TREATMENT FOR BONE LOSS, PSEUDOARTHROSIS, ARTHRODESIS AND BENIGN TUMORS BY USING MEXICAN XENOGRAFT (CLINICAL TRIAL).


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Summary
Objective: Bone loss as results of arthrodesis, pseudarthrosis, benign tumors and bone defects were treated using a xenograft (Nukbone).
Methods: The effectiveness of the material was evaluated through a longitudinal and observational study in the Hospital Regional “General Ignacio Zaragoza” (HHRGIZ) ISSSTE. The Mexican xenograft is a patent of the National Autonomous University of Mexico (UNAM).
Results: Fifty two patients were considered regardless age or gender. Of these patients, 28 were male and 24 female. Average age of the patients was 47.7 years (9-84 years). Twenty eight patients had arthrodesis, 16 were treated with pseudarthrosis, three patients had benign tumors and five patients presented bone defects, which were implanted with Nukbone at the site and was the correct treatment of the problem. The xenograft is fully integrated during a period of 3-18 months, depending on the size of the pathology and the region where it was placed. The fracture healing was evaluated radiographically according to the classification of Montoya. No patient had clinical signs of rejection.
Conclusions: In Mexico, bony xenografts (osseous) have been used, all of foreign origin due to the high degree of technological dependence in this country. In this study, we describe the use, for the first time, of a Mexican xenograft whose patent is from the Universidad Nacional Autónoma de México (UNAM). The Mexican xenograft is biocompatible and can be adapted to treat pathologies where bony (osseous) material is needed.
Key words: Xenograft, bone healing, arthrodesis.
INTRODUCTION

There are different causes that provoke the continuity of bone loss, which is an injury that goes through a healing process called osseous consolidation (formation of tissue of granulation, soft and hard callus and remodeling). Tumors, pseudoarthrosis and arthrodesis are some pathologies in which the loss of osseous consolidation exceeds the capability to be consolidated in a right way and time. The xenografts (Greek: xenos-strange) that come from bovine bones help the capability of osseous reconstruction and they also diminish the risk of transmission of diseases such as hepatitis and AIDS, which may appear in when employing allograft of bone. Another advantage is to avoid a double surgical procedure to take autologous bone (golden standard) because there is a chance of having got less tissue than the necessary for treatment, so the recovery time will be longer (1,2).

Arthrodesis is a surgery that integrates, through bone, skeletal joints. Held in conjunction with other surgical procedures such as discectomy. In general an arthrodesis procedure employs a bone graft with or without osteosynthesis or fixation (3-5), which may be removed or not when it is done. The incidence of complications as pseudoarthrosis is a common problem, particularly after ankle arthrodesis is considered that reaches up to 50% (6).

Pseudoarthrosis is the lack of definite bone consolidation of a fracture or arthrodesis. It is a pathological process that corresponds to the formation of a scar tissue through a non-ossified fibrous tissue, this is an irreversible and definite process, and the scar tissue is absolutely normal, pathological alteration shows up when there is no osteoblast integration to give fibrous scar tissue characteristics of bone tissue. All this happens because of different situations: the lack of perfect and uninterrupted immobilization, by the interposition of soft tissue, excessive separation of bone fragments, not enough vascularization or fracture of pathological bone.

Benign bone tumors have cells that tend to maturation and differentiation, are generally well defined respect to the tissues around. Its healing is guaranteed by a full resection. Malignant bone tumors are sarcomas that show a tendency to grow up quickly and disorderly, infiltrating neighboring organs, with a tendency to spread a distance in the form
of metastasis also occurs, treatment involves large affected bone resections, with wide security margins (7), but they are not considered in the current study.

The incidence of primary bone tumors is relatively low, reliable epidemiologic studies show that 1 out of 100 000 male inhabitants and 0.7 out of 100 000 female inhabitants suffer of this problem (World Health Organization) (8).

Only giant cell tumors represent about 4 or 5 % of the total primary bone tumors. Tumors located in the phalanges of the hand rarely appear and affect young patients, they are more common in third decade of life, the average age is 32 (7).

