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Research Article

The Clinical and Radiological Outcome of Bovine Hydroxyapatite (Bio Hydrox) as Bone Graft

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ABSTRACT

Background: A bone graft is a transplanted material to enhance the bone healing response through the osteogenic, osteoconductive, and osteoinductive process on the tissue. Bone autograft has long been the gold standard with the susceptibility of limited supply from the donor and the morbidity risk. The limitation presented by both autograft and allograft has led to the development of bovine hydroxyapatite (BHA). This research was conducted to evaluate the clinical and radiological outcomes of bovine hydroxyapatite as a bone graft.
Methods: This research is a descriptive study using a consecutive sampling design of all trauma patients who received bovine hydroxyapatite in our hospital institution between the period of 2016 to 2018 as the samples. The bovine hydroxyapatite was obtained from the tissue bank in our hospital institution. The results were evaluated clinically and radiologically. The data was tabulated and analyzed descriptively.
Results: From the 56 patients who underwent surgery and were given the bovine hydroxyapatite, most of the results were 80.36% excellent, 12.5% good, 3.57% fair, and 3.57 % poor.
Conclusion: Bovine hydroxyapatite can be considered as an alternative for bone graft in supporting the bone healing process.

Keywords: Bone graft, Bovine hydroxyapatite; Osteoconductive; Bone healing; Human and Medicine

INTRODUCTION

The bone graft is defined as the material transplanted into the recipient to increase the bone healing response through the osteogenetic, osteoconductive, and osteoinductive process in the soft tissue.[1,2] The osteogenetic process is the cellular quality of the graft, which allows the graft apposition using the replaced bone. Osteoconductive is the process where the graft reinforces the adhesion of osteoblast and progenitor cells, and also to provide the necessary interconnected structure where the migration of new cells and the formation of new systemic vessels are formed. The osteoinductive property is the capability of the graft to stimulate the differentiation of the non-differentiated stem cells or the osteoprogenitor cells into osteoblast.[3]

Currently, the use of bone graft is in high demand, where the procedural incidents of bone graft in the US have reached 1 million cases per year with a growth rate of 13% per year.[2] According to the data from the tissue bank, some varieties of bone grafts have been produced. The usage of bone graft from the tissue bank in our hospital institution is quite

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widely spread all over Indonesia. In 2017, the usage of about 3763 pack of bovine bone graft, 282 human/allograft, and 362 pack bovine hydroxyapatite was recorded.[3]

The organic bone graft is divided into three types: autograft, allograft, dan xenograft. The autogenous bone graft is considered to be the gold standard. It remains to show that in fact, it has a minimum immunological rejection reaction, an excellent complete histocompatibility, and allowing the best osteoinductive, osteoconductive, and osteogenetic properties.[4] The disadvantages of autograft are the morbidity rate and the limited number of donors. Due to the high number of morbidity and the limited donors, one alternative considered is a bone allograft. Bone allografts is widely known to be the organic alternatives to fill in the bone defects, as the substitute for limited bone autograft.[5] The advantages of the bone allograft are the possibility to adjust the size of the graft and mass production. In contrast, bone allograft can also lead to disease transmission, rejection reaction, delayed union, and the limited number of donors.[6–8]A proper and meticulous process is essential to produce bone allografts.

To address the issue, we develop bone xenograft as the alternative for the abundant availability where it has the osteoconductive property for mechanical support and low production cost. Incineration furnacing at 1000ºC to eliminate all components of protein from the bovine bone graft.[9] Xenograft is obtained from other species such as bovine through freeze-drying, demineralization, and deproteination process. However, the freeze-drying process generates a considerable degradation of the bone strength; therefore, the tested method from Professor Frank Dexter of Tissue Bank Yorkshire which has been adapted by distinct tissue banks in the Asia Pacific still indicate the reduction of bone strength.[10,11]

Bovine hydroxyapatite is obtained from the freeze-drying process. The material is harvested from bovine bones where all organic components have been extracted (deproteinized) by the furnacing process. The process consists of several steps: dissection, division, cleansing, freeze-drying, washing, and finally oven-dried. Hydroxyapatite produced from bovine bone has been completed a series of tests such as biocompatibility, the microstructure, and the composition test.[9]

Bovine hydroxyapatite has been developed in our hospital institution and has been widely used in orthopedic cases. Concerning the fact that previously mentioned, the author intends to evaluate the outcome of bovine hydroxyapatite as a bone graft from the clinical and radiological view.

METHODS

This is a descriptive study with the total samples examined the clinical and radiological outcomes. Samples were obtained by consecutive sampling, the patients who underwent surgery with bovine hydroxyapatite from January 2016 to December 2018, which consented to attend a scheduled check-up in the Orthopedic Outpatient Clinic or to be home-visited. Due to the limitation of the total number of the subject, the authors decided to evaluate all subjects that underwent orthopedic surgery

with bovine hydroxyapatite in the study period. The follow up was done for minimal 6 months before the clinical and radiological assessments were performed.

