ORIGINAL ARTICLE

Increased Fat Graft Survival with Mesenchymal Stem Cell Recruiting Effect of PRP: In Vitro and In Vivo Study of Application Techniques

PRP'nin Mezenkimal Kök Hücre Çağırıcı Etkisi ile Yağ Grefti Sağkalımında Artış: Uygulama Tekniklerinin İn Vitro ve İn Vivo Çalışması

[1]Gokce Yildiran [iD], [2]Osman Akdag [iD], [3]Gulsemin Cicek [iD], [4]Z. Esin Celik [iD], [5]Hasibe Artac [iD], [5]Hulya Ucaryılmaz [iD], [6]Selcuk Duman [iD], [2]Mustafa Sutcu [iD], [6]T. Murad Aktan [iD], [2]Zekeriya Tosun [iD]

[1]Konya City Hospital, Department of Hand Surgery, Konya, Turkey

[2]Selcuk University Medical Faculty; Department of Plastic, Reconstructive and Aesthetic Surgery, Konya, Turkey

[3]Kanuni Sultan Süleyman Training and Research Hospital, Department of Histology and Embryology, Istanbul, Turkey

[4]Selcuk University Medical Faculty; Department of Pathology, Konya, Turkey
[5]Selcuk University Medical Faculty; Department of Pediatric Immunology and Allergy, Konya, Turkey

[6]Necmettin Erbakan University Meram Medical Faculty; Department of Histology and Embryology, Konya, Turkey

Correspondence

Gokce Yildiran, Konya City Hospital, Department of Hand Surgery, Akabe, 42020, Konya, Turkey

E-Mail: ggokceunal@gmail.com

Note: This study was orally online presented in FESSH Congress 2021 by the first author.

How to cite ?

Yildiran G, Akdağ O, Cicek G, Celik ZE, Artaç H, Ucaryilmaz H, Duman S, Sutcu M, Aktan TM, Tosun Z. Increased fat graft survival with mesenchymal stem cell recruiting effect of PRP: in vitro and in vivo study of application techniques. Genel Tıp Derg. 2022; 32(2): 207-214

ABSTRACT

Aim: Adding platelet-rich plasm (PRP) or mesenchymal stem cells are the most accepted methods to increase fat graft's permanence. However, there is no consensus on timing and whether the effect of stem cells or PRP is observed more in the recipient area or in the donor area.

It is aimed to present the application method and localization of PRP to be combined with fat graft to increase the survival.

Material and Methods: in vitro part: Fat grafts were kept in a medium containing PRP. Cell output from the fat graft to the Petri dishes was examined every day. The time to recruit the maximum number of stem cells to the medium was determined (day 10). in vivo part: Eight group of rats were received PRP in different concentrations either to recipient or donor areas of fat grafts. After ten days, fat grafts were transferred to the recipient area. Ninety days after the transfer, histopathological examination and immunohistochemical staining were performed.

Results: The group which had received the full-dose PRP to the recipient area showed the highest cellular integrity and vascularity ($p < 0.05$). Vascularity was superior in the half-dose PRP group compared to the control group ($p < 0.05$); cellular integrity did not increase. Donor site groups did not show increase in cellular integrity.

Conclusion: Although PRP starts to increase fat graft permanence by increasing vascularity, it acts by preserving the cellular integrity of the fat cells as the concentrations increase. The PRP injection to the recipient area 10 days before fat grafting may provide higher survival rates.

Keywords: fat graft, PRP, stem cell, survival

ÖZ

Amaç: Yağ greftinin kalıcılığını artırmak için trombositten zengin plazma (PRP) veya mezenkimal kök hücre eklenmesi en çok kabul gören yöntemlerdir. Ancak zamanlama ve bölge açısından kök hücrenin mi yoksa PRPnin mi etkisinin daha çok gözlendiği konusunda bir fikir birliği yoktur.

Sağkalımı artırmak için yağ grefti ile kombine edilecek PRP'nin uygulama yöntemi ve lokalizasyonunun sunulması amaçlanmaktadır.

