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Effectiveness of Vancomycin-Impregnated Bone Graft Substitutes for the Treatment of Chronic Osteomyelitis in Long Bones: Comparative Analysis

Alexander P. Antipov, Svetlana A. Bozhkova, Ekaterina M. Gordina, Alexander V. Afanasyev, Magomed Sh. Gadzhimagomedov

Vreden National Medical Research Center of Traumatology and Orthopedics, St. Petersburg, Russia

Abstract

Background. Replacement of bone defects in the surgical treatment of chronic osteomyelitis is a key step to prevent recurrence of infection and potential fractures at the site of rehabilitation. Bone cement, biodegradable synthetic materials, as well as autologous, allogeneic, and xenogeneic bone tissue have become widespread in surgical practice. Giving these materials antibacterial properties will expand their use in the treatment of bone and joint infections, shorten the treatment time, and improve the patients' quality of life.

The aim of the study — to analyze the mid-term results of the second stage of surgical treatment for chronic osteomyelitis in long bones, depending on the type of used vancomycin-impregnated bone graft material: original biodegradable mineralized material based on allogeneic bone or a commercialy available biocomposite material consisting of β-tricalcium phosphate and hydroxyapatite.

Methods. The study included 25 patients who underwent the second stage of surgical treatment for chronic osteomyelitis. After removal of the cement spacer, the defect was replaced in Group 1 (n = 14) with a biocomposite material ReproBone® Granules with the addition of vancomycin, while in Group 2 (n = 11) — with an original mineralized allograft impregnated with vancomycin. Laboratory tests, vancomycin concentration in the drainage fluid, and the presence of infection recurrence within 1-3 years after surgery were evaluated.

Results. The groups did not differ in gender, age, and duration of the disease. The volume of the cavity defect was significantly higher in Group 2 (50 ml vs 14 ml; p = 0.0004). The vancomycin concentration in the drainage fluid from the first day after surgery in Group 2 was more than 10 times higher than in Group 1 (p = 0.0300) and remained at a high level until the 5th day. Osteomyelitis recurrence was observed in 14% of patients in Group 1 and was absent in Group 2.

Conclusions. Standard approach to the treatment of chronic osteomyelitis using antimicrobial spacers does not ensure complete eradication of microbial pathogens that continue to persist in bone tissue. The original biodegradable mineralized bone graft material based on allogeneic bone creates significantly higher local vancomycin concentrations and demonstrates clinical efficacy in all applications.

Keywords: chronic osteomyelitis, bone graft substitutes, vancomycin, allogeneic bone, local antibiotic therapy.

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✉ *Alexander P. Antipov*; e-mail: a.p.antipov@yandex.ru

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Сравнительный анализ эффективности костнопластических материалов, импрегнированных ванкомицином, при лечении хронического остеомиелита длинных костей

А.П. Антипов, С.А. Божкова, Е.М. Гордина, А.В. Афанасьев, М.Ш. Гаджимагомедов

ФГБУ «Национальный медицинский исследовательский центр травматологии и ортопедии им. Р.Р. Вредена» Минздрава России, г. Санкт-Петербург, Россия

Реферат

Актуальность. Замещение костных дефектов при хирургическом лечении хронического остеомиелита является ключевым элементом для предотвращения рецидивов инфекции и потенциальных переломов в месте санации. Широкое распространение в хирургической практике получили костный цемент, биодеградируемые синтетические материалы, а также аутологичная, аллогенная и ксеногенная костные ткани. Придание таким материалам антибактериальных свойств позволит расширить их применение при лечении инфекции костей и суставов, сократить сроки лечения, улучшить качество жизни пациентов.

Цель исследования — проанализировать среднесрочные результаты второго этапа хирургического лечения пациентов с хроническим остеомиелитом длинных костей в зависимости от типа используемого костнопластического материала, импрегнированного ванкомицином: оригинального биодеградируемого минерализованного материала на основе аллогенной кости или официнального биокомпозитного материала, состоящего из β-трикальцийфосфата и гидроксиапатита.

