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Research Article

Comparison of Bone Regeneration of Mandibular Bone Defects Using Natix and Bio_oss with Autogenous Bone in Dogs

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Abstract

Statement of the Problem: Discovery of bone substitute that enhance bone formation or improve bone healing is needed for the treatment of bone trauma and surgery. The use of autogenous bone grafts requires a harvesting procedure at a donor site, which means increased morbidity. In addition, graft resorption is a problem. One way to overcome this problem would be to use bone substitutes as a osteoconductive scaffold for bone regeneration from the residual bone.

Purpose: The aim of this study is to evaluate the effect of bovine inorganic bone (Bio-Oss) and Natix (Tigran PTG) and Autogenous Bone on bone regeneration.

Materials and Methods: In this interventional *in-vivo* study, bone cavities with 3 × 5 mm in diameter were prepared in both sides of the mandible of 4 male adult Terrier dogs. The cavities were divided into 4 groups according to the filling material as follows: Bio-oss, Natix, autogen and control. The animals were sacrificed after 14 days and histological and histomorphometrical analysis was performed.

Results: There was no significant differences between groups in inflammatory response,bone vitality and new bone type with use of Kruskal-wallis analysis. There was statistical difference, in bone formation between autogenous group and others.

Conclusion: According to this study, There was no significant differences between control group and biomaterial groups(Bio-oss and Natix) in amount of bone formation. It means that use of bone materials can't be effective in non-pathologic and non-critical defects.

Keywords: *Bone Regeneration; Bio-oss; Natix; Animal Study*

Introduction

Severe recessions usually occur in alveolar ridges of persons with periodontal problems which can cause side effects such as tooth hypersensitivity due to pulp exposure, or esthetic problems specially in anterior teeth and the most important one loss of periodontal support. In addition in multi root teeth which have furcation involvement or dental implants with periimplantitis, the ability to bone defect regeneration will improve treatment prognoses [1,2].

To solve these problems, bone grafts for regeneration purposes are used so that bone ridges with adequate bone level will be made [1,3].

Grafts and materials can be divided into four groups [2]: 1. Autogenous bone grafts 2. Allografts 3. Xenografts 4. Alloplastic bone substitutes.

Autogenous bone grafts from intra or extra oral donor sites are considered as gold standard for regeneration of cranofacial defects [2,4]. Although their problem is some damage to donor site, it can be solved by using bone substitute [2,3]. As the result, invention of bone substitutes which can speed up bone healing for treatment of bone trauma is needed [5].

Bio_oss is available as a xenograft. This material is a bovine anorganic mineral bone matrix which has a vast use in bone augmentation and several animal studies have revealed that this material is reliable in comparison with other bone substitutes [5,6].

Natix (Tigran PTG: Tigran Porous Titanium Granules), an alloplastic bone substitute made from pure titanium with 1 - 7 mm granul size is porous and unabsorbable. Porosity causes the bone material grow between the particles so that a scaffold is made for osteointegration. Unabsorbability causes a stable structural unit after intergration with surrounding bone so that there is no need to be overfilled in bone defect regeneration [7].

In a histological and histomorphometric evaluation study using Natix, it no foreign body reaction at the site of the newly formed bone or around the biomaterial residue was observed. Newly formed bone was fully vital with large lacunae containing osteocytes [8].

In another study comparing Natix with Nanobone, it was concluded that Both PTG and Nanobone® have osteoconductive properties and are effective in healing bone defects, but the histomorphometric analysis quantified the bone volume with both PTG and Nanobone® and revealed that the maximum amount of the total regenerated bone was seen in the PTG group [9].

According to this fact that no material has the ability for a reliable reosteointegration in periimplantitis defects yet, maybe Natix could be compromising for periimplantits defects, because of its material similariti to implants and on the other hand its osteoconductivity feature.

As the result in this studty we consider the bone regeneration ability of Natix as a new alloplastic bone substitute and Bio_oss as a xenograft bone regeneration material in comparison with autogenous bone graft as gold standard.

