

# Autologous platelet plasma: promising method in the osteoarthritis treatment

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The investigations of the platelet-derived biologic agents in osteoarthritis treatment had shown promising but often controversial results.

**The objective:** to study the efficacy and safety of the PAP use in knee OA (stages I-II) treatment.

**Patients and methods.** Study included 146 patients with I-II stages of knee OA who were divided into 2 groups: group 1 (68 persons) received standard treatment plus 3 weekly intra-articular injections of APP (total 2 courses in 12 months); group 2 (78 patients of comparable age and stage of OA) – received only standard OA treatment. All participants underwent clinical, X-ray and OA questionnaire (WOMAC) assessments.

**Results.** Patients from group 1 demonstrated better results in WOMAC and less frequent exacerbations of OA in 12 month than patients from group 2.

**Conclusion.** Repeated intraarticular APP injections lead to better results of knee OA treatment and decrease number of OA exacerbations in 12 months.

**Key words:** autologous platelet plasma, knee osteoarthritis.

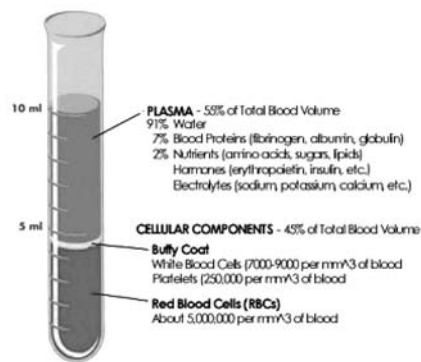
Osteoarthritis (OA) is a chronic degenerative progressive pathology of hyaline cartilage. OA accounts for profound morbidity, pain and health care expenses. The consequences to the individual and to the population as a whole are very significant, particularly with our aging population [2]. There are few validated interventions that can improve the functional state of patients once the degenerative process becomes symptomatic. Taking into account the lack of response of the body's healing mechanisms to degenerative conditions generally, local use of the stimulating and growth factors to activate cartilage regeneration is sensible. At the moment the stem cells therapy, PRP and mixed techniques are intensively investigating for OA treatment [1, 2].

Autologous platelet plasma (APP) is a novel therapeutic tool of autologous nature that has emerged in recent years. The application of APP in different tissues has given promising results in different pathologies such as acute and chronic injuries of bone and cartilage [1, 3]. APP treatment has demonstrated a quite prominent potential in rheumatology, orthopedics and sport medicine. Its therapeutic target eminently comprises chronic processes, although the range of indications is constantly expanding; PAP has been successfully used in many ailments, including knee osteoarthritis. Its low cost, ease of use, usefulness in pathological processes and high safety put it at the center of the researchers interest [3, 4].

PAP owes its therapeutic interest to the crucial role of platelets in the wound healing and tissue regeneration [4, 5, 8]. This role is not related to the repairing properties of the platelets themselves but, rather, to growth factors (GF) released by its  $\delta$  granules, which possess multiple regenerative properties (diagram 1).

Tissue wound repair is a complex process in which a variety of cellular functions such as chemotaxis, angiogenesis, cell proliferation, extracellular matrix formation and the «cleansing»

macrophage coexist, sequentially and covertly [5, 6]. These functions form a complex in which three relatively distinct phases are classically distinguished: inflammation, proliferation and remodeling 3, 4, 5, 6, 7. All GF content of the PAP is involved in the phases described, but all of their functions are still fully unknown. It is speculated that some of them play a role, but it is conceivable that each individual prominence varies depending on the type of tissue wound (ruptured, inflammation, degeneration, etc.) and the type of tissue (tendon, muscle, bone, etc.). PAP efficacy for the cells repair process activation was demonstrated experimentally and confirmed in few clinical studies but researches used different PAP preparations so results often are not comparable [6]. Also platelet quantification and the growth factor content definition must be defined in order to understand molecular mechanisms behind PRP regenerative strength. Standardization of PRP preparations is thus urgently needed [6–8].



**The objective:** to study the efficacy and safety of the PAP use in knee OA (stages I–II) treatment.

## PATIENTS AND METHODS

The study was performed at the Department of Family Medicine of the P.L. Shupyk National Medical Academy of Postgraduate Education (Kyiv, Ukraine) and Traumatology and Orthopedic Department of the O.O. Bogomolets National Medical University (Kyiv, Ukraine) and included 146 patients with diagnosed knee OA (radiological stage I–II). The severe comorbidities, previous trauma, knee surgery, other joint diseases were the exclusion criteria for the study. 146 patients (58 men (39,7%) and 88 women (60,3%), mean age  $41,7 \pm 1,2$  years) were divided into 2 groups. Group 1 included 68 patients who consented to receive standard OA treatment and 3 weekly intra-articular injections of APP (total 2 courses in 12 months) (plasma volume 12–15 ml/course, total platelets number per injection  $1260,24 \pm 22,1 \times 10^9$ ); Group 2 consisted of 78 patients with the same diagnosis who received only standard OA treatment (non-steroidal anti-inflammatory drugs (NSAID), physiotherapy, massage, exercises). Both groups were of comparable age, gender and initial WOMAC data (Group 1 –  $40,9 \pm 0,7$