Материал и методы. В исследование включены 25 пациентов, которым был выполнен второй этап хирургического лечения хронического остеомиелита. После удаления цементного спейсера пациентам группы 1 (n = 14) дефект замещали биокомпозитным материалом ReproBone® Granules с добавлением ванкомицина, пациентам группы 2 (n = 11) — оригинальным минерализованным аллотрансплантатом, импрегнированным ванкомицином. Оценивали показатели лабораторных исследований, концентрацию ванкомицина в дренажном отделяемом и наличие рецидивов инфекции в течение 1–3 лет после операции.

Результаты. Группы не различались по полу, возрасту и длительности заболевания. Объем полостного дефекта был значительно больше в группе 2 (50 мл против 14 мл; p = 0,0004). Концентрация ванкомицина в дренажном отделяемом с первого дня после операции в группе 2 превышала более чем в 10 раз данный показатель в группе 1 (p = 0,0300) и сохранялась на высоком уровне до 5-го дня. Рецидивы остеомиелита наблюдались у 14% пациентов в группе 1 и отсутствовали в группе 2.

Заключение. Стандартный подход к лечению хронического остеомиелита с использованием антимикробных спейсеров не обеспечивает полной эрадикации микробных возбудителей, которые продолжают персистировать в костной ткани. Оригинальный биодеградируемый минерализованный костнопластический материал на основе аллокости создает значительно более высокие локальные концентрации ванкомицина и демонстрирует клиническую эффективность во всех случаях применения.

Ключевые слова: хронический остеомиелит, костнопластические материалы, ванкомицин, аллогенная кость, локальная антибиотикотерапия.

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Антипов Александр Павлович; e-mail: a.p.antipov@yandex.ru

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INTRODUCTION

The replacement of bone cavities formed during radical surgical debridement of an infection site is a key element in the successful treatment of chronic osteomyelitis. This is due to several critical factors. On the one hand, any residual bone defect left after debridement that was not adequately drained becomes filled with a hematoma, creating a favorable environment for microorganism proliferation, which may lead to infection recurrence in 10-20% of cases [1]. On the other hand, such a defect increases the risk of fractures under critical loads on the operated segment. Furthermore, it is well known that achieving effective local antibiotic concentrations after radical surgical debridement of an osteomyelitis site through systemic antibiotic therapy alone is impossible [2]. The presence of microorganisms in the form of small colony variants (SCVs) and biofilms necessitates a significant increase — by tens to hundreds of times — in the minimum inhibitory concentration of antimicrobial agents [3]. A solution to this problem involves creating local antibiotic depots by using bone graft materials with antimicrobial properties [4, 5, 6, 7]. Various materials are widely used in surgical practice to replace bone defects, including autologous and allogeneic grafts supplemented with antibiotics, bone cements based on polymethylmethacrylate (PMMA) and calcium phosphate, biopolymer- and ceramic-based composites with antibacterial agents, and xenografts.

The main disadvantage of non-biodegradable materials (bone cement, biopolymer- and ceramic-based composites) is the need for a second surgical procedure to remove the spacer [5, 7, 8]. Additionally, such operations may present technical challenges and require specialized instruments, particularly if the material remains implanted for an extended period.

The local concentration of antibacterial agents is determined by the rate of dissolution and drug elution from the implanted material into the surrounding tissues. When mixed intraoperatively with autografts or composite materials that initially lack antibiotics, there is a high likelihood of rapid elution, resulting in only short-term antibiotic action at the defect site [9].

Allografts are widely used for bone defect replacement in orthopedics. However, they carry a risk of contamination when implanted into an infectious site, even after debridement [10]. In our opinion, the most promising approach for treating patients with infectious bone lesions is the use of an antimicrobial osteoplastic material based on purified allograft bone, which is characterized by a standardized duration of antibiotic elution. These materials have been approved for medical use in the European Union, but no such product is currently registered in Russia, nor does it have any analogs. At the same time, using this material in the one-stage complex treatment of patients with osteomyelitis has achieved infection control in 90% of cases over a two-year follow-up period [11], demonstrating a high potential for developing an original domestic material with similar properties. At present, there is a technology for allogeneic bone purification (patent RU 2722266 C1), which could serve as the basis for creating a material with the necessary antibacterial properties.

