purpose of this research was to study the safety of the PRP injections into the facial skin and assess its effect on immune system according to the routine laboratory tests. **Subjects and Material:** The research involved 50 women aged 20 to 52 years who received intradermal PRP injections into the facial skin. General examination, complete blood count before the procedure, and 1, 3, and 6 months after it, rheumatoid factor, lupus anticoagulant, and D-dimer in the blood serum before the procedure and 6 months after it were conducted for all the subjects involved in the research. **Results:** According to the studied indicators of autoimmune diseases (rheumatoid factor and lupus anticoagulant), there were no differences 6 months after the PRP injection procedure (P = 0.139 and P = 0.208, respectively). A small number of patients (6–20%) had a slight increase in lymphocytes (up to a maximum of 47.8%) and monocytes (up to a maximum of 11.4%) in the blood after 1, 3, and 6 months, which tended to normalise over time (P = 0.0001). No undesirable local or systemic reactions after the procedure as well as during the observed period were recorded. **Conclusion:** An algorithm for laboratory examination of patients before and after the PRP injections into the facial skin was proposed to exclude undesirable adverse reactions after the procedure. The safety research should be continued, taking into account the multiplicity of the procedure and its combination with other cosmetic effects.

Key Words: *Cosmetology, dermatology, facial skin, platelet-rich plasma, PRP, safety*

Introduction

Autologous platelet-rich plasma (PRP) is widely used in various fields of medicine today.[1] PRP is presently in great demand in aesthetic dermatology and cosmetology,[2] including the treatment of scars, stretch marks, alopecia,[3] vitiligo, photoaging,[4] and skin rejuvenation.[5] According to a systematic review, PRP had some positive effect in the aesthetic treatment and correction of scars as well as androgenic alopecia (88% based on 21 studies).[6] Most of the conducted studies have shown some positive local effects of PRP. The long-term effects in the studies have not been achieved, suggesting that the effect of PRP is limited.[2] In addition, the studies failed to include the patient-related factors, such as demographic variables (age, sex), the presence or absence of comorbidities, and any use of medication. All these factors must be taken into account as they can cause changes in the body and therefore affect the quality of PRP received from patients.[7]

Access this article online

Quick Response Code:

Website: https://journals.lww.com/ijd

DOI: 10.4103/ijd.ijd_785_24

Most of the research focusses exclusively on the numerous growth factors present in PRP. In PRP, numerous chemokines, cytokines, and growth factors are released from platelet alpha granules, which improve tissue regeneration, angiogenesis, extracellular matrix remodelling, and stem cell differentiation and proliferation.[8-10] However, the pro- and anti-inflammatory effects of PRP should not be excluded.[11] Platelets not only are involved in haemostasis and thrombosis but also play a regulatory role in both innate and adaptive immune responses.[12,13] Due to the release of a large number of secretory molecules (inflammatory mediators and cytokines), platelets are the main factor contributing to the proliferation and differentiation of lymphocytes, activation of neutrophils, and induction of CD16 expression on monocytes.[14,15] The CD16+ monocytes have been

How to cite this article: Koshkinbayeva AR, Ogizbayeva AV, Ponamareva OA, Omarkulov BK. Injections of autologous platelet-rich plasma into the facial skin: Assessing safety and influence on the immune system according to the routine laboratory tests. Indian J Dermatol 0;0:0.

Received: September, 2024. **Accepted:** August, 2025.

proven to get increased in patients with inflammatory diseases, including autoimmune diseases.[16] Some studies have shown that activated platelets producing serotonin, TGF-b, and IL-1 are involved in the pathophysiology of some autoimmune diseases (rheumatoid arthritis, systemic lupus erythematosus).[17-19] In a study by Lee SJ e*t al.*,[18] the authors found that in patients with rheumatoid arthritis, the plasma level of sCD62P (a marker of activated platelets) was significantly increased. Therefore, CD14 + CD16 + monocytes were increased and the plasma level of sCD62P positively correlated with the clinical parameters of rheumatoid arthritis. In a number of other studies, the authors revealed that PRP has anti-inflammatory effects due to the production of RANTES (Regulated upon Activation, Normal T-Cell Expressed and Presumably Secreted) by blocking the release of MCP-1 (Monocyte chemotactic protein-1) from monocytes and the concentration of lipoxin A4 in it, which suggested that PRP accelerated healing by controlling the local inflammatory response.[20,21]

