HSSJ (2017) 13:75–80
DOI 10.1007/s11420-016-9519-3

HSS Journal®
The Musculoskeletal Journal of Hospital for Special Surgery

ORIGINAL ARTICLE

Commercial Separation Systems Designed for Preparation of Platelet-Rich Plasma Yield Differences in Cellular Composition

Ryan M. Degen, MD · Johnathan A. Bernard, MD · Kristin S. Oliver, MD · Joshua S. Dines, MD

Received: 25 April 2016/Accepted: 15 July 2016/Published online: 19 August 2016

Abstract *Background:* The role of platelet-rich plasma (PRP) in the treatment of sport-related injuries is unclear, largely due to the heterogeneity of clinical results. This may relate to compositional differences in PRP from different separation systems. *Questions/Purposes:* This study aims to compare the composition of PRP produced with five different commercially available systems, focusing on cellular concentrations and pH. *Methods:* Seven donors (41 ± 12 years) provided blood for PRP preparation using five systems (Arthrex Angel, Emcyte Genesis CS, Arteriocyte Magellan, Harvest SmartPrep, and Biomet GPS III). Post processing, cellular composition was measured including platelets (PLT), white blood cells (WBC), neutrophils (NE), and red blood cells (RBC), as well as pH. *Results:* Platelet concentration and capture efficiency were similar between systems, except the Angel 7% preparation had a greater concentration than Genesis CS (2310 ± 524 vs. 1129 ± 264 k/μL). WBC concentration was variable between systems; however, significant differences were only found between the Angel 2% and GPS III preparations (11.0 ± 4.5, 27.3 ± 7.1 k/μL). NE concentration was significantly lower in the Angel 2% and 7% preparations compared with GPS III (0.6 ± 0.6 and 1.8 ± 1.3 k/μL vs. 9.4 ± 7.0 k/μL). RBC concentration was highest in SmartPrep (3.2 ± 0.6 M/μL) and Genesis CS systems (3.1 ± 0.6 M/μL) compared with all other systems (≤1.1 ± 1.2 M/μL). Finally, pH was significantly lower with the SmartPrep system (6.95 ± 0.06) compared with all others (≥7.26 ± 0.06). *Conclusion:* Aside from platelet concentration and capture efficiency, significant compositional differences were identified between preparation systems. Caution should be employed when interpreting clinical results of studies utilizing PRP, as the role of compositional differences and their effect on outcome are unknown. Further study is necessary to determine the clinical significance of these differences.

Keywords platelet-rich plasma · platelet-rich plasma separation system · cellular concentration

Level of Evidence: Therapeutic Study: Level IV

Electronic supplementary material The online version of this article (doi:10.1007/s11420-016-9519-3) contains supplementary material, which is available to authorized users.

R. M. Degen, MD (✉) · J. A. Bernard, MD · J. S. Dines, MD
Sports Medicine and Shoulder Service,
Hospital for Special Surgery,
535 East 70th Street,
New York, NY, USA
e-mail: ryan.degen@gmail.com

K. S. Oliver, MD
Blue Tail Medical Group,
St Louis, MO, USA

Introduction

Sports-related injuries are frequently associated with disability and time away from work and sport. Consequently, efforts are being directed towards identifying possible autologous or recombinant agents that can stimulate or augment the healing process to expedite return to activities [3, 9, 19]. One such agent that has been vastly studied in recent years is platelet-rich plasma (PRP). In orthopedics alone, its use has been studied in the treatment of non-unions, diabetic fractures, spinal fusions, as well as soft-tissue healing which includes tendinopathy, tendon-to-bone and ligament-to-bone healing [4, 6, 9, 12–14, 22, 24, 27, 29, 31, 32, 34].