Gereç ve Yöntem: in vitro çalışma: Yağ greftleri PRP içeren besiyerinde tutulmuştur. Yağ greftinden Petri kaplarına hücre çıkışı her gün incelendi. Ortama en fazla sayıda kök hücre alma zamanı belirlendi (10. gün).

in vivo çalışma: Sekiz grup sıçana, yağ greftlerinin alıcı veya verici alanlarına farklı konsantrasyonlarda PRP uygulandı. On gün sonra alıcı bölgeye yağ greftleri transfer edildi. Transferden doksan gün sonra histopatolojik inceleme ve immünohistokimyasal boyama yapıldı.

Bulgular: Alıcı alana tam doz PRP uygulanan grup en yüksek hücresel bütünlük ve damarlanma gösterdi ($p < 0.05$). Yarım doz PRP grubunda vaskülarite kontrol grubuna göre daha üstündü ($p < 0.05$); hücresel bütünlük artmadı. Alıcı alan grupları, hücresel bütünlükte artış göstermedi.

Sonuç: PRP damarlanmayı artırarak yağ grefti kalıcılığını artırmaya başlasa da konsantrasyonlar arttıkça yağ hücrelerinin hücresel bütünlüğünü koruyarak etki eder. Yağ greftlemesinden 10 gün önce alıcı bölgeye PRP enjeksiyonu daha yüksek hayatta kalma oranları sağlayabilir.

Anahtar kelimeler: kök hücre, PRP, sağkalım, yağ grefti

Introduction

Fat grafting applications are used for lipofilling and rejuvenation in aesthetic surgery, as well as to correct craniofacial contour irregularities, for breast reconstruction, and for scar treatment (1). Throughout its widespread use for many years, its most important complication is the 20–80% resorption rate. Many methods have been tried to prevent this complication and to increase fat graft permanence (2). Adding concentrated growth factors, adipose-derived mesenchymal stem cells, or platelet-rich plasma (PRP) to the fat graft are the most accepted methods (3, 4).

However, the excessive time and cost required to purify and obtain mesenchymal stem cells and concentrated growth factor brought PRP to the fore. Many clinical and experimental studies have discovered its various effects. Some have shown that PRP increases regeneration when combined with mesenchymal stem cells (5). There are also studies in current literature showing that PRP-supplemented scaffolds can attract and/or enrich dermal stem cells to the peripheral tissue (6).

In the literature available, few publications discuss the administration of PRP, and there is no up-to-date

Increased fat graft survival with mesenchymal stem cell.. - Yildiran et al.

Genel Tıp Dergisi

literature on whether the effect of stem cells or PRP is observed more in the recipient area or in the donor area.

The aim of this study is to present the application method and application localization of PRP to be combined with fat grafts to increase their survival.

Materials and Methods

This study was carried out in two phases, *in vitro* and *in vivo*. Ethics committee approvals were obtained separately for each phase (Local Ethical Committee Approval for in vitro study no. 2017/94 and Animal Institutional Review Board identification for in vivo study no. 2019-14). It was carried out in accordance with the principles of the Guide for the Care and Use of Laboratory Animals.

The purpose of the *in vitro* experiment was to determine the time required for PRP to recruit the maximum number of stem cells to the medium. In this step, fat grafts were kept in an *in vitro* medium containing PRP, and the day the PRP had absorbed the maximum amount of stem cells was determined (day 10).

The *in vivo* phase was conducted on the recipient area to determine the concentration required for PRP injection to achieve the most effective results. Toward this end, fat grafts were transferred to these areas 10 days after the PRP was applied to the fat graft recipient and donor areas, and the survival of the fat graft was evaluated at the end of 90 days (Figure 1).

Part I: in vitro Study

Obtaining Fat Grafts

After obtaining consent from a 45-year-old female patient who underwent liposuction, a fat graft was obtained from abdomen manually under general anesthesia using a medium-sized fat-removal cannula and a low-pressure injector; 150 cc of fat was irrigated with saline solution and phosphate-buffered saline.

