

Review Article

Does platelet-rich plasma enhance the survival of grafted fat? An update review

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Abstract: Autologous fat grafting enables repair and augmentation of soft tissues and is increasingly used in plastic and reconstructive surgery. The main limitation of fat grafting is unpredictable graft resorption. To obviate this disadvantage, several studies have searched for new ways of increasing the viability of the transplanted tissue. One promising approach has been to mix the fat graft with Platelet-Rich Plasma (PRP) before transplantation. The purpose of this article is to review systematically the available comparative evidence about PRP-assisted fat grafting.

Keywords: Fat grafting, platelet-rich plasma (PRP), comparative study

Autologous fat grafting enables repair and augmentation of soft tissues and is increasingly used in plastic and reconstructive surgery. Autologous fat tissue has been considered to be an ideal filler for augmentation of soft tissue because it is biocompatible, versatile, natural-appearing, nonimmunogenic, inexpensive, and readily obtainable with low donor site morbidity [1, 2].

The main limitation of fat grafting is unpredictable graft resorption. To obviate this disadvantage, several studies have searched for new ways of increasing the viability of the transplanted tissue. One promising approach has been to mix the fat graft with Platelet-Rich Plasma (PRP) before transplantation. The purpose of this article is to review systematically the available comparative evidence about PRP-assisted fat grafting.

Limitations of lipotransfer

Autologous fat grafting is a well established technique in plastic and reconstructive surgery [3]. Illouz was the first to describe fat grafting in 1983, where the transplant was obtained from the donor site by liposuction followed by immediate injection of the fat graft through syringes [4]. Fat grafting was primarily used in recon-

touring of the body and face to correct defects after congenital defects, trauma, or cancer surgery, but has been widened to include treatment of burns, scars after radiotherapy, hypertrophic scars, and wrinkles.

The disadvantage of using autologous fat grafting to correct soft tissue defects is the unpredictable rate of resorption, which ranges from 25%–80% [5-9]. Histological analyses of fat grafts have shown acute necrosis as well as oily cysts, calcification, and the formation of connective tissue [10, 11]. To obviate these drawbacks, some strategies have been advanced to improve graft viability [12-17]. Among these, most recently, autologous platelet-rich plasma assisted fat grafting is attracting many surgeons.

Strategy for searching for relevant publications

We searched PubMed (from inception to October 2012) for original studies using the following search strategy: ("platelet-rich plasma" [MeSH Terms] OR ("platelet-rich" [All Fields] AND "plasma" [All Fields]) OR "platelet-rich plasma" [All Fields] OR ("platelet" [All Fields] AND "rich" [All Fields] AND "plasma" [All Fields]) OR "platelet rich plasma" [All Fields]) AND ("fat" [All

Fields] AND (“transplantation” [Subheading] OR “transplantation” [All Fields] OR “grafting” [All Fields] OR “transplantation” [MeSH Terms] OR “grafting” [All Fields]). There were totally 20 studies meet the criteria. After a sensitive read of all the publications, we found 5 animal and 2 human studies that investigated the subject with control group.

Experimental and clinical trials of PRP assisted fat grafting

Here we have reviewed 7 update original studies published on fat transplantation assisted with PRP compared with fat grafting only (Table 1).

In two human studies, PRP assisted lipotransfer were used in breast augmentation compared with lipotransfer only. In Gentile's study [18], the patients treated with PRP (n=50) added to the autologous fat grafts showed a 69% maintenance of the contour restoring and of 3-dimensional volume after 1 year, whereas the patients of the control group treated with centrifuged fat grafting (n=50) showed a 39% maintenance. While in Salgarello's study [19], it was revealed that fat grafting plus platelet-rich plasma (n=17) is not superior to Coleman fat grafting alone (n=25) by the rate of liponecrosis at breast ultrasound, and the need for further fat grafting.

The animal studies are more promising for PRP assisted fat grafting. In two rabbit study, Rodríguez et al [20] found the infiltration of adipose tissue plus PRP (n=8) presented less inflammatory reaction and fewer oil cysts than the infiltration of adipose tissue without PRP (n=8). Pires et al [21] observed three major effects of the addition of PRP in the free fat graft: PRP Group (n=30) showed a significantly higher fat survival weight as compared with the control group (n=30). Histopathological investigations revealed that the number of viable adipocytes and blood vessels was higher in PRP group, and a larger number of necrotic areas and fibrosis were detected between control group. In Nakamura's study [22] on rats, PRP group (n=64) showed a significantly higher of fat survival weight and the number of viable adipocytes and blood vessels than the control group (n=64). In two nude mice study, one research team [23] found fat graft volume and

weight were significantly higher in the PRP group (n=10) than in the control group (n=10), and histologic evaluation revealed greater vascularity, fewer cysts and vacuoles, and less fibrosis in the PRP group than in the control group. The cellular integrity and inflammation were not statistically different between the two groups. Another team [24] found the weight, volume and histological parameters between the PRP group (n=12) and control group (n=12) were not statistically significant.