The aim of the study — to analyze the mid-term outcomes of the second stage of the surgical treatment for patients with long bone chronic osteomyelitis, depending on the type of bone graft material impregnated with vancomycin: an original biodegradable mineralized material based on allograft bone or a commercially available biocomposite material consisting of β-tricalcium phosphate and hydroxyapatite.

METHODS

Study design

This study was a comparative, non-randomized clinical trial with sequential patient allocation into comparison groups.

The study included 25 patients who were admitted for the second stage of the surgical treatment of chronic osteomyelitis at the septic surgery department from January 2018 to January 2022.

Inclusion criteria:

– diagnosed chronic osteomyelitis of long bones, classified as anatomical type III or IV, physiological class B according to the Cierny-Mader classification);

– completed first stage of the surgical treatment of chronic osteomyelitis, which involved radical debridement of infection site with the removal of necrotic and clearly non-viable tissues, formation of a bone cavity defect,

and its replacement with an antimicrobial spacer in the form of PMMA beads;

– no signs of recurrent chronic infection upon admission, based on clinical and laboratory data (complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and no local signs of inflammation at the site of previous operation);

– ability to undergo prolonged (at least 6-8 weeks) antibiotic therapy, including oral administration, based on microbial sensitivity data obtained from the microbiological analysis of intraoperative tissue biopsies and removed metal implants during the first stage of treatment;

– patient's informed consent to the use of a patient-specific implant based on an original biodegradable mineralized bone graft material impregnated with vancomycin.

Comparison groups and materials

Patients were sequentially allocated into comparison groups. Group 1 included 14 patients (2018-2020). During the second stage of surgical treatment, the bone cavity defect was filled with ReproBone® Granules (Ceramisys UK), a biocomposite material consisting of β-tricalcium phosphate and hydroxyapatite, with intraoperative addition of vancomycin (1 g vancomycin per 10 g material). Group 2 included 11 patients (2020-2022). The bone defect was filled with a patient-specific implant using an original biodegradable mineralized bone graft material (patent RU 2722266 C1), impregnated with vancomycin (1 g vancomycin per 10 g material) following a proprietary methodology (patent RU 2839413).

Based on the CT findings about the shape and volume of the defect obtained after the first stage of the surgical treatment, blocks of allogeneic bone graft material of different size and configuration in the form of cubes with faces of 5-20 mm, plates of 3-5 mm thickness, crumbs with a fraction of 0.5-10 mm, as well as hemispheres were made in advance, which allowed to adapt the material to the specific parameters of the defect.

Surgical technique and perioperative management

The extent of surgical intervention during the second-stage operation was identical in both groups, including the removal of the PMMA bead spacer, radical surgical debridement, filling of the resulting bone defect with one of the two described material, and placement of drainage systems (Redon drains). In Group 2, a patient-specific allograft made of the original biodegradable mineralized bone graft material was used, tailored to the anatomical characteristics of each patient's defect. Depending on the clinical picture and drainage output volume, the duration of drainage ranged from 2 to 5 days. In all cases, five tissue biopsies (scar and bone tissue from the bone defect area) were collected intraoperatively for microbiological analysis. The study was conducted according to standard microbiological diagnostic protocols. Samples were homogenized and cultured on standard nutrient media, followed by incubation under aerobic and anaerobic conditions for 14 days.

All patients received intravenous empirical or targeted etiotropic antibiotic therapy from the day of operation, based on preoperative microbiological findings or microbiological results from previous admissions. If intraoperative biopsy results warranted, antimicrobial therapy was adjusted accordingly, followed by a switch to oral antibiotics for a total duration of 6-8 weeks.

The following parameters were analyzed: medical history (infection duration, number of previous operations, number of relapses), type of pathogen, laboratory parameters upon admission (white blood cell count, CRP, hemoglobin, red blood cell count), surgery duration, intraoperative blood loss, bone defect volume, and drainage duration. Bone defect volume was measured using a fluid displacement method, where the cavity was filled with sterile saline and measured using a 100 ml Janet syringe.

