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Results of using various types of implants in experimental management of long bone osteomyelitic defects

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Relevance Chronic osteomyelitis makes about 10 to 25 % in the structure of locomotion system diseases. Moreover, osteomyelitis recurs in 20 to 30 % of the affected patients and results in secondary amputations and limb functional deficiency in 10.3 to 57 % of them. Management of secondary cavities and defects under such conditions is a challenge that does not have a uniform solution to date. Nano-composite carbon materials combine sufficient strength with possible biological integration and seem to be promising materials for filling bone defects of osteomyelitic origin. **Purpose** To study experimentally the results of using a nano-composite carbon-based material and compare it with allologous bone and porous ceramic implants for filling osteomyelitic long bone defects. **Materials and method** Experimental studies were performed on 20 normal rabbits. One cortical layer of the anterior shaft surface of their left radius was perforated by drilling. St. Aureus suspension of 0.5 ml in the concentration of 10–5 CFU/ml was injected into the medullary canal. The events of a local inflammatory reaction such as swelling, local hyperemia, temperature elevation, fistula formation were observed by day 7 in all the animals. Necrosequestrectomy was performed two weeks later. A standard defect of 0.5-cm was filled in with three different materials. A carbon nanostructured implant, a ceramic implant and allogenic bone bio-implant were used. **Results** X-ray and biomechanical studies during the experiment found that the use of the carbon implant for filling osteomyelitic defects provided optimization of bone tissue regeneration as compared with the use of allogenic bone and ceramic implants. Complete consolidation and formation of a block at the implant to bone border occurred by the end of week 4. Radiographic borders between the bone and the nano-carbon implant disappeared by week 6. The results of the biomechanical study revealed the comparable parameters of the breaking force in Group 1 and the control group of normal animals but a significant reduction in breaking force in Groups 2 and 3. **Conclusion** The use of nano-structured carbon material for filling osteomyelitic defects accelerated regenerated bone formation and provided positive osseointegration at the bone-to-implant border when compared with the other bone-substitute materials studied.
Keywords Chronic osteomyelitis, defect, nano-structured carbon implant, long bone, filling, substitution

INTRODUCTION

Chronic osteomyelitis makes up about 10 to 25 % in the structure of the diseases of the locomotion system [6, 7]. Moreover, osteomyelitis recurs in 20 to 30 % of the affected patients and results in secondary amputations and limb functional deficiency in 10.3 to 57 % of them [1, 18]. Secondary changes that are conditioned by a severe inflammatory process lead to serious disorders in the bone tissue structure and regenerative abilities [5, 8, 11]. Management of secondary cavities and defects in such conditions is challenging. The problem has not been solved yet [6, 11]. An important element of surgical treatment in chronic osteomyelitis is debridement of cavities and management of the defects that are formed due to the pathological process and surgical treatment [3, 13, 15]. Along with the classical method of bone regenerate formation with the Ilizarov distraction osteosynthesis, variants of bone defect management with allogenic bone or materials that possess an osteoconductiove potential that are based on calcium sulfate, hydrohyapatite, tri-calcium phosphate and some others have been under investigation [6, 14, 16, 17]. However, their insufficient mechanical strength requires prolonged immobilization. Porous metals such as nitinol and tantalum or implants on a coral base have a high degree of resistance to mechanical loads [3]. Nevertheless, their use results in problems of osteointegration with the surrounding bone tissue. Nano-composite carbon materials combine a sufficient strength with a possible biological integration and are believed to be promising for management of bone defects that are of osteomyelitic origin [9, 19].

Purpose of study was to investigate the results of an experimental use of a nano-composite carbon material for management of osteomyelitic bone defects and compare its results with the results of the use of allogenic bone and porous ceramic implants.

Goals:

1. Develop long bone osteomyelitis in experimental animals and create bone defects.

2. Work out a technology of osteomyelitic bone defect filling by implantation of augments made of a nano-structured carbon material, allogenic bone or porous ceramics.

3. Study the dynamics of bone regenerate formation by clinical examination and radiographic parameters in the implantation area.

4. Conduct a comparative assessment of the mechanical strength of the experimental blocks of the “bone-implant” junction.

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MATERIAL AND METHODS

Experimental study was conducted using 20 healthy rabbits of both sexes that matched in their physical parameters. The experiments conformed to the requirements of animal protection stated in the EU guidelines (86/609/EEC) and Helsinki declaration.

