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CLINICAL FEATURES OF REPARATIVE REGENERATION OF BONE TISSUE AND OPTIMIZATION OF TREATMENT FOR COMPRESSION FRACTURES OF THE THORACIC AND LUMBAR VERTEBRAL BODIES AGAINST THE BACKGROUND OF POSTMENOPAUSAL AND SENILE OSTEOPOROSIS

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Abstract

Introduction. Bone-destructive processes and injuries of the vertebral bodies of the thoracic and lumbar localization are a significant part of the pathology of this localization. According to etiological factors, mechanisms of pathogenesis and the nature of the course, they are a very heterogeneous groups of diseases.

Objective: to identify the main factors that determine the development of disorders in compression fractures of vertebral bodies of thoracic and lumbar localization against the background of postmenopausal and senile osteoporosis for improving the prognostic criteria of the disease on the basis of an integrated assessment of the clinical course of the disease and

optimizing treatment by activating reparative bone tissue regeneration according to the literature sources analyzed.

Material and research methods. Depending on the treatment method used, patients were divided into 3 groups: in group 1 (control group) were 20 patients with compression fractures of vertebrae of thoracic and lumbar localization against a background of postmenopausal and senile osteoporosis, where we used standard methods of therapy. Group 2 (main group) consisted of 20 patients with compression fractures of vertebrae of thoracic and lumbar localization against the background of postmenopausal and senile osteoporosis, in the treatment of which platelet-rich plasma was also used in addition to standard methods of therapy.

Research results. Based on the obtained results of the study, we developed an algorithm for surgical treatment of patients with pathological vertebral fractures against the background of osteoporosis. The choice of the method of surgical treatment depends on: the type of fracture, the level of damage, the degree of loss of bone mineral density, the degree of deformation of the spine, the general somatic state of the patient, the presence of stenosis of the spinal canal and signs of neurological deficit, the severity of the pain syndrome.

Conclusion. The introduction of platelet-rich plasma to the area of the bone wound shortens the duration of the healing process, in our opinion, by eliminating the phase of inflammation, low intensification of the phase of formation of tissue-specific elements that are present in large amount in platelet growth factors. In order to accelerate the restoration of damaged bone, we used a platelet-rich plasma in addition to standard therapy, and found a positive effect on compressive fractures of the thoracic and lumbar vertebrae against the background of postmenopausal and senile osteoporosis, which justifies the advisability of further use platelet-rich plasma in clinical practice.

Key words: Platelet-Rich Plasma; reparative regeneration; osteogenesis; bone remodeling; mineral metabolism; osteoporosis.

Introduction. Bone-destructive processes and injuries of the vertebral bodies of the thoracic and lumbar localization are a significant part of the pathology of this localization. According to etiological factors, mechanisms of pathogenesis and the nature of the course, they are a very heterogeneous groups of diseases [1]. Surgical interventions performed for compression fractures of the vertebral bodies of the thoracic and lumbar localization are performed in a complex topographic relationship and quite close to the vital organs. The high functional and social significance of the spinal column necessitates not only the fullest

possible restoration of the anatomical integrity and function of organs and tissues, but also the prevention of aesthetically unfavorable results [2].

Literature data and everyday clinical practice indicate significant differences in the course of reparative processes on the background of postmenopausal and senile osteoporosis. Traumatologists are constantly studying bone tissue, the conditions of reparative regeneration, there is a search for causes that lead to a slowdown or complete absence of fusion of bone fragments. It is well known that a certain percentage of compression fractures of the thoracic and lumbar vertebrae on the background of postmenopausal and senile osteoporosis during treatment is complicated by delayed consolidation, and in some cases – nonunion fracture or false joint (pseudoarthrosis), even with modern treatments. High material costs for treatment, repeated surgical interventions, which in some cases do not lead to recovery, prolonged disability – these are just some aspects of the whole complex of problems of medical and social rehabilitation of such victims [3].

Prevention of disorders of reparative osteogenesis on the background of postmenopausal and senile osteoporosis, optimization of the conditions of its course is an urgent task of scientists. There are a large amount of works on the problem of optimizing the processes of reparative regeneration, but mostly they contain solutions to biomechanical problems. They are based on stable fixation and restoration of the anatomical ratio of bone fragments. To solve these problems, work is underway to develop a large number of supraosseous, transosseous and intraosseous fixators [4].

