Efficacy of Ultrasound-guided Intra-articular Injections of Platelet-rich Plasma Versus Hyaluronic Acid for Hip Osteoarthritis

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abstract

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Intra-articular injections of platelet-rich plasma (PRP) and hyaluronic acid (HA) represent efficacious medical treatments for osteoarthritis (OA), although no comparative study on long-term efficacy in hip OA exists. The goals of the current study were to compare the clinical efficacy of PRP vs HA at 12 months of follow-up in patients with hip OA and evaluate the influence of the type of infiltration and patient age, sex, body mass index, and degree of OA on temporal clinical evolution. One hundred patients with chronic unilateral symptomatic hip OA were consecutively enrolled and randomly assigned to 1 of 2 groups: group A received PRP and group B received HA administered via intra-articular ultrasound-guided injections. Patients were evaluated at baseline and after 1, 3, 6, and 12 months using the Harris Hip Score (HHS) and visual analog scale (VAS). An overall improvement was detected in both groups between 1- and 3-month follow-up. Despite a slightly progressive worsening between 6- and 12-month follow-up, the final clinical scores remained higher compared with baseline ($P<.0005$), with no significant differences between PRP and HA. Regarding clinical temporal evolution, multivariate analysis showed that HHS was not influenced by the type of infiltration, patient age, sex, body mass index, or degree of OA, whereas a significant association was detected between OA grade IV and VAS evolution ($P<.0005$). Intra-articular injections of PRP are efficacious in terms of functional improvement and pain reduction but are not superior to HA in patients with symptomatic hip OA at 12-month follow-up.

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Osteoarthritis (OA) is the most common joint disorder, with a higher prevalence in women, characterized by chronic pain and functional limitation, and responsible for long-term disability in the elderly population. It typically affects weight-bearing joints; the hip is the second most frequently involved large joint after the knee. An aging and overweight population with reduced physical activity is responsible for the increasing prevalence of OA and its complications, with a significant social and economic impact.[1,2]

Treatments include nonpharmacological (eg, reduced activity, weight loss, supports, physiotherapy) and pharmacological (eg, analgesic, steroids, nonsteroidal anti-inflammatory drugs [NSAID]) therapies administered topically, orally, or intra-articularly.[3-7] The most important limitations of these treatments are the unpredictable efficacy, the side effects, and the inability to affect disease progression.[5,7] Hyaluronic acid (HA) injectable preparations of different molecular weights have been produced with the goal of restoring the viscoelastic properties of synovial fluid, which is reduced in OA.[8] In the majority of the studies, the variability of samples and procedures, the absence of a control group, and the shortness of follow-up limit the interpretation of results on HA's efficacy and the validity of recommendations about type, dose, and frequency of administration.[4,6,9-13]

More recently, an increasing knowledge of OA pathogenesis has elucidated new possible therapeutic targets. Some studies have shown that the ability to produce and repair extracellular matrix is compromised in aging chondrocytes.[13,14] The reduction of locally available growth factors and chondrocytes' response to stressful stimuli, associated with an increased production of inflammatory mediators and matrix degrading enzymes, are the major factors responsible for cartilage degeneration.[14,15] Platelet-rich plasma (PRP) is a natural concentrate of autologous platelets containing high levels of several growth factors, including platelet-derived growth factor (PDGF), transforming growth factor beta (TGF-ß), insulin-like growth factor 1 (IGF-1), epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), and fibroblast growth factor (FGF), which are stored in platelets' alpha-granules and are released on platelet activation to be delivered to the injured site and facilitate healing.[16-18]

Platelet-rich plasma was initially proposed as a biological therapy in other medical fields, such as dentistry, dermatology, and ophthalmology.[16,19] More recently, its use has been investigated in orthopedics for the treatment of tendon and ligament injuries, chronic wounds, muscle injuries, fractures, and OA.[16,20]

To date, a few studies have investigated the therapeutic efficacy of PRP intra-articular injections on knee OA,[21,22] whereas few data are available about its effects on hip OA.[23,24] To the current authors' knowledge, no prospective, randomized study comparing the efficacy of PRP and HA on hip OA exists.

