Chronic osteomyelitis is pathology of the bone system, accompanied not only by local manifestations, but changes in the whole body. Taking into account that the average age of the patients with chronic osteomyelitis (CO) is 30–40 years old. In the whole structure of diseases of locomotor organs, CO constitutes 3–6.5 %, occupying the first place among the complications after the operational treatment of closed fractures [1, 2]. In recent years a tendency is noticed towards the increase in the frequency of the disease. Among other purulent-septic diseases, CO is characterized by long-lasting and progressive development, resistance to treatment, predisposition to relapses [3]. Besides, during the last two decades, the number of patients with post-operational osteomyelitis increased dramatically – up to 34 % among the observed patients [4]. At present, there are no unique criteria in the assessment of efficiency of methods of treating CO, in particular, the elimination of osteomyelitis bone cavities. The opinions of surgeons [2, 5] coincide in the question of radical surgical manipulation with osteomyelitis.

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APPLICATION OF POROUS TITANIUM NICKELIDE FOR TREATMENT OF PATIENTS WITH CHRONIC OSTEOMYELITIS

Shtofin A. S., Shegolev M. B., Trushin P. V., Golovnev V. A., Golovnev A. V., Shtofin S. G.
Novosibirsk State Medical University, Russian Federation

ПРИМЕНЕНИЕ ПОРИСТОГОНИКЕЛИДАТИТАНАДЛЯЛЕЧЕНИЯБОЛЬНЫХХРОНИЧЕСКИМОСТЕОМИЕЛИТОМ

А. С. Штофин, М. Б. Щеголев, П. В. Трушин, А. В. Головнев, С. Г. Штофин
Новосибирский государственный медицинский университет, Российская Федерация

The research covered patients with chronic osteomyelitis. 55 patients underwent an original operation of single stage sequestrectomy and grafting the residual bone cavity with fine-grain titanium nickelide. There was demonstrated clinico-roentgenologic efficiency of this treatment method in early rehabilitation period and further follow up. Clinical effects were characterized by the absence of relapses of chronic osteomyelitis in 94.6 % of patients during the follow-up period. The inductive influence of titanium nickelide in the formation of trabecular bone tissue was experimentally based on 20 animals (dogs). Thus, our work confirms that the use sequestrectomy with the following grafting with the granules of titanium nickelide gives more positive results than the traditional method of treatment of the chronic osteomyelitis.

Keywords: chronic osteomyelitis, titanium nickelide, bone grafting, surgical treatment

В исследование включены 83 пациента с хроническим остеомиелитом (ХО), из них 55 больным была проведена оригинальная операция одномоментной секвестрэктомии и пластики остаточной костной полости мелкогранулированным никелидом титана. Продемонстрирована клинико-рентгенологическая эффективность данного метода лечения в раннем реабилитационном и в отдаленном периоде наблюдения. Клинические эффекты характеризовались отсутствием рецидивов ХО у 94,6 % больных в течение всего срока наблюдения. Экспериментально на 20 животных (собаках) было установлено индуцирующее действие никелида титана в процессе формирования зрелой костной ткани. Полученные результаты свидетельствуют о том, что применение метода лечения ХО путем секвестрэктомии с последующей пластикой гранулами никелида титана дает большее количество положительных результатов в сравнении с традиционным методом лечения.

