Журнал клінічних та експериментальних
JC&EMR
медичних досліджень

УДК 616-08-035:612.111.7:611-018.54:616.832-089

Abstract

E. G. Pedachenko[1],
M. V. Khyzhnyak[1],
O. O. Potapov[2],
Yu. E. Pedachenko[1,3],
O. F. Tanasiichuk[1],
O. P. Krasylenko[1*],
A. M. Furman[1],
I. G. Vasylieva[1],
N. G. Chopyk[1],
N. P. Oleksenko[1],
[1]State Institution «Institute of Neurosurgery named after acad. A. P. Romodanov of AMS of Ukraine», Kyiv, Ukraine;
[2]Medical Institute, Sumy State University, Sumy, Ukraine;
[3]National Medical Academy of Postgraduate Education named after P. L. Shupyk, Kyiv, Ukraine

THE RESULTS OF AUTOTRANSFUSION WITH PLATELET RICH PLASMA IN SPINAL NEUROSURGERY

Introduction. Platelet-rich plasma (PRP), a blood plasma separated by centrifugation with highly abundant platelets, has multiple applications in many healthcare fields for the improvement of soft and bone tissues regeneration. The studies of PRP implementation results in spine neurosurgery are of high demand in case of pathologies related to the degeneration or injury of living *bone* and cartilaginous elements of vertebral column, which require the installation of vertebral interbody fusion system.

Purpose. Improvement of surgical treatment outcomes by means of improving postoperative wound healing and reducing pain severity after the installation of transpedicular fixation systems in the lumbar spine using a biotechnological method which has a multimodal effect on regeneration processes and is simple and cost-effective

Materials and Methods. The results of transpedicular stabilization in lumbar spine vertebral column were assessed within the early postoperational period in two groups of patients comparable in age and health status with spondylolisthesis and spinal motion segment instability. Patients from the main group (n = 20, average age 47.8 ± 6.6 years) received PRP during the operation as compared to the control one (n = 30, average age 46.9 ± 5.6 years) without PRP injections.

Results. It was found that during the first day post-operation the pain severity in the main group was significantly reduced (1.6 ± 0.7 points according to the visual analogous scale) as compared to the control (3.8 ± 0.9 points). Moreover, these characteristics before the discharge of the patients were 0.3 ± 0.3 and 2.0 ± 0.4 points respectively. It is noteworthy that the swelling and wound edges hyperemia were remarkably reduced after the PRP use. Finally, no complications, side-effect or systemic consequences of PRP were observed.

Conclusions. Therefore, the local injections of PRP during the installment of transpedicular stabilization system in lumbar spine is easy-to-handle and safe approach favoring the quick recovery in early postoperational period.

Keywords: lumbar spine; transpedicular interbody fusion; platelet-rich plasma.

Corresponding author: *elena.krasylenko@gmail.com*

Резюме

Є. Г. Педаченко[1], М. В. Хижняк[1], О. О. Потапов[2], Ю. Є. Педаченко[1,3], О. Ф. Танасійчук[1], П. Красиленко[1*], А. М. Фурман[1], І. Г. Васильєва[1], Н. Г. Чопик [1], Н. П. Олексенко[1],

[1]ДУ «Інститут нейрохірургії ім. акад. А. П. Ромоданова НАМН України», Київ, Україна;

[2]Медичний інститут Сумського державного університету, м. Суми, Україна;

[3]Національна медична академія післядипломної освіти ім. П.Л. Шупика МОЗ України, м. Київ, Україна

РЕЗУЛЬТАТИ ЗАСТОСУВАННЯ ЗБАГАЧЕНОЇ ТРОМБОЦИТАМИ АУТОПЛАЗМИ У СПИНАЛЬНІЙ НЕЙРОХІРУРГІЇ

Досліджено ефективність інтраопераційного місцевого застосування збагаченої тромбоцитами аутоплазми (ЗТА) при встановленні систем транспедикулярної стабілізації в поперековому відділі хребта – за динамікою регресу больового синдрому (використовували візуальну аналогову шкалу) та станом післяопераційної рани.