PRP is a concentrate of autologous blood, with a higher concentration of platelets than in whole blood, ranging from as low as 200,000 platelets/μL [20] to equal or greater than 1,000,000 platelets/μL in a 5-mL volume of plasma [9, 12, 13, 17, 19, 26, 33]. Platelets contain α-granules that consist of various substances including proteins, cytokines, and growth factors that aid in regulating the healing process [4, 9, 13, 34]. When platelets come to an area of injury, they undergo degranulation, expelling these substances, aiding in the healing process by stimulating cell proliferation,

chemotaxis, angiogenesis, and cell differentiation [34]. Platelets also release histamine and serotonin, which increase local capillary permeability to improve access for additional inflammatory cells to start the reparative process [9]. While platelet concentration has been the primary focus when studying PRP in the past, other important constituents have been identified that also contribute to the healing process, including white blood cells, red blood cells, and neutrophils, all thought to propagate the local inflammatory response [13].

To date, results in the literature have been highly variable regarding the success of PRP injections [34]. Both Castillo et al. and Mazzocca et al. expressed concerns that it may relate to the underlying heterogeneity of available PRP produced by different separation systems, affecting the generalizability of reported results [3, 19]. They, in turn, studied the cellular composition of PRP produced from several commercially available separation systems. While they noted only slight differences in platelet concentrations between separation systems, they identified marked differences in the concentration of the additional components of PRP, including white blood cells, neutrophils, and red blood cells, whose roles are largely unknown in the healing process. The variability of the concentrations of these substances may affect the clinical response to PRP, and as a result, they emphasized the need for further study to determine the clinical relevance of these compositional differences in order to define the optimal PRP composition and better define its clinical application [3, 19].

In recent years, separation systems have continued to evolve in their technologic capabilities, including the ability to alter the processing protocol to produce different concentrations of various components within the concentrate. The purpose of this study was to compare the compositional differences of PRP from five different commercially available separation systems specifically assessing platelet concentration, white blood cell concentration, neutrophil concentration, red blood cell concentration, and pH of the final preparation.

Patients and Methods

Institutional review board approval (Salus IRB, IRB #1057) was obtained for this study. The participant group consisted of seven healthy volunteers (four males and three females,) with a mean age of 41 (±12) years old, without preexisting medical conditions requiring routine medication usage. All participants presented electively to donate blood for medical research purposes, and provided informed written informed consent, indicating their participation in this study was voluntary. Each donor underwent venipuncture and provided ~360 cc sample of blood. The five most commonly used separation systems at our center were obtained and utilized for comparison: Arthrex Angel (on both a 2% and 7% hematocrit setting), Emcyte Genesis CS, Arteriocyte Magellan PRP, Harvest SmartPrep APC+, and Biomet GPS III.

Before processing, a sample of whole blood was aliquotted for control purposes. Manufacturer's instructions were then closely followed for each separation system in processing the blood to produce the PRP product. The specific volume requirements, spin properties, and resultant volumes are reported in Table 1.

The aliquotted whole blood and PRP were then analyzed for specific cell concentrations: platelets (PLT), white blood cells (WBC), neutrophils (NE), red blood cells (RBC), and hematocrit percentage (HCT%) (Sysmex XE-5000, Lincolnshire, IL). Platelet capture efficiency, represented by the total number of platelets in the PRP sample divided by the total number of available platelets in the starting sample of blood, was also calculated. A pH measurement (SympHony Meter, VWR, Chicago, IL) was also taken for each system's PRP immediately following sample preparation.

Statistical analysis was done utilizing SPSS 17.0 (SPSS Inc., Chicago, Illinois), comparing differences in concentration of platelets, white blood cells, neutrophils, and red blood cells using a one-way analysis of variation (ANOVA) with a significance level of 0.05. Pairwise multiple comparisons were performed with Holm-Sidak testing.

Results

The results of whole blood analysis and subsequent PRP preparation analysis from the various systems can be found in Table 2.

Platelet concentrations increased significantly for all systems compared with whole blood ($p < 0.009$), but were largely the same between all separation systems, with the only significant difference coming between the Angel 7% HCT preparation and the Genesis CS preparation, with the Angel system producing a significantly greater concentration of platelets ($p = 0.04$). Platelet capture efficiency, also referred to as the system's recovery rate, did not demonstrate any significant differences between systems ($p \geq 0.089$) (Table 2).