The unicameral bone cyst corresponds to 3% of injuries primary bone is more common in male patients in a relation 3:1; its predominant location is diaphyseal proximal humerus and femur. It presents pain, swelling and stiffness of the proximal joint; the fracture is considered the first sign of a lesion and it happens in 66% of cases. The treatment consists of curettage of bone and placement of bone graft, with osteosynthesis or immobilization (9).

Bone loss from trauma (fractures) are due to various causes such as work and traffic accidents, which involve high-energy trauma collapse, displacement, exposed bone, tumor resections or infectious processes. Due to the frequency of these problems in third level public medical centers, in the National Autonomous University of Mexico had developed a bone xenograft (Nukbone®, patent PA/a/2002/009719) according to international standards ISO-137779 and American Society for Testing and Materials’, and the national ones set on NOM-059-SSA1-1993 (10-15).

The main objective of this work was to evaluate the efficiency of this xenograft for treatment of bone loss in arthrodesis, pseudoarthrosis and benign bone tumors.

**MATERIAL AND METHODS.**

An observational, longitudinal and descriptive study was carried out in the Regional Hospital Orthopaedics Service “General Ignacio Zaragoza” of the Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado(ISSSTE) between March 1, 2006 and July 30, 2007 (16).
Fifty-two patients were selected from external consultation orthopedic emergency and hospitalization with the following diagnoses: pseudoarthrosis, benign bone tumors, loss posttraumatic bone, spinal instability, lumbar spinal stenosis and cervical spinal stenosis.

Based on the interview and clinical record was prepared a format for collecting the following data: age, gender, diagnosis, treatment, geometry of the xenograft used, date of the surgical procedure, dates for outpatient consultation and radiographic control from the preoperative stage to discharge.

**INCLUSION CRITERIA**

a) Patient who requires a graft due to a bone loss because arthrodesis, pseudoarthrosis, trauma or benign bone tumor.
b) Male or female without an age limit.
c) To be a right holder of ISSSTE
d) To agree in writing with the placement of the xenograft under informed consent.

**EXCLUSION CRITERIA**

a) Do not accept xenograft placement.
b) Patients with malignant tumors.
c) Patients who did not continue outpatient control.

**NUKBONE® XENOGRAFT**

The implants donated by Biocriss were elaborated according to specified geometrical shapes, which were specified by the orthopedist and the cabinet studies. They could be cube-shaped, rectangular or polygonal blocks, ingots and plates, see Figure 1.

**PREOPERATIVE PLANNING**

- A clinical and radiological analysis was done to select the type of implant, which is essential for quick and effective management of the injury, so that radiographs were taken the affected bone in anteroposterior and lateral projections. In some cases CAT scanning and NMR were necessary.
- An evaluation of soft and scar tissues was carried out to determine the surgical approach.
• If necessary, it is determined the type of osteosynthesis material to be used in the surgical procedure.
• Clinical and preoperative studies were done by services of internal medicine and anesthesiology.
• The surgical approach was planned for each patient. In general, two surgical techniques were applied: arthrodesis and open reduction with internal fixation.
• Montoya’s classification, which establishes the different stages of bone repair, was used. It is helpful in radiographic study evaluation to determine the degrees of consolidation, which goes from 0 to IV grades (G0 – GIV) (17).

Figure 1. Different geometric shapes that can be showed by the xenograft Nukbone ®, according to the specification of the treating physician.

SURGICAL ARTHRODESIS SURGERY PROCEDURE

Asepsis and antisepsis of the affected area were realized whilst a patient was undergoing selective anesthesia, sterile fields were placed in order to surgical approach. Was dissected by planes, the periosteum of bone was removed, was performed bone surfaces decortication was done until bleeding tissue was obtained. After that the xenograft was placed, the bone stabilization was performed using osteosynthesis material. Sutures and drainage for counter-opening were placed.
OPEN REDUCTION INTERNAL FIXATION SURGERY PROCEDURE

With the patient under selective anesthesia, asepsis and antisepsis of the affected region were done, fields sterile were placed and proceeded to surgical bone. Was dissected by planes, the periosteum of bone was removed, in order to reduce bone fragments and the bone stabilization was done using osteosynthesis material. Then the xenograft was placed in the site of the defect or bone loss. Sutures and drainage for counter-opening were carried out.