The current studies on the clinical efficacy of PRP are not definitive and homogeneous. The number of patients is often insufficient, while heterogeneous PRP preparations, different methods of PRP preparation, the number of them, their frequency, intervals and duration, and use of combined treatment methods have been used to cause different reactions that cannot be compared with each other. The clear criteria for setting indicators for this procedure have also not been defined.[22,23] All these factors add some variability to the results obtained, which makes it difficult to judge the effectiveness of PRP. All the molecular mechanisms of PRP's action that promote tissue regeneration as well as systemic reactions to the PRP administration have not been studied sufficiently. There are very few studies on the safety of PRP's use, and most of them focussed on studying local immune and inflammatory responses.

Therefore, the purpose of this research was to study the safety of the PRP injections into the facial skin and assess its effect on immune system according to the routine laboratory tests and also to propose an examination algorithm before the procedure of PRP injections into the facial skin, in order to ensure safety and reduce side effects from the procedure.

Subjects and Methods

Patients

This pilot study involved 50 women aged 20 to 52 years who received intradermal PRP injections into the facial skin.

The following studies were conducted for all the subjects involved in the research:

- General examination with anamnesis to exclude any systemic diseases, acute viral/bacterial infectious diseases;
- After the procedure, the presence/absence of undesirable local and systemic reactions were checked (pain, itching, allergic reactions, bleeding, skin infections, etc.);
- Complete blood count before the procedure, and 1, 3, and 6 months after it with the determination of lymphocytes and monocytes to assess the immune and inflammatory response and platelets to exclude coagulation disorders;
- Indicators of autoimmune diseases – rheumatoid factor and lupus anticoagulant before the procedure and 6 months after it;
- To exclude coagulation disorders – D-dimer in the blood serum before the procedure.

These laboratory tests were chosen because they are widely available and can be performed in a short time.

The patients with the following criteria were excluded from the research:

- age under 20;
- pregnancy or lactating women;
- deviations from normal values in blood tests before the procedure (especially thrombocytopenia, changes in the number of lymphocytes/monocytes (low/high));
- the presence of the concomitant diseases such as coagulopathy, thyroid dysfunction, autoimmune and infectious diseases, diabetes mellitus, any other severe concomitant diseases affecting well-being and quality of life;
- taking any medications (especially receiving anticoagulant therapy).

Blood tests were done to assess the safety of the procedure after 1 month in order to identify acute inflammatory processes and after 3 and 6 months to identify possible side effects on the immune system.

All patients signed an informed consent before the examination and the procedure itself.

PRP preparation methodology

Patients had their faces cleansed and anaesthesised using 2.5% lidocaine cream 30 min prior to the procedure. At this time, venous blood was taken from the cubital vein in compliance with the rules of asepsis/antisepsis through a butterfly catheter with a 23G adapter into 3 tubes with heparin and a 9 ml separating gel. The tubes were then centrifuged at 3200 rpm for 5 min on a Plasmolife (China) centrifuge for plasma separation. Plasma was taken from the test tubes into sterile syringes with a volume of 3 ml. On average, the subjects received 13–14 ml of plasma.

PRP injection technique into facial skin

After the onset of anaesthesia, the facial skin was cleansed from cream and treated three times with a solution of chlorhexidine. Afterwards, intradermal PRP injections were performed using needles with a diameter

of 32G and a length of six mm. Injections were injected into the hypodermic and dermis layers in a uniform dose (0.2-0.3 ml) with an interval of 1-1.5 cm between injections over the entire surface of the face, including the area around the eyes. Skin was then cleansed with chlorhexidine solution, and dexpanthenol cream was applied in the area.

Ethics statement

The research was conducted in accordance with the principles of the Helsinki Declaration and approved by the Local Bioethics Commission (MOM No. 15 with assigned number No. 98 dated 17.11.2023). Written informed consent was obtained from all participants included in the research.

Statistical analysis

The statistical analysis was carried out by the STATISTICA 8.0. (StatSoft) software (StatSoft Inc., USA). The median (Me) and lower and upper quartiles (25%, 75%) were calculated. Changes in dynamics were evaluated using Friedman's ANOVA and Wilcoxon's non-parametric criterion. Spearman's non-parametric rank correlation method was used to identify the correlation relationship. To determine the optimal threshold values, ROC curves are constructed and the Yuden index is also determined. The results were considered statistically significant at $P < 0.05$.