Comparative evaluation component of disease severity in patients knee OA I-II during treatment

Duration of treatment		WOMAC results			
		Components clinical evaluation, intensity in points			W Points
		pain	stiffness	activity	
Day 0	Group 2 n=78	52,8±3,3	44,4±2,3	34,3±1,0	36,9±0,9
	Group 1 n=68	60,0±3,5	46,1±2,3	38,6±0,9	43,7±0,9
Day 17±3	Group 2 n=78	26,0±2,3 <sup>b</sup>	31,2±3,5 <sup>b</sup>	19,8±1,1 <sup>b</sup>	22,1±0,6 <sup>b</sup>
	Group 1 n=68	18,2±1,7 <sup>b,c</sup>	16,9±2,1 <sup>b,c</sup>	12,0±0,4 <sup>b,c</sup>	13,7±0,5 <sup>b,c</sup>
Day 180±3	Group 2 n=78	36,1±1,4 <sup>b</sup>	28,7±1,9 <sup>b</sup>	20,7±0,9 <sup>b</sup>	24,5±0,8 <sup>b</sup>
	Group 1 n=68	22,0±2,4 <sup>b,c</sup>	18,7±3,0 <sup>b,c</sup>	13,2±1,0 <sup>b,c</sup>	15,5±0,6 <sup>b,c</sup>
Day 365±3	Group 2 n=78	32,3±1,2 <sup>b</sup>	30,1±1,4 <sup>b</sup>	20,8±0,6 <sup>b</sup>	24,0±0,5 <sup>b</sup>
	Group 1 n=68	17,4±1,1 <sup>b,c</sup>	16,6±1,3 <sup>b,c</sup>	12,0±0,4 <sup>b,c</sup>	13,5±0,4 <sup>b,c</sup>
overall rate	before treatment	55,1±1,3 <sup>a</sup>	45,4±1,0	37,4±0,4	41,8±0,4 <sup>a</sup>
	after treatment	25,2±1,1 <sup>b</sup>	23,7±1,2 <sup>b</sup>	16,6±0,6	19,0±0,6 <sup>b</sup>

Note: a - significant difference between the rate depending on the duration of treatment, with  $p < 0.05$ ; b - significant difference before and after treatment in appropriate timing of treatment, with - reliable indicator of difference within the period of treatment depending on the applied therapy,  $p < 0.05$ ; W - general osteoarthritis severity index (points).

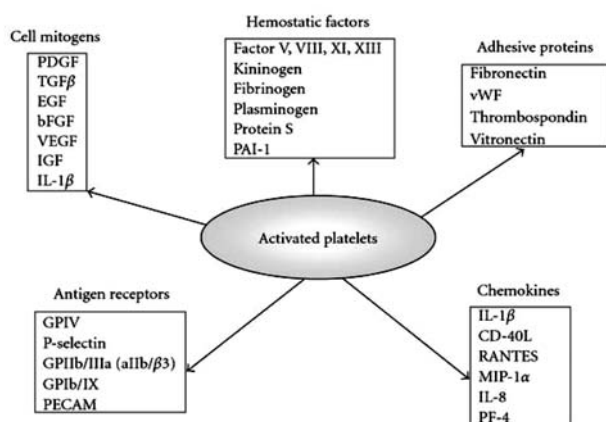


Diagram 1. Platelet components involved in the coagulation cascade and the atherosclerotic process.

PDGF, platelet-derived growth factor; TGFβ, transforming growth factor β; EGF, endothelial growth factor; bFGF, fibroblast growth factor; VEGF, vascular endothelial growth factor; IGF, insulin-like growth factor; IL-1β, interleukin-1β; PAI-1, plasminogen activator inhibitor 1; vWF, von Willebrand factor; GP, glycoproteins; PECAM, platelet and endothelial cell adhesion molecule; CD40L, CD40 ligand (CD154); RANTES, regulated on activation, normal T-cell expressed and secreted; MIP-1α, macrophage inflammation protein 1α; IL-8, interleukin-8; PF4, platelet factor 4 [8].

Group 2 – 39,7±0,9;  $p > 0,05$ ). The CRP-level and WOMAC scale parameters were analyzed before treatment and after 3 weeks; 6 and 12 months after course of treatment in both groups.

### RESULTS

According to current guidelines, the effectiveness of treatment of osteoarthritis determined by decreasing the duration of morning stiffness, indicators of inflammatory activity (CRP), a decrease in the intensity of joint pain in WOMAS and improv-

ing the functional activity of 20% or more of the initial value (Clegg O. et al., 2006; Bob H. et al., 2007; Haynes S., Gemmill H., 2007). Based on these criteria, we conducted a comparative assessment component displays of disease severity and gonarthrosis-IIst. the stages of differential treatment based on the results WOMAC.