Ключевые слова: хронический остеомиелит, никелид титана, пластика, хирургическое лечение
focus. It is the fulfillment of sequestrectomy, which must include four stages: a) the removal of necrotic tissues, pus, granulations from a sequestral cavity; b) the removal of a scleroid sequestrum capsule to the appearance of sharply margined areas of bone supplied with blood; c) the opening of the marrowy canal and its lumina above and below the affected area; d) the filling of the residual cavity with biological or other plastic material. The frequency of relapses of the disease after bone grafting with hemo-filling is 3.2–20.6 %, after grafting with muscle flap – 3.8–28.5 %, with dermatic-periosteal bone flap 3.9–31.3 %, with free bone grafting – 4.9–38.4 % of observations [1, 3, 4]. Various biological, mineral, synthetic or other materials are assessed as debride [5, 6, 7]. All this prompts to search actively to improve the methods of plastic restoration of residual bone cavity in the case of CO. In recent years, a new class of porous super-elastic materials on the basis of titanium nickelide has been developed, which possess unique properties: biochemical compatibility (bio-inertia), physical-chemical properties, close to the parameters of bone tissue, good anti-corrosion properties. Besides, they are not carcinogenic, not toxic, are well sterilized; they possesspreset porous structure, penetrance, wetting ability [9, 10, 12]. Living tissues easily germinate into the pores of titanium nickelide, at the same time direct connection is formed between the bone and the implant [6, 8, 11]. It allows them to function in the tissues of the body for a long time, without being rejected, which provides stable regeneration and permits to use implants from porous permeable alloys on the basis of titanium nickelide in the conditions of an infected bone bed.

The goal of research: to study and compare the processes of regeneration of bone tissue in animals while grafting bone cavities with titanium nickelide granules and free plastics in experiment, and also to assess the efficiency of surgical treatment of patients with CO by the use of grafting post-osteomyelitis cavity with fine-grain porous titanium nickelide.

Material and Methods. To realize the set goal, the results of research were analyzed, which were made on experimental animals (dogs), as well as the results of reconstructive operations with CO by the use of grafting with fine-grain titanium nickelide.

Experimental procedure. All the research was carried out with the observation of Rules of works with the use of experimental animals. To assess the speed of regeneration of bone tissue of dogs’ two methods of bone grafting were experimentally reproduced: a traditional one – with bone crumbs, and the method of filling the bone cavity with fine-grain titanium nickelide, which has been developed lately. In the first group consisting of 20 dogs, granules of porous titanium nickelide were placed in the formed cavity of shin bone epiphysis. In the second (control) group (consisting of 10 dogs) flank-bone crumbs were introduced into the form cavity of shin bone. The volume of sequestral cavities was on average 18.6 cm³. For an objective assessment of the patients’ condition, the complex examination was carried out, which included clinic-laboratory, bacteriological, roentgenological and morphological methods of research. Bacterial cultures were inoculated in 81.1 % of patients: Staphylococcus aureus – in 57 (69.7 %), Streptococcus haemolyticus – in 9 (11.6 %), Pseudomonas aeruginosa – in 7 (9.3 %), E. coli – in 4 (4.7 %) and mixed flora Enterococcus faecalis + Staphylococcus pyogenes – in 4 (4.7 %). All 55 patients from the group of clinical study on the basis of surgical clinical picture were treated with single stage plastic restoration of residual bone cavities, which included syringeectomy, sequestrectomy with grafting a sequestrum cavity with the granules of titanium nickelide. When the patients were admitted urgently (with phlegmons), the opening was made, then the draining of the phlegmon, the sanation during 8–10 days, then, as the second stage, the operation of sequestrectomy with grafting with the granules of titanium nickelide. The operation began with determining the fistulous tract and the syringeectomy to the bone, the resection of peri-ostemum, the opening of the sequestrum box, the removal of sequesters with granulated tissue. Then there was carried out curettage to the appearance of pinpoint bleeding. Then the sequestrum cavity was rinsed with the solution of antiseptic and filled with dry sterile granules of titanium nickelide in the amount not less than one third of the volume of the sequestrum cavity. The wound was stitched up completely with a rubber tube drainage left for 24 hours. In the post-operative period, antibiotics were prescribed for 5−7 days and physiotherapy. The stitches were taken out on the 7th-10th day. If necessary, there was carried out plaster immobilization of the limb in the physiological rest position for 3–4 months.

Analysis of the significance of differences in the groups was carried out in variational statistics methods.