WBC concentration was significantly elevated in all PRP samples compared with whole blood ($p < 0.018$), with the exception of the Angel 2% sample, which demonstrated a similar WBC concentration to whole blood ($p = 0.182$). The only statistically significant difference in WBC concentration in comparisons between the separation systems was between the Angel 2% preparation and the GPS III preparation, with a significantly lower concentration of WBC in the Angel 2% preparation compared with GPS III ($p = 0.017$) (Table 2).

Pairwise comparisons between the systems noted a significantly greater concentration of neutrophils in the GPS III preparation than that produced by the Angel system at 2% and 7% HCT settings ($p = 0.007$ and 0.027, respectively) (Table 2).

Comparing RBC concentration between PRP samples, both the SmartPrep and Genesis CS separation systems were less efficient at RBC separation, resulting in significantly greater concentrations of RBC compared with the Angel 2%, Angel 7%, Magellan, and GPS PRP samples ($p < 0.003$) (Table 2).

Comparison of the pH of the PRP preparations revealed that the SmartPrep system produced a sample that was significantly more acidic than all other preparations, with

Table 1 PRP preparation system properties

Manufacturer	Device	Whole blood volume (mL)	Anticoagulant	Procedure	Centrifuge	Centrifuge time	mL
Arthrex	Angel 2% HCT	52	ACD-A, 8 mL	Double spin	3500 RPM × 2:56 min 3000 RPM × 8:32 min	17 min	2.9 ± 0.5
Arthrex	Angel 7% HCT	52	ACD-A, 8 mL	Double spin	3500 RPM × 2:56 min 3000 RPM × 8:32 min	17 min	3.5 ± 0.7
Emcyte	GenesisCS	54	ACD-A, 6 mL	Single spin	3600 RPM × 10 min	10 min	6.0 ± 0.0
Harvest	SmartPRP	54	ACD-A, 6 mL	Double spin	2500 ± 150 RPM × 1–3 min 2300 ± 140 RPM × 6–9 min	14 min	7.0 ± 0.0
Arteriocyte	Magellan	52	ACD-A, 8 mL	Double spin	2800 RPM 3800 RPM	17 min	5.3 ± 1.6
Biomet	GPS III	54	ACD-A, 6 mL	Single spin	3400 RPM × 15 min	15 min	6.1 ± 0.2

Table 2 Composition of whole blood and PRP preparations (symbols denote statistically significant differences [$p < 0.05$] between pairs; asterisk (*) denotes statistically significant difference compared to all other samples)

Manufacturer	Device	mL	WBC (k/μL)	RBC (M/μL)	HCT %	PLT (k/μL)	NE (k/μL)	pH	Platelet capture efficiency
Whole blood	–	–	5.2 ± 1.0	4.4 ± 0.2	38.7 ± 1.9	206.1 ± 37.4	2.8 ± 0.8	–	–
Arthrex	Angel 2% HCT	2.9 ± 0.5	11.0 ± 4.5$^{\alpha}$	0.2 ± 0.1	1.1 ± 0.4	2064 ± 526	0.6 ± 0.6^{Y}	7.44 ± 0.11	0.56 ± 0.12
Arthrex	Angel 7% HCT	3.5 ± 0.7	16.9 ± 4.4	1.0 ± 0.3	8.8 ± 2.0	2310 ± 524$^{\beta}$	1.8 ± 1.3$^{\delta}$	7.34 ± 0.12	0.75 ± 0.13
Emcyte	GenesisCS	6.0 ± 0.0	20.6 ± 3.9	3.1 ± 1.6*	27.4 ± 14.1*	1129 ± 264$^{\beta}$	7.4 ± 3.1	7.28 ± 0.08	0.61 ± 0.12
Harvest	SmartPRP	7.0 ± 0.0	22.9 ± 4.3	3.2 ± 0.6*	28.9 ± 4.4*	1508 ± 406	4.2 ± 2.0	6.95 ± 0.06*	0.94 ± 0.12
Arteriocyte	Magellan	5.3 ± 1.6	19.8 ± 17.7	1.1 ± 1.2	9.8 ± 12.1	1989 ± 1225	4.1 ± 6.6	7.26 ± 0.06	0.86 ± 0.41
Biomet	GPS III	6.1 ± 0.2	27.3 ± 7.1$^{\alpha}$	1.0 ± 0.9	9.1 ± 8.0	1343 ± 670	9.4 ± 7.0 $^{\delta, Y}$	7.32 ± 0.06	0.73 ± 0.30