In recent years, the attention of surgeons has been drawn to Platelet-Rich Plasma (PRP) – plasma in which the number of platelets is several times higher than normal. This term is valid at a platelet concentration from 700 thousand to 1 million in 1 μ l of plasma [5]. Currently, PRP is widely used in dentistry for hemostatic purposes, to accelerate tissue regeneration, reduce scarring, stimulate angio- and osteogenesis. These features of the action of PRP are due to the presence in the alpha granules of platelets of numerous growth factors and other biologically active substances. It should be noted that information about the use of PRP in other areas of surgery and traumatology has not been studied carefully enough [6].

The most available source of autogenous growth factors are platelets. All these factors are found in the alpha granules of platelets. Among them – Platelet Derived Growth Factor (PDGF), Transforming Growth Factor (TGF-beta, 1, 2), Insuline like Growth Factor (IGF), Epidermal Growth Factor (EGF), Fibroblasts Growth Factor (FGF), endothelial growth factor, antiheparin factor, platelet activating factor [7].

Autogenous platelet mass stimulates collagen formation, accelerates skin and mucosal regeneration, induces vascular growth, stimulates rapid and complete bone formation, provides hemostasis, reduces pain, reduces the risk of infectious complications, promotes the best results of surgery [8]. It can be used to cover soft tissue wounds and fill bone defects. Autogenous platelet mass contains a high concentration of platelets and fibrinogen, as well as leukocytes and macrophages, which determines the very broad indications for use in otorhinolaryngology, cardiology, neurosurgery, vascular surgery, urology, gynecology, orthopedics, cosmetic surgery, ophthalmology, general surgery and dentistry [9].

However, being a powerful osteoinductor, autogenous platelet mass does not have osteoconductive properties, which was the basis for a series of experiments in which various osteoconductive materials were used [10].

The data presented in the literature on the treatment of bone fractures using plasma and platelet-enriched fibrin are ambiguous and sometimes contradictory. Along with the positive results, the scientific literature presents experimental and clinical data on the ineffectiveness of the use of PRP for the treatment of fractures and complications after fracture. On the one hand, this is due to the peculiarities of obtaining and using different concentrations of platelet-enriched plasma, on the other – the use of different matrices in conjunction with plasma (PRP) and fibrin (PRF) [11, 12].

Existing and described by us ideas about the course of bone regeneration in the case of its fracture determine the nature and content of the standards of their treatment. It is based on fixing the fragments in one way or another and providing functional rest to the damaged limb. Activation of the regeneration process is achieved by the outpouring of blood at the fracture site, the appearance of foci of inflammation. The activity of calcium metabolism, and the impact on its regulatory role is taken into account very poorly. In addition, natural factors that affect the intensity of regeneration (plasma, which is enriched by platelets) are not actively used. The latter circumstance is due to insufficient study of the mechanisms of its influence on bone regeneration processes.

This work is a fragment of the research "Diagnosis and treatment of patients with injuries and diseases of the musculoskeletal system" (№ state registration 0113U000796).

The aim of the study is to identify the main factors that determine the development of disorders in compression fractures of vertebral bodies of thoracic and lumbar localization against the background of postmenopausal and senile osteoporosis for improving the prognostic criteria of the disease on the basis of an integrated assessment of the clinical

course of the disease and optimizing treatment by activating reparative bone tissue regeneration according to the literature sources analyzed.

Materials and methods of research. Depending on the method of treatment, patients were divided into 2 groups: group 1 (control group) included 20 patients with compression fractures of the vertebral bodies of the thoracic and lumbar localization on the background of postmenopausal and senile osteoporosis, in the treatment of which were used standard traditional methods. Group 2 (main group) consisted of 20 patients with compression fractures of the vertebral bodies of the thoracic and lumbar localization on the background of postmenopausal and senile osteoporosis, in the treatment of which PRP was also used in addition to conventional therapies. Patients of both groups were treated in the Department of Traumatology with beds of polytrauma, City Hospital of Urgent and Emergency Medical Care under Zaporizhia City Council in 2017-2019.

The groups were equivalent in age, body mass index, course and radiological features of the underlying disease, as well as concomitant pathology and standard therapy.

There were conducted a clinical examination of patients, assessed the features of the manifestations of pain, functional activity. Also were performed instrumental studies (radiography, ultrasound, magnetic resonance imaging), general clinical laboratory studies. The study was performed before treatment, after 1, 6 and 12 months.

