Wiadomości Lekarskie

Publisher:
ALUNA Publishing
ul. Przesmyckiego 29, 05-510 Konstancin – Jeziorna
www.aluna.waw.pl www.wiadomoscilekarskie.pl
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PRACA ORYGINALNA
ORIGINAL ARTICLE

MORPHOLOGICAL DYNAMICS OF BONE TISSUE REPARATIVE REGENERATION DURING THE IMPLANTATION OF BIOCOMPOSITE "SYNTEKOST" INTO THE CAVITY OF THE TRAUMATIC DEFECT OF THE ILIAC CREST OF A RABBIT IN THE EXPERIMENT

MORFOLOGICZNA DYNAMIKA REGENERACJI NAPRAWCZEJ TKANKI KOSTNEJ PO IMPLANTACJI BIOKOMPOZYTU "SYNTEKOST" W MIEJSCE POURAZOWEGO UBYTKU GRZEBIENIA BIODROWEGO W MODELU EKSPERYMENTALNYM U KRÓLIKA

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ABSTRACT

Introduction: The problem of bone tissue regeneration and the development of the methods of directional influence on bone healing processes are one of the most urgent problems of modern medicine. The question of bone tissue posttraumatic regeneration is particularly important with regard to military conflicts, ecological and technological disasters, and has social and economic relevance, connected with the necessity of long-term treatment and medical rehabilitation.

The aim: The objective of the work is the experimental evaluation of bone tissue reparative regeneration during the implantation of biocomposite "Syntekost" (patent for invention №98573 dated 25.05.2012 Ukraine), and also dynamics determination of bone tissue reparative regeneration after its application during a year.

Materials and methods: The experiment was carried out on 24 rabbits. All the rabbits were divided into three groups. Penetrating bone damages on the edge of the proximal tibial metaphysis and diaphysis with the diameter of 2,2 mm were formed in the rabbits of the first group using intravenous anesthetic and the dynamics of the reparative regeneration of bone tissue of the iliac crest was studied in 6, 9 and 12 months, without using composite "Syntekost" (control group – 8 rabbits). Penetrating bone damages on the edge of the proximal tibial metaphysis and diaphysis with the diameter of 2,2 mm were formed in the rabbits of the second group and biocomposite "Syntekost" was implantated into them (8 rabbits). Penetrating bone damages on the edge of the proximal tibial metaphysis and diaphysis with the diameter of 2,2 mm were formed in the rabbits of the third group and biocomposite "Syntekost" was implantated into them together with blood plasma and ossein-hydroxyapatite (8 rabbits).

Results: In all stages the research showed the significantly higher percentage of splenial bone tissue both in the rabbits that had biocomposite "Syntekost" implanted without blood plasma and ossein-hydroxyapatite and in the rabbits that had biocomposite "Syntekost" implanted with blood plasma and ossein-hydroxyapatite in comparison with the one of the rabbits that didn't have biocomposite "Syntekost" implanted after having been injured ($p < 0,05$). In all stages of the research the rabbits that had biocomposite "Biokost" implanted together with blood plasma and ossein-hydroxyapatite had the significantly higher percentage of neogenic splenial bone tissue and the significantly lower percentage of biocomposite "Syntekost" comparing to the ones of the rabbits that had biocomposite "Syntekost" implanted without blood plasma and ossein-hydroxyapatite ($p < 0,05$).

Conclusions: The application of blood plasma and ossein-hydroxyapatite accelerates bone tissue regeneration and the process of biodegradation of biocomposite "Syntekost" throughout the experiment. In all stages of the experiment no toxic influence of biocomposite "Syntekost" on the surrounding bone tissue was found.

KEY WORDS: biocomposite "Syntekost", posttraumatic regeneration of bone tissue, ossein-hydroxyapatite, osteogenesis, iliac bone, biodegradation

Wiad Lek 2018, 71, 7, 1281-1288

INTRODUCTION

The problem of bone tissue regeneration and the development of the methods of directional influence on bone healing processes are one of the most urgent problems of modern medicine. The question of posttraumatic regeneration of bone tissue is particularly important with regard to military conflicts, ecological and technological disasters, and has social and economic relevance, connected with the necessity of long-term treatment and medical rehabilitation [1]. The usage of biomaterials for the production of bone tissue substitutes is of a particular importance for bone tissue posttraumatic regeneration. Biomaterials, used for transplantation, must meet chemical, mechanical and biological characteristics of bone tissue [2-5]. Chemical criteria require absence of undesirable chemical reaction with tissues and corrosion [6-8]. Mechanical characteris-

