CiSE
Clinics in Shoulder and Elbow

Clinics in Shoulder and Elbow Vol. 18, No. 2, June, 2015
http://dx.doi.org/10.5397/cise.2015.18.2.113

Platelet-rich Plasma in Arthroscopic Rotator Cuff Repair

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Rotator cuff tear is a common reason for shoulder pain. Although the surgical technique of rotator cuff repair is developing, high retear rate requires additional supplementary methods. Among these supplementary methods, as a kind of biologic augmentation, platelet-rich plasma (PRP) has been spotlighted and has recently been studied by many researchers. PRP, a concentrate of platelet extract obtained from whole blood, contains numerous growth factors. As this is known to play an important role in the tissue recovery process, it had been used for research in a variety of fields including orthopedics. Use of PRP has been attempted in surgical treatments of rotator cuff tear for better results; however, only a few large-scale research studies on the effect of PRP have been reported. Clinical results of each study are also variable. Therefore research using large-scale randomized, double-blind trials should be conducted in order to prove the application range, safety, and clinical effects of PRP.
(Clin Shoulder Elbow 2015;18(2):113-118)

Key Words: Shoulder; Rotator cuff; Platelet-rich plasma

Introduction

Rotator cuff lesion, which was reported from 14% to 50% of adults over the age of 60 years and 80% of adults over the age of 80 years, is the main reason for shoulder pain and causes much discomfort in daily life by causing decreased range of motion or muscular weakness of shoulder.[1,2] Numerous cases of rotator cuff lesion require surgical treatment. Surgical techniques for rotator cuff tear have been continuously developed for decades, from open repair with transosseous suture to all-arthroscopic single row technique or double row suture bridge technique.[3] Despite development of surgical techniques, the reported retear rate is still high. Single row technique, the most commonly used technique, showed retear rates of 30% to 94%.[4,5] According to a recent meta-analysis, double row suture bridge technique showed a lower retear rate when compared to single row technique, yet 27.3% of patients in whom double row suture bridge technique was performed also suffered from retear.[3,6] Because chronic rotator cuff tear makes attachment of the terminal part of the tendon to the bone difficult and prolongs the process, additional biologic augmentation other than suture methods are needed to help the tissues recover.[7]

Usage of platelet-rich plasma (PRP) is a form of biologic augmentation. PRP could be directly injected inside the joint, or may be applied by suturing organized PRP directly to the ruptured site during surgery.[8] Because numerous kinds of growth factors secreted from platelets have been regarded as having a positive effect on tendon recovery, studies researching the usage of PRP on rotator cuff repair have been conducted by many researchers for several years. In this study, the role of PRP on rotator cuff tear will be discussed and the effect of PRP will be analyzed by investigating existing literature.

Platelet-rich Plasma

Platelet is a component of blood plasma that takes part in hemostasis. Its life expectancy is 7 to 10 days and it contains intracellular structures including glycogen, lysosome, and two types of granules. Among these, alpha granule secretes growth factors involved in tissue repair. Activation of platelets in the

Received December 11, 2014. **Revised** January 23, 2015. **Accepted** January 28, 2015.

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Financial support: None. **Conflict of interests:** None.

pISSN 2383-8337
eISSN 2288-8721

resting state by thrombin leads to secretion of more than 1,500 kinds of materials, such as growth factors including transforming growth factor-β, platelet-derived growth factor, fibroblast growth factor, and vascular endothelial growth factor, and proteins that take part in hemostasis.[9,10] Once platelets are activated, 70% of restored growth factors are secreted within 10 minutes, and all restored growth factors are released within an hour. More growth factors are synthesized and secreted for the next 7 to 10 days until platelets die.[11]

PRP is a concentrate of platelets extracted from autologous blood. Whole blood is primarily centrifuged to separate red blood cells from plasma, and then undergoes secondary centrifugation to separate leukocytes and platelets together with a few red blood cells from platelet-poor plasma finely.[11] Average number of platelets within whole blood is 200,000 cells/μl. Optimal concentration of PRP that is effective for vascularization and tissue regeneration of 1.5 to 3 million cells/μl has been reported, which is around 7 to 10 times greater than the normal amount.[12]

First researched by Ferrari et al.[13] in 1987, the effect of PRP has been extensively researched in various fields for more than 20 years. Due to various kinds of platelet concentration methods and components, questions regarding the validity of correlation among research data have arisen. In order to standardize the result, Dohan Ehrenfest et al.[14] classified PRP according to four categories, depending on the presence of white blood cells and fibrin. The characteristics of classes and each protocol are shown in Table 1.[14-24] Although the effect of leukocytes in PRP has not yet been clearly determined, no effects that negatively affect PRP were found. In addition, when acromioplasty was performed in patients who suffered from subacromial impingement, the group that used leukocyte-rich PRP showed improvement of pain and inflammation.[25] Further research is necessary to study the effect of leukocyte-rich PRP, leukocyte-rich platelet-rich fibrin, pure PRP, and pure platelet-rich fibrin.