The groups were comparable in gender, age, disease duration, and the number of prior debridement operations (Table 1).

Table 1

Comparison group characteristics

Parameter		Group 1	Group 2	U test, p
Total, n		14	11	0.467
Male, n (%)		9 (64)	9 (82)	–
Female, n (%)		5 (36)	2 (18)	–
Disease duration, years, Me [25-75% IQR]		3.5 [1.0-8.5]	5 [2-19]	0.344
Age, y.o., Me [25-75% IQR]		34.5 [30-53]	44 [34-51]	0.572
No debridement interventions in the history, n (%)		1 (7)	1 (9)	
1-2 debridement interventions in the history, n (%)		7 (50)	5 (45.5)	0.687
More than 2 debridement interventions in the history, n (%)		6 (43)	5 (45.5)	
Localization:	shoulder	1 (7%)	0	–
	thigh	5 (36%)	6 (54.5%)	0.545
	leg	8 (57%)	5 (45.5%)	0.323

Determination of local vancomycin concentration

Local vancomycin concentration was measured using high-performance liquid chromatography (HPLC) in drainage fluid on postoperative days 1-5 in both groups. The analysis was performed on a Shimadzu chromatograph using a Shim-pack HR-ODS column. The methodology included transferring 1 ml of daily buffer to an Eppendorf tube, centrifugation (13.000 rpm for 5 minutes), and transferring the supernatant to a vial and placing it in the chromatograph. Injection volume was 100 µl. Run time was 25 minutes.

Treatment efficacy criteria

The primary efficacy criterion for both groups was the presence or absence of recurrent chronic infection over a follow-up period of at least 1 year (median 2.4 years [IQR 1.875-3.125] for Group 1, and median 2.2 years [IQR 1.95-2.78] for Group 2). Follow-up data were obtained via in-person examinations or remote assessments, including phone consultations, video/photo evaluation of the operated limb, and the review of X-ray or CT images with the descriptions of the treated segment.

Statistical analysis

Data were recorded in electronic spreadsheets, and statistical analysis was performed using Microsoft Excel 2019 (version 16.72, Microsoft, USA) and IBM SPSS Statistics (version 23.0.0.0) on a macOS Monterey 12.2.1 system. Due to the small sample size, the median (Me) was used as a measure of central tendency, and the interquartile range (IQR, 25-75%) was used to describe data dispersion. Comparisons of quantitative variables between groups were conducted using the Mann-Whitney U test. Categorical variables were analyzed using the χ^2 test. Differences were considered statistically significant at $p<0.05$. The Fisher's exact test was used to compare osteomyelitis recurrence rates between groups, as it is a non-parametric test suitable for small sample sizes and binary data (presence or absence of recurrence).

RESULTS

Groups 1 and 2 showed no statistically significant differences in terms of gender ($p = 0.467$), age ($p = 0.572$), or disease duration ($p = 0.344$). Upon admission for surgical treatment, no differences in blood laboratory test results were observed (Table 2), confirming the homogeneity of the study groups. The only significant difference was in the volume of the cavity defect. The median interval between surgical stages was comparable, being 178.5 days [97.75-272.00] in Group 1 and 130 days [76-169] in Group 2 ($p = 0.403$).

The bacteriological analysis of intraoperatively obtained tissue biopsies revealed microbial growth in 8 patients (57%) from Group 1 and 3 patients (27%) from Group 2. The predominant microorganisms were coagulase-negative staphylococci (n = 7): *Staphylococcus epidermidis* was identified

in 6 cases (5 MRSE strains and 1 MSSE strain), and *Staphylococcus saprophyticus* was found in 1 case. *Propionibacterium* spp. was detected in 4 patients, while *Burkholderia cepacia* complex (n = 1) and *Ochrobactrum anthropi* (n = 1) were also identified. Microbial associations were detected in 3 cases.

The average drainage duration was 2 days [IQR 1-2] in Group 1 and 5 days [IQR 4-5] in Group 2, which was attributed to the increased volume of hemorrhagic exudate. This may have been related to both the reaction to the allograft and the significantly larger bone defect volume. The concentration of vancomycin in the drainage fluid in Group 2 was more than 10 times higher on the first postoperative day compared to Group 1 (p = 0.030). Throughout the entire drainage period, patients in Group 2 exhibited vancomycin levels thousands of times higher than the minimum inhibitory concentration (MIC) for staphylococci (Table 3).