Results

Patient profiles

The results of the laboratory examination of patients (n = 50) before the procedure are presented in Table 1.

Fifty women aged 20 to 52 participated in the study: 8% of the subjects aged 20 to 24, 42% from 25 to 35, 32% from 36 to 45, and 18% from 46 to 52 years old.

In 16 patients (32%), blood platelets were elevated (329-492*109/l), and to exclude the active process of thrombosis, the D-dimer was studied, the levels of which in all patients were within the normal range.

The levels of lymphocytes and monocytes before the procedure in all patients were within the norms as were the studied markers of autoimmune diseases (rheumatoid factor and lupus anticoagulant).

Effects on the immune system were assessed according to the routine laboratory tests [Table 2].

No differences were seen in rheumatoid factor and lupus anticoagulant ($P = 0.139$ and $P = 0.208$, respectively) before and 6 months after the procedure (refer to Figure 1).

The number of lymphocytes and monocytes got increased 1 month after the procedure and then tended to decrease after 3 and 6 months ($P = 0.0001$). In seven patients (14%), lymphocytes were slightly increased in the range from 41 to 47.8% 1 month after the procedure and slightly increased in the range from 41 to 45% after 3 and 6 months in 4 patients (8%) [Figure 2]. In ten patients (20%), monocytes were slightly increased in the range from 9.1 to 11.4% 1 month after the procedure. The monocytes were slightly increased in the range from 9.3 to 10.8% after 3 months in four patients (8%), and after 6 months in three patients (6%), the monocytes

Table 1: Basic profiles of patients

Indicators	Median	Lower quartile	Upper quartile	Normal range[24]
Blood platelets (*10^9/l)	259.00	229.00	337.00	180-320
Blood lymphocytes (%)	33.75	28.00	38.00	18-40
Blood monocytes (%)	7.30	5.30	8.40	2.0-9.0
D –dimer (mcg/ml)	0.11	0.07	0.14	<0.243
Rheumatoid factor (IU/mL)	6.40	5.30	7.50	<14.0
Lupus anticoagulant (RU)	0.97	0.91	1.01	≤1.2

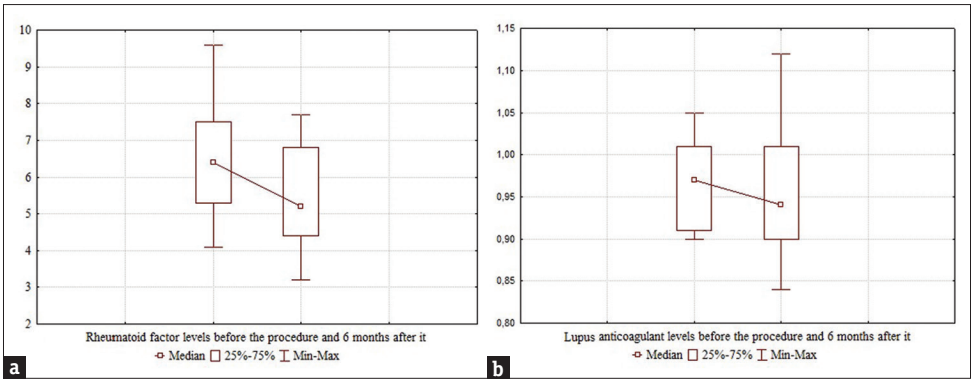

Figure 1: Rheumatoid factor (a) and lupus anticoagulant (b) before the procedure of intradermal PRP injections into facial skin and 6 months after it

Table 2: Dynamics of laboratory parameters after the PRP injections into the facial skin

Indicator	Median	Lower quartile	Upper quartile	Wilcoxon/Friedman ANOVA criterion	*P*-level
Lymphocytes before the procedure (%)	33.75	28.00	38.00	χ^2=26.421	0.0001
Lymphocytes 1 month after the procedure (%)	35.00	29.00	38.00		
Lymphocytes 3 months after the procedure (%)	29.00	26.00	35.00		
Lymphocytes 6 months after the procedure (%)	29.00	26.00	35.00		
Monocytes before the procedure (%)	7.30	5.30	8.40	χ^2=37.825	0.0000
Monocytes 1 month after the procedure (%)	7.80	6.50	8.90		
Monocytes 3 months after the procedure (%)	6.90	6.00	8.00		
Monocytes 6 months after the procedure (%)	6.90	5.10	7.90		
Rheumatoid factor before the procedure (IU/mL)	6.40	5.30	7.50	*Z*=1.481	0.139
Rheumatoid factor 6 months after the procedure (IU/mL)	5.20	4.40	6.80		
Lupus anticoagulant before the procedure (RU)	0.97	0.91	1.01	*Z*=1.260	0.208
Lupus anticoagulant 6 months after the procedure (RU)	0.94	0.90	1.01		