Інтенсивність болю у групі пацієнтів, яким вводилась ЗТА (n = 20), в першу ж післяопераційну добу була істотно нижчою (1,6 ± 0,7 балів), порівняно з контролем (n = 30) (3,8 ± 0,9 балів), і перед випискою склала, відповідно, 0,3 ± 0,3 та 2,0 ± 0,4 балів.

У всіх пацієнтів після введення ЗТА візуально відмічено значно меншу вираженість набряку та гіперемії країв рани.

Ускладнень, побічних реакцій, системного впливу біопрепарату не спостерігали.

Таким чином, місцеве введення ЗТА під час проведення відкритих хірургічних втручань на хребті є безпечною та ефективною процедурою, що дозволяє покращити перебіг раннього післяопераційного періоду.

Ключові слова: поперековий відділ хребта, транспедикулярна стабілізація, збагачена тромбоцитами аутоплазма.

Резюме

Е. Г. Педаченко[1], М. В. Хижняк[1], А. А. Потапов[2], Ю. Е. Педаченко[1,3], А. Ф. Танасийчук[1], Е. П. Красиленко[1*], А. Н. Фурман[1], И. Г. Васильева[1], Н. Г. Чопик[1], Н. П. Олексенко[1],

[1]ГУ «Институт нейрохирургии им. акад. А. П. Ромоданова НАМН Украины», г. Киев, Украина;

[2]Медицинский институт Сумского государственного университета, г. Сумы, Украина;

[3]Национальная медицинская академия последипломного образования им. П. Л. Шупика МЗ Украины, г. Киев, Украина.

РЕЗУЛЬТАТЫ ПРИМЕНЕНИЯ ОБОГАЩЕННОЙ ТРОМБОЦИТАМИ АУТОПЛАЗМЫ В СПИНАЛЬНОЙ НЕЙРОХИРУРГИИ

Исследована эффективность интраоперационного местного использования обогащенной тромбоцитами аутоплазмы (ОТА) при установке систем транспедикулярной стабилизации в поясничном отделе позвоночника – по динамике регресса болевого синдрома (применяли визуальную аналоговую шкалу) и состоянию послеоперационной раны.

Интенсивность боли в группе пациентов, которым вводилась ОТА (n = 20), в первые же послеоперационные сутки была значительно ниже (1,6 ± 0,7 бала) по сравнению с контролем (n = 30) (3,8 ± 0,9 баллов), и перед выпиской составила, соответственно 0,3 ± 0,3 и 2,0 ± 0,4 баллов.

У всех пациентов после введения ОТА визуально отмечена значительно меньшая выраженность отека и гиперемии краев раны.

Осложнений, побочных реакций, системного воздействия биопрепарата не наблюдали.

Таким образом, местное введение ОТА во время проведения открытых хирургических вмешательств на позвоночнике является безопасной и эффективной процедурой, которая позволяет улучшить течение раннего послеоперационного периода.

Ключевые слова: поясничный отдел позвоночника, транспедикулярная стабилизация, обогащенная тромбоцитами аутоплазма.

Автор, відповідальний за листування: *elena.krasylenko@gmail.com*

https://doi.org/10.21272/jcemr.2018.6(4):424–431

Introduction

The search for safe substances and methods to stimulate organism's regenerative potential more than three decades ago led to active research, and subsequently – to clinical application, of an endogenous substance such as centrifuged plasma with a given supraphysiological number of platelets – platelet rich plasma (PRP) [1].

Up to now, several hundreds of biologically active substances contained in platelets are known, including dozens of growth factors, particularly those that accelerate healing of damaged soft and bone tissues [2; 3].

With regard to soft tissues, researchers most often consider platelet-derived growth factor (PDGF), epidermal growth factor (EGF), transforming growth factor beta 1 (TGF-β1), vascular endothelial growth factor (VEGF, PDEGF), platelet angiogenic factor (PDAF), fibroblast growth factor (FGF), hepatocyte growth factor (HGF), insulin-like growth factor (IGF-I) [3; 4].

Changes in bone and cartilage tissues under the influence of PRP [5; 6] are also commonly associated with the factors such as TGF-β, IGF, FGFb, PDGF [7; 8; 9; 10]. In this case, the role of ADP (adenosine di-phosphate) and ATP (adenosine triphosphate), and fibronectin has been established in remodeling and regeneration of bone tissue; and the role of angiopoietin-2, vascular endothelial growth factors, thrombospondin-1 was shown in the processes of bone tissue vascularization [11].