The goals of this study were to compare the clinical efficacy of PRP vs HA at 12 months of follow-up in patients with hip OA and evaluate the influence of the type of infiltration and patient age, sex, body mass index (BMI), and degree of OA on temporal clinical evolution.

Materials and Methods

Approval for this study was obtained from the ethical committee and internal review board of Rizzoli Orthopaedic Institute. All participants provided written informed consent.

Of the 284 patients with hip OA evaluated between April 2010 and December 2011, a total of 164 were not eligible for the study and 16 refused to participate. Of the remaining 104 patients (66 men and 38 women) with symptomatic monolateral hip OA and enrolled in this prospective, randomized, controlled trial, 100 were available for 12-month follow-up and were included in the statistical analysis, whereas 4 (3 men and 1 woman) were lost to follow-up.

Randomization was conducted using computer-generated numbers from the Research Randomizer System.[25] Participants were randomly assigned in a 1:1 ratio to 1 of 2 groups: PRP or HA injections. Mean patient age was 53±12 years (range, 25-76 years), and mean BMI was 26±4 kg/m^2. Participants were blinded before randomization; thereafter, patients and the principal investigator (M.B.) were aware of the treatment. Data outcome assessors and collectors were blinded to the type of treatment received.

Inclusion criteria were a history of chronic monolateral hip pain lasting between 6 and 24 months, resistant to NSAID, and associated with radiological findings of hip OA. Previous HA hip injections were not considered an exclusion criterion if performed more than 12 months from study enrollment. Exclusion criteria were previous hip surgery at the affected hip, severe hip deformities following hip fractures, severe dysplasia, breastfeeding, diabetes mellitus, rheumatoid arthritis, severe cardiovascular diseases, infections and immunodepression, current consumption of drugs other than NSAID, current physical therapies for the treatment of OA, hematological diseases, coagulopathies, therapies with anticoagulant or antiaggregant drugs, hemoglobin levels less than 11 mg/dL or platelet levels less than 150,000/µL, and previous ipsilateral hip prosthesis.

The presence of ipsilateral or contralateral knee/ankle OA was not investigated. No patient in this series reported pain in areas other than the hip.

At baseline, all patients underwent anteroposterior radiography of the pelvis and were classified for the degree of OA according to Kellgren-Lawrence score[26]: 39 patients presented with early OA (grade II), 44 patients with moderate OA (grade III), and 17 patients with severe OA (grade IV). They were also clinically evaluated using the Harris Hip Score (HHS)[27] and the visual analog scale (VAS).

Platelet-rich Plasma Preparation

In agreement with a previously published standardized protocol,[21] 150 mL of venous blood was taken from each patient and collected in a bag containing 21 mL of sodium citrate, and 2 centrifugations were performed (the first cycle was run at 1800 rpm for 15 minutes to separate erythrocytes, and the second cycle was run at 3500 rpm for 10 minutes to concentrate platelets) to obtain 4 units of 5 mL each of PRP.[21-23] One unit was sent to the hospital laboratory to perform a platelet count and bacteriological tests, and the other three units were stored at -30°C. After this procedure, the number of platelets per microliter in the PRP had increased an average of 600% compared with the whole blood value, and each unit (corresponding with a single dose) contained an average of 6 to 8 million platelets. Mean final number of leukocytes was 8300/μL; no erythrocytes were present.[21-23,28]

Each PRP unit was thawed in a dry-thermostat at 27°C for 30 minutes. Before injection, 10% calcium chloride (Ca^{++}=0.22 mEq×dose) was added to the PRP unit to activate the platelets.

Treatment Procedure and Follow-up

All patients underwent 3 consecutive (once every 2 weeks) intra-articular ultrasound-guided injections of 5 mL autologous PRP (group A) or a vial (30 mg/2 mL) of high-molecular-weight (1500 kD) HA (Hyalubrix; Fidia Farmaceutici Spa, Padova, Italy) (group B).[5,19] Follow-up evaluation and treatment were performed in the Department of Radiology.