Patients with chronic osteomyelitis

<table>
<thead>
<tr>
<th>Localization of osteomyelitis focus</th>
<th>Study group (n=55)</th>
<th>Comparison group (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>abs.</td>
<td>%</td>
<td>abs.</td>
</tr>
<tr>
<td>Thigh bone</td>
<td>15</td>
<td>27.3</td>
</tr>
<tr>
<td>Shin bone</td>
<td>24</td>
<td>43.6</td>
</tr>
<tr>
<td>Humerus</td>
<td>4</td>
<td>7.3</td>
</tr>
<tr>
<td>Heel bone</td>
<td>4</td>
<td>7.3</td>
</tr>
<tr>
<td>Splint-bone</td>
<td>2</td>
<td>3.6</td>
</tr>
<tr>
<td>Huckle bone</td>
<td>2</td>
<td>3.6</td>
</tr>
<tr>
<td>Finger nail-bone</td>
<td>2</td>
<td>3.6</td>
</tr>
<tr>
<td>Radial bone</td>
<td>2</td>
<td>3.6</td>
</tr>
</tbody>
</table>

The chronicity of the disease was from 3 months to 13 years. The patients with complications of the basic disease, like pseudarthrosis and unconsolidated fracture, were excluded. The formed groups were consistent in gender, age, the duration of the disease, the localization of the pathological process, the number of previously undergone operations, which allowed to validate the accuracy of the obtained results. The clinical form of CO was established for all the patients. They were chronic post-traumatic osteomyelitis for 62 (75.4 %) patients, chronic hematogenic osteomyelitis for 21 (22.6 %). 62 patients were taken to hospital in the planned manner, 21 – urgently, due to the exacerbation of chronic osteomyelitis, 11 of them had burning pus (phlegmon) in soft tissues in the affected area. 83 (76 %) patients had a fistula form of CO. The sizes of fistulas were from spot to extensive ulcer osteomyelitis ulceration of the bone tissue to the bottom. The volume of sequestral cavities was on average 18.6 cm³. For an objective assessment of the patients’ condition, the complex examination was carried out, which included clinic-laboratory, bacteriological, roentgenological and morphological methods of research. Bacterial cultures were inoculated in 81.1 % of patients: Staphylococcus aureus – in 57 (69.7 %), Streptococcus haemolyticus – in 9 (11.6 %), Pseudomonas aeruginosa – in 7 (9.3 %), E. coli – in 4 (4.7 %) and mixed flora Enterococcus faecalis + Staphylococcus pyogenes – in 4 (4.7 %). All 55 patients from the group of clinical study on the basis of surgical clinical picture were treated with single stage plastic restoration of residual bone cavities, which included syringeectomy, sequestrectomy with grafting a sequestrum cavity with the granules of titanium nickelide. When the patients were admitted urgently (with phlegmons), the opening was made, then the draining of the phlegmon, the sanation during 8–10 days, then, as the second stage, the operation of sequestrectomy with grafting with the granules of titanium nickelide. The operation began with determining the fistulous tract and the syringeectomy to the bone, the resection of peri-ostemum, the opening of the sequestrum box, the removal of sequesters with granulated tissue. Then there was carried out curettage to the appearance of pinpoint bleeding. Then the sequestrum cavity was rinsed with the solution of antiseptic and filled with dry sterile granules of titanium nickelide in the amount not less than one third of the volume of the sequestrum cavity. The wound was stitched up completely with a rubber tube drainage left for 24 hours. In the post-operative period, antibiotics were prescribed for 5–7 days and physiotherapy. The stitches were taken out on the 7th-10th day. If necessary, there was carried out plaster immobilization of the limb in the physiological rest position for 3–4 months.