Currently some mechanisms have been found for stimulation of differentiation, migration and proliferation of chondrocytes and osteoblasts, as well as inhibition of osteoclast formation, performed by these biologically active substances [3; 12-23]. It was also established that PRP induces proliferation of cartilage intercellular matrix [24; 25]. The influence of platelet concentration in PRP on chondrogenesis and osteogenesis has been observed. Thus, the degree of bone regeneration at low concentrations was minimal, and with excessively high concentrations there was inhibition of bone tissue regeneration [11]. Also the data were obtained demonstrating the dose-dependent action of PRP anabolic effect on the nucleus pulposus cells of animal intervertebral disc in culture: increased viability [26], increased proliferation of chondrocytes [17; 18], prevention of reduction of chondrogenic genes expression [26].

The experiment shows that PRP is able to modulate the natural healing processes of soft tissues [3], which is a key point in elimination of the consequences of any surgical trauma. It was established that PRP influences the processes of angiogenesis, stimulation of proliferation of vascular endothelial cells, keratinocytes, fibroblasts, and at later stages of healing – regulation of the balance between fibrosis and regeneration of myocytes, etc. [3; 4]. It is also important that, in addition to regenerative properties, PRP has anti-inflammatory and analgesic effect [27-29], as well as antibacterial effect with regard to some microorganisms [30].

The idea of using PRP as an autologous component for fast healing of postoperative wounds was first introduced during the heart surgery in 1987 by Ferrari M. [31], which initiated the clinical application of PRP. In 1998, Marx R.E. et al were the first to report on their experience of using PRP to improve bone regeneration in the reparative surgery of the jaw [32].

Over a long period of clinical use, the possibilities of PRP have been widely studied in relation to fractures of long bones, ligamentous apparatus damage, tendinopathies, degenerative and non-specific inflammatory diseases of the joints, fistulas and bedsores that do not heal for a long time, pathologies of intervertebral discs, stabilizing operations of the spine [33-42].

However, even in those medical fields where considerable experience has been gained: orthopedics and traumatology, sports medicine, combustiology, maxillofacial surgery, plastic surgery [33-42], today there are many unclear questions and there are no definite clinical protocols regarding the application of PRP.

A large number of publications on PRP use in spinal neurosurgery and spine surgery suggests positive experience based on preclinical studies in vitro and in vivo [43-47]. In this context, it is important to study the mechanisms of PRP effect not only on the processes involving degeneration or injury of the spine bone and cartilage structures, but also on the integration of allo- and autologous systems of spine stabilization.

In experimental works, where spondylosyndesis was studied in a variety of animal models [48-52], different strategies for obtaining and application of PRP were used. But, despite the non-unified experimental protocols, the results of most studies indicate the effectiveness of this biotechnology. The conclusions of these publications are based on histological and radiological methods for assessing the quality of spondylosyndesis, the density of the bone

https://doi.org/10.21272/jcemr.2018.6(4):424–431

mass surrounding the implant, and its biomechanical properties.

Elder B.D. et al. (2015) was the first to systematize the results of 15 clinical trials on PRP use in the anterior cervical discectomy with spondylosyndesis, posterior cervical stabilization, thoracolumbar stabilization, posterior-lateral lumbar stabilization (with or without instrumentation), in which the quality of the intervertebral fusion was evaluated according to static and functional radiography and CT [11]. The authors emphasize the possibility of dependence between the results of studies and concentrations of platelets and biologically active substances contained therein, which has been proved experimentally. Although the review outlines several studies that indicate no or negative impact of PRP on the rate and quality of spondylosyndesis [53; 54], the majority of the publications mentioned above indicate that given autologous and allogenic grafts in the cervical and lumbar spine, PRP accelerates fusion without significantly affecting its long-term overall level (after 3-12 months) [43-46].

Therefore, a number of experimental and clinical studies indicate the reasonability of PRP use in patients with traumatic and degenerative diseases of the spine, for whom one of the most invasive types of spinal surgical interventions is indicated, i. e. stabilizing system installation.