The first stage of the experiment was to model osteomyelitis [2]. A 3-cm skin incision was made on the anteromedial surface of the left forearm in all the animals under intravenous anesthesia after the operation field treatment. One cortical layer of the left radius diaphysis was perforated from the anterior surface. Then, the bone marrow canal was exposed and 0.5 ml of St. aureus suspension was injected into it [6]. The events of a local inflammatory reaction such as swelling, local hyperemia, temperature elevation, sinus formation, and radiographic swelling periostitis were observed by day 7 in all the animals. Necrsequestrectomy was performed two weeks later to get a standard defect that measured 0.5 cm. The rabbits were randomly divided into three groups (5 rabbits in each) to implant a nano-structured carbon implant in group 1, an allogenic bone bioimplant in group 2, and a ceramic implant in group 3. A nano-structured carbon implant (Fig. 1) was used that contains carbon bars connected with a carbon matrix in mutually perpendicular planes and which declared porosity was 15 % and a ceramic implant (**Fig. 2**) that was developed for experiments in the laboratory conditions at Omsk State Classical University. The implant was fabricated by molding and heat treatment according to the technical drawings developed by both participants of the experiment. Also, an allogenic bone bioimplant was used (**Fig. 3**) that was industrially fabricated from a demineralized bone composite. Implants were fixed in the defect area with a circular stitching to the intact ulna. Then, the wound was sutured by layers.

All the animals were administered antibiotic therapy according to microbial culture tests – intramuscular injection of 0.5 g of ceftriaxonum twice a day. Group 4 was a control group of five healthy animals. Additional immobilization of the operated limb was not used. Dressings and antibiotic therapy were performed in the early postoperative period. Limb weight bearing was not limited.

General health of the animals was examined by measuring body temperature, checking food consumption, observing their motor activity recovery and weight bearing, measuring limb volume and comparing it with a healthy limb at the same level for swelling control. Radiographs were taken at two, 4 and 6 weeks after the implantation. Presence of periositis as a manifestation of an inflammatory process, defect size, bone regenerate structure and the condition of the cortical layer and bone marrow canal were checked radiographically.

The animals were withdrawn from the experiment after 6 weeks by an intravenous injection of thiopental sodium in the dose of 200 mg/kg. Then, the strength of bone regenerate that included the augment was tested at the border of the bone-to-implant. Perforation of the bone with two wires above and lower the implantation site was produced and then the wires were fixed in special clamps of the breaking machine R-05 UXL 4.2. Gradual stretching of the macropreparaton along its axis was produced until the bone block broke. The results were bone strength in N/m.

Statistical processing of the results considered the number of examination units, the type of the studied data and study design. Kruskal-Wallis H-criterion for multiple independent samples and the Mann-Whitney U-criterion for matched quantitative independent populations were used for comparison of quantitative findings. In all the statistic tests, the critical p level was acquired with the Bonferroni error ($p < 0.05/n$, where n is a number of paired comparisons). The analysis of the results used the STATISTICA 6.0 software package and Microsoft Office.

Fig. 1 Carbon implant

Fig. 2 Ceramic implant

Fig. 3 Allogenic bone implant

RESULTS

The animals of all the studied groups were atonic in the early postoperative period of two days. They moved little and did not load the operated limb. Food consumption and motor activity recovered by days 3 or 4.

The signs of soft tissue swelling in the operation area were observed in three and 4 animals with ceramic and carbon implants respectively on days 7 to 10. Expressed swelling was seen in six animals of the group with allogenic bone implants. One rabbit had a sinus with a pus discharge.

Statistically significant differences in the parameters studied were obtained by their clinical evaluation with Kruskal-Wallis H-criterion for multiple independent samples (**Table 1**).

Mann-Whitney U-criterion was used for subsequent study according to these results. Thus, weight bearing recovered in group 1 with carbon implants in an earlier term according to the comparison of the clinical parameters in the groups. Normal temperature, wound healing and swelling subsidence also normalized faster in this group. There was no statistical difference in the results between groups 2 and 3 (**Table 2**).

Manifestations of periostitis, sequester formation and bone marrow canal narrowing were absent in the radiographs of group 1 by the end of week 2. There was a moderately marked darkening and signs of bone tissue formation (**Fig. 4**). Manifestations of marked periostitis were still present in the radiographs of the group with allogenic bone implants. Solitary sequesters undergoing formation and thickening of cortical layers were seen in several cases. The borders of the bone defect were clearly distinguished. No signs of bone regeneration were revealed (**Fig. 5**). Periostitis signs, soft tissue swelling, sequester formation and bone marrow canal narrowing were observed in the animals with ceramic implants (**Fig. 6**).