tics of bioceramics must be close to the ones of the bone. Biological criteria require absence of the organism's immune system's reaction, existence of through pores with the diameter of 100-150 μm for bone tissue to extend into the transplant and for the stimulation of the process of osstification. Some authors used body's response to transplantation as the criterion for their adaptability and divided all the materials into 3 groups [5]: 1) toxic (causing necrosis of surrounding tissues) – the majority of metals; 2) bioinert (nontoxic, but biologically inactive) – ceramic materials based on Al_2O_3 i ZrO_2; 3) bioactive (nontoxic, biologically active, attach to bone tissue) – calcium phosphate, ceramics based on calcium phosphate, bioglass. However, despite the wide variety of materials, most of them do not meet the requirements in chemical, biological, mechanical characteristics [9-11]. Recently, the usage of the composites based on organic matrix and biodegradable hydroxyapatite has become a promising area of the development of bioceramics [12-14] – LLC "Promtekhreserv" (the production of bioactive ceramic composite for bone tissue recovery "Syntekost", Technical Requirements of Ukraine 33.1-31280163-001 : 2005). The structure of biodegradable composites is similar to the structure of bone tissue and during bone tissue regeneration it is a source of mineral and organic matters. When using biodegradable implants, their rapid biodegradation and substitution by bone tissue take place [15-17]. However, despite the significant advances in the development and application of biodegradable composites during bone tissue regeneration, the influence of the internal and external environments on the bone tissue regeneration process remains unknown. Thus, finding optimal materials for the replacement of bone defects is an important medical and social problem and conducting complex experimental and clinical researches is required to solve it.

THE AIM

The objective of the work is the experimental evaluation of the reparative regeneration of bone tissue during the implantation of biocomposite "Syntekost" (patent for invention №98573 dated 25.05.2012 Ukraine), and also dynamics determination of the reparative regeneration of bone tissue after its application during a year.

MATERIALS AND METHODS

The experimental part of the research was carried out on 24 rabbits. All the rabbits were divided into three groups. Penetrating bone damages on the edge of the proximal tibial metaphysis and diaphysis with the diameter of 2,2 mm were formed in the rabbits of the first group using intravenous anesthetic and the dynamics of reparative regeneration of bone tissue of the iliac crest was studied in 6, 9 and 12 months, without using composite "Syntekost" (control group – 8 rabbits). Penetrating bone damages on the edge of the proximal tibial metaphysis and diaphysis with the diameter of 2,2 mm were formed in the rabbits of the second group and biocomposite "Syntekost" was implantated into them (8 rabbits). Penetrating bone damages on the edge of the proximal tibial metaphysis and diaphysis with the diameter of 2,2 mm were formed in the rabbits of the third group and biocomposite "Syntekost" was implantated into them together with blood plasma and ossein-hydroxyapatite (8 rabbits).

The percentage of neogenic compact bone tissue and rough fibrous bone tissue in the rabbits of the control group and the percentage of neogenic compact bone tissue and rough fibrous bone tissue as well as the fragments of biocomposite "Syntekost" in the regeneration focus of the rabbits that had biocomposite "Syntekost" implanted and the rabbits that had biocomposite "Syntekost" implanted together with blood plasma and ossein-hydroxyapatite were ascertained in 6, 9 and 12 months.

Surgical interventions were carried out according to the rules of the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes. To study the histological structure of the regenerate the rabbits had their tibia separated from soft tissues, after that the area intended for damage and implantation of biocomposite "Syntecost" was excised, fixed in a solution of 10% neutral formaldehyde, decalcified with a 5% formic acid solution, dehydrated in alcohols of increasing concentration and embedded in paraffin. Histologic sections, 10-12 μm thick, were prepared, coloured with hematoxylin and eosin and studied with a light microscope. 100 point measuring grid was used for a morphometric research (Avtandilov G.G.). The morphometry programme included determinations of the relative amount of bone lamellae in the implant, rough fibrous bone tissue area, as well as the area with implant fragments. The research protocol envisaged the complete examination programme directly in the postsurgical period, as well as in 6, 9 and 12 months after performing the operation.

RESULTS AND DISCUSSIONS

Immature rough fibrous bone tissue and bone lamellae, disposed in the form of cords, which formed wide loop-shaped reticulum were identified by microscopy of the histological sections of the control group rabbits' iliac crest in the area of regeneration in 6 months after causing damage. Neogenic splenial bone tissue is more pronounced in the peripheral zones of the focus of damage on the border with undamaged bone, whereas rough fibrous bone tissue fragments are located in the central zone of the regeneration focus. The structure of the bone tissue of the iliac crest of the rabbits of the control group beyond the regeneration zone was similar to the structure of the one of the intact rabbits, focuses of destruction or resorption were not discovered (pic. 3.1). The morphometric analyses showed that bone lamellae amounted to 41,4±0,9%, neogenic splenial bone tissue 58,2±0,9; (table I).

