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Intra-articular Platelet-Rich Plasma Injections for Treating Knee Pain Associated with Articular Cartilage and Degenerative Meniscal Lesions

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Abstract

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Keywords: Platelet-rich plasma; Articular cartilage; Degenerative meniscal lesions; Safety method; Intra-articular application

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BACKGROUND: Platelet-rich plasma (PRP) is an autologous concentration of platelets that contain a large number of growth factors. These growth factors play a role in the regeneration, repair, and acceleration of the biochemical process, thereby reducing the pain associated with injuries of the articular cartilage and meniscus

AIM: The purpose of this study is to evaluate the effect of the PRP method in the treatment of knee joint cartilage injuries and degenerative meniscus lesions as well as pain relief.

MATERIAL AND METHODS: The process of obtaining PRP begins by taking 15 ml of blood from the patient with a special system called Arthrex Double Syringe system. The test tube is centrifuged at 4000 rpm for 5 minutes. From the separated plasma, 5-6 ml PRP is taken and prepared for application. PRP is administered intra-articularly.

RESULTS: At the Jan Mitrev Clinic in Skopje in 2018, PRP procedures were performed on 126 patients, 56 (44.4%) of whom were male, and 70 (55.6%) were female. The patients were evaluated by the Tegner Lysholm Knee Scoring Scale (TLKSS) before applying 3 doses of PRP for 7 days as well as 3 and 6 months after the application of PRP. The results showed considerable improvement 3 months after the PRP application, and 6 months after the application the results remained approximately identical.

CONCLUSION: The application of PRP in the field of medicine is widely applied, and it will continue to be because the understanding of PRP therapy is increasingly refined. This therapy represents a potential and latest method in short-term pain reduction, but additional studies are needed to prove its long-term effectiveness.

Introduction

The most recent research and findings in the treatment of knee pain in articular cartilage injuries and degenerative meniscus lesions are increasing the need for biology and its association with the inflammatory process. The normal function and preservation of articular cartilage and meniscus morphology depend primarily on the balance between aggressive and protective factors [1]. Biology and its use are extremely important for the balance between these factors [2], [3], [4]. Platelet-rich plasma (PRP) is increasingly used in articular cartilage injuries and

degenerative meniscus lesions. PRP is an autologous concentration of platelets that contain a large number of growth factors [5], [6], [7], [8]. These growth factors play a role in the regeneration, repair, and acceleration of biochemical processes, thereby reducing the pain associated with injuries of the articular cartilage and meniscus [9]. The latest world research shows excellent results in reducing pain by using PRP [10], [11], [12], [13], [14]. In the Republic of Macedonia, the PRP application has been used for the last decade.

The purpose of this study is to evaluate the effect of the PRP method in the treatment of knee joint cartilage injuries and degenerative meniscus lesions

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as well as pain relief.

Material and Methods

A prospective six-month study involved 15 patients treated at the Zan Mitrev Clinic in Skopje in 2018. All patients underwent a clinical examination, X-ray examinations and magnetic resonance imaging of the knee. They all received 3 doses of PRP applied over 7 days.



Figure 1: Taking 15 ml blood sample

The process of obtaining PRP begins by taking 15 ml of blood from the patient (Figure 1) with a special system called Arthrex Double Syringe system (Figure 2).



Figure 2: Arthrex Double Syringe System

The test tube is centrifuged at 4000 rpm for 5 minutes (Figure 3).



Figure 3: Centrifuge at 4000 rpm

From the separated plasma, 5-6 ml PRP is

taken and prepared for application (Figure 4). PRP is administered intra-articularly (Figure 5). The Tegner Lysholm Knee Scoring Scale was used for evaluating the patients at the first and sixth month after the treatment with PRP.



Figure 4: PRP ready for application

All patients included in the study signed a consent to participate in the study, as well as consent for publishing the results.



