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Original Article

Treatment of knee osteoarthritis with platelet-rich plasma plus hyaluronic acid in comparison with platelet-rich plasma only

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Abstract: Background: The exact outcome of the combined use of hyaluronic acid (HA) and platelet-rich plasma (PRP) in the treatment for osteoarthritis remains unclear. The goal of this paper was to compare the efficacy of PRP + HA with those of a cohort of patients treated with platelet-rich plasma only. Materials and methods: A total of 126 Subjects with knee osteoarthritis were enrolled: 63 cases in PRP plus HA group and 63 cases in PRP group. After clinical and radiographic evaluation, patients received a weekly intra-articular injection of HA added with PRP or of only PRP for 3 weeks. Follow-up was carried out at 1, 3, 6, and 12 months. Results: In the participants treated with PRP plus HA and with PRP only, VAS scores decreased significantly, and accordingly, knee function (WOMAC) improved, compared to the status of patients prior to treatment. Regarding to VAS and WOMAC, no significant difference were observed between the two groups; however, there is a trend that could obtain better functional scores in PRP plus HA group (VAS, $P = 0.392$; WOMAC, $P = 0.082$). Six failures occurred in the PRP plus HA group and 11 in PRP group. No major adverse events or complications were observed in both groups. Conclusions: The association of PRP and HA is effective and safe in the management of patients suffering from mild to moderate KOA. Although no differences in functional outcomes were shown between the groups, there is a trend that PRP plus HA could obtain relatively better functional scores.

Keywords: Hyaluronic acid (HA), platelet-rich plasma (PRP), osteoarthritis, outcome

Introduction

Knee osteoarthritis (KOA) is a degenerative joint disease characterized by biochemical and biomechanical alterations of articular cartilage, which is very common in the elderly population [1-3]. It is the more common cause of chronic pain and the loss of mobility, which can undermine overall health and quality of life of the affected patients [4, 5]. Currently, available drugs including analgesics, nonsteroid and steroid anti-inflammatory drugs (NSAIDs), glucosamine, chondroitin sulphate, and hyaluronic acid (HA), were applied for the treatment of KOA to release pain and inflammation, and to improve knee function and quality of life [6]. Unfortunately, none of managements above can halt OA progression and reverse any existing damage.

In view of the above reasons, the use several novel drugs, including platelet-rich plasma (PRP) and HA injections, which is able not only to manage clinical symptoms but also to provide an instructional environment for stimulating joint repair, was managed for KOA patients [7, 8]. The injections of platelet-rich plasma (PRP) and HA have been extensively applied to regulate the complex spatiotemporal signaling within and between the joint tissues and to improve lubrication and modulate inflammation, which can restore a natural healing microenvironment [8, 9]. Several studies [10-14] have shown superior results of intra-articular PRP injections than HA. A meta-analysis has also showed that PRP injection is more efficacious than HA injection and placebo in reducing symptoms and improving function and quality of life [15]. However, the exact efficacy of the

Table 1. Patient Demographic Characteristics

	PRP + HA	PRP	*P* value
Sample size (n)	63	63	-
Age (years)	61.2 ± 9.6	60.7 ± 10.1	.834
Gender (f/m)	45/18	51/12	.722
Body mass index (kg/m^2)	24.2 ± 4.2	24.6 ± 3.9	.755
Side, No. left/right	25/38	29/34	.614
Kellgren-Lawrence, No (n, %)			.818
I	17 (27.0)	15 (23.8)	-
II	28 (44.4)	31 (49.2)	-
III	18 (28.6)	17 (27.0)	-
Symptoms (months)	26	29	-
VAS	7.2 ± 3.2	6.9 ± 3.8	.517
WOMAC	39.9 ± 13.50	41.1 ± 12.7	.439
Follow-up (months)	14.2	15.7	-

Abbreviations: PRP, platelet-rich plasma; HA, hyaluronic acid; f, female; m, male; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

combination of the two therapeutic agents ---PRP and HA, remains unclear.