Bone lamellae, fragments of rough fibrous bone tissue and fragments of the mineral component of the biocomposite were detected by microscopy of the histological

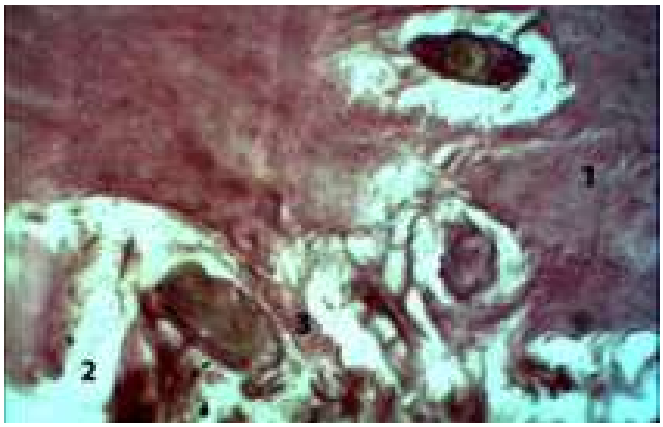

Fig. 1. The histological structure of the neogenic bone tissue and the transplant by the implantation of biocomposite "Syntekost" into the bone tissue of the iliac crest of a rabbit without adding blood plasma and ossein-hydroxyapatite in a 6-month period. Hematoxylin-eosin, ob. 10., oc. 10. Keys: 1 – bone lamae; 2 – fragments of bioceramics; 3 – rough fibrous bone tissue.

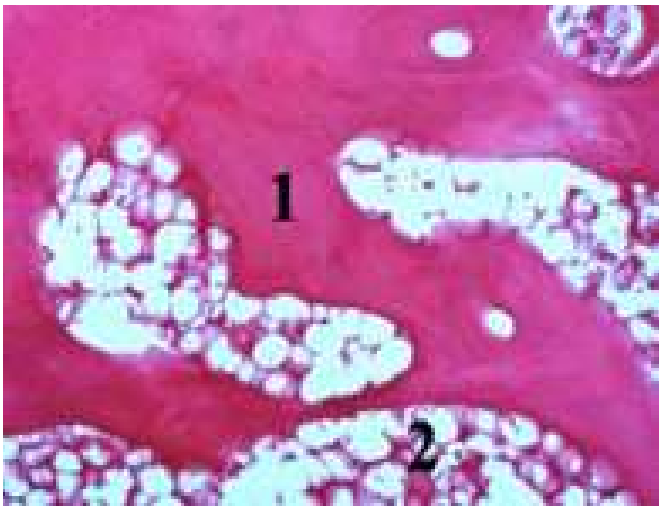

Fig. 2. The bone tissue of the iliac crest of an intact rabbit: 1 – bone trabecules; 2 – red marrow. Hematoxylin-eosin, ob. 10., oc. 10.

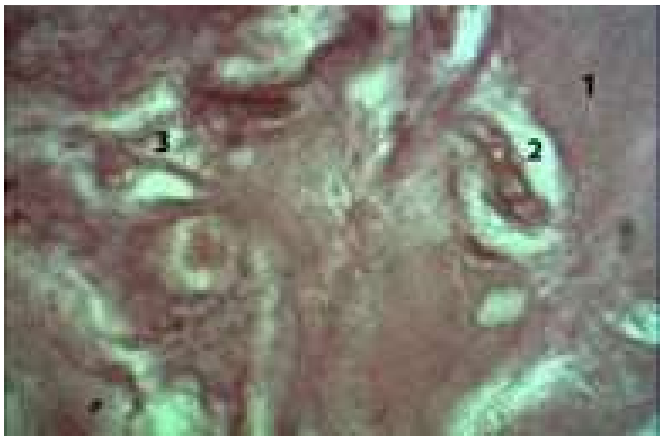

Fig. 3. The histological structure of the neogenic bone tissue and the transplant by the implantation of biocomposite "Syntekost" into the bone tissue of the iliac crest of a rabbit with blood plasma and ossein-hydroxyapatite in a 6-month period. Hematoxylin-eosin, ob. 10., oc. 10. Keys: 1 – bone trabecules; 2 – fragments of bioceramics; 3 – rough fibrous bone tissue.

Fig. 4. The bone tissue of the iliac crest of the rabbits beyond the implantation zone in 6 months after the implantation of biocomposite "Syntekost" with the addition of blood plasma and ossein-hydroxyapatite into the iliac crest of a rabbit. Hematoxylin-eosin, ob. 10., oc. 10. Keys: 1 – bone lamae; 2 – red marrow; 3 – yellow marrow.

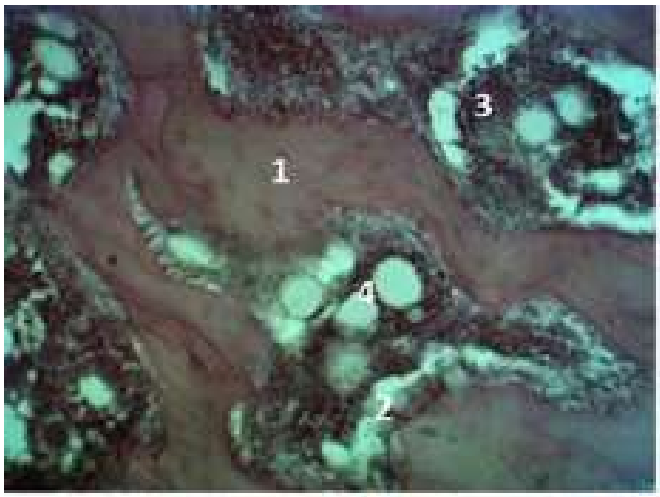

Fig. 5. The bone tissue of the rabbits' iliac crest beyond the implantation zone in 9 months after the implantation of biocomposite "Syntekost" into the bone tissue of the iliac crest with blood plasma and ossein-hydroxyapatite. Hematoxylin-eosin, ob. 10., oc. 10. Keys: 1 – bone lamae; 2 – fragments of bioceramics; 3 – red marrow; 4 – yellow marrow.