In the treatment of patients of group 2 was used PRP – the concentration of biologically active molecules – growth factors in plasma obtained from the patient's own blood.

Arthrex ACP System is method of concentrating growth factors for therapeutic use. The use of a double syringe provides its own enriched plasma in a closed system. 15 ml of venous blood is drawn into the syringe, and a red protective cap is put on the cannula. For blood sampling it is recommended to use a butterfly needle with a diameter of 18-20G. When used with an anticoagulant before centrifugation, the blood is mixed with gentle movements of the syringe in a circle.

The syringe is placed in the socket of the centrifuge rotor, in the opposite socket – a counterweight or a second syringe of equal volume. Centrifugation is carried out for 5 minutes at 1500 rpm (revolutions per minute). The syringe is then drawn upright so that the plasma does not mix with the precipitated erythrocytes. To transfer 3-5 ml of plasma from a large outer syringe to a small inner syringe, slowly push down on the outer syringe while slowly pulling up the plunger of the small inner syringe. The small inner syringe is unscrewed, the needle is put on, after which the plasma will be ready for use – injection.

When used in conjunction with an anticoagulant, use plasma up to 4 hours after blood collection.

When studying the processes of reparative osteogenesis, it is important to study specific markers of bone metabolic processes. The main structural component of the extracellular space of bone tissue is collagen fibers. Among the methods of assessing the condition of bone tissue, in particular the intensity of the processes of biosynthesis and collagen breakdown, the method of determining the fractions of oxyproline in urine is one of the priority places.

In our study, gender was dominated by women – 14 and 16 people, respectively, in the first and second groups (70 and 80%). By localization, the majority (12 and 13 people – 60 and 65%) were vertebral injuries of the transitional thoracolumbar spine.

The main complaint in all patients was pain. The intensity of the pain syndrome was assessed on a visual analog scale VAS-100. At the time of admission to the hospital, the average score on the VAS scale was 59.1 ± 12.4 and 62.2 ± 13.8 points in the first and second groups, which corresponded to the assessment of severe pain. Only 1 and 2 patients from the first and second groups (5 and 10%) did not complain of pain in the spine.

The mechanism of injury was dominated by low-energy injuries – 75 and 80% (15 and 16 patients in the first and second groups, respectively), when the fracture occurred under the influence of light load. Neurological disorders as a consequence of osteoporotic vertebral fractures were found in 5 and 7 (25 and 35%) patients. These disorders were represented by radicular pain from the level of the fracture, and in some patients there were phenomena of lower paraparesis with sensitive disorders.

The main role in the diagnosis of vertebral fractures and verification of osteoporosis belongs to radiological methods of research. Until now, the X-ray method with the performance of standard spondylograms in 2 projections has not lost its relevance. This method allows you to determine the level and nature of the vertebral fracture, the degree of kyphosis of the fractured vertebra and the sagittal balance of the spine as a whole. Helical (spiral) computed tomography (CT) of the spine were performed in 16 and 18 (80 and 90%) patients of the first and second groups, respectively. During the CT scan, the level and nature of the damage, the number of damaged vertebrae, the presence and magnitude of the displacement of bone fragments of the damaged vertebra into the lumen of the spinal canal were specified. Spinal canal stenosis were found in 4 and 6 victims (20 and 30%). Magnetic resonance imaging (MRI) examination of the damaged spine were performed in patients with

neurological symptoms to determine the degree of compression of the spinal cord and its roots, and when it was necessary to clarify the etiology of pathological fracture of the spine.

To assess the nature of the vertebral fracture and the degree of its destruction as a result of injury, we used the universal classification of vertebral fractures proposed by Magerl F. et al. (1994). According to this classification, vertebral fractures on the background of osteoporosis are type A injuries, when a vertebral body fracture occurs without damage to the posterior structures. Most patients had type A1 injuries (50 and 55%) and A2 (10 and 15%) without displacement of fragments, and only 40 and 30% of patients in the first and second groups had explosive fractures of type A3, respectively.

To diagnose osteoporosis, the method of dual-energy X-ray absorptiometry (DEXA) was used, which is currently considered the "gold standard" worldwide. Patients with T-score in the range from -2.5 to -3.5 SD – 40 and 55% patients predominated. A significant proportion of patients had a pronounced degree of osteoporosis (below -3.5 SD) – 6 and 7 (30 and 40%) patients. At the same time, both men and women with aging showed progression of osteoporosis with a decrease in T-score.