The inclusion criteria include 1) Patient with fracture in single bone; 2) Patient with non-union fracture. The exclusion criteria include 1) Patient with multiple fracture; 2) Patient with pathologic fracture due to bone tumor; 3) Patient with osteomyelitis; 4) Patient with Open fracture Grade 3B based on Gustilo-Anderson Criteria.

The first step was to find the patient's data, which were operated using the bone graft from January 2016 until December 2018. After the data recapitulation was acquired, the tracing of the data was conducted in the medical record base of our hospital institution. In the patients' medical record, the patient's identity, the address, and the result of the clinical and the radiological routine check-up from the Orthopedic Outpatient Clinic or home-visit were gathered. The assessment was done by the single person for preventing the observation biased. Regarding the outcome, the category of the assessment on the usage of bone graft was evaluated from the clinical and the radiological are comprised of A) Excellent: Good radiologic union with complete graft incorporated, complete functional recovery; B) Good: Radiologic union with partial graft incorporation and does not require orthotic protection; C) Fair: Poor graft incorporation with the need for orthotic protection; D) Poor: Market fragmentation of the graft, no radiologic incorporation. Functionally no improvement over the preoperative condition.[12]

This study was approved by our hospital institution ethics committee. The data were recorded and tabulated according to demographic characteristics. The descriptive analysis was done to elaborate on the clinical and radiological outcomes of this study without using comparative statistical analysis.

RESULTS

There were eighty-six trauma patients who were operated using bovine hydroxyapatite in our hospital institution from January 2016 until December 2018. However, there were only 56 eligible patients who had complete data from medical records and were possibly evaluated. Other patients could not be evaluated since they did not come and could not be called for a routine check-in in the Orthopedic Outpatient Clinic at our hospital institution.

Based on Table 1 showed the age distribution data of the patients, the highest percentages (39.28%) were the patients with a range of age 41-50 years old. Meanwhile, there were only two subjects in the >60 years old group. The most frequent defect locations were 55.36% in metaphysis. According to the results presented in Table 1, most of the patients (80.36%) were excellent, 12.5% were good, 3.57% were fair, and 3.57 % were poor.

Based on the bone regions, the highest distribution was in the femur region which encountered from 22 patients (39.28 %). However, the most common fractures were tibial plateau fractures (13 cases), followed by intercondylar femur fractures 9 cases, which shown in Table 2. There were complications

post-surgical infections of two patients and implant failure of two patients (Table 3).

DISCUSSION

Bone grafts have four essential functions, which are consisted of increasing the osteogenesis process, creating a union between 2 bone fragments, restoring the contour of the bone, and provide the bone skeletal structures. Bovine hydroxyapatite is a material that has been used replacing autograft and allograft for bone regeneration process in the orthopedic field since it has many benefits such as the numerous quantities and minimal complication of the bovine hydroxyapatite usage.[13]

The tissue bank at our hospital institution has developed lots of varieties of bone grafts. A fresh-frozen bone allograft is one of the bone allografts used for more significant bone defect reconstruction. It was quite challenging to be distributed due to the cold chain needs, which had to be stored in -80^{o}C.

Another bone graft produced from the tissue bank in our hospital institution is a freeze-dried bone allograft. This bone graft has a small percentage of water, which is less than 8% because of the sublimation process. It makes the storage easier since this bone graft can be stored in the room temperature and can be easily distributed.[9]

There are several types in the processing of freeze-dried bone allograft, where these organic and inorganic compounds remain in the beginning. Moreover, by the deproteinizing process, grafts only contain inorganic compounds (mineral hydroxyapatite) inside. Lastly, the demineralization process only demonstrates the organic compounds

Table 1. Patient Demographics

Groups	N	Percentage (%)
Age		
▪ < 20 years old	5	8.92
▪ 21-30 years old	9	16.07
▪ 31-40 years old	10	17.86
▪ 41-50 years old	22	39.28
▪ 51-60 years old	8	14.28
Bone		
▪ Humerus	11	19.64
▪ Radius	4	7.14
▪ Femur	22	39.28
▪ Tibia	17	30.36
▪ Metacarpal	1	1.78
▪ Phalanges	1	1.78
Location		
▪ Metaphysis	31	55.36
▪ Shaft	25	44.64
Outcome		
▪ Excellent	45	80.36%
▪ Good	7	12.5%
▪ Fair	2	3.57%
▪ Poor	2	3.57%

Table 2. Patient distribution based on cases

Pathology	Bone region	Numbers
Tibial plateau fracture	Tibia	13
Lower end radius fracture	Radius	3
Upper-end humerus fracture	Humerus	5
Intercondylar fracture	Femur	9
	Humerus	4
Non-union	Femur	4
	Humerus	2
	Tibia	2
Comminuted fracture	Femur	9
	Tibia	2
	Radius	1
	Metacarpal	1
	phalanx	1
Total		56

Table 3. Patient distribution based on the complication.