PURPOSE. Improvement of surgical treatment outcomes by means of improving postoperative wound healing and reducing pain severity after the installation of transpedicular fixation systems in the lumbar spine using a biotechnological method which has a multimodal effect on regeneration processes and is simple and cost-effective.

MATERIALS AND METHODS. The results of transpedicular fixation (TPF) in early postsurgical period were assessed in 50 patients aged 33 to 65 years. The patients with spondylolisthesis and instability of spinal motion segment in the lumbar spine were subject to surgical treatment. Indications for surgical treatment were determined taking into account the correlation between clinical and neurological data and MRI data and functional spondylography of the lumbosacral spine.

All patients were divided into 2 homogeneous groups by somatic status and age. The patients in the treatment group (n = 20, mean age 47.8 ± 6.6) had PRP during TPF; the control group patients (n = 30, mean age 46.9 ± 5.6) received no PRP. Contraindications to PRP included diabetes mellitus, blood-clotting disorder, hepatitis.

The operation was performed with a patient in ventricumbent position using endotracheal anesthesia. To install TPF system 2 paravertebral approaches were used in the projection of the pedicle of vertebral arches. After aponeurosis dissection and muscle separation under the control of electron-optical image intensifier, screws were implanted into the vertebral bodies with subsequent fixation with rods. Further, the tissues were closed layer by layer. After the operation the treatment group patients received 1.5 mL PRP into the surgical wound soft tissues damaged during the surgery using a syringe for injection with a needle.

To prepare PRP, patients' venous blood was taken immediately before surgery. PRP was obtained immediately after blood collection by differential centrifugation in PRP tubes (CRSI, China) for 10 minutes at 850 g under sterile conditions [2]. Platelet count in obtained PRP samples amounted 1 million (920-1050 thousand) cells per μl. Counting and viability assessment for the platelets obtained were carried out in Gorjaev's count chamber after preliminary staining with a 0.2% solution of trypan blue using a light microscope.

After the surgery, the regimen of medication in both groups traditionally included antibacterial and non-steroidal anti-inflammatory drugs, corticosteroids.

A comprehensive clinical, laboratory, and instrumental (spondylographic) examination was performed in all patients prior to the operation and at the time of discharge (3-4 days later) to evaluate the safety of PRP use.

RESULTS AND DISCUSSION. The efficacy of PRP was evaluated in the early postoperative period by subjective (pain severity by visual analogue scale) and objective (postoperative wound condition) indices (Table 1).

Table 1 – Over-time severity of pain syndrome after transpedicular fixation in the lumbar spine (VAS score)

Groups of patients	Observation period		
	preoperative	early postoperative	
		1st postoperative day	3rd postoperative day
Treatment group	8.3 ± 0.9	1.6 ± 0.7	0.3 ± 0.3
Control group	7,9 ± 1.1	3.8 ± 0.9	2.0 ± 0.4

https://doi.org/10.21272/jcemr.2018.6(4):424–431

The severity of pain in PRP group of patients was significantly lower on the first postoperative day (1.6 ± 0.7 points) compared to the control group (3.8 ± 0.9 points), and before the discharge it was 0.3 ± 0.3 and 2.0 ± 0.4 points, respectively. At the same time, 85.0 % of patients in the treatment group refused additional administration of analgesics in the first day, while in the control group this portion was 6.7 %.

The next day after the operation and later, the patients who had received PRP presented with much better visual state of the wound due to the lack of edema and hyperemia in the area of postoperative wound.

During the entire stay of patients at the inpatient department, there were no signs of negative effect of PRP on laboratory parameters and general condition.

Conclusions

Thus, local administration of PRP during transpedicular stabilization system installation in the lumbar spine is a technically simple and safe procedure, not accompanied by adverse reactions and causing no systemic effects on the organism.

The patients, who had PRP in the postoperative period, during the entire stay at the inpatient department presented with a significant decrease in pain syndrome severity, as compared to the control group, and significant improvement of early regeneration.

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(received 01.11.2018, published online 25.12.2018)

(одержано 01.11.2018, опубліковано 25.12.2018)

https://doi.org/10.21272/jcemr.2018.6(4):424–431