Each patient was placed supine with the hip in a neutral position or slightly intrarotated (15°-20°). A 1- to 4-MHz convex transducer (Acuson Sequoia Ultrasound System; Siemens Healthcare, Malvern, Pennsylvania) with a lateromedial and caudocranial inclination was used to assist the injection.[29] No topic skin refrigeration or local anesthetic infiltration was used.

A standard B-mode with color Doppler was used to identify the hip along the axis of the femoral neck, laterally to the femoral vessels. Under real-time ultrasound guidance, intra-articular injection was sterilely performed by inserting a spinal needle (20 gauge, 0.9×90 mm) at the level of the femoral head-neck junction using a classic anterior approach, and the intra-articular spreading was monitored.[30] At the conclusion of the procedure, the patient moved the hip a few times to facilitate the distribution of the injected substance in the joint. The patient was then discharged with the advice to limit use of the leg for a few days and then to gradually perform light exercise. Nonsteroidal anti-inflammatory drug consumption was forbidden for 48 hours after treatment. Thereafter, NSAID consumption was allowed for pain control but had to be recorded, together with all possible posttreatment side effects.

All patients were clinically reevaluated at 1, 3, 6, and 12 months after the third injection using the HHS and VAS. Patients were also asked to report repetitive NSAID consumption (omitting dosage and frequency of consumption) at baseline and follow-up to provide a supplementary indirect parameter of therapeutic efficacy. Finally, possible side effects related to the procedure were recorded to assess the treatment's safety.

Sample Size Calculation

The difference in HHS at 12-month follow-up between the 2 groups of patients was established as the parameter to be used to assess the superiority of PRP vs HA, which represents the primary aim of this study. Based on the results of a previous study on the efficacy of PRPs in hip OA showing that standard deviation for HHS at 12-month follow-up was 15 points,[5] the authors assessed the cutoff for statistical significance at 10 points; for an alpha standard error of 0.05 and a power of at least 0.8, the minimum sample size for each group was 38.

Statistical Analysis

Statistical analysis was performed using SPSS version 19.0 statistical software (SPSS Inc, Chicago, Illinois). For all tests, a *P* value less than .05 was considered statistically significant. Continuous variables were expressed as mean±SD.

The Mann-Whitney *U* test was used to assess age and BMI differences between the 2 groups; differences in terms of sex, OA grade, and NSAID consumption were defined by Fisher's chi-square test. Univariate general linear model (GLM), corrected for age and OA grade, was used to define the influence of the type of injection on HHS and VAS at baseline and at 12-month follow-up. General linear model repeated measures were used to evaluate the influence of the type of injection and patient age, sex, BMI, and OA grade on HHS and VAS scores' evolution. General linear model with log-linear Poisson distribution, corrected for age and OA grade, was used to determine the influence of the type of injection over the use of NSAID. Results of GLM analysis were expressed in terms of mean percentage and 95% confidence interval (CI).

RESULTS

Baseline

The 2 groups were homogeneous for BMI (26±5 vs 27±4 kg/m^2) and sex (F:M=20:30 vs 17:33). Group A had a significantly lower age (51±12 vs 56±12 years; *P*=.035) and greater NSAID consumption (*P*=.03).

Group A showed a lower prevalence of grade II OA (32% vs 46%) but a higher prevalence of grade IV OA (26% vs 8%) (*P*=.047), whereas no difference was found for grade III OA.

According to univariate GLM analysis corrected for age, OA grade, and NSAID consumption, the 2 groups did not significantly differ for HHS (group A, 58% [95% CI, 54%-62%]; group B, 63% [95% CI, 59%-67%]) and VAS (group A, 5.5% [95% CI, 5%-6%]; group B, 6% [95% CI, 5.5%-6.5%]) scores at baseline (**Figure 1**).