Complication	Numbers	Percentages
Infection	2	3%
Implant failure	2	3%
Nerve lesion	0	-

Demineralized Bone Matrix (DBM) in grafts.[9]

The supplies of bone grafts could not afford the high demands for the usage of the bone grafts. Therefore, the tissue bank installation in our hospital institution produces bovine hydroxyapatite (bio hydrox) as a new alternative solution. Bovine hydroxyapatite has a high success rate and a lower expense for bone transplantation in orthopedic surgeries.[14]

This research evaluated the efficacy of the bovine hydroxyapatite as a bone graft in 56 patients in our hospital institution. The age distribution of the patient data is varied from 11 until 68 years old. Ages and genders are essential factors affecting pain sensation. Children, elder, and women feel more pain sensation than men does. These factors affected the pain evaluation for the patients who underwent surgeries using bovine hydroxyapatite.

The most frequent cases using bone grafts in this research are metaphyseal fracture (56%), comminuted fracture (31%), and tibial plateau fracture (20%). It is similar to the research conducted by Shibuya et al. of which the bovine hydroxyapatite could reconstruct, elevate, to restore the joint depression contour. Hence, good structural strength, especially for leg and ankle surgeries, could be achieved. The new ranges of motions, exercises, and weight-bearing are the primary success keys of the rehabilitation process.

The success rates of bone hydroxyapatite in this research were tremendously high. Most of the patients were 80.36% excellent, 12.5% good, 3.57% fair, and 3.57 % poor. Mahyudin et al. conducted research using rabbits, which had similar results with this research. It was stated that bovine hydroxyapatite had the same results in the bone healing process compared to allograft.[15] Hydroxyapatite with or without the combination of bone marrow, become a compelling choice for cancellous bone, while no evidence for cortical bone regarding to the bone in-growth.[1,16]

A study by Tsai et al. where the x-ray image series which were obtained from 27 of the 33 patients with HA bone substitute showed proper bone healing and an 81.8% fusion rate after 6–12 months of follow up. An important discovery is that most of the sintered bovine HA was placed outside the cortex in this study, but the sintered bovine HA was still able to incorporate relatively well into the bone.[17]

There are several merits of HA: its chemical similarity to the bone; its excellent biocompatibility, which can stimulate osteoconduction; and its ability to be integrated into the bone without provoking an immune reaction. Further study by Kotobuki et al. explained that microenvironment HA could provide its calcium ions and alkaline ions for osteoblasts to cause mineralized extracellular mesenchymal and to secrete ATPase. It can also encourage cells to show an osteoblastic phenotype and form bone tissue.[18]

There was a non-union case in an external fixator application shown in figure 1a.

Therefore, six months post-application of the external fixation and addition of *bone hydroxyapatite* inside the fracture site. The results were excellent (Figure 1B).

Figure 1. (A) Non-union Case of tibial fracture in external fixator application and (B) The results of 6 months post-application of the external fixation and addition of *bone hydroxyapatite* inside the fracture site.

There is a fracture of the tibial plateau that needs to restore joint-depressed. Bone graft implanted to filled defect and restored the joint surface (Figure 2). Pre ORIF (Figure 2A) dan post ORIF with *plate* and *screw* also added *bone graft* (Figure 2B). The fractured lines were united, and joint depression was reduced.

There are four complications that we found. From further investigation, that patient with open fracture supracondylar femur with bone loss and patient with open fracture intercondylar humerus who was conducted with ORIF using the double plate and adding bone graft showed poor results. We suspected that the infection as the leading cause of both non-union cases in this research since they were both open fracture cases that had high risks of getting the infection. According to the research conducted by Tsai *et al.* also stated that the infection was the cause of the bone graft failure.[17]

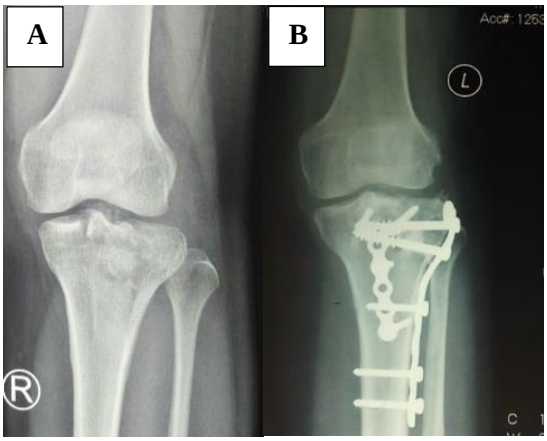

Figure 2. (A) Tibial Plateau Fracture Pre ORIF and (B) post ORIF with plate and screw also added bone graft.

The usage of bovine hydroxyapatite is relatively saved and showed a satisfying result on fractured patients. This is because *bovine hydroxyapatite* has been deproteinized, and humans growing up have been long exposed to the bovine protein, from the meat and the dairy products. Infection cases were found in 2 patients with open fracture cases. This infection results in the bad outcome of the healing process (non-union).[19]

This study had several limitations that include the number and variety of cases provided in this study had not fulfilled every specific type of possible injury. This study had not included comparative statistical analysis to evaluate the outcome based on the type of injury. The longer follows uptime should be done to provide a better understanding of the long-term outcome of bovine hydroxyapatite usage in trauma patients.

CONCLUSION

This study showed promised potency of bovine hydroxyapatite as a bone graft substitute based on clinical and radiological outcome descriptively. The BHA can become an alternative in increasing the bone healing process, filling in the bone defect, repairing the contour, and the structure.

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