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Bone Xenografts in Trauma and Orthopaedics (Analytical Review)

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Abstract

Purpose of the analytical review — to evaluate the application experience of bone xenografts in trauma and orthopaedics surgery. ***Methods.*** Data search was performed in the electronic databases of PubMed and eLIBRARY with depth of 20 years. ***Results.*** The authors identified 13 papers which described the application experience of bone xenografts in trauma surgery and orthopaedics. The highest efficiency (from 92 to 100%) was reported for cases of xenografts use to replace defects in intraarticular fractures and revision arthroplasty. Unsatisfactory outcomes were related to cases with no integration and graft rejection. The least efficiency (from 41,9 to 46,1%) was reported in reconstructive foot surgery. No effect of bone xenografts was observed for replacement of defects in cases of pseudoarthrosis. The most frequent complication was graft material infection. The summarized literature data provided the calculated share of complications following xenograft use of 7,53% (18 out of 239 cases, CI 5–95%, 4,53–11,21). Two areas were identified for improvement of technical and biological properties of bone xenografts: 1. Modification of original xeno-matrix (enhancement of purification technique, alteration of structure of chemical composition of the bone matrix); 2. Augmentation of matrix volume by additional elements (biologically active agents, stem cells). It's noted that demand for xenografts in traumatology and orthopaedics can increase after refining and expanding the indications for clinical use. ***Conclusion.*** Bone xenografts used in the modern trauma surgery and orthopaedics to replace bone defects in revision arthroplasty as well as in certain fracture types. Such material is relatively safe and its ability to be modified allows to improve its biological properties.

Keywords: bone allograft, bone xenografts.

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Introduction

Currently the tasks to replace deficient bone tissues in trauma and orthopaedic surgery can't be solved without use of allo and xenogenic grafting materials [1, 2]. Both those graft types differ from the autologous bone in inferior osteogenic properties, potential antigenic response and disease transfer, as well as in altered biological and mechanical properties due to their processing [3].

Despite the fact that a series of publications demonstrated a comparable or even superior efficiency of xenogenic vs allogenous materials for bone defects replacement [4, 5, 6], currently allogenous grafts are given preference in the national clinical practice [7, 8, 9, 10, 11, 12, 13]. In the authors' opinion the xenografts are underestimated although their accessibility allows to:

– cover the increasing demand for osteoplastic materials mainly for application in revision joint replacement [14];

– reduce cost of the end products (production of xenomaterials has a significant potential for cheaper mass production and, by some estimates, could be three times more cost effective than production of allografts [15]);

– substantially modify the material to improve their biological features (osteoconduction, osteoinduction, safety) and to increase shelf life [16];

– ensure better process of sorting and rejection and to select the materials with the optimal physical and mechanical properties.

Those advantages are currently utilized in dental practice and maxillofacial surgery where xenografts feature rather wide application [17, 18, 19, 20, 21, 22, 23, 24, 25]. In contrast, the data on bone xenografts in trauma and orthopaedic surgery are quite fragmented.

The purpose of this analytical review — to evaluate the experience of bone xenogenic materials in trauma and orthopaedic surgery.

Data collection and extraction

The sources search was performed in open databases of scientific literature PubMed and eLIBRARY with the depth of 20 years. The keywords used were 'xenobone', 'xenograft', 'xenomatrial', 'bone AND xenograft'.

The authors established inclusion and exclusion criteria for further analysis and evaluation of the literature.

Inclusion criteria were as follows: availability of the full text of publication or structures abstract with indication of particular quantitative data.

Exclusion criteria:

1. Clinical cases, report thesis, unpublished papers.

2. Research with "duplicaton" indicators (similar research protocol, groups and number of patients, etc). In case of "duplicating" papers the authors chose a later source.

3. Papers dedicated to dental and maxillofacial surgery.

Results

Clinical application. The authors identified 13 sources describing clinical application of bone xenografts in practical trauma and orthopaedic surgery (Table 1).