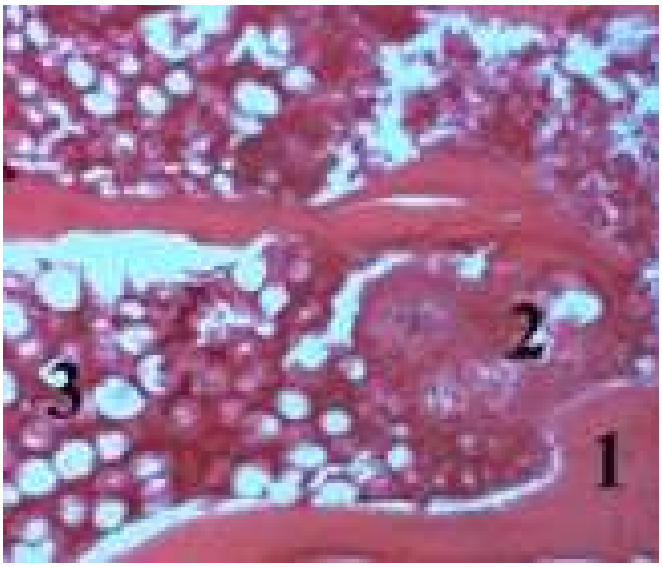

Fig. 6. Bone tissue of the animals of the control group, 9-month period: 1 – bone trabecules; 2 – rough fibrous bone tissue; 3 – red marrow. Hematoxylin-eosin, ob. 10., oc. 10.

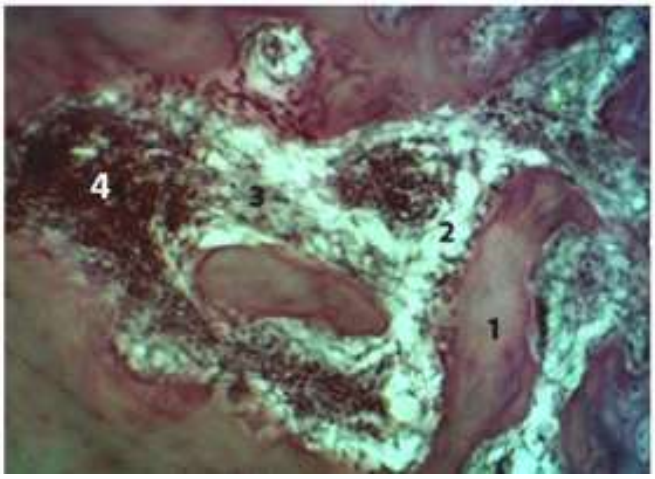

Fig. 7. The histological structure of the neogenic bone tissue and the transplant by the implantation of biocomposite "Syntekost" into the bone tissue of the iliac crest of a rabbit without adding blood plasma and ossein-hydroxyapatite in 9 months. Hematoxylin-eosin, ob. 10., oc. 10. Keys: 1 – bone lamae; 2 – blood vessels; 3 – rough fibrous bone tissue; 4 – red marrow.

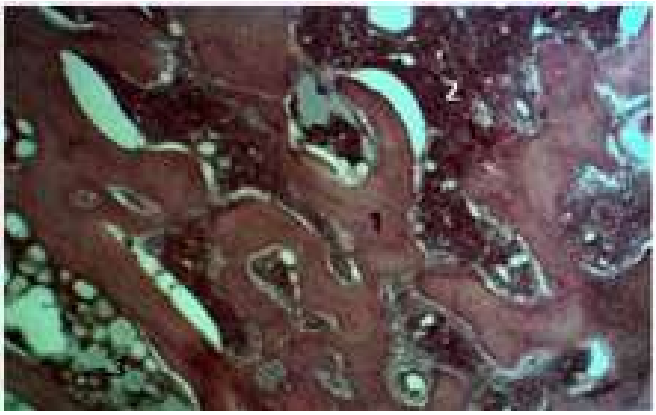

Fig. 9. The histological structure of the neogenic bone tissue and the transplant after the implantation of biocomposite "Syntekost" into the bone tissue of the iliac crest of a rabbit without adding blood plasma and ossein-hydroxyapatite in 12 months. Hematoxylin-eosin, ob. 10., oc. 10. Keys: 1 – bone lamae; 2 – red marrow; 3 – yellow marrow.