Follow-up

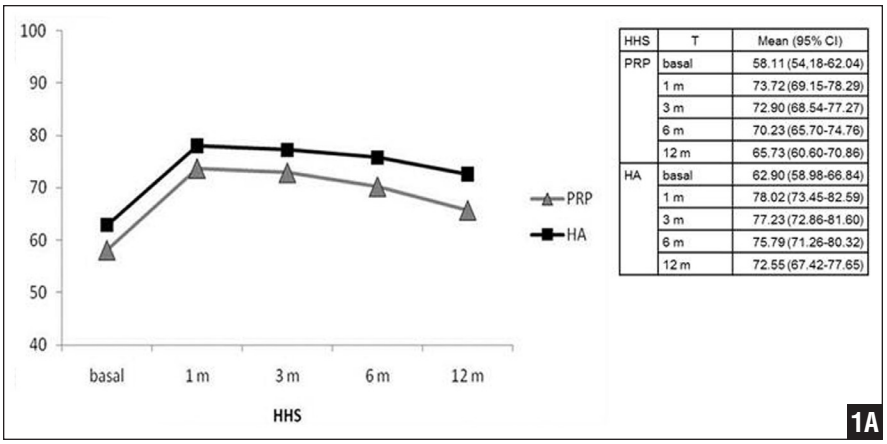
Univariate GLM analysis corrected for age, OA grade, and NSAID consumption showed no significant difference for HHS (group A, 66% [95% CI, 61%-71%]; group B, 72% [95% CI, 67%-77%]) and VAS (group A, 4.7% [95% CI, 4%-5.4%]; group B, 4.6% [95% CI, 4%-5.3%]) scores at 12-month follow-up (**Figure 1**).

General linear model repeated measures analysis revealed a variable percentage of clinical improvement (HHS and VAS) according to the different time points, independent from the type of injection and patient age, sex, and BMI. The best results were registered between 1- and 3-month follow-up ($P<.0005$), followed by a slightly progressive worsening from 6- to 12-month follow-up ($P=.005$), although the final scores remained higher than baseline ($P<.0005$) and similar between the 2 groups (**Figure 1**).

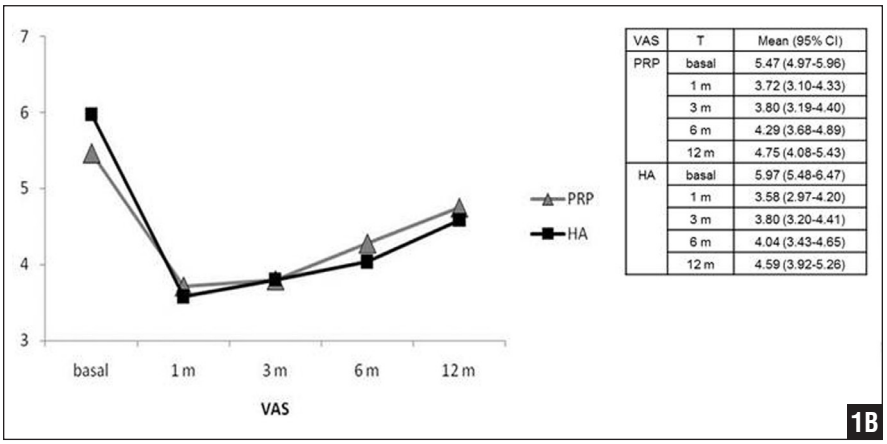
The temporal evolution for both HHS and VAS scores (GLM repeated measures analysis corrected for age) was not influenced by the type of infiltration in any of the different arthritis degrees (**Tables 1-2**). At the same time, temporal variation of VAS score (partial $\eta^2=0.111$; $P<.0005$), but not HHS (partial $\eta^2=0.03$; $P=.15$), was significantly influenced by the OA grade. Patients affected by OA grades II and III had a similar temporal evolution for HHS and VAS scores. For patients with OA grade IV, HHS trend was similar to that of patients with OA grade III, whereas VAS score showed an immediate pain reduction at 1-month follow-up (more dramatic than that of patients with OA grade III) and then a rapid increase; the trend becomes similar to OA grade III at 12-month follow-up (**Figure 2**).

General linear model analysis with log-linear Poisson distribution corrected for age and OA grade showed a significant variability in NSAID consumption over time ($\eta^2=0.193$; $P<.0005$) and between groups ($\eta^2=0.104$; $P=.035$). Compared with baseline, NSAID consumption was significantly lower at all follow-up times in both groups ($P<.0005$), with no major final differences between them. A drastic reduction was observed in group A at 1-month follow-up (17% [95% CI, 5%-30%] vs 92% [95% CI, 81%-100%]), whereas in group B, the decrease was more gradual and reached the nadir at 6-month follow-up (35% [95% CI, 22%-47%] vs 74% [95% CI, 64%-85%]), followed by a progressive increase toward 12-month follow-up (**Figure 3**).