Materials and Methods

In this interventional *in-vivo* study, 4 male Terrier dogs of about 8 years old with average weight of 14.4 kg were chosen. Before surgery, dogs went on a same standard diet and condition for a week, and were feeded with soft meals and water twice a day [10].

After general anaesthesia with a mixture of Xylosin 2% (5 mg/kg) (Alfansan: Woreden_Holland) and Ketamin 10% (40 mg/kg) (Tritan: Germany) via IM injection in quadceps, in each dog a horizontal incision was made according to muccogingival line from mesial of second

premolar to distal of first molar, and a full-thickness flap was made by a periost elavator in envelope shape. Then 4 monocortical defects of 5 mm diameter and 3 mm thickness via 5 mm trephine bur on external surface of mandiblar bones with a 5 mm distance from incision line and each other (2 defects on the right side and 2 defects on the left side) (Figure 1). Graft materials were placed in the defects randomly (Figure 2). Defects were categorized in 4 groups in each dog:

Figure 1: *Making defects.*

Figure 2: *Filling defects using natix and bio-oss.*

1. Filled by Bio_oss (Bio_oss powder was mixed with sterillized physiologic serum).
2. Filled by Natix (Natix powder was mixed with sterillized physiologic serum).
3. Filled by autogenous bone (positive control group).
4. Leaved without treatment (negative control group).

It's necessary to mention that autogenous bones were collected from trephine burs.

After making flaps tension free, incision sites were sutured using a 3-0 suture in continuous design.

Dogs have received 50000 UI Penicilin Benzatin and 75 mg/kg Diclofenac Sodium IM every 12 hours for 2 days [10]. Then each dog was considered regularly for well being and health condition.

2 weeks after surgery, dogs were uteanized with general anaesthesia drug overdose. Sutures were removed and a full-thickness flap was made and defect sites were located. Samples were collected sylinderically in 7 mm diameter and 5 mm thickness using 7 mm trephine burs (Figure 3). And were fixed with Formaline 10% for 4 days (Figure 4). Tissue samples were prepared for histologic analysis with H&E staining[10]. Samples were handled to pathologist blindly to consider bone formation, existance of osteoclasts and osteocytes.