Table 1

Results of animal health condition in the postoperative period

Parameter	Time of recovery (days, Me)			H-criterion of Kruskal – Wallis ($p < 0.017$)
	Carbon implant	Allogenic bone implant	Ceramic implant	
Limb weight bearing	2.0	3.0	3.0	6.48 ($p = 0.04$)
Wound healing	10.5	12	12	4.2 ($p = 0.12$)
Body temperature normalization	13.5	14.5	15	3.64 ($p = 0.16$)
Swelling subsidence	12	14	14.5	7.79 ($p = 0.02$)

Table 2

Mann-Whitney U-criterion values after comparison of clinical results

Groups compared	Mann-Whitney U-criteria values for clinical parameters studied			
	Weight-bearing recovery	Wound healing	Temperature normalization	Swelling subsidence
1-2	4 ($p = 0.02$)	7.5 ($p = 0.09$)	8.5 ($p = 0.13$)	3.5 ($p = 0.02$)
1-3	6 ($p = 0.05$)	7.5 ($p = 0.09$)	8 ($p = 0.11$)	3.5 ($p = 0.02$)
2-3	17 ($p = 0.87$)	17.5 ($p = 0.93$)	15 ($p = 0.63$)	16.5 ($p = 0.81$)

Fig. 4 Radiographs of forearm bones at 2 weeks after implantation of carbon implants

Fig. 5 Radiographs of forearm bones at 2 weeks after implantation of allogenic bone implants

Fig. 6 Radiographs of forearm bones at 2 weeks after implantation of ceramic implants

By the end of week 4, expressed regeneration process and growth of bone tissue around the nano-structured carbon implants were observed in group 1. Manifestations of periostitis were absent (**Fig. 7**). In the same period, remodeling of bone tissue was absent in group 2. The regeneration process was less expressed, signs of periostitis were preserved, sequesters were under formation, thickening of cortical layers and soft tissues swelling were seen (**Fig. 8**). Structural destruction of the ceramic implant associated with the start of axial loading and response to the interaction of the implant with the tissues that were involved into the inflammation process happened in group 3 by week 4. Periostitis signs, soft tissues swelling, sequesters under formation as well as bone marrow canal narrowing were also observed (**Fig. 9**).

By week 6, complete bone tissue regeneration with defect consolidation and viable bone callus formation were revealed in group 1 (**Fig. 10**). Slow regeneration was detected in group 2. The borders of the defect zone remained clear and the allogenic bone implant contrasted within them (**Fig. 11**). The radiographic study in group 3 at this time point of the experiment was not done as the implant had destructed in the earlier period.

Fig. 7 Radiographs of forearm bones at 4 weeks after implantation of a carbon implants

Fig. 8 Radiographs of forearm bones at 4 weeks after implantation of allogenic bone implants

Fig. 9 Radiographs of forearm bones at 4 weeks after implantation of ceramic implants

Fig. 10 Radiographs of forearm bones at 6 weeks after implantation of carbon implants

Fig. 11 Radiographs of forearm bones at 6 weeks after implantation of allogenic bone implants

Upon the withdrawal of the animals from the experiment, the blocks of bone tissue were tested for breakage with the break machine.

The statistical comparison enabled to reveal statistical differences between the groups (H = 15.74658, p = 0.0013). By the subsequent paired comparison of the biomechanical test results in the groups, it was established that the differences revealed were conditioned by the presence of such at the significance level set between the groups 1–3, 1–4, 2–3, 2–4 and that they were statistically significant. Differences between the groups 1–2 and 3–4 were absent (**Table 3, Fig. 12**).

Table 3

Mann-Whitney U-criteria values upon biomechanical study comparison

Groups compared	U	p-level
1-2	11.50	0.841270
1-3	0.00	0.007937
1-4	0.00	0.007937
2-3	0.00	0.007937
2-4	0.00	0.007937
3-4	2.00	0.031746

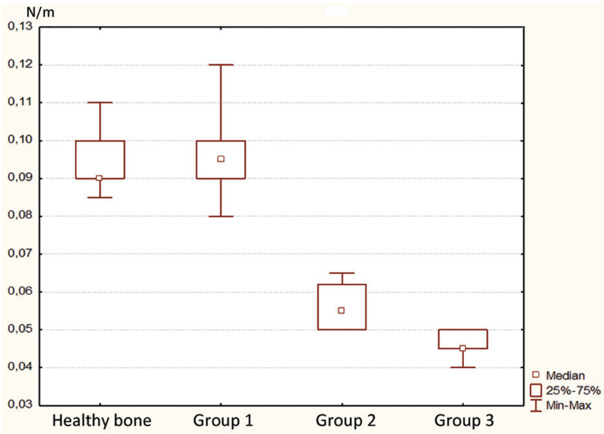

Fig. 12 Results of the median test of the biomechanical study data in the groups after 6 weeks (N/m)