Analysis of the significance of differences in the groups was carried out in variational statistics methods.
Results and Discussion. Results of the experimental research. After 1 postoperative month, impregnations of metal and a slight shadow of tissue, connecting the granules, were radiologically determined in the animals of the first group in the area of grafting of shin bone epiphysis. In control samples, bone fragments were surrounded with a capsule. Macroscopically it was hard to draw out the granules from the cavity in the first group of dogs by destroying bone structures. In control samples lose connective tissue was located between the fragments of bone tissue. Microscopically, on the prepared slices of shin bone, we discovered that, inside metal pores, bone cells, surrounded with osteomucoid, were located. Nuclei and basophilic cytoplasm were well contoured in them. Thin bone trabeculas developed anastomosis with bone structures formed in the pores of the implant. Besides, bone trabeculas surrounded the granules, connecting them, and anastomosed with bone tissue, surrounding the cavity. After 3 months in the first group of animals, the granules of titanium nickelide in the zone of operational intervention were surrounded with bone trabeculas forming anastomosis. Macroscopically in the study group the granules in the researched zone of bone tissue were tightly knitted together with the maternal bed by bone trabeculas. Microscopically (slices of shin bone) it was found out that between metal granules and around them trabeculae of bone tissue were surrounded with traces of alteration was located: irregular gluing line and a large number of osteoblasts. Around some trabeculas were seen Gaupschit’s lacunas and osteoclasts. Between trabeculas, bone marrow of myeloid structure was formed. The border between the formed bone structure and maternal bed was absent. There was an organotypic copmplex: bone tissue and the granules of titanium nickelide in the form of single structure. After 3 months in the second group there was discovered of the epiphysis cavity the primitive bone tissue of trabecular structure against the background of osteoclastic resorption of bone fragments, osteoid substance with collagenous fibrils. The complete contact with the maternal bed was not observed. Thus, in the first group of animals, accelerated formation of trabecular bone tissue was observed and, as a result, the filling of a bone defect. Pathogenetic mechanism of apparent osteogenic reaction is the possibility to form bone tissue in the pores of the implant. The corresponding temperature and, probably, the stimulating inductive influence of titanium nickelide contributed into the differentiation of bone marrow stem cells into osteogenic ones and the formation of bone tissue. In the pores of the implant, trabecular bone tissue was formed with the structure analogous to metrical bone. The germination and growth of bone tissue in the porous structure of the implant occurred simultaneously in many pores in the form of separate nuclei (zones), which then proliferated and united into a single tissue system, filling the pores of the implant and connecting their canals [7].

Two months later the regenerate consisted mainly by the end of the third month after the operation. The structure pattern of tissue in the pores did not practically change with the time.

Results of clinical research. During early post-operative period, it was determined that 4 (8.0 %) patients of the study group had post-operative wound pyogenesis and 2 (4.0 %) patients revealed the formation of hematomata in the zone of postoperative wound. In the comparison group, these figures were correspondingly 4 (14.3 %) and 2 (7.1 %); 3 (10.7 %) patients had necrosis of wound edges. The post-operative complications were evaluated as a consequence of the presence of a vast defect of tissues before the operation and, as a result of resection of cicatrical wound edges, the lack of tissues for closing the defect. Conservative measures allowed eliminating these complications. All the patients were discharged from hospital in a satisfactory condition. Healing by first intention was observed in 50 patients (92.0 %) in the study group and in 19 patients (67.9 %) in the comparison group. The average duration of treatment in hospital for the study group was 11.6 days for planned admittance and 17.7 days for urgent admittance, in the comparison group – 14.8 and 23.6 days, correspondingly. Distant results were followed during the period from 6 months to 5 years. In the study group 52 patients did not have limb pains; there were no relapses of the exacerbation. 3 patients (5.4 %) had fistulas formed in the operational zone, in the comparison group 14 (4.3 %) patients had periodic pains in the limb. 5 (17.9 %) patients had fistulas, 5 (17.9 %) patients had exacerbation of the process. Rh-investigations revealed that the regeneration of bone occurred in both groups, however it considerably predominated in the study group. All the patients in the study group had periosteal bone reaction in the destruction zone, and in the comparison group – 24 patients (85.7 %). A month after the operation, roentgenological research revealed that all the patients of the study group determined the shadow of implant material in the zone of former bone defects, the sharpness of their contours was disappearing. Further the intensity of the shadow from the side of the defect edges increased, and by the time of the 6th month it achieved the criteria of normal bone tissue, which did not alter later. In the comparison group by this time, no patient manifested complete obliteration of bone cavity. Clinical and roentgenological examination determined the relapse of osteomyelitis in 5 (5.4 %) patients in the study group, the result of the realized treatment could be evaluated as good. The function of operated limbs was restored completely, a good cosmetic effect was achieved. In the comparison group the relapse of CO was determined for 3 (10.7 %) patients.