Analysis of the literature data demonstrate that:

– Clinical application of bone xenomaterials in traumatology and orthopaedics is rather limited;

– The greatest efficiency (from 92 to 100%) was observed for cases where materials were used to replace defects in intraarticular fractures and revision arthroplasty, unsatisfactory outcomes were related to absence of material integration and rejection of material;

– The least efficiency (from 41.9 to 47.2%) was observed for reconstructive foot surgery;

– No effect was observed after use of xenogenic bone materials for defects replacement due to pseudoarthrosis;

– Infection is the most frequent complication after use of bone xenografts.

Table 1

Literature data on clinical application of bone xenografts in trauma and orthopaedic surgery

Applications (number of cases)	Treatment efficiency*	Implant associated complications	Source
Fracture of the tibial plateau (*n* = 19)	19 (100%)	No	[26]
Intraarticular fractures (*n* = 19)	18 (94.7%)	2 cases of infection (10.5%)	[27]
Evans calcaneal osteotomy (*n* = 29)	Comparable to allograft	No	[28]
Bone defects (*n* = 116)	107 (92.2%)	16 cases of infection (13.8%)	[29]
Replacement of iliac crest defect after autobone harvesting (*n* = 16)	15 (93.8%)	No	[30]
Revision arthroplasty (*n* = 27)	27 (100%)	No	[31]
Revision arthroplasty (*n* = 15)	14 (93.3%)	No	[32]
Wedge tibial osteotomy (*n* = 4); revision arthroplasty (*n* = 3)	7 (100%)	No data	[33]
Wedge tibial osteotomy (*n* = 31)	24 (77.4%)	5 cases (16.1%): 2 infections and 3 cases of discharge at the implantation site	[34]
Revision arthroplasty using xeno- and autografts (*n* = 27)	21 (77.8%)	1 case of infection (4.8%)	[35]
Reconstructive foot surgery (*n* = 31)	13 (41.9%)	No data	[36]
Reconstructive foot surgery (*n* = 13)	6 (46.2%)	No data	[37]
Pseudarthrosis (*n* = 2)	0 (osteolysis)	No data	[38]

* Treatment efficiency was estimated as the number of positive outcomes in percentage to the overall number of cases.

Basing on the literature containing complications data the estimated percentage of complications for use of xenomaterials amounts to 8.45% (24 of 284 cases, CI 5–95%: 5.50–11.96) [26, 27, 28, 29, 30, 31, 32, 34, 35]. However, it should be noted, that complications reported in the publications of Levai et al. and Charalambides et al. [34, 35] dated 2003 and 2005 can be due to imperfect processing technologies at that time. So, by excluding such data from the statistics, it's possible to obtain percent of complications equal to 7.53% (18 of 239 cases, CI 5–95%: 4.53–11.21).

Detailed analysis of complications was given in the paper of Kubosch et al. where it was demonstrated on the large data volume that complications rate in use of xenomaterials for bone defects replacement depended on localization of defect and integration rate decreased with patient age [29]. This research allows to consider the fact that percentage of complications can be reduced when elaborating contraindications for use of xenografts related to defect site and age of patient.

Performance improvement of bone xenografts. Despite the available experience of clinical application of xenomaterials and availability of sufficient number of materials approved for use [2, 39, 40], improvement of their efficiency and safety continues.

Table 2 presents the key experimental works in this area.

Table 2

Areas for improvement of performance features for bone xenografts

Area	Modification type	Source
Impregnation by biologically active agents	Growth factors	[41, 42, 43, 44, 45]
	Antibiotics	[46, 47]
	Antibiotics + Growth factors	[48]
	Bisphosphonates	[49]
	Platelet rich plasma	[50]
Tissue engineering	Enrichment of xenomatrix by stem cells	[51, 52, 53, 54, 55, 56, 57]
Chemical modification of xenomatrix	Inclusion of fluorine ions	[58]
	Inclusion of chlorine ions	[59]
	Inclusion of magnesium ions	[60]
	Chemical cross-link of biopolymer	[61]
Physical modification of xenomatrix	Change in porosity	[62, 63]
	Change in crystallinity	[64]
Improvement of purification technologies	Deproteinization	[65]
	Lipids extraction	[66]
New sources of xenomaterials	Horns	[67]
	Rabbits, horse	[68]

Two main areas for improvement of technical and biological properties of bone xenomaterials can be identified among the analyzed papers:

Modification of original xenomatrix (improvement of purification technology, change in the structure and chemical composition of bone matrix) [58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68];

Introduction of additional elements into the matrix bulk (biologically active agents, stem cells) [41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57].