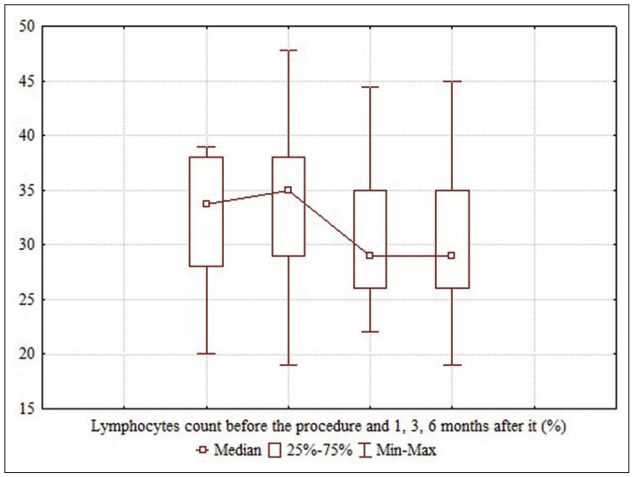

Figure 2: Lymphocytes before the procedure of intradermal PRP injections into facial skin and 1, 3, and 6 months after it

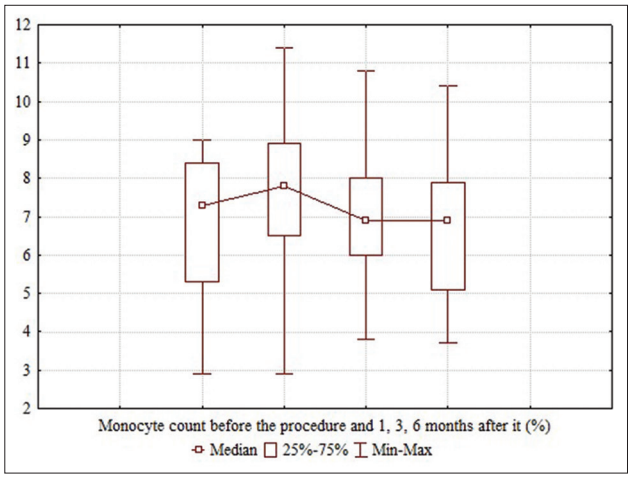

Figure 3: Monocytes before the procedure of intradermal PRP injections into the facial skin and 1, 3, and 6 months after it

were slightly increased in the range from 10.0 to 10.4% [Figure 3]. At the same time, the levels of lymphocytes and monocytes did not correlate with each other in any way ($P > 0.05$).

No undesirable local or systemic reactions after the procedure as well as during the observed period were recorded.

Discussion

The development of platelet-rich plasma to stimulate tissue repair and regeneration has been an important area of research in various fields of medicine for over 30 years.[25] The fact that PRP is an autologous product eliminates concerns about immunogenic reactions from the body. According to the conducted studies and systematic reviews, adverse events of PRP therapy, such as injection site pain, itching, infections, bleeding, and nerve damage, are minimal (less than 1%).[26-28] In this study, no undesirable local or systemic reactions after the procedure as well as during the observed period were recorded.

Coagulation activation markers can be elevated in many inflammatory diseases, including rheumatoid arthritis and autoimmune cutaneous disorders.[29] High platelets and their activation were found to occur in some skin inflammatory disorders, such as atopic dermatitis and psoriasis. Authors suggested platelets as a possible link between chronic inflammation and hypercoagulantion.[30] The relationships between the activation or dysfunction of the immune system and the coagulation system are evident in systemic autoimmune diseases including lupus erythematosus[31] and rheumatoid arthritis,[32] which show an increased thrombotic risk. The increase of D-dimer was noticed in patients with skin disorders like chronic spontaneous urticaria, angioedema, and bullous pemphigoid.[33-35] Hypercoagulation can play a local pathogenic role in inducing the skin lesions by increasing endothelial vascular permeability and a systemic role in increasing the risk of thrombosis.[29] Therefore, in this study, we also examined the state of the coagulation system to exclude patients with hypercoagulation and reduce the possibility of side effects. In 16 patients, blood

platelets were elevated (329-492 * 109/l), but D–dimer level in all patients was within the normal range.