Regarding side effects, 1 patient developed a superficial hematoma during the first infiltration due to transitional damage of a peripheral branch of the great saphenous vein presenting with an abnormal course, which spontaneously resolved in 2 weeks. No other major peri- or posttreatment complications occurred. Sixteen patients (10 in group A, 6 in group B) reported moderate pain during or after treatment that spontaneously resolved in 1 to 2 days.



HHS	T	Mean (95% CI)
PRP	basal	58.11 (54.18-62.04)
	1 m	73.72 (69.15-78.29)
	3 m	72.90 (68.54-77.27)
	6 m	70.23 (65.70-74.76)
	12 m	65.73 (60.60-70.86)
HA	basal	62.90 (58.98-66.84)
	1 m	78.02 (73.45-82.59)
	3 m	77.23 (72.86-81.60)
	6 m	75.79 (71.26-80.32)
	12 m	72.55 (67.42-77.65)



VAS	T	Mean (95% CI)
PRP	basal	5.47 (4.97-5.96)
	1 m	3.72 (3.10-4.33)
	3 m	3.80 (3.19-4.40)
	6 m	4.29 (3.68-4.89)
	12 m	4.75 (4.08-5.43)
HA	basal	5.97 (5.48-6.47)
	1 m	3.58 (2.97-4.20)
	3 m	3.80 (3.20-4.41)
	6 m	4.04 (3.43-4.65)
	12 m	4.59 (3.92-5.26)

Figure 1: Graphs showing Harris Hip Score (HHS) (A) and visual analog scale (VAS) score (B) evolution at different follow-up times (T) in patients treated with platelet-rich plasma (PRP) vs hyaluronic acid (HA). Abbreviation: CI, confidence interval.

Discussion

Hip OA is a common cause of chronic pain and disability.[1,2] Medical treatment can temporarily reduce pain but does not affect the disease's natural progression and often presents important side effects (mainly gastrointestinal bleeding with NSAID, higher risk of infections, and osteonecrosis with corticosteroids).[3-7] The rationale for intra-articular administration of HA is the restoration of viscoelastic properties of the synovial fluid with the subsequent

Table 1

HHS and OA Grade

Treatment Type	OA Grade	Follow-up, mo	Mean HHS (95% CI)
PRP	2	Basal	63.312 (56.345-70.280)
		1	77.602 (69.604-85.599)
		3	78.195 (70.581-85.809)
		6	76.536 (68.497-84.575)
		12	73.056 (64.045-82.066)
	3	Basal	55.163 (49.224-61.101)
		1	71.706 (64.890-78.523)
		3	69.023 (62.534-75.513)
		6	68.285 (61.433-75.137)
		12	62.137 (54.457-69.817)
	4	Basal	54.312 (46.766-61.858)
		1	71.946 (63.285-80.608)
		3	71.423 (63.177-79.669)
		6	62.415 (53.708-71.121)
		12	60.794 (51.036-70.553)
HA	2	Basal	66.187 (60.514-71.859)
		1	79.195 (72.684-85.706)
		3	80.690 (74.492-86.889)
		6	79.763 (73.218-86.307)
		12	73.761 (66.425-81.096)
	3	Basal	60.734 (54.876-66.592)
		1	75.010 (68.286-81.734)
		3	73.263 (66.862-79.665)
		6	73.432 (66.673-80.190)
		12	71.081 (63.505-78.657)
	4	Basal	63.587 (49.980-77.193)
		1	89.380 (73.762-104.997)
		3	84.241 (69.373-99.109)
		6	76.895 (61.197-92.593)
		12	79.634 (62.039-97.230)

Abbreviations: CI, confidence interval; HA, hyaluronic acid; HHS, Harris Hip Score; OA, osteoarthritis; PRP, platelet-rich plasma.