Obtaining PRP

The 40 cc venous blood obtained from the same patient was centrifuged at 1100 rpm for 20 min at 17° Celsius and at 3800 rpm for 10 min at 16° Celsius. Serum was added at 2× and 4× dilution of the PRP. Antibiotic solutions (penicillin/streptomycin and L-glutamine, Capricorn Scientific GmBH, Germany) and DMEM (Dulbecco's Modified Eagle's Medium, Life Technologies, Ghent, Belgium) were added.

Composition of Petri Dishes

Under laminar flow, 40 mg fat was placed in standard Petri dishes with sterile pipettes (Figures 2 a-b). Only antibiotics and DMEM were added to the first (control) group; 4× diluted PRP was added to the second group (DF4), and 2× diluted PRP to the third group (DF2).

Evaluation

Under a microscope, cell output from the fat graft to the Petri dishes was examined. The days when the first output started were recorded. On days 1, 2, 3, 4, 5, 7, 8, 9, 10, 11 and 12, stem cells emerging around each fat graft in all three groups were recorded by manually counting under a microscope. Since the increases after day 10 were disproportionate, counting was terminated after day 12.

On day 12, in the control group, the DF2 group, and the DF4 group, stem cells that adhered to the plastic Petri dishes were removed, incubated, and subjected to flow cytometric analysis by labeling with CD 45, CD 73, CD 90, and CD 105, and validated. In flow cytometry, 10,000 mesenchymal stem cells were counted. All mesenchymal stem cells (MSCs) were examined for expression of cell surface markers by flow cytometry. All MSCs expressed CD105, CD90, and CD73 markers and were negative for expression of CD45 surface antigen.
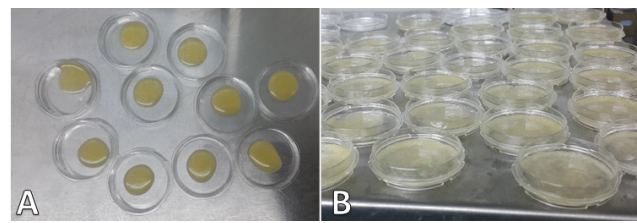

Figure 2 a: After the fat grafts were irrigated, they were placed in the middle of the Petri dishes

Figure 2 b: Petri dishes after drying under laminar flow

Part II: in vivo Study

Obtaining PRP

For the in vivo experiment, 10 Wistar-Albino rats, 8–12 weeks old, were used for blood collection to prepare the PRP. Intracardiac blood was collected under ether anesthesia and centrifuged at 1100 rpm at 17° C for 20 min and at 3800 rpm at 16° C for 10 min. PRP revealed a platelet count of $2 \times 10^5/\mu L$. PRP/2 and PRP/4 were prepared by diluting the PRP with serum by 2 × and 4 ×, respectively. In this way, three different concentrations of PRP were obtained.

Materials and Surgical Procedures

Sixty-four rats were divided into eight groups. Four groups received 0.2 ml serum, 0.2 ml PRP/4, 0.2 ml PRP/2, and 0.2 ml PRP injected into the right inguinal fat pad. As these injections were made into the donor area (D), these four groups were designated 1D, 2D, 3D, and 4D, respectively.

In the other four groups, 0.2 ml serum, 0.2 ml PRP/4, 0.2 ml PRP/2, or 0.2 ml PRP was injected into the right dorsum

Increased fat graft survival with mesenchymal stem cell.. - Yildiran et al.

Genel Tıp Dergisi

subscapular area of each rat. As these injections were made into the recipient area (R), the groups were designated 1R, 2R, 3R, and 4R, respectively.

Because the maximum stem cell output was detected on day 10 in the *in vitro* phase, 10 days after the injections in all groups in the *in vivo* phase, the right groin fat pack was irrigated with PBS and cut into small pieces of less than 1 mm, made injectable, and transferred to the rat dorsum. Fat grafts of 1.2 ml were transferred to all recipient areas.