Discussion

Platelet-rich plasma is a concentration of autologous human platelets (three to five times higher than baseline platelet count) in a small volume of plasma, containing the nine main growth factors proved to be actively degranulated by platelets to start the wound-healing process. These include transforming growth factor (TGF- β 1 and - β 2), platelet-derived growth factor (PDGF-AA, -AB and -BB), vascular endothelial growth factor (VEGF A and C), insulin growth factor (IGF-1) and epidermal growth factor (EGF). In addition to these growth factors, platelet-rich plasma also contains fibronectin, vitronectin, fibrinogen, osteocalcin, and osteonectin, known to act as cell adhesion molecules and as a matrix for cellular processes. The active secretion of these growth factors is initiated by the clotting process of blood. The natural process can be started by adding thrombin or calcium chloride. The active secretion of these growth factors by platelets begins within 10 minutes after clotting, with more than 95 percent of the presynthesized growth factors secreted within 1 hour. After this initial burst, the platelets synthesize and secrete additional proteins for the balance of their lives (5 to 10 days) [13]. Successful clinical applications have been reported using platelet-rich plasma, such as periodontal [25] and oral surgery [26], cosmetic surgery [27], spinal fusion [28], cardiac bypass surgery [29], and treatment of soft tissue ulcers [30].

Positive effects of platelet-rich plasma in favoring angiogenesis processes and proliferation of adipose-derived stem cells have been demonstrated experimentally. In relation to angiogenesis, Eppley et al. reported that platelet-rich plasma growth factors stimulate endothelial cells near their application site, favoring prolif-

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Table 1. Publications that investigate PRP assisted fat grafting with control group

Year	Author	Title	Object	Fat+PRP	Fat only	Follow-up	Result	Conclusion	Level of Evidence
2012	Gentile P, Di Pasquali C, Bocchini I, Floris M, Eleonora T, Fiaschetti V, Floris R, Cervelli V.	Breast Reconstruction With Autologous Fat Graft Mixed With Platelet-Rich Plasma	human	50 patients	50 patients	1 year	69% maintenance over 39%	positive	II
2011	Salgarello M, Visconti G, Rusciani A.	Breast fat grafting with platelet-rich plasma: a comparative clinical study and current state of the art.	human	17 patients	25 patients	3 months and 6 months	not superior to Coleman fat grafting alone	none	II
2011	Oh DS, Cheon YW, Jeon YR, Lew DH	Activated platelet-rich plasma improves fat graft survival in nude mice: a pilot study	nude mice	10 mice	10 mice	10 weeks	PRP treatment improved the survival and quality of fat grafts	positive	V
2011	Rodríguez-Flores J, Palomar-Gallego MA, Enguita-Valls AB, Rodríguez-Peralto JL, Torres J.	Influence of platelet-rich plasma on the histologic characteristics of the autologous fat graft to the upper lip of rabbits.	New Zealand rabbits	8 rabbits	8 rabbits	8 weeks and 12 weeks	The infiltration of adipose tissue plus PRP presented less inflammatory reaction and fewer oil cysts	positive	V
2010	Pires Fraga MF, Nishio RT, Ishikawa RS, Perin LF, Helene A Jr, Malheiros CA.	Increased survival of free fat grafts with platelet-rich plasma in rabbits.	New Zealand rabbits	30 rabbits	30 rabbits	6 months	significantly higher of fat survival weight and the number of viable adipocytes and blood vessels	positive	V

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2010	Nakamura S, Ishihara M, Takikawa M, Murakami K, Kishimoto S, Nakamura S, Yanagibayashi S, Kubo S, Yamamoto N, Kiyosawa T	Platelet-rich plasma (PRP) promotes survival of fat-grafts in rats	rats	64 rats	64 rats	10, 20, 30, and 120 days	The percentage area occupied by normal adipocytes in the PRP group was significantly higher. By 30 days, significantly more capillaries were seen in the PRP group	positive	V
2009	Por YC, Yeow VK, Louri N, Lim TK, Kee I, Song IC.	Platelet-rich plasma has no effect on increasing free fat graft survival in the nude mouse	nude mice	12 mice	12 mice	16 weeks	The weight, volume and histological parameters between the two groups were not statistically significant	none	V

eration and formation of new capillaries [31]. A second potential mechanism by which PRP enhances fat graft survival is greater proliferation of adipose stromal cells (ASCs) or stimulation of ASCs to differentiate into adipocytes. PRP stimulates the proliferation of ASCs and adipose tissue in vitro [32]. ASCs are generally included in the fat harvesting procedure, and thus some ASCs are usually present in fat grafts [33]. In addition, PRP has a mitogenic effect on endothelium [34], and other mesenchymal stem cells [35-37]. Kakudo et al. showed that activated platelet-rich plasma contains large amounts of PDGF-AB and TGF- β 1 and that they promoted the proliferation of human adipose-derived stem cells and human dermal fibroblast in vitro [38]. Lastly, Bendinelli et al. report the antiinflammatory effect of PRP by a reduction of COX2 and CXCR4 gene expression [39].

Implications for current research and future practice

The role of PRP in fat grafting and its clinical application is a fast developing area for plastic surgeons. Although, the effect of PRP on fat tissues has been studied within in vitro and animal models, clinical applications are still lacking the support of purposely designed randomised controlled trials. However, because the current two clinical pilot studies have shown encouraging outcomes, further controlled clinical trials to elucidate the effects of PRP in pragmatic settings are warranted. The trials also need to take into account the quality control of the various PRP preparations utilised to ensure that optimal concentrations of relatively pure platelets are injected with high concentrations of endogenous growth factors that are releasable during or soon after injection. Once the mechanism of PRP tissue regeneration becomes fully elucidated it may also become possible to use individual or combinations of recombinant or purified alpha granular growth factors with similar efficacy.

In conclusion, PRP theoretically has the potential for enhancing the survival of grafted fat.

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Disclosure

The authors have no financial interest in any products, devices, or drugs mentioned in this article.

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