Table 2

VAS and OA Grade

Treatment Type	OA Grade	Follow-up, mo	Mean VAS (95% CI)
PRP	2	1	4.930 (4.048-5.812)
		2	3.617 (2.565-4.668)
		3	3.344 (2.288-4.399)
		4	3.571 (2.502-4.640)
		5	3.827 (2.645-5.009)
	3	1	5.626 (4.874-6.377)
		2	4.054 (3.158-4.950)
		3	4.352 (3.452-5.252)
		4	4.683 (3.771-5.594)
		5	5.445 (4.438-6.453)
	4	1	6.237 (5.282-7.192)
		2	3.006 (1.868-4.145)
		3	3.403 (2.259-4.546)
		4	4.708 (3.550-5.866)
		5	4.939 (3.659-6.219)
HA	1-2	1	5.437 (4.720-6.155)
		2	3.481 (2.625-4.337)
		3	3.573 (2.713-4.432)
		4	3.702 (2.832-4.573)
		5	4.529 (3.566-5.491)
	3	1	6.251 (5.510-6.992)
		2	4.252 (3.368-5.136)
		3	4.284 (3.396-5.172)
		4	4.393 (3.494-5.292)
		5	4.604 (3.610-5.598)
	4	1	6.264 (4.543-7.986)
		2	1.264 (-0.789-3.317)
		3	2.541 (0.479-4.603)
		4	3.285 (1.197-5.373)
		5	4.287 (1.978-6.595)

Abbreviations: CI, confidence interval; HA, hyaluronic acid; OA, osteoarthritis; PRP, platelet-rich plasma; VAS, visual analog scale.

reduction of inflammation and functional improvement.[8] Some reviews and meta-analyses have demonstrated HA's safety, whereas its efficacy is still debated.[4,6,9-13,22] More recently, intra-articular injection of PRP, an autologous product rich in growth factors stored in platelet granules, has been proposed for OA treatment, with the aim of stimulating chondrogenesis and reducing OA catabolism and intra-articular inflammation.[16-18,20] The use of PRP has gained increasing popularity over time, although the definition of PRP itself is still far from being established in terms of optimal concentration, possible paradoxical inhibitory effects of higher concentration, and leukocyte presence.[31,32]

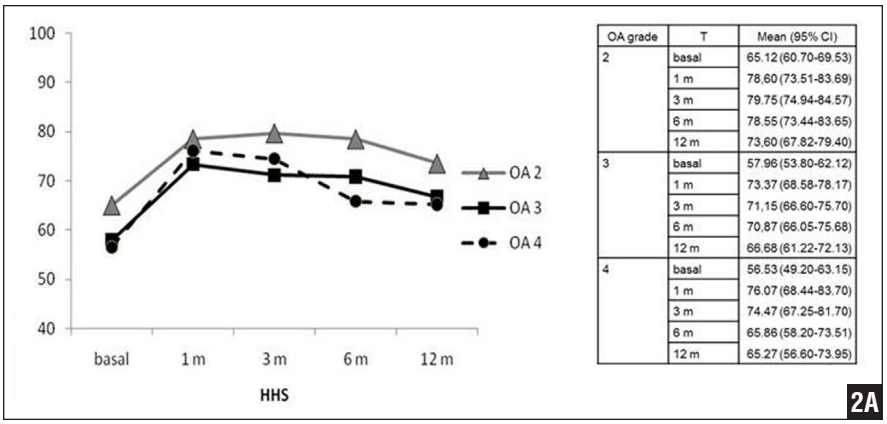
The use of frozen PRP is sometimes cause for concern, although its use is well documented. The alteration of the morphology and decrease of platelet

functional properties—which includes degranulation of alpha-granules—after storing platelets in freezing conditions is well-known, but no data exist on the effect of freezing on the clinical results of platelet injections, and freeze-thawing is one of the methods used for releasing intracellular growth factors.[33,34] Freezing PRP allows time to proceed with quality analysis, so it may be considered an advantage of this technique. No major health problems have been reported in association with its use, and its use is not precluded by the presence of concomitant disorders.[16]