Histopathological Evaluation

Rats were sacrificed after 90 days. The fat grafts were excised with dorsal skin. Fat tissue sections were fixed in buffered 10% formalin for 24 hours and then embedded in paraffin. Sections 4-µm thick were obtained from the paraffin blocks. Following deparaffinization, slides were stained with hematoxylin-eosin and Masson's trichrome and evaluated under an Olympus BX-53 light microscope. The degree of cellular integrity of adipocytes, necrosis, cysts and vacuoles were assessed and scored as indicated in the literature: 0, none; 1, mild; 2, mild–moderate; 3, moderate; 4, moderate–severe; and 5, severe (7).

Immunohistochemistry

For assessment of vascularity, immunohistochemical VEGF staining was performed. For this purpose, anti-VEGF antibody (1:100, Dako, USA) was used. The staining was performed with a Ventana Benchmark XT (Roche Diagnostics, UK) automatic staining machine. The degree of staining was evaluated on three different areas of each slide at 200× magnification. The total number of stained vessels was calculated on each slide, and the degree of vascularity was scored as above.

Statistical Analysis

The SPSS 26.0 (IBM Corporation, Armonk, New York, US) program was used for analysis of variables. The compatibility of univariate data to normal distribution was evaluated using the Kolmogorov-Smirnov test. In comparing more than two independent groups according to quantitative data, the Kruskal-Wallis H Test, a nonparametric test, was used with Monte Carlo simulation technique results, and Dunn's Test was used for post hoc analyses. Variables were analyzed at a 95% confidence level, and a p value of less than 0.05 was considered significant.

Results

Part I: in vitro Study

While no stem cell output was observed in the control group until day 12, a gradually increasing cell output was detected in both groups to which PRPs were added. Day 10, the last day on which the cell output increased proportionally, was determined to be the day when maximum stem cell output was observed.

Part II: in vivo Study

One rat each in the 1R and 2R groups was excluded from the study because they died before the study was completed.

It was determined that the group with a high degree of cellular integrity (3.7/5), low cyst and vacuolization formation (1/5), less necrosis (0.8/5) in adipose cells, and the highest vascularization (76) was the 4R group (Table 1).

Compared to the 1R group, higher cellular integrity and vascularization were observed in the 4R group (p< 0.05) (Figures 3 a-d). Although it was observed that vascularity was superior in the 3R group compared to the 1R group, cellular integrity did not increase (Figures 4 a-d). All parameters were similar between the 3R and 4R groups (p> 0.05). The 2R group showed similar results to the 1R group (p> 0.05).

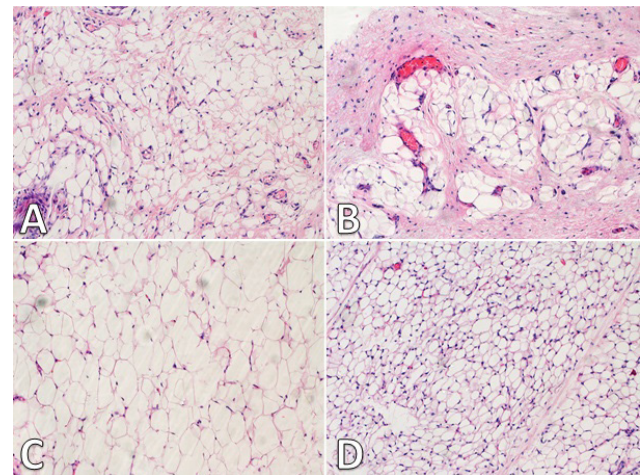**Figure 3 a:** Cellular integrity of fat cells in group 1R (lower), hematoxylin-eosin staining, x200 magnification
Figure 3 b: Cellular integrity of fat cells in group 2R, hematoxylin-eosin staining, x200 magnification
Figure 3 c: Cellular integrity of fat cells in group 3R, hematoxylin-eosin staining, x200 magnification
Figure 3 d: Cellular integrity of fat cells in group 4R (higher), hematoxylin-eosin staining, x200 magnification
Compared to the 1D group, the 4D group statistically showed fewer cysts, vacuoles, and necrosis and higher vascularization but no increase in cellular integrity (Figures 5-7). In the 3D group, higher vascularization was observed than in the 1D group, but cellular integrity did not increase. It was observed that cellular integrity was higher in the 4D group compared to the 3D group (p< 0.05). The 2D group showed similar results to the 1D group (p> 0.05).