The Effect of Applying Platelet-rich Plasma in Rotator Cuff Repair; Review of Literature

Laboratory Study

Jo et al.,[26] who harvested human tenocytes during degenera-

Table 1. Classification of the Platelet Concentrates Protocols

PC	Method	LC	FD	Brief of technique	Drawback
P-PRP					
MP	Anitua's PRGF[15,16]	_	Low	Pipetting lower part of acellular plasma using only 'eyeballing' as a measuring tool	Lack of ergonomy and reproducibility
AP	Cell separator PRP[17]	_	Low	Cell separation with optical reader	Contained residual RBC or leukocyte
	Vivostat PRF[18]	_	Low	Using specific kit	Expensive
L-PRP					
MP	Friadent PRP[19]	+	Low	1st step centrifugation ; PPP and buffy coat collected	Expensive
	Curasan PRP[17]	+	Low	2nd step centrifugation ; PPP layer is discarded using the 'eyeballing' method	Contained residual RBC
	Plateltex PRP[20]	+	Low	Simillar method to Friadent's and Curasan's and using gelifying agent	Lack of reproducibility
AP	PCCS PRP[16,18]	+	Low	1st step centrifugation; PPP and buffy coat collected	Expensive
	Smart PRP[18,19]	+	Low	2nd step centrifugation; PPP layer is discarded	Cubersome centrifugations
	Magellan PRP[21]	+	Low	Cell separation with optical reader	
	GPS PRP[22]	+	Low	1st step centrifugation; PPP layer is discarded	
				2nd step centrifugation; Aspiration of buffy coat on the surface of RBC layer	
P-PRF					
MP	Fibrinet PRFM[18]	_	High	Buffy coat and PPP are transferred to tube containing $CaCl_2$ for clotting process	Difficult and expensive
L-PRF					
MP	Choukroun's PRF[23,24]	+	High	Without any anticoagulant or gelifying agent After centrifucation, PRF clot formed at the layer of buffy coat	Platelets are already activated during the process

PC: platelet concentrates, LC: leukocyte collection, FD: fibrin density, P-PRP: pure platelet-rich plasma, L-PRP: leukocyte rich platelet-rich plasma, P-PRF: pure platelet-rich fibrin, L-PRF: leukocyte-rich platelet-rich fibrin, MP: manual protocol, AP: automatized protocol, PRGF: preparation rich in growth factors, PCCS: platelet concentrate collection system, GPS: gravitational platelet separation system, PPP: platelet-poor plasma, PRFM: platelet-rich plasma fibrin matrix, RBC: red blood cell.

Table 2. Controlled Clinical Studies Dealing with the Surgical Use of PRP in Rotator Cuff Tears

Author (year)	Evidence level and study design	Sample size (persons) (PRP/control)	Tear size	Material	Surgical technique	Mean F/U (mo)	Clinical outcome	Imaging outcome
Barber et al. (2011)[32]	Level 3 Case-control	20/20	All size	PRFM Sutureable	Single row	31	No significant differences found	Lower retear rate in PRP group
Castricini et al. (2011)[33]	Level 1 RCT	43/45	Isolate supraspinatus tear	PRFM Sutureable	Double row	16	No significant differences found	No significant differences found
Jo et al. (2011)[34]	Level 2 Prospective cohort	19/23	All size	PRP gel Sutureable	Double row/suture bridge	20	No significant differences found	No significant differences found
Randelli et al. (2011)[35]	Level 1 RCT	26/27	All size	PRP Injectable	Single row	24	Initial difference, but no significant difference at final F/U	Lower retear rate for smaller tear with PRP
Bergeson et al. (2012)[36]	Level 3 Cohort	16/21	Small to medium	PRFM Sutureable	Single or double row	12	No significant differences found	Higher retear rate in PRP group
Gumina et al. (2012)[37]	Level 1 RCT	39/37	Large	L-PRFM Sutureable	Single row	13	No significant differences found	Lower retear rate in PRP group
Rodeo et al. (2012)[38]	Level 2 Prospective RCT	40/39	All size	PRFM Sutureable	Single or double row/ suture bridge	12	No significant differences found	No significant differences found
Antuña et al. (2013)[39]	Level 2 Prospective RCT	14/14	Massive	PRF Injectable	Single row	24	No significant differences found	No significant differences found
Jo et al. (2013)[40]	Level 1 RCT	20/18	Large to massive	PRP gel Sutureable	Double row/suture bridge	12	No significant differences found	Lower retear rate in PRP group
Ruiz-Moneo et al. (2013)[41]	Level 1 RCT	32/31	All size	PRP Injectable	Double row	12	No significant differences found	No significant differences found
Weber et al. (2013)[42]	Level 1 RCT	30/30	All size	PRFM Sutureable	Single row	12	No significant differences found	No significant differences found
Charousset et al. (2014)[43]	Level 3 Case-control	35/35	Large to massive	L-PRP Injectable	Double row	24	No significant differences found	No differences of retear rate ; retear size was smaller in L-PRP group
Malavolta et al. (2014)[44]	Level 1 RCT	27/27	Small to medium	PRP Injectable	Single row	24	No significant differences found	No significant differences found
Zumstein et al. (2014)[45]	Level 1 RCT	10/10	All size	L-PRF Suturable	Double row	12 Weeks	No significant differences found	No significant differences found
Hak et al. (2015)[46]	Level 2 RCT	12/13	Small to medium	PRP Injectable	Single row	6 Weeks	No significant differences found	Not performed