an average pH of 6.95 ($p < 0.001$). In addition, the Genesis and Magellan systems were also found to be significantly more acidic than the Angel 2% system, with average pH of 7.28 and 7.26 compared with 7.44 ($p = 0.003$ and 0.014) (Table 2).

Discussion

The primary purpose of this study was to quantify the characteristics of PRP derived from different commercially available separation systems to identify potential differences in composition. Clinical outcomes following PRP injections have been variable, with few clear clinical indications. This heterogeneity may stem from the underlying differences in the composition of PRP identified in this study, which may therefore limit data pooling from different systems and affect the generalizability of reported results. The results of this analysis revealed similar platelet concentration and capture efficiency between preparation systems. However, the concentration of the remaining constituents was variable between systems. Additionally, pH varied between systems, with several producing a concentrate with a non-physiologic pH.

Limitations of this study are consistent with those in similar studies, where sample size was limited, potentially impacting study results and introducing type II error. However, this sample size is consistent with similar, widely quoted studies investigating compositional differences in PRP [3, 18]. Additionally, a single-donor model was utilized, which allows for stronger comparisons between the different separation systems. Unfortunately, given the study design with our desire to compare multiple systems, we did not have sufficient volume of blood to test repeatability with each system, which represents an additional limitation. Secondly, the concentration of various growth factors was not included in this study as the focus was primarily on the different cellular concentrations produced by these different systems, and the volume of data with growth factor analysis would make interpretation and reporting of results challenging. Lastly, this was not an inclusive study, as several other PRP preparation systems exist, although studying all systems with a single-donor model would not be feasible given the volume of blood required for each system, making the cumulative blood donation excessively large and potentially unsafe. As a result, this study included the most common clinically utilized systems at our institution for comparison.

With the exception of a difference between the Angel 7% preparation and the Magellan preparation, all systems produced a concentration of platelets meeting the definition outlined by Marx of >1 million cells/μL. In theory, each would provide a sufficient concentration to augment the healing response. However, all systems produced a different end volume, and therefore a different total cumulative dosage of platelets per sample. The clinical significance of this is unknown, as there is currently little to no evidence on the total platelet dosage required to treat various pathologic entities. Therefore, we cannot make clinical recommendations on which of these systems is superior based on platelet concentration alone.

Looking at WBC concentration, there was only slight variation between the various separation systems. By the standards outlined by Dohan Ehrenfest et al., all preparations contained WBC concentrations above that in whole blood, classifying them as leukocyte-rich PRP [8]. These findings may allow for pooling of data from select studies utilizing these systems to aid in determining the utility of leukocyte-rich PRP, which has been highly debated. Several studies have supported leukocyte-rich PRP, arguing that the WBC potentiate the release of cytokines from platelets to improve healing, and also confers antimicrobial properties to reduce infection rates, as demonstrated in vitro [4, 15, 24, 25]. Others argue that the release of these cytokines causes a highly inflammatory reaction, predisposing to fibrosis and structurally weaker tissue, while the purported antimicrobial effects have not been noted in in vivo studies [1, 11, 16, 21, 30]. Additionally, as it pertains to intra-articular use, leukocyte-rich PRP has been shown to cause increased post-injection pain, cell death, and synoviocyte activation than leukocyte-poor PRP [2]. At present, no clear consensus exists regarding the utility of WBC in PRP and further study is warranted which may be facilitated by the results of this analysis.