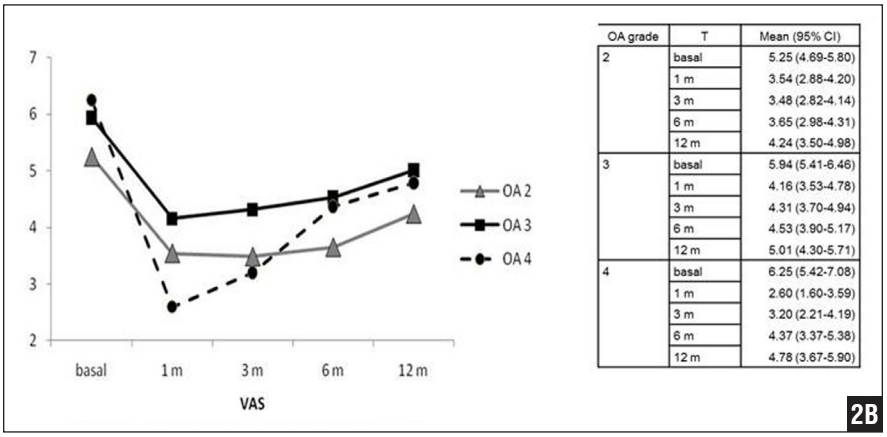
To the current authors' knowledge, this study is the first prospective, comparative, randomized, single-blind trial assessing the efficacy of ultrasound-guided intra-articular injection of PRP compared with HA in symptomatic patients with hip OA not responding to other types of oral therapies. An overall clinical improvement (in terms of HHS and VAS scores) was detected in both groups of patients, with the highest peak between 1- and 3-month follow-up, followed by a slightly progressive worsening between 6- and 12-month follow-up. However, in both groups, the final scores remained higher than baseline with no significant differences between PRP and HA efficacy.

The pattern of HHS values over time was not influenced by the type of infiltration, patient age, sex, BMI, and degree of OA. Degree of OA influenced VAS evolution. At 1-month follow-up, pain was significantly more reduced in patients with OA grade IV compared with grades II and III, although pain rapidly recurred and no major differences were found at 12-month follow-up among groups. These results are in contrast to those reported by Qvistgaard et al[12] and Kon et al,[22] who found better results in younger patients affected by early knee OA.

Regarding NSAID consumption, a drastic reduction was evident in the PRP group at 1-month follow-up, whereas in the HA group, the decrease was more

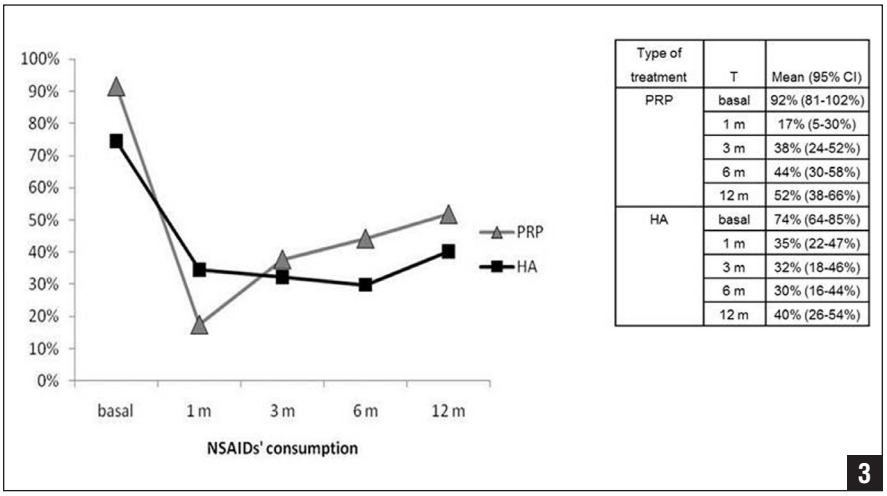


OA grade	T	Mean (95% CI)
2	basal	65.12 (60.70-69.53)
	1 m	78,60 (73.51-83.69)
	3 m	79.75 (74.94-84.57)
	6 m	78.55 (73.44-83.65)
	12 m	73,60 (67.82-79.40)
3	basal	57.96 (53.80-62.12)
	1 m	73.37 (68.58-78.17)
	3 m	71,15 (66.60-75.70)
	6 m	70,87 (66.05-75.68)
	12 m	66.68 (61.22-72.13)
4	basal	56.53 (49.20-63.15)
	1 m	76.07 (68.44-83.70)
	3 m	74.47 (67.25-81.70)
	6 m	65.86 (58.20-73.51)
	12 m	65.27 (56.60-73.95)