The mean follow-up duration was 2.4 years [IQR 1.875-3.125] for Group 1 and 2.2 years [IQR 1.95-2.78] for Group 2. The recurrence of osteomyelitis was observed in 2 out of 14 patients (14%) in Group 1, while no recurrences were reported in Group 2 (p>0.05). In both cases of chronic infectious process recurrence, intraoperatively obtained materials showed diagnostically significant microbial growth: *Staphylococcus saprophyticus* and *Propionibacterium* spp. in one case, and *Ochrobactrum anthropi* with *Propionibacterium* spp. in the other.

DISCUSSION

A review of the scientific literature indicates that the key criteria for selecting materials to treat chronic osteomyelitis include their ability to maintain prolonged local concentrations of antibacterial agents above the MIC for pathogens and the absence of undesirable systemic and cytotoxic local effects. Table 4 presents a comparative analysis of the main materials used for bone defect replacement in chronic osteomyelitis.

Table 2

Investigated parameters of perioperative period in comparison groups, Me [25-75% IQR]

Parameter		Group 1	Group 2	U test, p
Preoperative period				
WBC, $\times 10^9$/l		6.3 [4.9-8.45]	6.3 [5.5-7.5]	0.727
CRP, mg/ml		2.025 [0.5-3.3]	3.21 [0.88-6.52]	0.134
RBC, $\times 10^{12}$/l		4.98 [4.7-5.19]	4.81 [4.63-5.1]	0.219
Hb, g/l		142 [131.25-153.25]	137 [127-151]	0.536
Intraoperative period				
Defect volume, ml		14 [8.75-26.25]	50 [35-55]	**0.0004**
Defect size depending on the localization, ml	shoulder	10 [10-10]	–	
	thigh	25 [15-35]	47.5 [17.5-66.2]	0.247
	leg	11 [7.25-22.50]	50 [40.0-152.5]	**0.002**
Blood loss, ml		125 [50-300]	100 [30-150]	0.244
Surgery duration, min.		82.5 [71.25-128.75]	50 [40-65]	**0.0003**
Wound drainage, n (%)		7 (50)	7 (64)	
Postoperative period				
Drainage timing, days		3 [1-4]	3 [2-5]	0.434
WBC, $\times 10^9$/l		5.95 [5.0-7.7]	7.1 [5.950-7.675]	0.437
CRP, mg/ml		3.145 [1.9-5.6]	27.275 [10.02-64.35]	**0.0002**
RBC, $\times 10^{12}$/l		4.21 [4.03-4.71]	4.39 [4.2-4.5]	0.585
Hb, g/l		122 [114.0-138.5]	127.5 [112.75-137.75]	0.841

Bold font indicates statistically significant values.

Table 3

Concentration of vancomycin in drainage fluid determined by high-performance liquid chromatography method

Day	Concentration, μg/ml, Me [25-75% IQR]		U test, p
	Group 1	Group 2	
1st	280 [265-430]	3119.5 [868.75-6990]	**0.030**
2nd	185 [95-215]	447 [181.9-1511.0]	0.106
3rd	–	2000.5 [307.75-4078.75]	–
4th	–	3225 [2681-3225]	–
5th	–	2402.5 [2187.0-2402.5]	–

Bold font indicates statistically significant values.