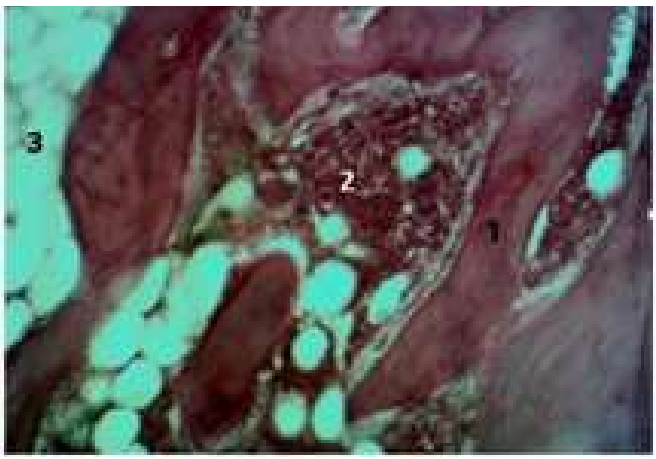

Fig. 11. The histological structure of the neogenic bone tissue and the transplant after the implantation of biocomposite "Syntekost" into the bone tissue of the iliac crest of a rabbit with blood plasma and ossein-hydroxyapatite in 12 months. Hematoxylin-eosin, ob. 10., oc. 10. Keys: 1 – bone lamae; 2 – red marrow; 3 – yellow marrow.

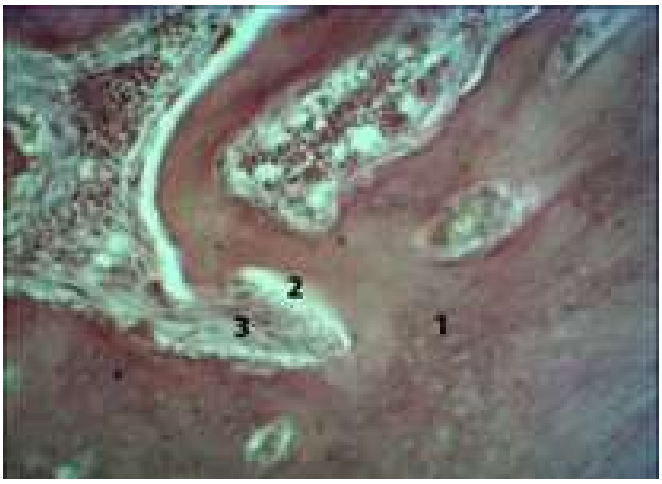

Fig. 8. The histological structure of the neogenic bone tissue and the transplant by the implantation of biocomposite "Syntekost" into the bone tissue of the iliac crest of a rabbit with blood plasma and ossein-hydroxyapatite in 9 months. Hematoxylin-eosin, ob. 10., oc. 10. Keys: 1 – bone lamae; 2 – fragments of bioceramics; 3 – rough fibrous bone tissue.

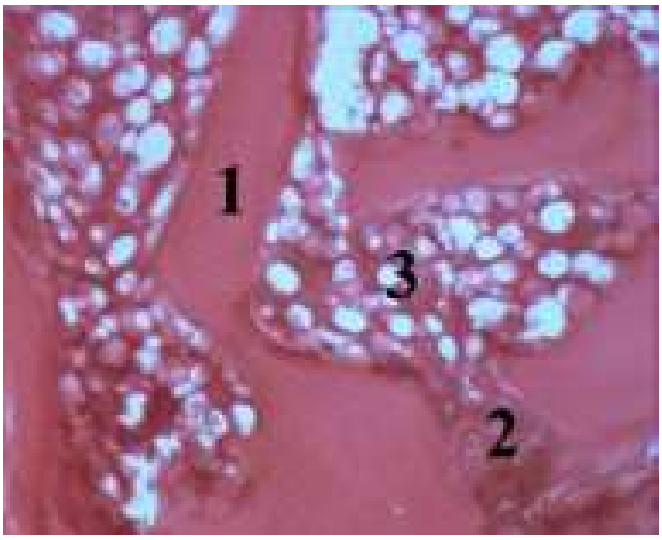

Fig. 10. Bone tissue of the animals of the control group, 12-month period: 1 – bone trabecules; 2 – rough fibrous bone tissue; 3 – red marrow. Hematoxylin-eosin, ob. 10., oc. 10.

sections of the transplants of biocomposite "Syntekost" in the rabbits of the second group in 6 months. The fragments of the mineral component of the biocomposite can be seen in the form of cavities between bone lamellae and rough fibrous bone tissue after decalcification. Neogenic blood vessels ingrow deeply from the bone tissue of the iliac crest into the transplant, which points at the active process of bone tissue regeneration, which is closely connected with vascularization. Neogenic bone tissue is located in all parts of the ceramic implant, however, splenial bone tissue is more pronounced in its peripheral sections, whereas the fragments of rough fibrous bone tissue are more pronounced in the areas of the transplant, which are farther from the border between biocomposite "Syntekost" and iliac crest bone tissue. Neogenic bone

Table I. The percentage of bone lamellae and rough fibrous bone tissue in the rabbits of the control group and also the content of bone lamellae, rough fibrous bone tissue and the remains of the ceramic material in the rabbits that had biocomposite "Syntekost" implanted and in the rabbits that had biocomposite "Syntekost" implanted together with blood plasma and ossein-hydroxyapatite within the period of 6 months (M ±m).