Similar to the role of WBC within PRP, there is conflicting evidence regarding the role of neutrophils in the inflammatory and reparative processes stimulated by PRP. In our study, the concentration of neutrophils widely varied between the different separation systems. Some studies have suggested that they are important in providing an antimicrobial effect, via release of a bactericidal acid, while other studies suggest that there is a positive correlation between their presence and the quantity of IL-1β, an inflammatory cytokine, which may or may not have deleterious effects on the healing process [19, 21, 25]. The specific effect must be further investigated, and as such, few conclusions can be drawn regarding the differential concentration among these systems, other than to say that caution should be employed when comparing the clinical effects of these different preparations as they varied significantly in neutrophil concentration.

The role of RBC in PRP injections is also largely unknown, with little data on the specific effects of this component of PRP. In recent years, there has been evidence to suggest that RBCs can be deleterious, particularly with intra-articular PRP injections, as they may be harmful to synoviocytes as identified by Braun et al., resulting in the release of catabolic mediators that may increase cartilage damage and contribute to joint degeneration [2]. Concentrations of RBC in this study varied, with some separation systems (SmartPrep and Genesis CS) inefficiently removing this component during the filtration process. While the Genesis CS system is a single-spin system, which could potentially explain the inability to separate the RBC component [7], SmartPrep is a double-spin system which should be capable of removing RBC. Instead, it may relate to the spin time as both of these systems had the shortest duration of spin cycle, which may have prevented further RBC separation. Regardless of the underlying processing difference attributable for this compositional difference, caution should

be exercised when utilizing PRP preparations that are RBC-rich, as further study is necessary to determine the clinical effect of RBC within PRP for the treatment of soft-tissue pathology.

Comparing the cellular concentrations between single-spin systems (Emcyte Genesis, Biomet GPS) and double-spin systems (Arthrex Angel, Harvest Smartprep, Arteriocyte Magellan), there were no consistent, statistically significant differences between the methods of PRP preparation. However, we do note that the single-spin systems produced lower concentrations of platelets (1129 ± 264 and 1343 ± 670 k/μL) compared with the double-spin systems ($\geq 1508 \pm 406$ k/μL), although the only statistically significant differences were between the Emcyte Genesis and Arthrex Angel 7% preparations (Table 2). Similarly, the single-spin systems also had higher concentrations of NE (7.4 ± 3.1 and 9.4 ± 7.0 k/μL), compared with the double-spin systems ($\leq 4.2 \pm 2.0$ k/μL), although the only significant differences were between both single-spin systems and the Arthrex Angel 7% preparation (Table 2).

Unique to this study, the pH of each PRP sample was also analyzed, revealing that several of the systems produced acidic PRP samples (pH = 6.95–7.32), falling outside of the normal physiologic range of 7.35 to 7.45. Several studies have previously correlated increased subjective pain with the injection of acidic substances, falling below a pH of 7.35 [5, 10, 28]. Consequently, the injection of these acidic PRP preparations may be a potential source of pain for patients. As a result, this data may be useful as it informs the clinician of a potential harm to their patients, as several of the systems produced relatively acidic preparations, falling below this physiologic range. Consideration should be given to buffering these PRP preparations with bicarbonate solution to bring it to a physiologic pH prior to injection, limiting the discomfort associated with this injection, as performed by Mishra et al. in their study investigating the efficacy of PRP in the treatment of chronic lateral epicondylitis [23].

In conclusion, PRP preparations from different separation systems demonstrated similar platelet concentration and capture efficiency; however, they otherwise demonstrated significant differences in WBC, neutrophil, and RBC concentration, as well as pH. The results from this study should caution physicians from pooling data from studies utilizing different separation systems, as differences in cellular composition may contribute to heterogeneous clinical outcomes. These results may also help to guide selection of separation systems for clinicians based on desired preparation properties. Further basic science studies are necessary to delineate the role of these different cellular constituents to determine if these measured differences are clinically meaningful.

Compliance with Ethical Standards

Conflict of Interest: Ryan M. Degen, MD, Johnathan A. Bernard, MD, and Kristin S. Oliver, MD have declared that they have no conflict of interest. Joshua S. Dines, MD reports personal fees from Arthrex, Conmed Linvatec and Ossur, outside the work.

Human/Animal Rights: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5).