Table 4

Materials for creating a local depot of antibacterial agents

Material	Advantages	Disadvantages
Autografts with the addition of antibacterial agents	– high biocompatibility; – osteoinductive and osteoconductive properties [41]	– limited material volume due to the patient's physiological constraints; – additional surgical trauma; – rapid reduction of local concentration [9]
Bone cement (PMMA)	– high material strength for filling segmental defects; – extensive accumulated experience in clinical use; – wide selection of commercially available materials containing antibacterial agents [2, 5, 7]	– non-biodegradable (necessitating repeated intervention); – insufficient duration of antibiotic elution; – risk of antibiotic resistance (in case of low local antibiotic concentrations); – limited spectrum of antibacterial agents [5, 7, 8, 25, 26, 27, 28]
Calcium phosphate-based bone cements	– high biocompatibility; – biodegradable material = prolonged release of antibacterial agents [6, 17, 18, 19, 20]	– lower mechanical strength compared to PMMA-based cements; – creating a uniform dispersion of antibiotics within the material is a technically challenging process [12, 13, 14, 15, 16]
Biopolymer- and ceramic-based composites with antibacterial agents	– ensure slow and prolonged antibiotic release; – high biocompatibility; – availability of commercial products containing antibacterial agents: CERAMENT G (BONESUPPORT), Herafill G (Heraeus Medical), Osteoset-T (Wright Medical) [12, 19, 37]	– high cost – hard-to-predict resorption rate [12, 13, 14, 15, 16]
Xenografts	– good biocompatibility; – potential for large-scale production: readily available in large volumes [40, 46]	– high risk of a pronounced immune response if insufficiently processed; – use of animal-derived tissues may be unacceptable for some patients due to religious or ethical reasons [40, 46];
Allogeneic cancellous bone	– ability to create a local depot with sustained high concentrations of antibacterial agents for an extended period (over 7 days); – complete filling of long bone defects; – preservation of bone's structural and mechanical properties; – high material biocompatibility [10, 11, 21, 22]	– no registered medical products with antimicrobial activity available in Russia

Modern materials for bone defect replacement in chronic osteomyelitis can be categorized into several groups: autologous grafts, synthetic materials (PMMA, calcium phosphates), biopolymer- and ceramic-based composites, as well as allo- and xenografts. Particular attention is given to allogeneic cancellous bone, which combines the advantages of maintaining high local antibiotic concentrations while preserving the structural and mechanical properties of native bone. However, major limiting factors for most materials include insufficient mechanical strength or difficulties in predicting resorption and drug elution rates [12, 13, 14, 15, 16]. Additionally, high costs and the lack of registered forms with antimicrobial activity remain significant barriers to the widespread clinical use of some promising materials.

The use of a biocomposite material based on β-tricalcium phosphate and hydroxyapatite, intraoperatively impregnated with vancomycin, resulted in sustained infection remission in 86% of cases, aligning with literature data [17, 18, 19, 20]. The replacement of osteomyelitic defects with the original biodegradable mineralized bone graft material impregnated with vancomycin was effective in all cases. Similar results have been reported for osteoplastic materials based on allogeneic bone impregnated with antibiotics [21, 22].

The study groups were homogeneous in baseline parameters except for the median cavity defect volume, which was significantly larger in Group 2 than in Group 1 ($p = 0.0003975$). Despite the larger defect area in Group 2, intraoperative blood loss and surgical time were lower, while the need for drainage persisted longer, which may be related to the surgical technique or the material used.

Diagnostically significant microbial growth in intraoperative biopsy tissue samples was detected in 57% of cases in Group 1 and 27% in Group 2. Coagulase-negative staphylococci, including methicillin-resistant strains (MRSE), were predominant. Along with the absence of clinical and laboratory signs of infectious inflammation this may suggest the low efficacy of antimicrobial spacers. Apparently, the antibiotic concentrations achieved in the bone defect area, particularly vancomycin, are insufficient against staphylococcal cells that penetrate the osteocyte lacunar-canalicular network and can persist intracellularly in osteoblasts for a prolonged period [23, 24]. The negative impact of a prolonged interval between the stages of surgical treatment cannot be ruled out, as it is known that after the cessation of antibiotic elution from the spacer, microbial biofilms form on its surface, as on any foreign body [25, 26, 27, 28]. According to scientific literature, one of the reasons for the insufficient eradication of MRSE in the infection site is patients' non-compliance with the regimen of prolonged antibacterial therapy in the postoperative period [29], though further research is needed.

The leading causative agents of osteomyelitis are Gram-positive microorganisms [30, 31, 32, 33, 34], which in the vast majority of cases are susceptible to vancomycin. At the same time, vancomycin exhibits low cytotoxic activity and minimal systemic effects when locally deposited, making it the drug of choice for impregnating bone graft materials in the treatment of chronic osteomyelitis [35, 36, 37, 38, 39].