Up to now, only one study by Abate et al [1] has been perform to investigate the association of these two therapeutic agents in patients suffering from KOA. In their study, they demonstrated that the association of PRP plus HA has the same efficacy of platelet-rich plasma only, administered in higher volume. However, there were several limitations in it, including small sample size and short follow-up period. Therefore, it is necessary to perform more studies to confirm this result.

The purpose of this study was to investigate compare the clinical response to PRP plus HA and PRP treatment in 2 groups of patients affected by KOA.

Materials and methods

This study was approved by the Institutional Board Review of Provincial Hospital Affiliated to Shandong University. Each subject provided his or her written informed consent.

The patient were included if he or she met with the following diagnostic criteria: patients suffering for more than 3 months from KOA (Kellgren-Lawrence [16] 0 to III at X-ray evaluation or MRI findings of degenerative changes in patients presenting with no OA X-ray findings). Exclusion criteria were the following: patients older than 80 years; Kellgren-Lawrence score > III; systemic diseases (diabetes, renal, hepatic, cardiac, infections, endocrinopathies, malignancies); immunodepression; anticoagulant or antiaggregant therapies; use of NSAIDs in the 5 days before blood donation; and patients with Hb values < 11 g/dl and/or platelet values < 150,000/mm^3. Based on the criteria above, a total of 63 cases who received PRP plus HA injections for the treatment of KOA at Provincial Hospital Affiliated to Shandong University from January 2012 to July 2014 and the same number of cases who received only PRP injections were enrolled.

All demographic and anthropometric data, including age, gender, body mass index (BMI), visual analogue scale (VAS), and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), were collected from hospital records.

The procedure for preparing PRP that is described by Abate et al. [1]. Patients received a weekly intra-articular injection (lateral approach) of the compound PRP plus HA or only PRP for 3 weeks. At the time of injection the syringe was appropriately covered to prevent patients from discovering the substance they were receiving. After each injection, the patients were kept under observation for approximately 30 min (monitoring early side effects) and then sent home with instructions to restrict the use of the leg for at least 24 hours. And all patients were suggested to use cold therapy/ice on the affected area to relieve pain. During this period, the use of NSAIDs was forbidden. Moreover, patients were permitted to take rest or mild activities (such as using an exercise bike or mild exercise in a pool), and were allowed to participate in a gradual resumption of normal sport or recreational activities as tolerated. Evaluation was repeated after 1, 3, 6, and 12 months. In order to compare the outcomes obtained in the PRP plus HA group, the same clinical and functional parameters were retrospectively employed from a group of patients who received PRP only for the treatment of KOA and the same standard assessment protocol.

Table 2. Clinical outcomes

	PRP + HA	PRP	*P* value
VAS	1.3 ± 1.1	1.6 ± 1.9	.392
WOMAC	14.6 ± 6.9	15.7 ± 8.5	.082
Satisfaction			.192
Excellent/good	57 (90%)	52 (83%)	-
Fair/poor	6 (10%)	11 (17%)	-

All statistical analyses were carried out with the Statistical Package for the Social Sciences (SPSS) software version 19.0 (SPSS Inc., Chicago, USA). All continuous data were reported as mean ± standard deviation (SD). Dichotomous data are expressed as frequencies and percentage. The two-sample Student's t test was used to compare continuous variables, when the distribution of data was normal; the Wilcoxon's rank sum test was used otherwise. The χ^2 test was used to evaluate associations between categorical data. For all tests, $P < 0.05$ was considered significant.

Results

All demographic characteristics of the subjects are listed in **Table 1**. There were no significant difference between the two groups, in term of age, gender, and BMI. At baseline, no significant demographic and clinical differences were observed among groups, with regarding to VAS and WOMAC.