Animal groups	Content,%		
	Bone trabecules	Rough fibrous bone tissue	The remains of the ceramic material
Group 1. The control group without the implantation of biocomposite "Syntekost"	41,4 ± 0,9	50, 2 ± 1,1	0
Group 2. The implantation of biocomposite "Syntekost" without blood plasma and ossein-hydroxyapatite	45,4 ± 0,7	50,7 ± 0,8	3,2 ± 0,2
Group 3. The implantation of biocomposite "Syntekost" with blood plasma and ossein-hydroxyapatite	46,1 ± 0,3	50,5 ± 0,8	3,2 ± 0,2

lamellae are closely connected with the ceramic matrix of biocomposite "Syntekost", which points at the high rate of biocompatibility of the transplant. The morphometric analyses showed that neogenic bone lamellae amounted to 41,4 ± 0,90%. Cavities, corresponding to the fragments of the bioceramics, were detected between the neogenic bone lamellae. The fragments of the bioceramics amounted to 3,5 ± 0,4%, and were surrounded by rough fibrous bone tissue ± 1,1% correspondingly. Thus, in 6 months neogenic splenial bone was located at the periphery of the transplant, whereas rough fibrous bone tissue was in the centre of the implanted material. We also noted the complete conglutination of biocomposite "Syntekost" without adding blood plasma and ossein-hydroxyapatite with the bone tissue of the iliac crest. The bone structure of the iliac crest beyond the implantation zone is similar to the bone structure of the iliac crest of the intact rabbits, the areas of its destruction and resorption were not detected, which points at the absence of signs of toxicity of biocomposite "Syntekost".

In 6 months rabbits of the 3 group, which had biocomposite "Syntekost" implanted into the cavity of the defect of the iliac crest bone tissue together with blood plasma and ossein-hydroxyapatite, had neogenic splenial bone tissue and rough fibrous bone tissue located irregularly all over the implanted material. Bone lamellae, disposed in the form of cords, ingrew into biocomposite "Syntekost" from the bone tissue of the iliac crest and formed a wide loop-like net on the border between the defect and undamaged bone, whereas rough fibrous bone tissue is located in the centre (pic. 3.3). The structure of the bone tissue of the iliac crest beyond the implantation zone was similar to the structure of the bone tissue of the intact rabbits' iliac. Bone lamellae formed a wide loop-like net, in the meshes of which red and yellow marrows were located. Dystrophic changes of the bone tissue, the formation of a connective tissue capsule around the transplant, inflammatory reaction or reject phenomena were not observed in the implantation zone.

The morphometric analyses of the regeneration focus of the control group rabbits and of the rabbits of the second and the third groups showed a higher percentage of bone lamellae in the rabbits of the second and third groups, which had biocomposite "Syntekost" implanted.

By morphometric analyses of the transplant of biocomposite "Syntekost" with the addition of blood plasma and ossein-hydroxyapatite as the osteogenesis stimulant, the significantly higher percentage of bone lamellae was determined in these samples in a 6-month period, while the percentage of rough fibrous bone tissue was significantly lower than in the rabbits that had the transplant of biocomposite "Syntekost" implanted without blood plasma and ossein-hydroxyapatite. The percentage of bioceramics' fragments in these samples was significantly lower than in the rabbits that had the transplant of biocomposite "Syntekost" implanted without blood plasma and ossein-hydroxyapatite.

Thus, in 6 months the significantly higher percentage of splenial bone tissue was discovered both in the rabbits that had biocomposite "Syntekost" implanted without blood plasma and ossein-hydroxyapatite and the rabbits that had biocomposite "Syntekost" implanted with blood plasma and ossein-hydroxyapatite in comparison with the one of the rabbits that didn't have biocomposite "Syntekost" implanted after having been injured. In 6 months the rabbits that had biocomposite "Syntekost" implanted with blood plasma and ossein-hydroxyapatite as the osteogenesis stimulant had the significantly higher percentage of neogenic splenial bone tissue in comparison with the one of the rabbits that had biocomposite "Syntekost" implanted without blood plasma and ossein-hydroxyapatite and the significantly lower percentage of biocomposite "Syntekost" comparing to the one of the rabbits that had biocomposite "Syntekost" implanted without blood plasma and ossein-hydroxyapatite, ($p < 0,05$). This proves the stimulant effect of the components of blood plasma and ossein-hydroxyapatite on the bone tissue regeneration and also on the process of biodegradation of biocomposite "Syntekost" in 6 months. In 6 months together with the active osteogenesis a significant decrease of the amount of biocomposite "Syntekost" – from 100% to 3,2% ($p < 0,05$) – takes place in the implant.

In 9 months neogenic splenial bone tissue and rough fibrous bone tissue of the rabbits of the control group were located regularly all over the defect zone. The neogenic lamellae were closely connected with the splenial bone tissue

Table. II. The percentage of bone lamellae and rough fibrous bone tissue in the rabbits of the control group and also the content of bone lamellae, rough fibrous bone tissue and the remains of the ceramic material in the rabbits that had biocomposite "Syntekost" implanted and in the rabbits that had biocomposite "Syntekost" implanted together with blood plasma and ossein-hydroxyapatite within the period of 9 months (M ±m).