We identified significant differences in vancomycin concentration in the drainage fluid between the groups. The use of an original bone graft material impregnated with vancomycin allowed for the creation of higher local antibiotic concentrations compared to Group 1. Moreover, the high vancomycin level detected on day 5 suggests the possibility of maintaining elevated antibiotic concentrations in the infectious focus over an extended period. The significantly higher initial concentration of vancomycin in the drainage fluid in Group 2 may be due to the highly porous structure of allogeneic bone, which has a considerably larger total surface area and pore volume compared with β-TCP and HAp granules.

It is important to note that after the application of the original allogeneic bone graft material, patients in Group 2 exhibited a statistically significant increase in CRP levels in the postoperative period compared to Group 1. This could be attributed to the body's natural response to a larger surgical intervention, as patients in Group 2 had significantly larger bone defects.

Additionally, the increase in CRP levels may be associated with several factors reflecting the body's specific immunological and inflammatory response to allograft [40, 41]. Despite processing, bone allografts may still contain small amounts

of residual antigens or other biologically active substances that are recognized by the patient's immune system as foreign. This can lead to an immune response involving the activation of macrophages and other immune cells, which, in turn, triggers an increase in CRP levels [42, 43, 44]. Furthermore, the resorption process of allografts involves the activation of osteoclasts — cells that play a key role in bone tissue degradation. During resorption, various inflammatory mediators, including cytokines such as interleukin-1 and tumor necrosis factor-alpha (TNF-α), are released, stimulating hepatic cells to produce CRP [45].

It is also known that some allograft components, especially if they are partially decalcified or have undergone other processing, may independently initiate an inflammatory response by releasing remnants of bone matrix proteins or other biomolecules that stimulate the immune response [46]. The local inflammatory reaction likely determines the tissue exudative response, necessitating prolonged drainage of the defect area replaced with the original allograft. These aspects highlight the need for a careful control and monitoring of bone graft materials based on allo- and xenografts, which are currently under active development.

Compared to synthetic bone substitutes, the unique porous structure of bone-derived materials offers significant advantages, providing the ability for prolonged antibiotic elution to maintain an effective drug concentration over the required period. Proper impregnation of allografts with antibiotics ensures sustained local antibiotic presence, which is critically important for infection control [21]. Additionally, allografts serve as an excellent scaffold for subsequent osteogenesis, facilitating the gradual filling of the formed bone defects.

CONCLUSIONS

The standard approach to treating chronic osteomyelitis by filling the post-debridement bone defect with antimicrobial bead spacers fails to achieve complete pathogen eradication. This suggests that bacteria may persist in the bone tissue and/or intracellularly. The high vancomycin concentrations achieved with the original biodegradable mineralized bone graft material, as well as its clinical efficacy in all cases, indicate its potential for further research.

DISCLAIMERS

Author contribution

All authors made equal contributions to the study and the publication.

All authors have read and approved the final version of the manuscript of the article. All authors agree to bear responsibility for all aspects of the study to ensure proper consideration and resolution of all possible issues related to the correctness and reliability of any part of the work.

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Authors' information

✉ *Alexander P. Antipov*
Address: 8, Akademika Baykova st., St. Petersburg, 195427, Russia
https://orcid.org/0000-0002-9004-5952
e-mail: a-p-antipov@ya.ru

Svetlana A. Bozhkova — Dr. Sci. (Med.), Professor
http://orcid.org/0000-0002-2083-2424
e-mail: clinpharm-rniito@yandex.ru

Ekaterina M. Gordina — Cand. Sci. (Med.)
http://orcid.org/0000-0003-2326-7413
e-mail: emgordina@win.rniito.ru

Alexander V. Afanasyev — Cand. Sci. (Med.)
https://orcid.org/0000-0002-3097-7846
e-mail: afanasyev1307@mail.ru

Magomed Sh. Gadzhimagomedov
https://orcid.org/0009-0001-6113-0277
e-mail: orthopedist8805@yandex.ru