Informed Consent: Informed consent was obtained from all patients for being included in the study.

Required Author Forms Disclosure forms provided by the authors are available with the online version of this article.

References

1. Anitua E, Zalduendo MM, Prado R, Alkhraisat MH, Orive G (2015) Morphogen and proinflammatory cytokine release kinetics from PRGF-Endoret fibrin scaffolds: Evaluation of the effect of leukocyte inclusion. J. Biomed. Mater. Res. A 103:1011–1020.
2. Braun HJ, Kim HJ, Chu CR, et al. The Effect of Platelet-Rich Plasma Formulations and Blood Products on Human Synoviocytes: Implications for Intra-articular Injury and Therapy. *Am J Sports Med*. 2014; 42: 1204-1210.
3. Castillo TN, Pouliot MA, Kim HJ, et al. Comparison of growth factor and platelet concentration from commercial platelet-rich plasma separation systems. *Am J Sports Med*. 2011; 39: 266-71.
4. Cavallo C, Filardo G, Mariani E, et al. Comparison of platelet-rich plasma formulations for cartilage healing: an in vitro study. *J Bone Joint Surg Am*. 2014; 96: 423-9.
5. Cepeda MS, Tzortzopoulou A, Thackrey M, Hudcova J, Arora Gandhi P, Schumann R (2012) Cochrane Review: Adjusting the pH of lidocaine for reducing pain on injection. Evidence-Based Child Heal. 7:149–215.
6. Cervellin M, de Girolamo L, Bait C, et al. Autologous platelet-rich plasma gel to reduce donor-site morbidity after patellar tendon graft harvesting for anterior cruciate ligament reconstruction: a randomized, controlled clinical study. *Knee Surg Sports Traumatol Arthrosc*. 2012; 20: 114-20.
7. Dhurat R, Sukesh M. Principles and methods of preparation of platelet-rich plasma: A review and author's perspective. *J Cutan Aesthet Surg*. 2014; 7: 189.
8. Dohan Ehrenfest DM, Andia I, Zumstein MA, et al. Classification of platelet concentrates (Platelet-Rich Plasma-PRP, Platelet-Rich Fibrin-PRF) for topical and infiltrative use in orthopedic and sports medicine: current consensus, clinical implications and perspectives. *Muscles Ligaments Tendons J*. 2014; 4: 3-9.
9. Foster TE, Puskas BL, Mandelbaum BR, et al. Platelet-rich plasma: from basic science to clinical applications. *Am J Sports Med*. 2009; 37: 2259-72.
10. Frank SG, Lalonde DH. How acidic is the lidocaine we are injecting, and how much bicarbonate should we add? *Can J Plast Surg*. 2012; 20: 71-73.
11. Giovanini AF, Deliberador TM, Tannuri Nemeth JE, et al. Leukocyte-platelet-rich plasma (L-PRP) impairs the osteoconductive capacity of the autograft associated to changes in the immunolocalization of TGF-β1 and its co-expression with Wnt10b and CD34 cells. *J Craniomaxillofac Surg*. 2013; 41: e180-6.
12. Hall MP, Band PA, Meislin RJ, et al. Platelet-rich plasma: current concepts and application in sports medicine. *J Am Acad Orthop Surg*. 2009; 17: 602-8.
13. Hsu WK, Mishra A, Rodeo SA, et al. Platelet-rich plasma in orthopaedic applications: evidence-based recommendations for treatment. *J Am Acad Orthop Surg*. 2013; 21: 739-48.
14. Jenis LG, Banco RJ, Kwon B (2006) A prospective study of Autologous Growth Factors (AGF) in lumbar interbody fusion. Spine J. 6:14–20.