Animal groups	Content,%		
	Bone trabecules	Rough fibrous bone tissue	The remains of the ceramic material
Group 1. The control group without the implantation of biocomposite "Syntekost"	78,7±1	21,3±0,6	0
Group 2. The implantation of biocomposite "Syntekost" without blood plasma and ossein-hydroxyapatite	82,5±1,1 (p <0,05)	18,1±0,6	0,43±00,2
Group 3. The implantation of biocomposite "Syntekost" with blood plasma and ossein-hydroxyapatite	88,7±0,7 (p <0,05)	9,8±0,5	0,25±0,07

of the iliac crest. As in the previous stage of the research dystrophic changes of the bone tissue of the iliac crest, the formation of a connective tissue capsule around the regeneration focus of the bone tissue, inflammatory reaction were not observed beyond the defect zone. The structure of the bone tissue of the iliac crest beyond the defect zone was similar to the one of the intact rabbits (pic. 3.5).

Thus, in 9 months both the rabbits of the second group that had biocomposite "Syntekost" implanted without blood plasma and ossein-hydroxyapatite after having been injured and the rabbits that had biocomposite "Syntekost" implanted with blood plasma and ossein-hydroxyapatite had neogenic splenial bone tissue and rough fibrous bone tissue located evenly all over the implanted material, their complete conglutination with the bone tissue of the iliac crest took place as well. As in the previous stage of the research the bone tissue dystrophic changes, the formation of a connective tissue capsule around the transplant, inflammatory reaction or reject phenomena were not observed in the implantation zone of any rabbit.

Thus, in 9 months the significantly higher percentage of splenial bone tissue was discovered both in the rabbits that had biocomposite "Syntekost" implanted without blood plasma and ossein-hydroxyapatite and the rabbits that had biocomposite "Syntekost" implanted with blood plasma and ossein-hydroxyapatite in comparison with the one of the rabbits of the control group that didn't have biocomposite "Syntekost" implanted after having been injured. (Table II.).

In 9 months both the rabbits of the second group that had biocomposite "Syntekost" implanted without blood plasma and ossein-hydroxyapatite and the rabbits of the third group that had biocomposite "Syntekost" implanted with blood plasma and ossein-hydroxyapatite had the significantly higher percentage of neogenic bone lamellae in comparison with the one in the previous stage of the research ($p < 0,05$). As in the previous stage of the research the neogenic bone lamellae are closely connected with the ceramic matrix of biocomposite "Syntekost", which points at the high rate of biocompatibility of the transplant.

In 9 months both the rabbits of the second group that had biocomposite "Syntekost" implanted without blood plasma and ossein-hydroxyapatite and the rabbits of the third group that had biocomposite "Syntekost" implanted with blood plasma and ossein-hydroxyapatite had the significantly lower percentage of rough fibrous bone tissue and biocomposite "Syntekost" fragments in comparison with the one in the previous stage of the observation. (Table II)

In 12 months there was the significantly higher percentage of bone lamellae in biocomposite "Syntekost" without blood plasma and ossein-hydroxyapatite and in biocomposite "Syntekost" with blood plasma and ossein-hydroxyapatite in the implantation zone comparing to the one in the previous stages of the research (pic. 3.8.) The bioceramics remains were not discovered. (Table III).

In 12 months the control group rabbits' neogenic splenial bone tissue and rough fibrous bone tissue were located evenly. Like in the previous stages of the research they were closely connected with the bone tissue of the iliac crest. Dystrophic changes of the bone tissue of the iliac crest, the formation of a connective tissue capsule around the bone tissue regeneration focus, inflammatory reaction were not observed beyond the defect zone. The structure of the bone tissue of the iliac crest beyond the defect zone was similar to the one of the intact rabbits, focuses of destruction or resorption were not discovered, bone lamellae formed a wide loop-like net, in the meshes of which red and yellow marrows were located (pic. 3). Dystrophic changes of the bone tissue were not discovered beyond the regeneration centre. The formation of a connective tissue capsule around the transplant and inflammatory reaction were not observed too.

In 12 months both the rabbits of the second group that had biocomposite "Syntekost" implanted without blood plasma and ossein-hydroxyapatite 92,5±0,7% and the rabbits of the third group that had biocomposite "Syntekost" implanted with blood plasma and ossein-hydroxyapatite 98,7±0,4% had the significantly higher percentage of splenial bone tissue in comparison with the one of the rabbits that didn't have biocomposite "Syntekost" implanted 91,1± 0,5. In 12 months the rabbits that had biocomposite "Syntekost" implanted with blood plasma and ossein-hydroxyapatite as the osteogenesis stimulant had the significantly higher percentage of neogenic splenial bone tissue in comparison with the one of the rabbits that had biocomposite "Syntekost" implanted

Табл.III. The percentage of bone lamellae and rough fibrous bone tissue in the rabbits of the control group and also the content of bone lamellae, rough fibrous bone tissue and the remains of the ceramic material in the rabbits that had biocomposite "Syntekost" implanted and in the rabbits that had biocomposite "Syntekost" implanted together with blood plasma and ossein-hydroxyapatite within the period of 12 months (M ±m).