There was no significant difference in any parameter between the 4D and 4R groups (p> 0.05). Statistically higher cellular integrity and lower cyst and vacuole formation were found in the 3R group compared to the 3D group (p< 0.05). There was no difference in any parameter related to the survival of fat cells between
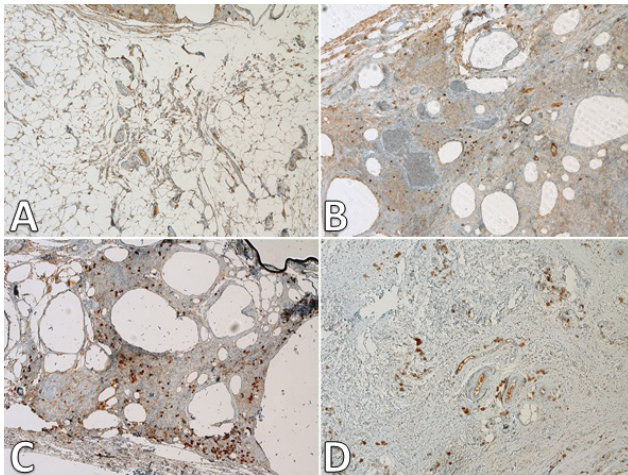
the 2R and 2D groups (p> 0.05).

Figure 4 a: Vascularization in group 1R (lower), VEGF, x100 magnification

Figure 4 b: Vascularization in group 2R (medium), VEGF, x100 magnification

Figure 4 c: Vascularization in group 3R (higher), VEGF, x100 magnification

Figure 4 d: Vascularization in group 4R (higher), VEGF, x100 magnification
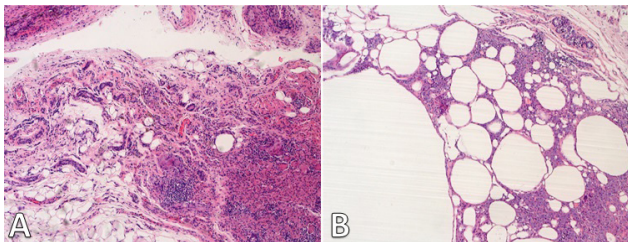

Figure 5 a: Lower cyst and vacuole formation in group 4D, hematoxylin-eosin staining, x100 magnification

Figure 5 b: Higher cyst and vacuole formation in group 1D, hematoxylin-eosin staining, x100 magnification
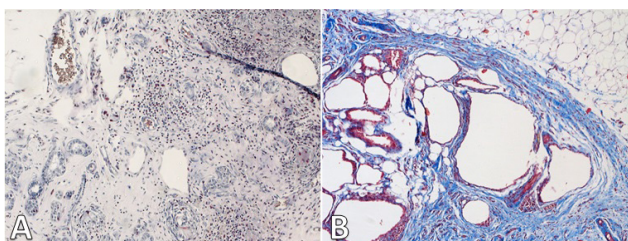

Figure 6 a: Lower fibrosis in group 4D, Masson's trichrome staining, x200 magnification

Figure 6 b: Higher fibrosis in group 1D, Masson's trichrome staining, x200 magnification

Figure 7 a: Ninety days after the fat graft transfer, black arrow shows the fat graft under the dorsal skin, group 4D.

Figure 7 b: Fat tissue (black arrow) 90 days after the transfer, group 4D.

Figure 7 c: Significant cyst formation (red arrow) 90 days after the transfer, group 1D.