15. Li G-Y, Yin J-M, Ding H, et al. Efficacy of leukocyte- and platelet-rich plasma gel (L-PRP gel) in treating osteomyelitis in a rabbit model. *J Orthop Res*. 2013; 31: 949-56.
16. Lopez-Vidriero E, Goulding KA, Simon DA, et al. The use of platelet-rich plasma in arthroscopy and sports medicine: optimizing the healing environment. *Arthroscopy*. 2010; 26: 269-78.
17. Marx RE. Platelet-rich plasma (PRP): what is PRP and what is not PRP? *Implant Dent*. 2001; 10: 225-8.
18. Mazzocca AD. Platelet-Rich Plasma Differs According to Preparation Method and Human Variability. *J Bone Jt Surg*. 2012; 94: 308.
19. Mazzocca AD, McCarthy MBR, Chowaniec DM, et al. Platelet-rich plasma differs according to preparation method and human variability. *J Bone Joint Surg Am*. 2012; 94: 308-16.
20. Mazzucco L, Balbo V, Cattana E, et al. Not every PRP-gel is born equal. Evaluation of growth factor availability for tissues through four PRP-gel preparations: Fibrinet, RegenPRP-Kit, Plateltex and one manual procedure. *Vox Sang*. 2009; 97: 110-8.
21. McCarrel TM, Minas T, Fortier LA. Optimization of leukocyte concentration in platelet-rich plasma for the treatment of tendinopathy. *J Bone Joint Surg Am*. 2012; 94: e143(1–8).
22. McCarthy ML, MacKenzie EJ, Edwin D, et al. Psychological distress associated with severe lower-limb injury. *J Bone Joint Surg Am*. 2003; 85-A: 1689-97.
23. Mishra A, Pavelko T. Treatment of chronic elbow tendinosis with buffered platelet-rich plasma. *Am J Sports Med*. 2006; 34: 1774-8.
24. Mishra AK, Skrepnik NV, Edwards SG, et al. Efficacy of platelet-rich plasma for chronic tennis elbow: a double-blind, prospective, multicenter, randomized controlled trial of 230 patients. *Am J Sports Med*. 2014; 42: 463-71.
25. Moojen DJF, Everts PAM, Schure R-M, et al. Antimicrobial activity of platelet-leukocyte gel against Staphylococcus aureus. *J Orthop Res*. 2008; 26: 404-10.
26. Nikolidakis D, Jansen JA. The biology of platelet-rich plasma and its application in oral surgery: literature review. *Tissue Eng Part B Rev*. 2008; 14: 249-58.
27. Nin JRV, Gasque GM, Azcárate AV, et al. Has platelet-rich plasma any role in anterior cruciate ligament allograft healing? *Arthroscopy*. 2009; 25: 1206-13.
28. Parham SM, Pasieka JL. Effect of pH modification by bicarbonate on pain after subcutaneous lidocaine injection. *Can J Surg*. 1996; 39: 31-35.
29. Peerbooms JC, Sluimer J, Bruijn DJ, et al. Positive effect of an autologous platelet concentrate in lateral epicondylitis in a double-blind randomized controlled trial: platelet-rich plasma versus corticosteroid injection with a 1-year follow-up. *Am J Sports Med*. 2010; 38: 255-62.
30. Portela GS, Cerci DX, Pedrotti G, et al. L-PRP diminishes bone matrix formation around autogenous bone grafts associated with changes in osteocalcin and PPAR-γ immunoexpression. *Int J Oral Maxillofac Surg*. 2014; 43: 261-8.
31. Sánchez M, Anitua E, Azofra J, et al. Comparison of surgically repaired Achilles tendon tears using platelet-rich fibrin matrices. *Am J Sports Med*. 2007; 35: 245-51.
32. Sánchez M, Fiz N, Azofra J, et al. A randomized clinical trial evaluating plasma rich in growth factors (PRGF-Endoret) versus hyaluronic acid in the short-term treatment of symptomatic knee osteoarthritis. *Arthroscopy*. 2012; 28: 1070-8.
33. Saucedo JM, Yaffe MA, Berschback JC, et al. Platelet-rich plasma. *J Hand Surg Am*. 2012; 37: 587-9. quiz 590.
34. Sheth U, Simunovic N, Klein G, et al. Efficacy of autologous platelet-rich plasma use for orthopaedic indications: a meta-analysis. *J Bone Joint Surg Am*. 2012; 94: 298-307.