To assess the quality of life, we used an adapted version of the general international questionnaire EuroQol-5D. In most patients, all components of quality of life had problems of moderate severity.

Analysis of the normality of the distribution was evaluated by Shapiro-Wilk (W) criteria. When it was impossible to reject the null hypothesis of statistically significant differences in the distribution of variables from normal, nonparametric data analysis methods were used, and in other cases, parametric methods.

Data are presented as mean and standard error of representativeness of the sample mean (in the case of normal distribution), and in the form of median and interquartile range (25-75 percentile, if there is a difference from the normal distribution). In the case of a non-normal distribution or analysis of ordinal variables, the Mann-Whitney U-test was used for 2 unrelated samples, and for a larger number of samples, the Kruskal-Wallis H test was followed by a Games-Howell comparison. Comparison of the two groups was performed by using the Wilcoxon test.

The results of the study were processed using the statistical package of the licensed program "STATISTICA® for Windows 6.0" (StatSoftInc., № AXXR712D833214FAN5), as well as "SPSS 17.0", "Microsoft Excel 2003". Some statistical procedures and algorithms are implemented in the form of specially written macros in the appropriate programs. Differences at $p < 0.05$ were considered statistically significant for all types of analysis.

Research results and their discussion. From the point of view of morphology of the process we can distinguish two stages of bone regeneration: the first stage includes the formation of regenerate, at this stage there is a phase of connective tissue callus and a phase of its subsequent transformation into bone, to the second – reorganization of primary callus. In the literature there is another view of this process, when there are five stages: 1 – the formation of tissue similar to the mesenchyme; 2 – differentiation of cellular elements of this tissue; 3 – formation of primary bone marrow cavities; 4 – restructuring of the temporary callus; 5 – reverse development of callus. In addition, based on morphological data on bone wound healing, we can differentiate six stages of recovery of a bone defect: 1 – destabilization of cellular elements; 2 – cell proliferation; 3 – differentiation of different types of tissues (cartilaginous, fibroblastic, osteoblastic, undifferentiated tissue similar to the mesenchyme, and fibroblastic connective tissue); 4 – epigenesis of osteogenic tissue, when all types of tissues by direct metaplasia and atypical enchondral ossification and osteoid modification pass into osteoid tissue; 5 – spongiation of osteoid tissue and formation of osteons; 6 – creation of a lamellar bone.

Depending on the nature of the load changes the nature of bone formation: desmal, chondral and angiogenic. In the first two variants, provisional tissues (precursor tissue) are formed, which later undergoes reorganization into bone tissue, in the third type, newly formed bone tissue is formed directly around the vessels. Thus, it is possible to fix the absence of a single, generally accepted point of view on the transformation of tissues formed in the process of healing of bone fractures and provide recovery of the defect.

It remains relevant to assume that in the regeneration of bone tissue in addition to heterogeneous cell sources of different localization and origin, which have different potentials for differentiation and osteogenic capabilities, involved elements of the blood clot – fibrocytes, platelets, histiocytes, fat cells, pericytes, pericytes myeloid series, endotheliocytes.

Terminologically correct it is considered to speak about PRP at concentration of thrombocytes from 700 thousand to 1 million in 1 μ l of plasma, and at the minimum content in it of erythrocytes. In addition, several other necessary conditions must be met. This is the sterility of the material and morphologically complete platelets. The relationship between the clinical properties of PRP with the content of a large number of platelets in it is confirmed in many studies. Their high concentration in the wound provides a large number of growth factors and is a necessary condition for both effective hemostasis and for a favorable course of the wound healing process.

Modern methods of obtaining PRP are quite perfect, they allow you to quickly get the required amount of material directly in the operating room. Numerous positive properties of PRP include: stimulation of fibroblast and osteoblast migration, acceleration of revascularization and regeneration of mesenchymal tissues, reduction of bleeding and reduction of bacterial contamination. The use of PRP can reduce the time of growth and maturation of bone tissue.

As a result of our clinical observation, we obtained the following results. In group I after vertebroplasty, all patients from the first days noted a regression of pain (compared to baseline), which continued. However, in patients with type A1 fractures and localization in the transition zone (Th-L) in the long term there was a greater increase in the deformation of the "cemented" vertebrae, and therefore, the regression of pain was less pronounced.