Animal groups	Content,%		
	Bone trabecules	Rough fibrous bone tissue	The remains of the ceramic material
Group 1. The control group without the implantation of biocomposite "Syntekost"	91,1± 0,5	8,6±0,9	0
Group 2. The implantation of biocomposite "Syntekost" without blood plasma and ossein-hydroxyapatite	92,5±0,7	7,3±0,8	0
Group 3. The implantation of biocomposite "Syntekost" with blood plasma and ossein-hydroxyapatite	98,7±0,4	1,4±0,2	0

without blood plasma and ossein-hydroxyapatite and the significantly lower percentage of biocomposite "Syntekost" comparing to the one of the rabbits that had biocomposite "Syntekost" implanted without blood plasma and ossein-hydroxyapatite. ($p < 0,05$).

In 12 months both the rabbits that had biocomposite "Syntekost" implanted without blood plasma and ossein-hydroxyapatite and the rabbits that had biocomposite "Syntekost" implanted with blood plasma and ossein-hydroxyapatite had the significantly higher percentage of neogenic bone lamellae in comparison with the one in the previous stage of the observation. ($p < 0,05$).(Table. III).

The percentage of rough fibrous bone tissue is significantly lower in comparison with the one in the previous stage of the research 7,3±0,8%; and 1,4±0,2% correspondingly. The remains of bioceramics were not detected.

The structure of the bone tissue of the iliac crest beyond the regeneration zone was similar to the one of the intact rabbits, focuses of destruction or resorption were not discovered, bone lamellae formed a wide loop-like net. Red and yellow marrows were located in its meshes (pic. 3.). Dystrophic changes of the bone tissue were not discovered beyond the regeneration centre. The formation of a connective tissue capsule around the regeneration centre and inflammatory reaction were not observed too. (pic.3.7.).

In 12 months the rabbits that had biocomposite "Syntekost" implanted without the addition of blood plasma and ossein-hydroxyapatite and the rabbits that had biocomposite "Syntekost" implanted with the addition of blood plasma and ossein-hydroxyapatite had splenial bone tissue located evenly with small zones of rough fibrous bone tissue in the areas that are distant from the edge of the biocomposite and the iliac crest splenial bone tissue. The structure of the bone tissue of the iliac crest beyond the implantation zone was similar to the splenial bone tissue of the iliac crest of the intact rabbits. Bone lamellae formed a wide loop-like net, in the meshes of which red and yellow marrows were located. The structure of the red and yellow marrows was similar to the one of the intact rabbits.

In 12 months the splenial bone tissue and the rough fibrous bone tissue of the rabbits that had biocomposite "Syntekost" implanted without blood plasma and the rabbits that had biocomposite "Syntekost" implanted with blood plasma and ossein-hydroxyapatite replaced the implanted biocomposite "Syntekost" completely. Like in the previous stages of the research dystrophic changes of the bone tissue and the rejection of biocomposite "Syntekost" were not observed.

Wilcoxon signed-rank test was used to evaluate the reliability of the difference in dynamics values. Values were considered reliable when ($p < 0,05$).

CONCLUSIONS

1. The significantly larger amount of biocomposite "Syntekost" is replaced by splenial bone tissue in the rabbits that had biocomposite "Syntekost" implanted with blood plasma and ossein-hydroxyapatite as the osteogenesis stimulant in comparison with the one of the rabbits that had biocomposite "Syntekost" implanted without blood plasma and ossein-hydroxyapatite.
2. The application of blood plasma and ossein-hydroxyapatite accelerates bone tissue regeneration and the biodegradation process of biocomposite "Syntekost" throughout the experiment.

In all stages the research showed the significantly higher percentage of splenial bone tissue both of the rabbits that had biocomposite "Syntekost" implanted without blood plasma and ossein-hydroxyapatite and of the rabbits that had biocomposite "Syntekost" implanted with blood plasma and ossein-hydroxyapatite in comparison with the one of the rabbits that didn't have biocomposite "Syntekost" implanted after having been injured ($p < 0,05$). In all stages of the research the rabbits that had biocomposite "Syntekost" implanted together with blood plasma and ossein-hydroxyapatite had the significantly higher percentage of neogenic splenial bone tissue and the significantly lower percentage of biocomposite "Syntekost" comparing to the ones of the rabbits that had biocomposite "Syntekost" implanted without blood plasma and ossein-hydroxyapatite ($p < 0,05$).

3. The application of biocomposite "Syntekost" with blood plasma and ossein-hydroxyapatite has no toxic influence on the surrounding bone tissues.

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Authors' contributions:
According to the order of the Authorship

Conflict of interest:
The Authors declare no conflict of interest

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Received: 15.07.2018
Accepted: 04.10.2018