In the participants treated with PRP plus HA and PRP only (**Table 2**), VAS scores decreased significantly, and accordingly, knee function (WOMAC) improved, compared to the status of patients prior to treatment. Regarding to VAS and WOMAC, no significant difference were observed between the two groups; however, there is a trend that could obtain better functional scores in PRP plus HA group (VAS, $P = 0.392$; WOMAC, $P = 0.082$).

Six failures occurred in the PRP plus HA group and 11 in PRP group: in eight cases with suspected intolerance to some components of PRP and HA, and so the injective treatment was stopped after the first administration. Nine patients were still complaining of intense pain and functional deficit and sought other treatment in another medical center. No major adverse events or complications were observed in both groups. We documented temporary mild worsening of pain in the knee joint after application of PRP in six cases, which was spontaneously resolved after 2 days.

Discussion

The conservative treatment of KOA has been well documented in the literature over the past 5 decades. Treatment with PRP restores the natural rheologic and metabolic homeostasis of the joints affected by the arthrotic process. The biochemical modifications induced by PRP treatment improve the protective, lubricating, and shock-absorbing effect of the synovial fluid. This therapeutic approach does not cause side effects such as inflammatory and pseudoseptic reactions, a great advantage. Moreover, improved centrifugation techniques have led to the ability to concentrate platelets as PRP, with the goal of delivering these concentrates as sources of growth factors to accelerate and support the healing of hard and soft tissue injuries naturally without subjecting the patient to significant risk.

PRP was first used in cardiac surgery by Ferrari et al. [17] in 1987 as an autologous transfusion component after open-heart surgery to reduce blood loss. PRP is a concentrate derived from peripheral blood, and it is now frequently used in different fields of medicine, including orthopedics, sports medicine, dentistry, dermatology, and ophthalmology, as well as in plastic, maxillofacial, and cosmetic surgery [18-20]. It is hypothesized to have regenerative, anti-inflammatory, analgesic, and antimicrobial properties [21]. As a result, PRP has been studied as an adjunct for healing of several structures, including bone healing [22-24], cartilage healing [25], and chronic tendinopathy [26, 27] and in the setting of surgical procedures such as rotator cuff repair [28], Achilles tendon repair [29], and anterior cruciate ligament reconstruction [30-32]. One potential advantage of platelet-rich preparations is that they are easily obtained from the patient's blood after a simple centrifugation process.

From previous systematic reviews [33-35], it has been concluded that PRP reduces pain and improves the osteoarthritis indices (WOMAC score, IKDC score, and adverse events) of PRP injection versus HA injection or placebo. In a recent study of Sampson et al. [36] including 14 patients with primary and secondary knee OA, treatment with PRP injections significantly

improved function and reduced pain. The study by Sanchez et al. [37] presented the preliminary results of the effectiveness of intra-articular injections of PRP in retrospective cohort study of 30 patients treated with PRP and 30 patients treated with HA. Few studies have evaluated the effectiveness of PRP plus HA in KOA. To our knowledge only one recent clinical trial [1] compared the effectiveness of PRP and HA. This trial showed that the association of PRP plus HA is effective and safe in the treatment for patients suffering from mild-to-moderate KOA. Similar findings have been observed also in our study. This current study showed that PRP plus HA injections could offer a significant clinical improvement.

In the present study, there are several limitations that need to be considered. First, it should be noted that this study was a retrospective analysis that might lower the evidence of the study. Second, the follow-up period was relatively too short to find out long-term effect of the two surgical managements. Third, relatively small sample size may affect the power in statistical analysis. Finally, some bias may have existed in the selection of the technique due to the choice of medications depending on the therapist's preference.

Conclusion

In conclusion, the association of PRP and HA is effective and safe in the management of patients suffering from mild to moderate KOA. Although no differences in functional outcomes were shown between the groups, there is a trend that PRP plus HA could obtain relatively better functional scores. A well-designed randomized controlled trial is urgently needed to identify an optimal treatment protocol.