In group II, in most patients, back pain significantly regressed, which allowed patients to return to normal physical activity. At X-ray control after operation we focused on an estimation of stability of fixing of the damaged part of spine by a metalwork and definition of sizes of correction of kyphotic deformation of bodies of vertebrae reached during operation.

In the long term after surgery in patients of groups I and II there were a slight loss of correction of kyphotic deformity, which did not depend on the type of fracture, and was largely determined by the type of surgery. Thus, in the combination of spondylosynthesis and vertebroplasty, the increase in deformation in the long term were almost absent, in contrast to patients with prolonged osteosynthesis, where wedge-shaped and kyphosis in the long term were significantly worse due to prolonged resorption of bone marrow tissue.

The main loss of the achieved deformation correction after prolonged osteosynthesis of the spine, as in vertebroplasty, were observed in fractures in the transition zone (Th-L). After the combined fixation of significant differences between fractures at different levels were not observed, which suggests the use of a combination of spondylosynthesis with vertebroplasty in the localization of fractures in this area.

When assessing the quality of life in all groups of patients after surgery, there were an increase in self-esteem for all components, most pronounced in the increased parameters of mobility (movement in space) and a decrease in pain and discomfort.

In the process of surgical treatment of patients with pathological vertebral fractures on the background of osteoporosis, we identified 3 groups of complications. The first group includes complications that occurred in the early postoperative period and are associated with the healing process of the postoperative wound. These complications occurred in one patient

from the first and one patient from the second group after a long spinal spondylosynthesis and were stopped by conservative measures.

The release of bone cement into the lumen of the spinal canal, which required revision surgery, occurred in only one patient after vertebroplasty in the first group. After removal of the cement there was a regression of neurological symptoms with the restoration of strength and sensitivity in the lower extremities.

In the third group, we identified complications associated with the development of instability of fixation and the emergence of migration of the metalwork.

Among patients with prolonged transpedicular fixation of the spine in 2 and 3 patients of the first and second groups (4 and 6%) in the early postoperative period and in 2 patients of the first group (4%) – in the late postoperative period, developed instability of osteosynthesis with screw dislocation in the vertebrae, which required repeated operations with additional strengthening of transpedicular screws in the vertebral bodies with bone cement.

At the combined plasticity with fixation of vertebrae by bone cement only at one patient (2%) of the first group in the remote period migration of a metalwork was noted. The complication was due to insufficient introduction of cement around the installed screws in an extrapedicular way without the formation of a full-fledged cement "mantle".

Good treatment results (complete or significant relief of pain, correction of spinal deformity and restoration of its viability, significant improvement of quality of life, absence of clinical and radiological signs of instability and migration of metalwork) were achieved in 10 and 14 patients (50 and 70%) of the first and second groups respectively.

Satisfactory treatment outcome (moderate pain, preservation of spinal support function, slight increase in deformation of the damaged spine in the long term after surgery, no signs of migration of the metalwork) were observed in 5 and 6 patients (25 and 30%) of the first and second groups, respectively.

Unsatisfactory result (increase in vertebrogenic pain syndrome, progression of deformity of the damaged part, impaired spinal support, low level of physical activity and quality of life after surgery, the phenomenon of instability of fixation and displacement of metalwork) were noted in 5 patients (25%) of the first group. The main reasons for the unsatisfactory results of treatment were the following complications: the release of cement into the lumen of the spinal canal, the instability of osteosynthesis of the spine with the migration of structures against the background of severe progressive osteoporosis.

Conclusion. Based on the results of the study, we developed an algorithm for surgical treatment of patients with pathological vertebral fractures on the background of osteoporosis.

The choice of surgical treatment depends on: type of fracture, level of damage, the degree of loss of bone mineral density, the degree of spinal deformity, the general somatic condition of the patient, the presence of spinal stenosis and signs of neurological deficit, pain.

The introduction of platelet-rich plasma into the bone wound reduces the duration of the healing process, in our opinion, by eliminating the inflammatory phase, low intensification of the phase of formation of tissue-specific elements, which are present in large numbers in platelet growth factors. In order to accelerate the recovery of damaged bone, we used PRP in addition to standard therapy and found its positive effect in compression fractures of the vertebral bodies of the thoracic and lumbar localization on the background of postmenopausal and senile osteoporosis, which justifies its further use in clinical practice.

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