Discussion

Since fat grafting is relatively easy, cost-effective, and readily available, it has become the favorite topic recently. However, the predictability of fat grafting application is limited, and there is controversy over its consistency. Some publications have reported resorption rates reaching 90% (8). After the development of liposuction in the 1980s, fat grafting gained popularity and various techniques were introduced to prevent resorption. Although the addition of adipose tissue-derived stem cells (ADSC), repeated injections, and microinjections have been used to prevent resorption, the problem has not yet been completely prevented. The causes of resorption include lack of structural support, negative factors in the recipient area, absence of angiogenesis, and early deficits in vascular supply (9).

Studies reporting the use of stem cells and PRP to prevent reduced survival, the biggest obstacle to fat grafting applications, have been published (10–12). This information in the literature is generally based on experimental information and requires mesenchymal stem cell isolation and serial passages, making fat grafting a difficult and expensive procedure not widely available. Houdek et al. observed that PRP-added collagen scaffolds accumulate dermal-derived mesenchymal stem cells in the environment better than collagen alone, thereby proving that PRP can attract mesenchymal stem cells to the environment (6). The current study showed that PRP alone could attract mesenchymal stem cells to the environment on the 10th day.

Missing in the literature was information as to whether PRP and fat grafting should be done at the same time and, if not, what the optimal interval would be. In this study, an exponential increase was observed after day 10, as the stem cells in the environment also showed division. It was thought that the proportional increase in stem cells in the first 10 days is due to migration of

Increased fat graft survival with mesenchymal stem cell.. - Yildiran et al.

Genel Tıp Dergisi

cells, and after day 10 the exponential increase was due to stem cell proliferation. For this reason, fat grafts were performed 10 days after PRP injection in this study.

There are many studies in which PRP and fat grafts are injected simultaneously as a mixture (2, 3, 12, 13). According to the results of this study, if the fat graft is combined with the stem cells, simultaneous injection can be performed, but if PRP is combined with the fat graft, it may be more favorable to inject the fat graft on day 10 when the PRP has recruited the stem cells in the environment.

When variables in the *in vivo* study were examined, the high cellular integrity of the fat cells, the low rates of necrosis, fibrosis, cysts, and vacuoles, and high vascularization rates were associated with the persistence of the fat graft. When these data were evaluated together, the best results were obtained with fat graft transfers applied 10 days after a full-dose PRP injection to the recipient area.

The effect of PRP doses diluted up to 4 × is no different from fat transfer without PRP, regardless of the area injected. This concentration is insufficient for PRP to affect the fat graft. The effect of 2 × diluted doses (10^5 platelets/µL) of PRP on the graft was increased vascularity regardless of the area in which it was injected.

PRP, which has proinflammatory properties, does not delay wound healing due to the inflammation it creates, on the contrary, it increases healing by increasing vascularity and providing an amount of inflammation that is absolutely necessary for wound healing. In this study, it was thought that the permanence of the fat graft was preserved by similar mechanisms (14).

In the group with full-dose PRP injected into the recipient area, the increase in cellular integrity of the fat graft as well as the increase in vascularity can be interpreted as increasing the survival of the fat graft by varying the effect mechanisms as concentration increases.

It was shown that full-dose PRP injections into the donor area only increased vascularity and did not affect cellular integrity compared to the serum-administered group. For this reason, although there is no difference in any parameter between the full-dose PRPs given to the recipient area and to the donor area, it is thought that injecting PRP into the recipient area will be more effective in patients for whom fat grafts will be applied, since it increases cellular integrity as well as vascularity. Ferraro et al. showed that different centrifugation methods change cellular integrity in fat cells (15). Son et al., on the other hand, showed that when storage techniques change, the cellular integrity also changes (16). In light of this information, it is thought that cellular integrity, which is a good criterion for evaluating fat graft persistence, is associated with mechanical events. In this study, PRP injection into the recipient area functioned as if fertilizing the recipient area and preparing the soil for planting. Since it also increases vascularity, PRP injection, acting as preconditioning, may have had a greater effect on the injectable fat tissue in the donor area compared to the fat pack.