Figure 5: Intra-articular application of PRP

Statistical method

The statistical series, according to the defined variables of interest, are tabulated and graphically presented. The distribution of the numerical statistical series (correct/incorrect) was tested with Kolmogorov Smirnov test, Lilliefors test and Shapiro-Wilk's W test. The numerical series structure was analysed with the central tendency (mean) and dispersion measures (standard deviation). The significance test of the difference between two arithmetic means in the independent samples was performed with the parametric Student-t-test. The significance test of the difference between the two-arithmetic means in the dependent samples was performed with the nonparametric Wilcoxon matched-pairs test.

Testing the significance of the differences between the three arithmetic meanings in the dependent samples was performed with Friedman ANOVA, the significance level for p < 0.05 at Cl = 95% is considered statistically significant. The database is analysed with the statistical program STATISTICA 12 for Windows.

Results

At the Zan Mitrev Clinic in Skopje in 2018, PRP procedures were performed on 126 patients, 56 (44.4%) of whom were male, and 70 (55.6%) were female. From the 126 patients, 15 were examined and evaluated in this study, 10 of them (66.7%) were female, and 5 (33.3%) were male. The average age of the total number of respondents was 49.3 ± 6.3 years.

Table 1: Mean Age Value of Examined Patients by Sex

Sex	Mean	Std. Dev.	Min	Max
Females	49.1	5.8	38	60
Males	49.8	7.8	36	55
Total	49.3	6.3	36	60

The average age of the female respondents was 49.1 ± 5.8 , and for males, it was 49.8 ± 7.8 years. There was no significant difference in age between the subjects of both sexes (There was no significant difference in age between the subjects of both sexes (Student-t-test: t = -0.196, p = 0.8475) (Table 1 and Figure 6).

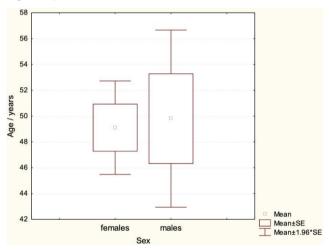


Figure 6: Mean Age Value of Examined Patients by Sex

The patients were evaluated by the TLKSS (Tegner Lysholm Knee Scoring Scale) before applying 3 doses of PRP for 7 days as well as 3 and 6 months after the application of PRP. The results showed considerable improvement 3 months after the PRP application, and 6 months after the application the results remained approximately identical.

The mean value of TLKSS before the intervention was 61.9 ± 7.4 after 3 months, and after 6 months, it was 83.4 ± 4.6 and 83.4 ± 4.3 , respectively. The variance analysis showed that there were statistically significant differences concerning the TLKSS at the three points of time (Friedman ANOVA: Chi. Sqr. = 24.54, p = 0.00001). There also was a statistically significant difference between the mean values of TLKSS before the intervention and after 3

months (Wilcoxon matched-pairs test: Z = 3.407, p = 0.00062). There was also a statistically significant difference between the mean values of TLKSS before the intervention and 6 months after (Wilcoxon matched-pairs test: Z = 3.411, p = 0.00065).

Table 2: Mean Value on the TLKSS at different points in time

Tegner lysholm knee scoring scale	Mean	Std.dev.	Min	Max
Before intervention	61.9		- IVIII I	74
		7.4	51	
After 3 months	83.5	4.6	//	92
After 6 months	83.4	4.3	75	90

The difference between the mean values of TLKSS after 3 and 6 months was insignificant (Wilcoxon matched-pairs test: Z = 3.411, p = 0.00065) (Table 2 and Figure 7).