As mentioned above, platelets play an important role in the proliferation and differentiation of lymphocytes, activation of neutrophils, and induction of CD16 expression on monocytes.[14,15] Based on research conducted to date, in some autoimmune diseases, there can be an increased level of CD16 + monocytes,[16] sCD62P[19] and serotonin, TGF-b, and IL-1 produced by activated platelets.[17,18] Therefore, when carrying out invasive procedures with PRP, we must not forget about its possible effect on the immune system.[11] However, when searching the bibliographic database of scholarly articles, we did not find any studies examining the systemic effects of PRP, including on the immune system. Most of the research has focussed on studying local immune and inflammatory responses, but never on the systemic effects when using PRP. Therefore, it is not possible to compare the data we obtained.

In this pilot study, no changes were found of the studied markers of autoimmune diseases (rheumatoid factor and lupus anticoagulant) 1, 3, and 6 months after the PRP injection procedure (P = 0.139 and P = 0.208, respectively). A small number of patients (6-20%) had a slight increase in lymphocytes (up to a maximum of 47.8%) and monocytes (up to a maximum of 11.4%) in the blood after 1, 3, and 6 months, which tended to normalise over time (P = 0.0001). There is the development of autoantigen-specific lymphocytes in autoimmune diseases. Different factors (genetics, environment, infections, stress, etc.) might influence the progression to autoimmune conditions. Autoimmune diseases can go unnoticed for a long time, and clinical manifestations may occur in the later stages of the disease.[36] PRP contains many active factors, which may also be potential risk factors for the occurrence of immune reactions. Lymphocytosis after the PRP injection procedure may indicate systemic immune reactions, or a hidden autoimmune process, or the risk of autoimmune disorders because alterations in immune homeostasis can lead to an accumulation of autoreactive lymphocytes which condition the patient to the development of autoimmunity, especially in genetically susceptible individuals.[37,38]

Despite the fact that in this study initially the procedure of PRP injections into the facial skin was carried out on patients without autoimmune diseases or other diseases affecting immune responses, when carrying out this procedure, one must take into account the risk of disorders of the immune system in patients with possibly hidden autoimmune diseases, or a predisposition to them. In this connection, we recommend an examination algorithm before the procedure of PRP injections into the facial skin, which includes routine laboratory tests: complete blood count with the determination of lymphocytes, monocytes and platelets, D-dimer, and a thorough history taking. This algorithm is needed for admission to the procedure in order to minimise the possible impact on the immune system. The algorithm we proposed is applicable not only in cosmetology but also in other areas of medicine (dentistry, orthopaedics, gynecology, etc.), where research on the safety of using PRP as a treatment procedure is also necessary.

The potential limitations of this pilot study may be the small number of patients studied, short observation period, a small set of studied parameters of immune status, and study of the effect of a single facial skin PRP injections procedure. More large prospective studies are needed in this field. Studies in patients with autoimmune and other diseases are also needed to evaluate the safety of this procedure because our study was conducted on relatively healthy patients.

As a result of this pilot study focussed on the safety of the PRP injections into the facial skin, no undesirable local effects were detected after 6 months of procedure. No effect on the immune system according to the routine laboratory tests was recorded as well. An algorithm for laboratory examination of patients before and after the PRP injections into the facial skin was proposed to exclude undesirable adverse reactions after the procedure. Since this was a pilot study with its limitations, more large prospective studies are needed taking into account the large sample, longer follow-up period, multiplicity of the procedure, its combination with other cosmetic effects, and more in-depth study of the systemic effects of PRP injections.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Ali SS, Ahmad I, Khurram MF, Chaudhury G, Karad S, Tripathi S, *et al*. The role of platelet-rich plasma in reducing pain, pruritis, and improving wound healing of skin graft donor site. Indian J Plast Surg 2022;55:376-82.
2. Leo MS, Kumar AS, Kirit R, Konathan R, Sivamani RK. Systematic review of the use of platelet-rich plasma in aesthetic dermatology. J Cosmet Dermatol 2015;14:315-23.
3. Chen JX, Justicz N, Lee LN. Platelet-rich plasma for the treatment of androgenic alopecia: A systematic review. Facial Plast Surg 2018;34:631-40.
4. Pixley JN, Cook MK, Singh R, Larrondo J, McMichael AJ. A comprehensive review of platelet-rich plasma for the treatment of dermatologic disorders. J Dermatolog Treat 2023;34:2142035.
5. Ulusal BG. Platelet-rich plasma and hyaluronic acid-an efficient biostimulation method for face rejuvenation. J Cosmet Dermatol 2017;16:112-9.
6. Damiá E, Chicharro D, Rubio M, Carrillo JM, Sopena J,