In view of the results of this study, it seems possible to get more efficiency from PRP with more concentrated PRP doses; not having tested higher concentrations is a limitation of this study. However, since this study is based on clinical applicability, techniques other than routine PRP acquisition methods in clinical practice were not used.

The highlights of this study are:

1. PRP increased the stem cells emerging from the fat graft, and the maximum presence of stem cells was observed on the 10th day.

2. Injection of PRP into the recipient area provided superior fat graft permanence rates.

3. Although PRP starts to increase fat graft permanence by increasing vascularity, it acts by preserving the cellular integrity of the fat cells as the concentrations increase.

Thus, in performing fat graft applications in which permanence is prioritized, the PRP injection to the recipient area 10 days before fat grafting may provide higher survival rates.

References

1. Simonacci F, Bertozzi N, Grieco MP, Grignaffini E, Raposio E. Procedure, applications, and outcomes of autologous fat grafting. Ann Med Surg (Lond) 2017;20:49-60.

2. Li F, Guo W, Li K, et. al. Improved fat graft survival by different volume fractions of platelet-rich plasma and adipose-derived stem cells. Aesthet Surg J 2015;35:319-33.

3. Xiong BJ, Tan QW, Chen YJ, et. al. The Effects of Platelet-Rich Plasma and Adipose-Derived Stem Cells on Neovascularization and Fat Graft Survival. Aesthetic Plast Surg 2018;42:1-8.

4. Hu Y, Jiang Y, Wang M, Tian W, Wang H. Concentrated Growth Factor Enhanced Fat Graft Survival: A Comparative Study. Dermatol Surg 2018;44:976-84.

5. Cervelli V, De Angelis B, Lucarini L, et. al. Tissue regeneration in loss of substance on the lower limbs through use of platelet-rich plasma, stem cells from adipose tissue, and hyaluronic acid. Adv Skin Wound Care 2010;23:262-72.

6. Houdek MT, Wyles CC, Stalboerger PG, et. al. Collagen and

Increased fat graft survival with mesenchymal stem cell.. - Yildiran et al.

Genel Tıp Dergisi

Fractionated Platelet-Rich Plasma Scaffold for Dermal Regeneration. Plast Reconstr Surg 2016;137:1498-506.

7. Sezgin B, Ozmen S, Bulam H, et. al. Improving fat graft survival through preconditioning of the recipient site with microneedling. J Plast Reconstr Aesthet Surg 2014;67:712-20.

8. Rohrich RJ, Sorokin ES, Brown SA. In search of improved fat transfer viability: a quantitative analysis of the role of centrifugation and harvest site. Plast Reconstr Surg 2004;113:391□7.

9. Kassolis JD, Reynolds MA. Evaluation of the adjunctive benefits of platelet-rich plasma in subantral sinus augmentation. J Craniofac Surg 2005;16:280-7.

10. Rasmussen BS, Sørensen CL, Kurbegovic S, et. al. Cell-Enriched Fat Grafting Improves Graft Retention in a Porcine Model: A Dose-Response Study of Adipose-Derived Stem Cells versus Stromal Vascular Fraction. Plast Reconstr Surg 2019;144:397e□408e.

11. Zhao J, Yi C, Zheng Y, et. al. Enhancement of fat graft survival by bone marrow-derived mesenchymal stem cell therapy. Plast Reconstr Surg 2013;132:1149-57.

12. Atashi F, André-Lévigne D, Colin DJ, et. al. Does non-activated platelet-rich plasma (PRP) enhance fat graft outcome? An assessment with 3D CT-scan in mice. J Plast Reconstr Aesthet Surg 2019;72:669□75.

13. Raposio E, Bertozzi N, Bonomini S, et. al. Adipose-derived Stem Cells Added to Platelet-rich Plasma for Chronic Skin Ulcer Therapy. Wounds 2016;28:126-31.