OA grade	T	Mean (95% CI)
2	basal	5.25 (4.69-5.80)
	1 m	3.54 (2.88-4.20)
	3 m	3.48 (2.82-4.14)
	6 m	3.65 (2.98-4.31)
	12 m	4.24 (3.50-4.98)
3	basal	5.94 (5.41-6.46)
	1 m	4.16 (3.53-4.78)
	3 m	4.31 (3.70-4.94)
	6 m	4.53 (3.90-5.17)
	12 m	5.01 (4.30-5.71)
4	basal	6.25 (5.42-7.08)
	1 m	2.60 (1.60-3.59)
	3 m	3.20 (2.21-4.19)
	6 m	4.37 (3.37-5.38)
	12 m	4.78 (3.67-5.90)

Figure 2: Graphs showing Harris Hip Score (HHS) (A) and visual analog scale (VAS) score (B) temporal evolution in relation to osteoarthritis (OA) grade independent of treatment type. Abbreviations: CI, confidence interval; T, time.



Type of treatment	T	Mean (95% CI)
PRP	basal	92% (81-102%)
	1 m	17% (5-30%)
	3 m	38% (24-52%)
	6 m	44% (30-58%)
	12 m	52% (38-66%)
HA	basal	74% (64-85%)
	1 m	35% (22-47%)
	3 m	32% (18-46%)
	6 m	30% (16-44%)
	12 m	40% (26-54%)

Figure 3: Graph showing the percentage of patients using nonsteroidal anti-inflammatory drugs (NSAIDs) at different follow-up times (T) in the platelet-rich plasma (PRP) vs hyaluronic acid (HA) groups. Abbreviation: CI, confidence interval.

gradual and reached the nadir at 6-month follow-up; both groups then progressively resumed NSAID consumption, although final levels remained significantly lower compared with baseline. No major differences were evident between the 2 groups. A previous study focusing on patients treated with intra-articular HA injections for hip OA showed a similar abrupt decrease in NSAID consumption in the first 3 months of follow-up, with a subsequent further improvement related to recurrent treatment.[30]

Finally, moderate peri- and posttreatment pain was the most commonly observed side effect; no major complications or adverse events occurred, except for a spontaneously resolving superficial hematoma in a patient presenting an abnormal venous anatomy. These safety data are in accordance with previously reported studies.[21-24]

Limitations of the current study are the homogeneity in terms of OA and the age range of patients in the series. The lack of strong experimental evidence derived from comparative, blind studies represents a major limitation in the evaluation of PRP vs HA efficacy and their validation for the treatment of hip OA. To the authors' knowledge, only 1 study has compared the efficacy of PRP and HA in patients with knee OA over a 6-month period,[23] and 2 other uncontrolled studies have assessed the efficacy of PRP on hip OA.[21,24] Previously reported studies investigating HA efficacy present a high variability in terms of sample size, therapy frequency and dose, control group, and short-period follow-up.[4,6,9-13]

The lack of a third control group treated by placebo is another limitation of the current study. An intra-articular injection of either lidocaine or saline may give a partial biologic effect due to intracapsular bleeding, so it may not be considered a true placebo. Patients selected for this study experienced uncontrolled pain, unresponsive to any other noninjective therapy, and for ethical reasons the authors decided to limit the comparison to 2 treatment groups and improve the study's evidence by increasing the number of enrolled patients.

Conclusion

Intra-articular PRP injections are as safe and efficacious as HA at 12-month follow-up in terms of functional improvement and pain reduction. However, the efficacy is temporary, as demonstrated by the gradual worsening of clinical scores toward the end of follow-up, even if these findings cannot be extended to all of the different PRP preparations available. The minimal invasiveness of the procedure could make the cyclical application of PRP injections suitable to delay surgery. Other controlled, randomized studies evaluating larger cohorts of patients for longer periods are warranted to validate these promising but preliminary data.

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