Cuervo B, *et al*. Can plasma rich in growth factors be safe for parental use? A safety study in the canine model. Int J Mol Sci 2018;19:2701.
7. Tey RV, Haldankar P, Joshi VR, Raj R, Maradi R. Variability in platelet-rich plasma preparations used in regenerative medicine: A comparative analysis. Stem Cells Int 2022;2022:3852898.
8. Gharibeh N, Aghebati-Maleki L, Madani J, Pourakbari R, Yousefi M, Ahmadian Heris J. Cell-based therapy in thin endometrium and Asherman syndrome. Stem Cell Res Ther 2022;13:33.
9. Etulain J, Mena HA, Meiss RP, Frechtel G, Gutt S, Negrotto S, *et al*. An optimised protocol for platelet-rich plasma preparation to improve its angiogenic and regenerative properties. Sci Rep 2018;8:1513.
10. Hajipour H, Farzadi L, Latifi Z, Keyhanvar N, Navali N, Fattahi A, *et al*. An update on platelet-rich plasma (PRP) therapy in endometrium and ovary related infertilities: Clinical and molecular aspects. Syst Biol Reprod Med 2021;67:177-88.
11. Koupenova M, Clancy L, Corkrey HA, Freedman JE. Circulating platelets as mediators of immunity, inflammation, and thrombosis. Circ Res 2018;122:337-51.
12. Repsold L, Joubert AM. Platelet function, role in thrombosis, inflammation, and consequences in chronic myeloproliferative disorders. Cells 2021;10:3034.
13. Tram E, Malesa K, Pomianowski S, Kami ski R. Role of platelets in osteoarthritis-updated systematic review and meta-analysis on the role of platelet-rich plasma in osteoarthritis. Cells 2022;11:1080.
14. von Hundelshausen P, Weber C. Platelets as immune cells: bridging inflammation and cardiovascular disease. Circ Res 2007;100:27-40.
15. Yoon BR, Yoo SJ, Choi Yh, Chung YH, Kim J, Yoo IS, *et al*. Functional phenotype of synovial monocytes modulating inflammatory T-Cell responses in Rheumatoid Arthritis (RA). PLoS One 2014;9:e109775.
16. Cloutier N, Allaeys I, Marcoux G, Machlus KR, Mailhot B, Zufferey A, *et al*. Platelets release pathogenic serotonin and return to circulation after immune complex-mediated sequestration. Proc Natl Acad Sci U S A 2018;115:E1550-9.
17. Burbano C, Villar-Vesga J, Orejuela J, Muñoz C, Vanegas A, Vásquez G, *et al*. Potential involvement of platelet-derived microparticles and microparticles forming immune complexes during monocyte activation in patients with systemic lupus erythematosus. Front Immunol 2018;9:322.
18. Lee SJ, Yoon BR, Kim HY, Yoo S, Kang SW, Lee W. Activated platelets convert CD14+CD16- Into CD14+CD16+monocytes with enhanced FcγR-Mediated phagocytosis and skewed M2 polarization. Front Immunol 2021;11:611133.
19. El-Sharkawy H, Kantarci A, Deady J, Hasturk H, Liu H, Alshahat M, *et al*. Platelet-rich plasma: Growth factors and pro- and anti-inflammatory properties. J Periodontol 2007;78:661-9.
20. Tejapira K, Yongpisarn T, Sakpuwadol N, Suchonwanit P. Platelet-rich plasma in alopecia areata and primary cicatricial alopecias: A systematic review. Front Med 2022;9:1058431.
21. Amable PR, Carias RB, Teixeira MV, da Cruz Pacheco I, Corrêa do Amaral RJ, Granjeiro JM, *et al*. Platelet-rich plasma preparation for regenerative medicine: Optimization and quantification of cytokines and growth factors. Stem Cell Res Ther 2013;4:67.
22. Everts P, Onishi K, Jayaram P, Lana JF, Mautner K. Platelet-rich plasma: New performance understandings and therapeutic considerations in 2020. Int J Mol Sci 2020;21:7794.