DISCUSSION

It is known that the debridement of cavities is an important part of the surgical management of chronic osteomyelitis followed by filling in post-resection defects. Bone tissue defect is formed due to elimination of the chronic infection focus in the bone and surrounding tissues after removal of sequesters, opening and debridement of all the osteomyelitic cavities along with their internal walls, dissection of all the purulent sinuses that is filled in with the use of Ilizarov compression distraction method, allo- or autografting materials, or with the use of various biopolymer materials impregnated with antibiotics. The use of composite materials for management of bone defects was also described.

There were studies that investigated a general response of the organism to a carbon implant and possibilities of circular defect management. These works showed good results in the experiments on dogs and rabbits but without an additional impact of infection agents [10]. The studies revealed that a viable bone-to-carbon block was formed by week 20 of the experiment [12]. A carbon material was also used in the spine surgery for treatment of inflammatory diseases. The advantages of its use were early functional restoration of the spine and prevention of different complications [4].

The results of our study are similar to the results of several authors. They showed that the use of nano-structured carbon augments provided reduction of the recovery period in the experimental animals. Regular consumption of food was resumed by the end of day 3. Normal temperature was detected in group 1 by the end of day 13 while in groups 2 and 3 it remained elevated on days 14 and 15 respectively. In group 1, partial weight bearing was observed by the end of day 1 and the animals fully used the operated limb by the end of day 2. On the contrary, limb weight bearing restored in groups 2 and 3 only by the end of days 3 or 4. Only 60 % of animals in group 3 could use their operated limb that proved that there was no consolidation in the area of the osteomyelitic defect.

The findings of the radiographic study fully correlated with the findings of the clinical examination of the animals. The radiographic data in the area of the osteomyelitic defect differed between the groups by the end of the second week. At that time point, the manifestation of periostitis was absent only the animals of the group with a nano-structured carbon augment and there were signs of bone callus formation. The filling of the post-resection bone defect in the subsequent series of X-rays ran the stage of paraosseous callus formation that gradually extended to the deepness of the implant position in the bone. Complete consolidation and formation of the bone-to-implant block was seen by the end of week 4. Gradual increase in density and structural remodeling of the peri-implant bone followed and the radiographic borders between the bone and the nano-carbon implant disappeared by the end of week 6. At the same time point, delayed formation of bone regenerate was observed in the group of allogenic bone implant. Its visual density was significantly lower. Destruction of ceramic implants happened in 60 % of cases in group 3.

The study of bone blocks for breakage revealed that the maximum strength of 0.097 ± 0.013N/m by the end of 6 weeks was obtained in the group of nano-structured carbon implants. It corresponded to the healthy bone strength (0.095 ± 0.008 N/m). The strength of macropreparations that were prepared after osteomyelitic defect filling with allobone grafts was 0.056 ± 0.006 N/m. The weakest results of the micropreparation tests for breakage were in the group of ceramic implants. It was 0.046 ± 0.003 N/m that made 44 % from the strength that featured group 1 (**Tables 3, 4**).

Table 4

Results of the biomechnical test in the groups studied (Me, lower Q1 and upper Q3 quartile)

Group	Number of samples (abs)	Median (N/m)	Q1	Q3
1	5	0.09	0.090	0.100
2	5	0.095	0.090	0.100
3	5	0.055	0.050	0.062
4	5	0.045	0.045	0.050

CONCLUSION

1. The proposed method of long bone defect creation in the experiment enables to model osteomyelitis and is suitable for assessment of treatment efficiency.

2. Better clinical results such as food consumption and temperature normalization, weight bearing recovery and swelling subsidence were obtained with the use of a nano-structured carbon implant.

3. According to radiographic findings, the use of a nano-structured carbon material for management of osteomyelitic defects accelerated bone regenerate formation and provided a positive osteointegration at the border between the bone and implant as compared with other types of bone substitution materials that were studied.

4. The mechanical strength of the regenerated bone for break at the border of the bone and implant of the experimental blocks with the nano-structured carbon implants was 0.097±0.013 N/m that corresponded to the mechanical parameters of healthy bone and was by 45 to 50 % higher of the strength that the allogenic bone and ceramic implants featured.

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