Disclosure of conflict of interest

None.

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References

[1] Abate M, Verna S, Schiavone C, Di Gregorio P and Salini V. Efficacy and safety profile of a compound composed of platelet-rich plasma and hyaluronic acid in the treatment for knee osteoarthritis (preliminary results). Eur J Orthop Surg Traumatol 2015; 25: 1321-1326.

[2] Dieppe PA and Lohmander LS. Pathogenesis and management of pain in osteoarthritis. Lancet 2005; 365: 965-973.

[3] Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, Ezzati M, Shibuya K, Salomon JA, Abdalla S, Aboyans V, Abraham J, Ackerman I, Aggarwal R, Ahn SY, Ali MK, Alvarado M, Anderson HR, Anderson LM, Andrews KG, Atkinson C, Baddour LM, Bahalim AN, Barker-Collo S, Barrero LH, Bartels DH, Basanez MG, Baxter A, Bell ML, Benjamin EJ, Bennett D, Bernabe E, Bhalla K, Bhandari B, Bikbov B, Bin Abdulhak A, Birbeck G, Black JA, Blencowe H, Blore JD, Blyth F, Bolliger I, Bonaventure A, Boufous S, Bourne R, Boussinesq M, Braithwaite T, Brayne C, Bridgett L, Brooker S, Brooks P, Brugha TS, Bryan-Hancock C, Bucello C, Buchbinder R, Buckle G, Budke CM, Burch M, Burney P, Burstein R, Calabria B, Campbell B, Canter CE, Carabin H, Carapetis J, Carmona L, Cella C, Charlson F, Chen H, Cheng AT, Chou D, Chugh SS, Coffeng LE, Colan SD, Colquhoun S, Colson KE, Condon J, Connor MD, Cooper LT, Corriere M, Cortinovis M, de Vaccaro KC, Couser W, Cowie BC, Criqui MH, Cross M, Dabhadkar KC, Dahiya M, Dahodwala N, Damsere-Derry J, Danaei G, Davis A, De Leo D, Degenhardt L, Dellavalle R, Delossantos A, Denenberg J, Derrett S, Des Jarlais DC, Dharmaratne SD, Dherani M, Diaz-Torne C, Dolk H, Dorsey ER, Driscoll T, Duber H, Ebel B, Edmond K, Elbaz A, Ali SE, Erskine H, Erwin PJ, Espindola P, Ewoigbokhan SE, Farzadfar F, Feigin V, Felson DT, Ferrari A, Ferri CP, Fevre EM, Finucane MM, Flaxman S, Flood L, Foreman K, Forouzanfar MH, Fowkes FG, Fransen M, Freeman MK, Gabbe BJ, Gabriel SE, Gakidou E, Ganatra HA, Garcia B, Gaspari F, Gillum RF, Gmel G, Gonzalez-Medina D, Gosselin R, Grainger R, Grant B, Groeger J, Guillemin F, Gunnell D, Gupta R, Haagsma J, Hagan H, Halasa YA, Hall W, Haring D, Haro JM, Harrison JE, Havmoeller R, Hay RJ, Higashi H, Hill C, Hoen B, Hoffman H, Hotez PJ, Hoy D, Huang JJ, Ibeanusi SE, Jacobsen KH, James SL, Jarvis D, Jasrasaria R, Jayaraman S, Johns N, Jonas JB, Karthikeyan G, Kassebaum N, Kawakami N, Keren A, Khoo JP, King CH, Knowlton LM, Kobusingye O, Koranteng A, Krishnamurthi R, Laden F, Lalloo R, Laslett LL, Lathlean T, Leasher JL, Lee YY, Leigh J, Levinson D, Lim SS, Limb E, Lin JK, Lipnick M, Lipshultz SE, Liu W, Loane M, Ohno SL, Lyons R, Mabweijano J, MacIntyre MF, Malekzadeh R, Mallinger L, Manivannan S, Marcenes W, March L, Margolis DJ, Marks GB, Marks R, Matsumori A, Matzopoulos R, Mayosi BM, McAnul-