The age and gender distribution of the patients and the level of the integral index WOMAC before and after treatment of people male and female patients with knee OA I-II stage depending on the day of treatment and therapy programs applied examined groups of patients are shown in Table 1.

3 weeks after course of treatment patients of Group 1 demonstrated better results than Group 2 as assessed by WOMAC: in Group 2 general index had decreased in 35.8%, and in Group 1 – in 74.1% - mostly on account of pain severity and stiffness.

After 6 months of follow-up (before second course of PAP treatment), the mean number of OA exacerbations was (0,7±0,02) in Gr. 1 and (1,6±0,04) in Gr. 2 ( $p < 0,05$ ) and general WOMAC index in Gr. 1 was significantly lower than in Gr. 2 (accordingly 22,8±0,3 and 36,5±0,8;  $p < 0,05$ ).

In the next 6 months again patients in Gr.1 had less exacerbations (0,51±0,03) then patients in Gr. 2 (1,4±0,03),  $p < 0,05$ ; and better WOMAC performance (Gr. 1 – 17,5±0,6 and Gr. 2 – 37,1±0,5;  $p < 0,05$ ). There were no adverse events due to use of PAP injections in group 1.

### CONCLUSION

Repeating intra-articular injections of PAP, added to the standard care in knee OA improves functional activity, reduces pain and number of OA exacerbations in 12 months of follow up. The course of 3 intra-articular injections added to the standard treatment of knee OA improves functional activity, reduces pain and probably can prolong remission in patients with the early stages of disease. The further studies are needed with ultrasound/MRI monitoring of the articular cartilage to obtain more accurate information and determine the most effective methods of its use in OA patients.

**Аутологическая тромбоцитарная плазма: новый метод в лечении остеоартроза**  
**Л.В. Химион, А.А. Бурьянов, Л.А. Смолина**

Исследования эффективности применения биологических препаратов на основе тромбоцитов в лечении остеоартрита показали впечатляющие, но часто противоречивые результаты.

**Цель исследования:** изучение эффективности и безопасности аутологичной тромбоцитарной плазмы (АТП) в лечении остеоартроза (ОА) коленного сустава ранних стадий.

**Материалы и методы.** Исследование проведено в двух группах пациентов с ОА коленных суставов I–II стадий. Группа 1 состояла из 68 пациентов, которые вместе со стандартной терапией ОА получали 3 внутрисуставных инъекции ТАП (еженедельно; всего 2 курса за 12 мес). Группа 2 состояла из 78 пациентов с таким же диагнозом, которые получали только стандартную терапию ОА. Всем участникам исследования проводили клинические и рентгенологические исследования, а также оценку эффективности лечения по шкале WOMAC.

**Результаты.** Пациенты группы 1 продемонстрировали лучшие результаты лечения и уменьшение количества обострений ОА за 12 мес по сравнению с пациентами группы 2.

**Заключение.** Повторные курсы внутрисуставного применения ТАП улучшают результаты лечения ОА коленных суставов I–II стадий и уменьшают количество обострений за 12 мес.

**Ключевые слова:** тромбоцитарная аутологичная плазма, остеоартроз коленных суставов.

**Аутологічна тромбоцитарна плазма: новий метод у лікуванні остеоартрозу колінних суглобів**  
**Л.В. Хіміон, О.А. Бур'янов, Л.О. Смоліна**

Дослідження ефективності застосування біологічних препаратів на основі тромбоцитів в лікуванні остеоартриту показали вражаючі але часто суперечливі результати.

**Мета дослідження:** визначення ефективності і безпеки застосування тромбоцитарної аутологічної плазми (ТАП) у лікуванні остеоартрозу (ОА) колінного суглоба на ранніх стадіях.

**Матеріали та методи.** Дослідження проведено в двох групах пацієнтів із ОА колінних суглобів I–II стадій. Група 1 складалась із 68 пацієнтів, які разом із стандартною терапією ОА одержали 3 внутрішньосуглобові ін'єкції ТАП (щотижня, усього 2 курси за 12 міс). У групу 2 увійшли 78 пацієнтів, які одержували лише стандартну терапію ОА. Усім пацієнтам, що увійшли в дослідження, проводили клінічне і рентгенологічне обстеження, а також оцінювали ефективність лікування за WOMAC.

**Результати.** Пацієнти групи 1 продемонстрували кращі результати лікування та меншу кількість загострень ОА за 12 міс порівняно із пацієнтами групи 2.

**Заключення.** Повторні курси внутрішньосуглобового введення ТАП покращують результати лікування ОА колінних суглобів I–II стадії та зменшують кількість загострень ОА за 12 міс.

**Ключові слова:** аутологічна тромбоцитами плазма, остеоартроз колінних суглобів.

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