23. Dos Santos RG, Santos GS, Alkass N, Chiesa TL, Azzini GO, da Fonseca LF, *et al*. The regenerative mechanisms of platelet-rich plasma: A review. Cytokine 2021;144:155560.
24. ABIM Laboratory Test Reference Ranges January 2024. American Board of Internal Medicine; 2024. Available from: https://www.abim.org/Media/bfijryql/laboratory-reference-ranges.pdf. [Last acessed on 2024 Sep 04].
25. Cognasse F, Hamzeh-Cognasse H, Mismetti P, Thomas T, Eglin D, Marotte H. The non-haemostatic response of platelets to stress: An actor of the inflammatory environment on regenerative medicine? Front Immunol 2021;12:741988.
26. Prodromidou A, Zacharakis D, Athanasiou S, Protopapas A, Michala L, Kathopoulis N, *et al*. The emerging role on the use of platelet-rich plasma products in the management of urogynaecological disorders. Surg Innov 2022;29:80-7.
27. Dankova I, Pyrgidis N, Tishukov M, Georgiadou E, Nigdelis MP, Solomayer EF, *et al*. Efficacy and safety of platelet-rich plasma injections for the treatment of female sexual dysfunction and stress urinary incontinence: A systematic review. Biomedicines 2023;11:2919.
28. El-Dawla RE, Abdelhaleem M, Abdelhamed A. Evaluation of the safety and efficacy of platelet-rich plasma in the treatment of female patients with chronic telogen effluvium: A randomised, controlled, double-blind, pilot clinical trial. Indian J Dermatol Venereol Leprol 2023;89:195-203.
29. Cugno M, Borghi A, Garcovich S, Marzano AV. Coagulation and skin autoimmunity. Front Immunol 2019;10:1407.
30. Ghasemzadeh M, Hosseini E. Platelet-leukocyte crosstalk: Linking proinflammatory responses to procoagulant state. Thromb Res 2013;131:191-7.
31. Kern A, Barabás E, Balog A, Burcsár S, Kiszelák M, Vásárhelyi B. Characterization of the thrombin generation profile in systemic lupus erythematosus. Physiol Int 2017;104:35-41.
32. Łukasik ZM, Makowski M, Makowska JS. From blood coagulation to innate and adaptive immunity: The role of platelets in the physiology and pathology of autoimmune disorders. Rheumatol Int 2018;38:959-74.
33. Takahagi S, Mihara S, Iwamoto K, Morioke S, Okabe T, Kameyoshi Y, *et al*. Coagulation/fibrinolysis and inflammation markers are associated with disease activity in patients with chronic urticaria. Allergy 2010;65:649-56.
34. Csuka D, Veszeli N, Imreh É, Zotter Z, Skopál J, Prohászka Z, *et al*. Comprehensive study into the activation of the plasma enzyme systems during attacks of hereditary angioedema due to C1-inhibitor deficiency. Orphanet J Rare Dis 2015;10:132.
35. Marzano AV, Tedeschi A, Berti E, Fanoni D, Crosti C, Cugno M. Activation of coagulation in bullous pemphigoid and other eosinophil-related inflammatory skin diseases. Clin Exp Immunol 2011;165:44-50.
36. Bieber K, Hundt JE, Yu X, Ehlers M, Petersen F, Karsten CM, *et al*. Autoimmune pre-disease. Autoimmun Rev 2023;22:103236.
37. Alberts B, Johnson A, Lewis J, *et al*. Molecular Biology of the Cell. 4th edition. New York: Garland Science; 2002. Lymphocytes and the Cellular Basis of Adaptive Immunity. Available from: https://www.ncbi.nlm.nih.gov/books/NBK26921/. [Last accessed on 2024 Sep 04].
38. Amaya-Uribe L, Rojas M, Azizi G, Anaya JM, Gershwin ME. Primary immunodeficiency and autoimmunity: A comprehensive review. J Autoimmun 2019;99:52-72.