In the opinion of the authors today the most developed area is the impregnation of various biologically active agents such as growth factors and drug substances into the bulk or/and on the surface of the xenomatrix [41, 42, 43, 44, 45, 46, 47, 48, 49]. Relevant enough is the area of tissue engineering where cell stems are implanted onto the surface of xenomaterial [51, 52, 53, 54, 55, 56, 57].

Search of new raw materials sources for obtaining bone grafts is continuing [67, 68].

The present analysis demonstrated that osteoplastic materials of xenogenic origin are currently used in practical traumatology and orthopaedic surgery to treat a limited range of pathologies in contrast to maxillofacial surgery and dentistry that have already accumulated large experience of such materials application for bone defects replacement and established own protocols for implantation. Nevertheless, we can expect a growing demand for xenomaterials in trauma and orthopaedics due to increased clinical need related to increasing number of revisions in arthroplasty requiring replacement of deficient bone stock.

Relatively rare application of xenomaterials in current traumatology and orthopaedics can be explained both by certain conservatism of surgeons unwilling to risk and implant biomaterials due to possible complications and by lack on information on availability of such materials on the market. Anyway, xenogenic materials are used sporadically, therefore, there is insufficient number of routine applications in cases that can be standardized. The amount of scientific evaluation for application of such materials is also insufficient.

Undoubtedly, such situation is also accounted to the fact that technical features and efficiency criteria of xenomaterials available on the market limit their demand in trauma and orthopaedics. Broadening of indications for application of xenografts can be achieved by additional modification of such materials, and first of all by improving their osteoinductive and osteoconductive properties. Relevance of this topic is verified by the number of experimental research undertaken lately in this area (Table 2).

The conducted literature analysis allows to conclude that reported advantages of xenomaterials (accessibility and modifiability, relatively low cost and acceptable safety) have rather high potential for its further application. In this regard, there are three main tasks to be solved for more popular application of xenografts.

1. Refinement of indications for application and development of treatment protocols for treatment of bone pathologies using xenomaterials (indicated by some authors in their publications [28, 69, 70]). This task can be solved by evidence-based clinical studies. The present review demonstrated that despite a growing availability of registered xenogenic materials on the market, there is still no evidence-based, well-structured and independent clinical research.

2. Broadening of indications for use of bone xenografts. Solution can be found in improvement of obtaining and modification of xenomatrix, that will allow to enhance technical and biological properties of the materials and expand indications for use in traumatology and orthopaedics. Creation of a material to replace large bone defect is the most relevant area [29, 41, 70].

3. Determination of the possibility to use xenomaterials in combination with other bone substitutes. Works in this area are also underway [71, 72].

Certainly, determining the advantages of bone xenomaterials over materials of allogeneic and even more so, of autogenous nature, requires evidence-based research. However, already now we can identify the scope of application for such materials: joint arthroplasty and replacement of small bone defects. We can also suggest that enhanced production technologies and growth of the market of bone xenogenic materials will make such grafts more accessible for practical use.

Conclusion

The performed analytical review demonstrated that xenogenic bone grafts in current traumatology and orthopaedics found its scope of application for replacement of bone deficiencies during revision joint arthroplasty as well as at some type of fractures. These materials can be modified to improve their biological properties. This opens up additional prospects for the use of xenogenic bone grafts in the practice of trauma and orthopaedic surgeons.

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Authors' contribution

M.V. Stogov — concept of the research, analysis and description of search results.

D.V. Smolentsev — selection of publications, analysis and description of search results.

E.A. Kireeva — selection of publications, preparing and design of the paper.

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