ty JH, McDermott MM, McGill N, McGrath J, Medina-Mora ME, Meltzer M, Mensah GA, Merriman TR, Meyer AC, Miglioli V, Miller M, Miller TR, Mitchell PB, Mock C, Mocumbi AO, Moffitt TE, Mokdad AA, Monasta L, Montico M, Moradi-Lakeh M, Moran A, Morawska L, Mori R, Murdoch ME, Mwaniki MK, Naidoo K, Nair MN, Naldi L, Narayan KM, Nelson PK, Nelson RG, Nevitt MC, Newton CR, Nolte S, Norman P, Norman R, O'Donnell M, O'Hanlon S, Olives C, Omer SB, Ortblad K, Osborne R, Ozgediz D, Page A, Pahari B, Pandian JD, Rivero AP, Patten SB, Pearce N, Padilla RP, Perez-Ruiz F, Perico N, Pesudovs K, Phillips D, Phillips MR, Pierce K, Pion S, Polanczyk GV, Polinder S, Pope CA 3rd, Popova S, Porrini E, Pourmalek F, Prince M, Pullan RL, Ramaiah KD, Ranganathan D, Razavi H, Regan M, Rehm JT, Rein DB, Remuzzi G, Richardson K, Rivara FP, Roberts T, Robinson C, De Leon FR, Ronfani L, Room R, Rosenfeld LC, Rushton L, Sacco RL, Saha S, Sampson U, Sanchez-Riera L, Sanman E, Schwebel DC, Scott JG, Segui-Gomez M, Shahraz S, Shepard DS, Shin H, Shivakoti R, Singh D, Singh GM, Singh JA, Singleton J, Sleet DA, Sliwa K, Smith E, Smith JL, Stapelberg NJ, Steer A, Steiner T, Stolk WA, Stovner LJ, Sudfeld C, Syed S, Tamburlini G, Tavakkoli M, Taylor HR, Taylor JA, Taylor WJ, Thomas B, Thomson WM, Thurston GD, Tleyjeh IM, Tonelli M, Towbin JA, Truelsen T, Tsilimbaris MK, Ubeda C, Undurraga EA, van der Werf MJ, van Os J, Vavilala MS, Venketasubramanian N, Wang M, Wang W, Watt K, Weatherall DJ, Weinstock MA, Weintraub R, Weisskopf MG, Weissman MM, White RA, Whiteford H, Wiebe N, Wiersma ST, Wilkinson JD, Williams HC, Williams SR, Witt E, Wolfe F, Woolf AD, Wulf S, Yeh PH, Zaidi AK, Zheng ZJ, Zonies D, Lopez AD, AlMazroa MA and Memish ZA. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012; 380: 2197-2223.

[4] Alshami AM. Knee osteoarthritis related pain: a narrative review of diagnosis and treatment. Int J Health Sci (Qassim) 2014; 8: 85-104.

[5] Prochazkova M, Zanvit P, Dolezal T, Prokesova L and Krsiak M. Increased gene expression and production of spinal cyclooxygenase 1 and 2 during experimental osteoarthritis pain. Physiol Res 2009; 58: 419-425.

[6] Handl M, Amler E, Braun K, Holzheu J, Trc T, Imhoff AB, Lytvynets A, Filova E, Kolarova H, Kotyk A and Martinek V. Positive effect of oral supplementation with glycosaminoglycans and antioxidants on the regeneration of osteochondral defects in the knee joint. Physiol Res 2007; 56: 243-249.

[7] Andia I and Abate M. Knee osteoarthritis: hyaluronic acid, platelet-rich plasma or both in association? Expert Opin Biol Ther 2014; 14: 635-649.