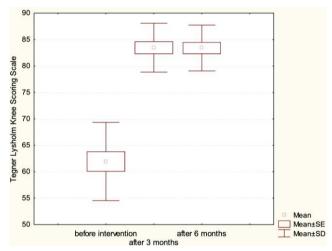


Figure 7: Mean Age Value on the TLKSS at different points in time

Discussion

The main purpose of PRP is to restore the balance between protective and aggressive factors through anti-inflammatory effects. Abrams et al., [15] state that the PRP therapy for patients that have osteoarthritis shows positive results in both clinical and pre-clinical trials. In their paper, these authors pointed out several limits in their research because of the selective selection of patients. In their research on the quality of PRP therapy in degenerative joint cartilage degeneration, Campbell at al., [16] indicated that the International Knee Documentation Committee (IKDS) achieved a six-month improvement. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), showed significant improvement compared to hyaluronic acid (HA) when it comes to pain in 3- and 6-month follow-ups. A large number of scientific studies have shown positive short-term results in the use of PRP treatment, while a relatively small number of studies have demonstrated a long-term efficacy [17]. The demographic data of patients such as body mass index, age and sex, play a role in the effectiveness of PRP [18], [19], [20].

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Several studies have failed to confirm the use of medications after the PRP treatment, while some studies have evaluated the effect of drugs on the effectiveness of PRP [21].

In conclusion, the application of PRP in the field of medicine is widely applied, and it will continue to be because the understanding of PRP therapy is increasingly refined. This study shows the effect of PRP in 15 patients, with a significant reduction in pain, following the administration of 2-3 doses of PRP evaluated on the TLKSS. Also, no side effects were observed in any of the patients that were studied. This therapy represents a potential and latest method in short-term pain reduction, but additional studies are needed to prove its long-term effectiveness.