Figure 3: *Collecting samples.*

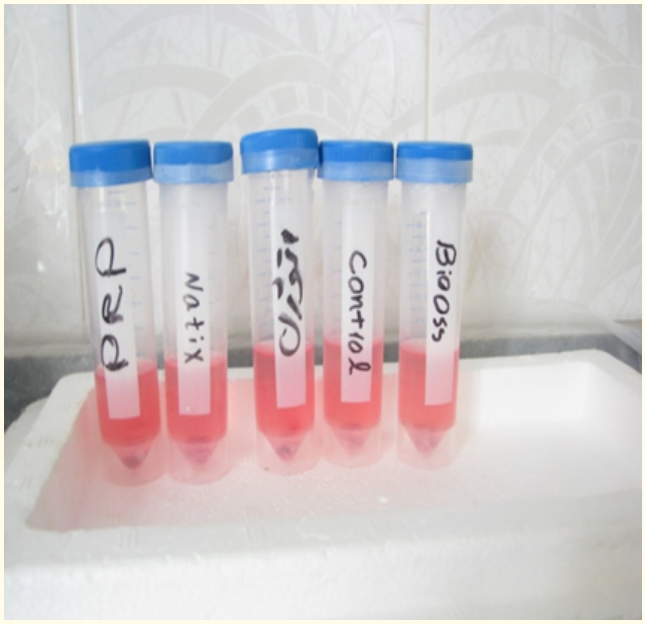

Figure 4: *Final samples.*

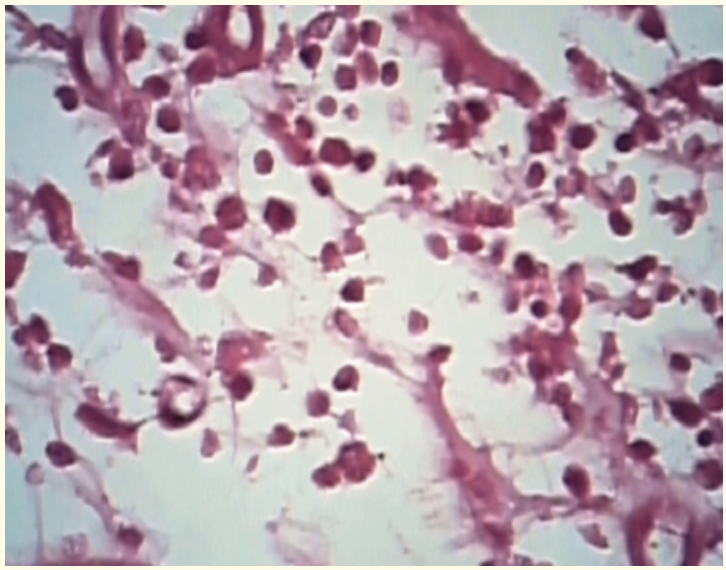

Figure 5: *Histologic view of inflamatory cells.*

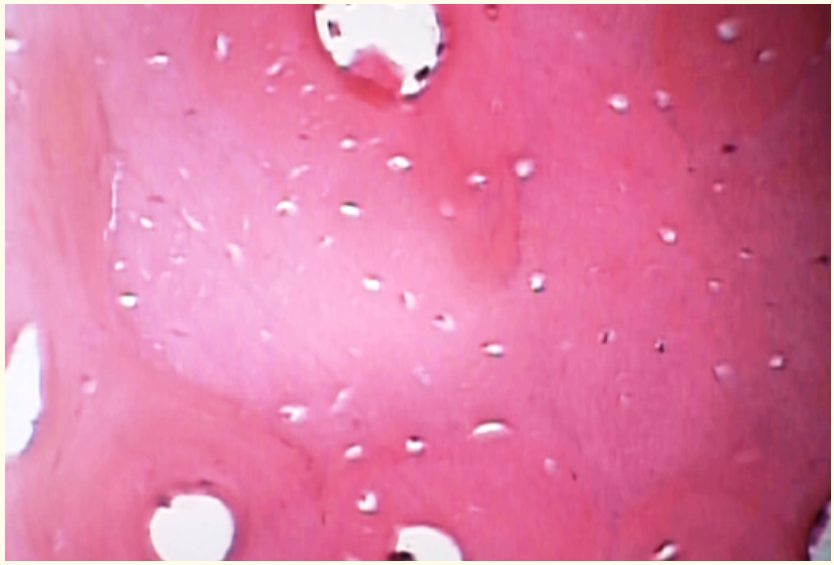

Figure 6: *Histologic view of osteocyte cells.*

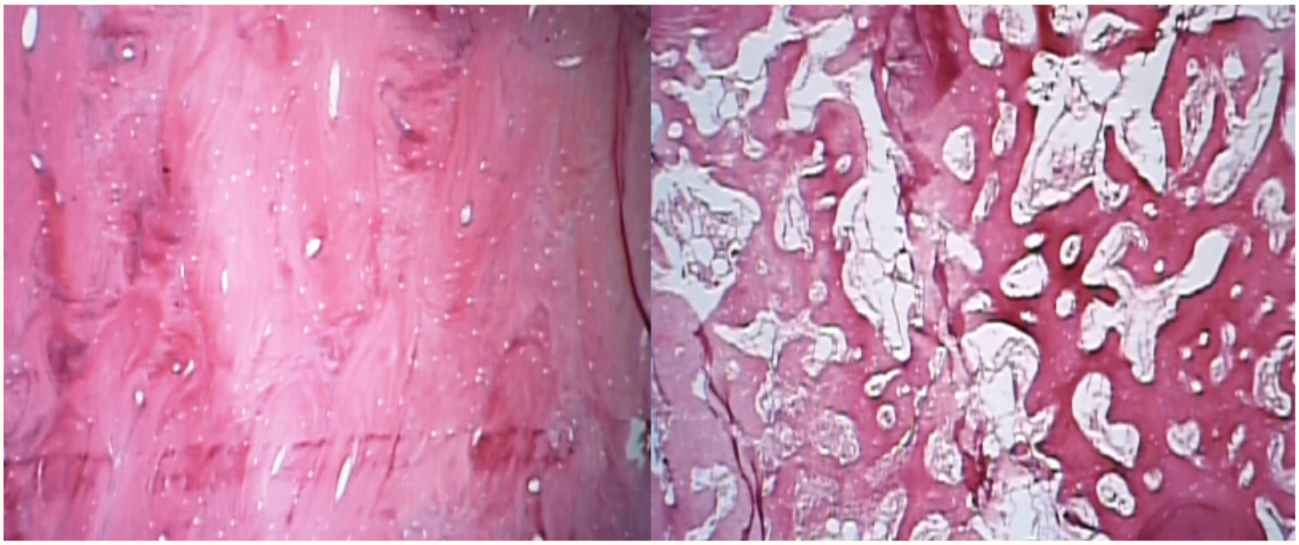

Figure 7: *Histologic view of bone type (right side woven and left side Lamellar).*

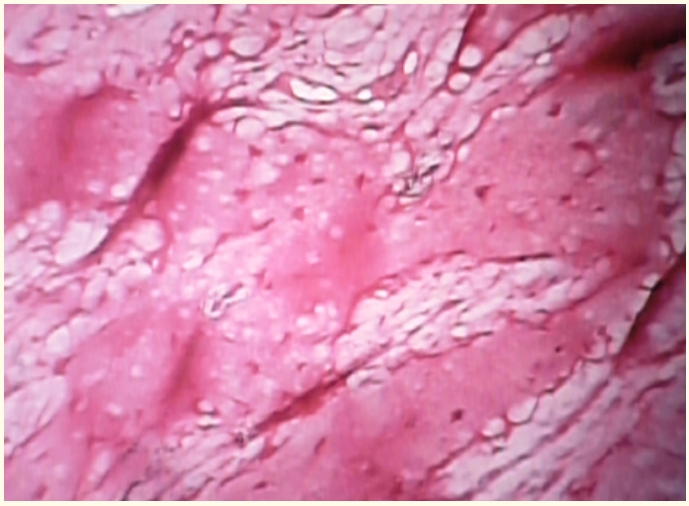

Figure 7: *Histologic view of bone formation.*

Analysis

For histologic analysis, optical microscope slides, were made with 10x, 40x and 100x magnitude for considering the existance inflammatory cells and osteoclasts and osteocytes [11].

For histomorphometric analysis we used microscope with polarized light with 40x magnitude and for quantitive analysis of bone formation in each group, we used digital pictures taken by Nikon camera (Nikon digital camera, Japan) and then for quantitive assessment we used a graphic software (Photoshop CS8) [11].

Results

During the study one dog died for unknown reason. Among 12 defects made, one sample was without inflammation, 7 samples were with low inflammation, 4 samples had moderate inflammation and no sample had severe inflammation.

Although all bio-oss samples showed low inflammation and Natix and autogenous samples showed one moderate inflammation each one, but using kruskal-wallis test showed that there is no statistical difference between groups according to inflamatory response.

According to bone vitality, there was no significant difference between groups and in all samples alive osteocyte was observed inside the lacunas. Also there was no significant difference between groups for bone type.

Kruskal-Wallis test for comparison of each factor in different groups revealed that only the bone formation observations were different among groups (chi = 9.614, df = 4, p = 0.047, and other factors showed no significant difference.

Then, Mann-Wittney test was used in order to define the groups with significant difference (Table 1).