RESULTS

Of the 52 cases, there were 28 male patients and 24 female ones whose average age was 47.7 years (9-84 years), the predominant age group 40 to 60 years. The most affected bones were vertebrae (cervical and lumbar) with 25 cases, 6 humerus, 5 shinbone, 4 clavicle, 4 femur, 3 radius, 4 hands and one hip.

About the treatments, 28 patients had arthrodesis (53.8%), 16 osteosynthesis were treated with xenografts for pseudarthrosis (30.8%), 3 patients had benign tumors (5.7%) and 5 patients presented posttraumatic bone defects in which internal fixation was required and xenograft application was implemented (9.6%). See Figure 1. All patients were implanted with Nukbone at the site of problem.

Descriptive statistics were used to assess the results (18). The patients with spinal arthrodesis were 26, one of ankle and one of wrist, showed bony consolidation in 6 weeks up to 6 months according to x-ray and CAT images, see Figures 2 and 3. The patients of spinal arthrodesis were monitored by CAT for 3, 6, 12 and 24 months after surgery. Patients who required column arthrodesis, were those in which showed commitment to the neurological structures or instability biomechanics secondary to trauma, degenerative nerve diseases or nervous system tumors.

Wrist arthrodesis corresponded to a patient with significant pain and deformity in the wrist as a result rheumatoid arthritis, and the last arthrodesis patient was a patient with a fracture ankle malunion.
Patients with pseudoarthrosis were 16, after two months treated with Nukbone, bone healing was observed with an evolution of GIII in the Montoya scale.

In bone tumors treated with Nukbone, GIII bone healing was observed after two months on average.

Figure 2. Spondyolitic spondylolisthesis L5-S1. A) male 51 years old diagnosed with lumbar spinal stenosis congenital degenerative etiology. B) Side view takeover postoperative six months duration; shows proper consolidation of the chips (cubes indicated by small arrow) integrated to form new bone. C) Back view of the same control; arrows indicate Nukbone® chips.

Figure 3. Tomographic control six months after surgery of the same patient that Figure 2. The post operative course shows the integration of Nukbone® forming tissue with a density
similar to the bone has partially covered the construct. A) Anterior view of surgical place. B) Rear view of surgical site.

**DISCUSSION**

Now, biological grafts are used to help the recovery function of the bone tissue, remaining as an alternative medical treatment for patients that require it. However, the integration of the graft depends on its material, the immune response of the patient and the surgeon’s skill.

It is true that the autologous bone is the gold standard of grafting, but its use increases the patient rehabilitation time and run the risk that be insufficient in quantity. Regarding to the xenograft integration, there are two key stages: the osteoinduction and the osteoconduction, which depend on age, pre-existing degenerative chronic diseases of the patient, the anatomical site where it is placed, and amount and geometrical shape of the xenograft.

In Mexico, bone xenografts have been used for decades, as osteoconductor biopolymer, coralline, xenograft, and so on, all of them foreign origin due to the high degree of technological dependence in this country. In this study, Mexican xenografts were used for the very first time, whose patent solitude is from UNAM.

The age range of patients was 9 to 84 years old, which shows that the biomaterial can be used in paediatric patients, who have a fast bony metabolic rate, as well as in geriatric patients, in whom the regeneration process are longer.

The most frequent cases in this study were arthrodesis (53.8%) and pseudoarthrosis (30.8%) quite related in a direct way to the most affected age group (40-60 years). The use of the xenograft allowed to observe the time differences in consolidation depending on the bone; the bone healing was grade III in Montoya’s classification in 90% of cases in a range 6 to 24 weeks. Should be noted that the time of consolidation xenografts bone from abroad varies from 5 to 24 weeks.

The Mexican xenograft is biocompatible and was described appropriate to treat diseases where bone contribution is required. Nukbone® is easily placed due to the geometric shape appropriate preoperative, which is clearly an advantage for the orthopedist, decreasing
intraoperative time in the design and adjustment of the piece to the surgical site, in case of using another implant (19–23).

CONCLUSIONS

There were no cases xenograft clinical rejections, confirming that it is biocompatible. In all patients the xenograft was fully integrated to the bone, becoming new bone formation. This was verified by clinical and radiographical studies during more than a year.

There were no surgical complications, fistulas or wound infections, which helped the reintegration patient to normal activities as soon as possible.

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REFERENCES