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References

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- 1. Kennedy MI, Whitney K, Evans T, LaPrade RF. Platelet-Rich Plasma and Cartilage Repair. Current reviews in musculoskeletal medicine. 2018; 11(4):573-82. https://doi.org/10.1007/s12178-018-9516-x PMid:30203333 PMCid:PMC6220001
- 2. Goldring MB, Otero M. Inflammation in osteoarthritis. Curr Opin Rheumatol. 2011; 23:471-478. https://doi.org/10.1097/BOR.0b013e328349c2b1 PMid:21788902 PMCid:PMC3937875
- 3. Mueller MB, Tuan RS. Anabolic/catabolic balance in pathogenesis of osteoarthritis: identifying molecular targets. PM R. 2011; 3:S3-11. https://doi.org/10.1016/j.pmrj.2011.05.009 PMid:21703577
- 4. Wojdasiewicz P, Poniatowski LA, Szukiewicz D. The role of inflammatory and anti-inflammatory cytokines in the pathogenesis of osteoarthritis. Mediat Inflamm. 2014; 2014:561459. https://doi.org/10.1155/2014/561459 PMid:24876674 PMCid:PMC4021678
- 5. Kon E, Filardo G, Di Martino A, Marcacci M. Platelet-rich plasma (PRP) to treat sports injuries: evidence to support its use. Knee Surg Sports Traumatol Arthrosc. 2011; 19:516-527. https://doi.org/10.1007/s00167-010-1306-y PMid:21082164
- 6. Jang SJ, Kim JD, Cha SS. Platelet-rich plasma (PRP) injections as an effective treatment for early osteoarthritis. Eur J Orthop Surg Traumatol. 2013; 23:573-580. https://doi.org/10.1007/s00590-012-1037-5 PMid:23412170
- 7. Halpern B, Chaudhury S, Rodeo SA, Hayter C, Bogner E, Potter HG, Nguyen J. Clinical and MRI outcomes after platelet-rich plasma treatment for knee osteoarthritis. Clin J Sport Med. 2013; 23:238-239. https://doi.org/10.1097/JSM.0b013e31827c3846 PMid:23238250
- 8. Sampson S, Reed M, Silvers H, Meng M, 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.
- https://doi.org/10.1097/PHM.0b013e3181fc7edf PMid:21403592
- 9. Joshi Jubert N, Rodríguez L, Reverté-Vinaixa MM, Navarro A. Platelet-rich plasma injections for advanced knee osteoarthritis: a prospective, randomized, double-blinded clinical trial. Orthopaedic journal of sports medicine. 2017; 5(2):2325967116689386. https://doi.org/10.1177/2325967116689386 PMid:28255569 PMCid:PMC5315239
- 10. Sanchez M, Anitua E, Azofra J, Aguirre JJ, Andia I. Intraarticular 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.
- 11. Kon E, Filardo G, Di Matteo B, Marcacci M. PRP for the treatment of cartilage pathology. Open Orthop J. 2013; 7:120-128. https://doi.org/10.2174/1874325001307010120 PMid:23730375 PMCid:PMC3664439
- 12. Filardo G, Kon E, Buda R, Timoncini A, di Martino A, Cenacchi A, Fornasari PM, Giannini S, Marcacci M. Platelet-rich plasma intra-articular knee injections for the treatment of degenerative cartilage lesions and osteoarthritis. Knee Surg Sports Traumatol Arthrosc. 2011; 19:528-535. https://doi.org/10.1007/s00167-010-1238-6 PMid:20740273
- 13. Filardo G, Kon E, Roffi A, Di Matteo B, Merli ML, Marcacci M. Platelet-rich plasma: why intra-articular? A systematic review of preclinical studies and clinical evidence on PRP for joint degeneration. Knee Surg Sports Traumatol Arthrosc. 2015; 23:2459-2474. https://doi.org/10.1007/s00167-013-2743-1 PMid:24275957 PMCid:PMC4541701
- 14. Kon E, Buda R, Filardo G, et al. Platelet-rich plasma: intraarticular knee injections produced favorable results on degenerative cartilage lesions. Knee Surg Sports Traumatol Arthrosc. 2010; 18:472-479. https://doi.org/10.1007/s00167-009-0940-8 PMid:19838676
- 15. Abrams GD, Frank RM, Fortier LA, Cole BJ. Platelet-rich plasma for articular cartilage repair Sports Med Arthrosc Rev. 2013; 21:213-219. https://doi.org/10.1097/JSA.0b013e3182999740 PMid:24212369
- 16. Campbell KA, Saltzman BM, Mascarenhas R, Khair MM, Verma NN, Bach BR, Jr, Cole BJ. Does intra-articular platelet-rich plasma injection provide clinically superior outcomes compared with other therapies in the treatment of knee osteoarthritis? A systematic review of overlapping meta-analyses. Arthroscopy. 2015; 31:2213-2221. https://doi.org/10.1016/j.arthro.2015.03.041 PMid:26033459
- 17. Huang PH, Wang CJ, Chou WY, Wang JW, Ko JY. Short-term clinical results of intra-articular PRP injections for early osteoarthritis of the knee. Int J Surg. 2017; 42:117-122. https://doi.org/10.1016/j.ijsu.2017.04.067 PMid:28476542
- 18. Weibrich G, Kleis WK, Hafner G, Hitzler WE. Growth factor levels in platelet-rich plasma and correlations with donor age, sex, and platelet count. J Craniomaxillofac Surg. 2002; 30:97-102. https://doi.org/10.1054/jcms.2002.0285 PMid:12069512
- 19. Weibrich G, Kleiss WK, Kunz-Kostomanolakis M, Loos AH, Wagner W. Correlation of platelet concentration in platelet-rich plasma to the extraction method, age, sex, and platelet count of the donor. Int J Oral Maxillofac Implants. 2001; 16:693-699.
- 20. Evanson JR, Guyton MK, Oliver DL, Hire JM, Topolski RL, Zumbrun SD, McPherson JC, Bojescul JA. Gender and age differences in growth factor concentrations from platelet-rich plasma in adults. Mil Med. 2014; 179:799-805. https://doi.org/10.7205/MILMED-D-13-00336 PMid:25003868
- 21. Schippinger G, Pruller F, Divjak M, et al. Autologous plateletrich plasma preparations: influence of nonsteroidal anti-inflammatory drugs on platelet function. Orthop J Sports Med. 2015: 3:2325967115588896.
- https://doi.org/10.1177/2325967115588896 PMid:26665098 PMCid:PMC4622369