[8] Musumeci G, Castrogiovanni P, Leonardi R, Trovato FM, Szychlinska MA, Di Giunta A, Loreto C and Castorina S. New perspectives for articular cartilage repair treatment through tissue engineering: A contemporary review. World J Orthop 2014; 5: 80-88.

[9] Jevsevar DS. Treatment of osteoarthritis of the knee: evidence-based guideline, 2nd edition. J Am Acad Orthop Surg 2013; 21: 571-576.

[10] Cerza F, Carni S, Carcangiu A, Di Vavo I, Schiavilla V, Pecora A, De Biasi G and Ciuffreda M. Comparison between hyaluronic acid and platelet-rich plasma, intra-articular infiltration in the treatment of gonarthrosis. Am J Sports Med 2012; 40: 2822-2827.

[11] Filardo G, Kon E, Di Martino A, Di Matteo B, Merli ML, Cenacchi A, Fornasari PM and Marcacci M. Platelet-rich plasma vs hyaluronic acid to treat knee degenerative pathology: study design and preliminary results of a randomized controlled trial. BMC Musculoskelet Disord 2012; 13: 229.

[12] Sanchez M, Fiz N, Azofra J, Usabiaga J, Aduriz Recalde E, Garcia Gutierrez A, Albillos J, Garate R, Aguirre JJ, Padilla S, Orive G and Anitua E. 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: 1070-1078.

[13] Rayegani SM, Raeissadat SA, Taheri MS, Babaee M, Bahrami MH, Eliaspour D and Ghorbani E. Does intra articular platelet rich plasma injection improve function, pain and quality of life in patients with osteoarthritis of the knee? A randomized clinical trial. Orthop Rev (Pavia) 2014; 6: 5405.

[14] Vaquerizo V, Plasencia MA, Arribas I, Seijas R, Padilla S, Orive G and Anitua E. Comparison of intra-articular injections of plasma rich in growth factors (PRGF-Endoret) versus Durolane hyaluronic acid in the treatment of patients with symptomatic osteoarthritis: a randomized controlled trial. Arthroscopy 2013; 29: 1635-1643.

[15] Kanchanatawan W, Arirachakaran A, Chaijenkij K, Prasathaporn N, Boonard M, Piyapittayanun P and Kongtharvonskul J. Short-term outcomes of platelet-rich plasma injection for treatment of osteoarthritis of the knee. Knee Surg Sports Traumatol Arthrosc 2016; 24: 1665-77.

[16] Kellgren JH and Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis 1957; 16: 494-502.