Material A	Material B	P.Value
Bio-oss	Natix	0.114
	Autogenous	*0.025
	Control	0.317
Natix	Bio-oss	0.114
	Autogenous	*0.034
	Control	0.099
Autogenous	Bio-oss	*0.025
	Natix	*0.034
	Control	*0.034
Control	Bio-oss	0.317
	Natix	0.099
	Autogenous	*0.034

Table 1: *Mann-Wittney test results.*

**: Statistical significant difference.*

Discussion

According to Torres., *et al*. [12] materials for bone regeneration should have some features such as osteoinductivity and osteoconductivity, biocompatibility, absorbability, causing no foreign body reaction and is of use.

Among these materials autogenous grafts have all these features and of course access to these grafts need an extra trauma and cost for the patient [12]. So that several studies are done using different bone regeneration materials to improve bone healing.

According to several studies on Bio-oss, this material is reliable in comparision with other bone substitutes [6].

Bio-oss is made from bovine bone which is processed to exclude the organic matter, so that it has only the organic matter. This material is used in bone cavities to help bone formation for many years, so in many articles it is considered as a standard for assessment of different bone regeneration materials. This material is well available and has a low cost.

Natix or porous titanium granules is a synthetic bone substitute made from pure titanium which has a granule size of 1 - 7 mm. This material is newly introduced as a graft for periodontal defects regeneration around teeth and implants.

Bio-oss and Natix are compared with autogenous bone which is gold standard for bone regeneration. In addition in this study a negative control defect was made which undergoes self healing mechanism and be compared with defects treated with grafts.

According to Etel., *et al*. [13] study, mature dog is the best animal model comparable to human.

To scallhorn opinion, one of the most important factors in biologic acceptance of a material is the inflammation around biomaterial particles which in this study, the inflammation around Bio-oss particles was similar to Aritz., *et al*. [5] study. Despite the little difference with some other studies [14], it seems that inflammation level around Bio-oss particles is acceptable.

According to histologic analysis, there were no significant difference between Bio-oss,Natix and autogenous bone.

After all, we can conclude that both Bio-oss and Natix are biocompatible.

In 2 weeks, there were no significant difference for average bone formation between Natix, Bio-oss and also control group which underwent self healing mechanism. This result was similar to Wohlfahrt study that showed there is no significant difference between Natix and control group in swines, but on the other hand it is in opposite of his results that showed there is a significant difference between bio-oss and Natix groups [10]. Also this result is against the results of Razavian study which showed that there is more bone formation in control group than biomaterials groups after a 2 week study on rabbits' skulls [11].

But average of bone formation showed a significant difference between autogenous group and all study groups which demonstrates that autogenous bone graft is the only gold standard for bone defects regeneration.

We can justify the cause of these differences as below:

- Animal type chosen and sample size.
- Difference between defects sizes and follow up periods.
- Lack of such articles which consider the effect of these materials simultaneously in 2 weeks.
- Existance of 4 simultaneous defect in dogs' mandibles with 3 different materials.
- Affecting these defects by self healing mechanism.

In 2 weeks, about the cause of similarity in bone formation among groups, we can say that although these materials are biocompatible and act like a scaffold for bone formation, but they need degradation (for Bio-oss) or osteoblasts attachment to particles (for Natix) in comparison with control group which has non-critical and non-pathogen defects, the bone formation starts rapidly.

Conclusion

At the end we should mention that if our study may continue for some other weeks or was using another animal or another site except mandible, our results may be different as other studies.

According to this study, we conclude that autogenous bone graft is the best method for bone defect regeneration.

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Competing Interests

There are no competing interests.

Authors' Contributions

Janet Moradihaghgoo: Supervision, conduct study.

Masoumeh khoshhal: Supervision, conduct study.

Bita Maleki: Operating study.

Mohammad Hosseinipanah: Operating study.

Ghasem Solgi: Data Analysis, interpretation.

Abbas Moghimbeigi: Data analysis**,** interpretation.

Nazli Rabienejad: Drafting, revising.

Fatemeh Cheraghi: Drafting.

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