PRP: platelet-rich plasma, F/U: follow-up, RCT: randomized controlled trial, PRFM: platelet-rich plasma fibrin matrix, L-PRFM: leukocyte-rich platelet-rich plasma fibrin matrix, PRF: platelet-rich fibrin, L-PRP: leukocyte rich platelet-rich plasma, L-PRF: leukocyte-rich platelet-rich fibrin.

tive rotator cuff repair, and cultivated them for 2 weeks using platelet-poor plasma and PRP with various concentrations, reported that the PRP applied group showed better cell proliferation, gene expression, and synthesis of tendon matrix.

Beck et al.[27] researched PRP application in rotator cuff tear using a rat model. Supraspinatus of rat model was detached and repaired using PRP. Follow-ups for 7, 14, and 21 days showed that while failure load showed no significant difference, the group that used PRP showed high stiffness of tendons and more organized collagen fiber. Hapa et al.,[28] who used PRP for rotator cuff tear on a rat model and followed for 2 weeks, reported that the group that used PRP showed less inflammation, and better vascularization and mechanical strength. Dolkart et al.,[29] who used PRP for rotator cuff repair on a rat model and observed for 3 weeks, reported that the group that used PRP showed significantly higher maximal load, stiffness and collagen birefrience. However they reported that no significant difference was shown in tendon organization and vascularization. Ersen et al.[30] also conducted research using a rat model and reported that even though maximal load and stiffness of the group that used PRP was significantly superior, no histological differences were shown.

Chung et al.[31] used a rabbit model to perform repair surgery 6 weeks after incising supraspinatus to imitate chronic rotator cuff tear and used PRP for rotator cuff repair and observed the results at 4 and 8 weeks after the surgery. They reported that the group that used PRP showed better tendon status in continuity and orientation of collagen, and higher maximal load of tendons.

In cases of cell level or animal experiments, results are mostly positive. However, these results came from a controlled situation and may not represent the status of the human body. In addition, current animal experiments could not reflect human's status of chronic rotator cuff tear or recovery ability. Therefore, application of the results of animal experiments to clinical situations is still limited.

Clinical Study

Clinically, PRP has been applied to tissues of repaired site during rotator cuff repair. The results of research that used PRP during surgeries are described in Table 2.[32-46]

Conclusion could not be made easily since the consistency of study design and PRP formula for each study has not been formulated. According to the study so far, clinical results of the usage of PRP for rotator cuff tear showed no significant difference, but some studies reported a low retear rate,[1,32,35,37] while the study conducted by Bergeson et al.[36] reported a higher retear rate.

A systemic review conducted by Chahal et al.[47] in 2012 which analyzed 5 studies[32-36] reported that PRP usage is not effective, and meta-analysis conducted by Zhao et al.[48] and Li et al.[49] on randomized controlled trials[33,35,37-42] in 2014 reported that PRP usage does not help clinical results or decrease rotator cuff retear rate. In meta-analysis conducted by Zhang et al.[50] in 2013, it was reported that PRP usage did not help clinical results, but retear rate showed a significant decrease in small and middle sized tears.

In response to these inconsistent results, some researchers who support PRP stated that 'All PRP is not created equal.' In other words, they suggested that the differences result from different methods of PRP manufacture, activation, and application. Therefore, more standardized criteria for manufacture, maintenance, dosage, and application of PRP will be required, and adequate additional large-scale randomized study should be conducted. Analysis of the effects of PRP is also necessary, considering the size and the condition of torn rotator cuff tendon.

Conclusion

Although surgical techniques for rotator cuff tear are being developed, retear rate is significantly high. For this reason, biologic augmentation that could enhance the recovery has become prominent. PRP, a concentration of platelets, could be useful for recovery of rotator cuff tear through secretion of numerous growth factors that could help in the recovery of tissues. Research has been conducted in order to prove the effectiveness of PRP. However, the effect of PRP has not been significantly proven. For the usage of PRP during rotator cuff repair surgery, it should be additionally necessary that large-scale research studies use the standardization of manufacture, dosage, and method for application of PRP.

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