[17] Ferrari M, Zia S, Valbonesi M, Henriquet F, Venere G, Spagnolo S, Grasso MA and Panzani I. A new technique for hemodilution, preparation of autologous platelet-rich plasma and intraoperative blood salvage in cardiac surgery. Int J Artif Organs 1987; 10: 47-50.
[18] Alsousou J, Thompson M, Hulley P, Noble A and Willett K. The biology of platelet-rich plasma and its application in trauma and orthopaedic surgery: a review of the literature. J Bone Joint Surg Br 2009; 91: 987-996.
[19] Anitua E, Andia I, Ardanza B, Nurden P and Nurden AT. Autologous platelets as a source of proteins for healing and tissue regeneration. Thromb Haemost 2004; 91: 4-15.
[20] Sanchez AR, Sheridan PJ and Kupp LI. Is platelet-rich plasma the perfect enhancement factor? A current review. Int J Oral Maxillofac Implants 2003; 18: 93-103.
[21] McCarrel TM, Mall NA, Lee AS, Cole BJ, Butty DC and Fortier LA. Considerations for the use of platelet-rich plasma in orthopedics. Sports Med 2014; 44: 1025-1036.
[22] Bibbo C, Bono CM and Lin SS. Union rates using autologous platelet concentrate alone and with bone graft in high-risk foot and ankle surgery patients. J Surg Orthop Adv 2005; 14: 17-22.
[23] Tsai CH, Hsu HC, Chen YJ, Lin MJ and Chen HT. Using the growth factors-enriched platelet glue in spinal fusion and its efficiency. J Spinal Disord Tech 2009; 22: 246-250.
[24] Arm DM. Re: Weiner BK, Walker M. Efficacy of autologous growth factors in lumbar intertransverse fusions. Spine. 2003; 28: 1968-1971. Spine (Phila Pa 1976) 2004; 29: 946-948; author reply 948-949.
[25] Spakova T, Rosocha J, Lacko M, Harvanova D and Gharaibeh A. Treatment of knee joint osteoarthritis with autologous platelet-rich plasma in comparison with hyaluronic acid. Am J Phys Med Rehabil 2012; 91: 411-417.
[26] Peerbooms JC, Sluimer J, Bruijn DJ and Gosens T. 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: 255-262.
[27] Gosens T, Peerbooms JC, van Laar W and den Oudsten BL. Ongoing positive effect of platelet-rich plasma versus corticosteroid injection in lateral epicondylitis: a double-blind randomized controlled trial with 2-year follow-up. Am J Sports Med 2011; 39: 1200-1208.
[28] Chahal J, Van Thiel GS, Mall N, Heard W, Bach BR, Cole BJ, Nicholson GP, Verma NN, Whelan DB and Romeo AA. The role of platelet-rich plasma in arthroscopic rotator cuff repair: a systematic review with quantitative synthesis. Arthroscopy 2012; 28: 1718-1727.
[29] Schepull T, Kvist J, Norrman H, Trinks M, Berlin G and Aspenberg P. Autologous platelets have no effect on the healing of human achilles tendon ruptures: a randomized single-blind study. Am J Sports Med 2011; 39: 38-47.
[30] Radice F, Yanez R, Gutierrez V, Rosales J, Pinedo M and Coda S. Comparison of magnetic resonance imaging findings in anterior cruciate ligament grafts with and without autologous platelet-derived growth factors. Arthroscopy 2010; 26: 50-57.
[31] Nin JR, Gasque GM, Azcarate AV, Beola JD and Gonzalez MH. Has platelet-rich plasma any role in anterior cruciate ligament allograft healing? Arthroscopy 2009; 25: 1206-1213.
[32] Magnussen RA, Flanigan DC, Pedroza AD, Heinlein KA and Kaeding CC. Platelet rich plasma use in allograft ACL reconstructions: two-year clinical results of a MOON cohort study. Knee 2013; 20: 277-280.
[33] Anitua E, Sanchez M, Aguirre JJ, Prado R, Padilla S and Orive G. Efficacy and safety of plasma rich in growth factors intra-articular infiltrations in the treatment of knee osteoarthritis. Arthroscopy 2014; 30: 1006-1017.
[34] Lai LP, Stitik TP, Foye PM, Georgy JS, Patibanda V and Chen B. Use of Platelet-Rich Plasma in Intra-Articular Knee Injections for Osteoarthritis: A Systematic Review. PM R 2015; 7: 637-648.
[35] Riboh JC, Saltzman BM, Yanke AB, Fortier L and Cole BJ. Effect of Leukocyte Concentration on the Efficacy of Platelet-Rich Plasma in the Treatment of Knee Osteoarthritis. Am J Sports Med 2016; 44: 792-800.
[36] Sampson S, Reed M, Silvers H, Meng M and Mandelbaum B. Injection of platelet-rich plasma in patients with primary and secondary knee osteoarthritis: a pilot study. Am J Phys Med Rehabil 2010; 89: 961-969.
[37] Sanchez M, Anitua E, Azofra J, Aguirre JJ and Andia I. Intra-articular injection of an autologous preparation rich in growth factors for the treatment of knee OA: a retrospective cohort study. Clin Exp Rheumatol 2008; 26: 910-913.