14. 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 Oct 21;21(20):7794. doi: 10.3390/ijms21207794. PMID: 33096812; PMCID: PMC7589810.

15. Ferraro GA, De Francesco F, Tirino V, et. al. Effects of a new centrifugation method on adipose cell viability for autologous fat grafting. Aesthetic Plast Surg 2011;35:341-8.

16. Son D, Oh J, Choi T, et. al. Viability of fat cells over time after syringe suction lipectomy: the effects of cryopreservation. Ann Plast Surg 2010;65:354-60.

Increased fat graft survival with mesenchymal stem cell.. - Yildiran et al.

Genel Tıp Dergisi

Table 1: Median values of parameters and p values between groups.

		Cellular integrity of adipocytes	Cyst and vacuole formation	Necrosis	Vascularity
		Med. (Min/Max)	Med. (Min/Max)	Med. (Min/Max)	Med. (Min/Max)
Groups					
	1D	1.7 (1 / 3)	3.3 (1 / 5)	0 (0 / 0)	29 (18 / 64)
	1R	2 (0 / 3)	2 (0 / 5)	0.1 (0 / 1)	37 (28 / 62)
	2D	2.4 (1 / 4)	3.7 (0 / 5)	3.4 (1 / 5)	43 (29 / 71)
	2R	2.3 (1 / 4)	3 (1 / 5)	2.8 (0 / 5)	45 (30 / 62)
	3D	1.4 (0 / 2)	4.2 (1 / 5)	1.8 (1 / 4)	54 (39 / 76)
	3R	3.2 (1 / 4)	1 (0 / 5)	1.7 (0 / 4)	60 (45 / 88)
	4D	2.6 (2 / 4)	0.3 (0 / 3)	1.4 (0 / 4)	58 (34 / 103)
	4R	3.7 (2 / 4)	1 (0 / 3)	0.8 (0 / 4)	76 (38 / 102)
P Value		0.003	0.001	<0.001	<0.001
Pairwise	**1D→1R**	0.747	0.362	0.770	0.445
	1D→2D	0.154	0.898	<0.001	0.161
	1D→2R	0.269	0.975	<0.001	0.181
	1D→3D	0.596	0.550	0.001	0.004
	1D→3R	0.035	0.103	0.007	0.001
	1D→4D	0.120	0.002	0.006	0.002
	1D→4R	0.002	0.058	0.065	<0.001
	1R→2D	0.291	0.300	<0.001	0.556
	1R→2R	0.448	0.361	0.002	0.578
	1R→3D	0.404	0.136	0.004	0.042
	1R→3R	0.087	0.507	0.020	0.021
	1R→4D	0.238	0.044	0.018	0.023
	1R→4R	0.007	0.359	0.136	0.001
	4D→2D	0.897	0.002	0.156	0.081
	4D→2R	0.692	0.003	0.368	0.089
	4D→3D	0.037	<0.001	0.611	0.803
	4D→3R	0.581	0.163	0.983	0.967
	4D→4R	0.112	0.258	0.371	0.258
	4R→2D	0.086	0.043	0.021	0.004
	4R→2R	0.053	0.063	0.078	0.005
	4R→3D	<0.001	0.013	0.161	0.168
	4R→3R	0.299	0.792	0.382	0.276
	3D→2D	0.050	0.638	0.363	0.134
	3D→2R	0.106	0.585	0.683	0.144
	3D→3R	0.008	0.026	0.596	0.771
	3R→2D	0.496	0.079	0.150	0.074
	3R→2R	0.353	0.108	0.357	0.081
	2D→2R	0.786	0.926	0.639	0.989

Kruskal Wallis Test(Monte Carlo), Post Hoc Test : Dunn's Test, Med.: Median, Min.:Minimum, Max.:Maximum

Increased fat graft survival with mesenchymal stem cell.. - Yildiran et al.

Genel Tıp Dergisi

Figure 1. Schematic description of the in vitro and in vivo parts of the study.