Conclusions. Clinical practice confirms that the use of the treatment method of CO by sequestrectomy with the following grafting with the granules of titanium nickelide gives more positive results than the traditional method. It is less traumatic, simpler in realization. The use of this technology allows to reduce the number of post-operative complications and negative results in distant periods, shortens the period of hospital treatment, provides the restoration of bone tissue defects in shorter time, decreases the number of relapses of the disease and improves the quality of patients’ lives. Thus, clinic-experimental research showed that porous titanium nickelide is a perspective material and can be used for different skeletal pathologies. In the experiment, its use for grafting bone cavity in comparison with bone crumps demonstrated the formation of bone organo-typical regenerate 3 months earlier. The use of bio-compatible fine-grain titanium nickelide contributes into rapid and efficient completion of the bone regeneration process in bone tissue, simplifies the methodology, reduces the time of operation and the time of rehabilitation period and, as a result, increases the efficiency of treating patients with chronic osteomyelitis.
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About authors:
Stofin Andrey Sergeevich, MD; Associate Professor, Department of general surgery;
tel.: +73832767464; e-mail: department.of.general.surgery@gmail.com
Shegolev Michail Borisovich, MD; Associate Professor, Department of general surgery;
tel.: +73832767464; e-mail: department.of.general.surgery@gmail.com
Trushin Pavel Victorovich, MD, CMSc; Associate Professor, Department of general surgery;
tel.: +73832767464; e-mail: tpv1974@rambler.ru
Shtofin Sergey Gridorevich, MD; PhD, Professor, Head of Department of general surgery;
tel. +73832767464; e-mail: department.of.general.surgery@gmail.com
Golovnev Andrey Vladimirovich, MD, CMSc; Associate Professor, Department of general surgery;
tel.: +73832767464; e-mail: department.of.general.surgery@gmail.com
Shegolev Michail Borisovich, MD; Associate Professor, Department of general surgery;
tel.: +73832767464; e-mail: department.of.general.surgery@gmail.com
Golovnev Vladimir Andreevich, MD; PhD, Professor, Professor of Department of general surgery;
tel.: +73832767464; e-mail: department.of.general.surgery@gmail.com
Stofin Andrey Sergeevich, MD; Associate Professor, Department of general surgery;
tel.: +73832767464; e-mail: department.of.general.surgery@gmail.com

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OSTEOPOROTIC SHEEP MANDIBULAR MODEL FOR COMPARATIVE ALVEOLAR BONE HEALING RESEARCH

Sirak S. V., Shchetinin E. V., Bobryshev D. V., Fritsch T. 2, Giesenhagen B. 3, Petrosyan G. G., Didenko N. N., Romanenko R. G., Grimm W.-D. 1,4

1 Stavropol State Medical University, Russian Federation
2 University of Arad, Romania
3 University of Frankfurt am Main, Germany
4 Witten/Herdecke University, Witten, Germany

ОРИГИНАЛЬНЫЕ ИССЛЕДОВАНИЯ
Экспериментальная медицина

С. В. Сирак 1, Е. В. Щетинин 1, Д. В. Бобрышев 1, Т. Фрич 2, Б. Гизенхаген 3, Г. Г. Петросян 1, Н. Н. Диденюк 1, Р. Г. Романенко 1, В.-Д. Гриим 1, 4

1 Ставропольский государственный медицинский университет, Российская Федерация
2 Университет Арад, Румыния
3 Университет Франкфурта-на-Майне, Германия
4 Университет Виттен – Хердекке, Виттен, Германия

In the study was investigated the suitability of the mandibular ridge in osteoporotic sheep for comparative dental implant research, to establish histological protocols for this model, to study the effect of variations in healing of tooth extraction sockets and of an acute 12mm bone defects. The hypothesis tested was the post-extraction osteoporotic sheep mandible and the acute 12mm bone defect in osteoporotic sheep is a suitable model for comparative dental