A comparison of using autogenous bone graft combined with deproteinized bovine bone and autogenous bone graft alone for treatment of alveolar cleft

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A comparison of using autogenous bone graft combined with deproteinized bovine bone and autogenous bone graft alone for treatment of alveolar cleft

Abstract

This study assessed the clinical results and the bone graft quantity of the two techniques of secondary alveolar cleft bone grafting. Thirty patients with a mean age 10.2 ±1.7 years were randomly divided into 2 groups of study, group I: the cancellous bone graft was harvested from the anterior iliac crests by the conventional trapdoor approach and group II: the bone graft was prepared by mixing the cancellous bone, harvested by a trephine bone collector and then mixed with deproteinized bovine bone in the ratio of 1:1 by volume. The patients in Group II recovered from uncomfortable walking significantly faster than Group I (p<0.05) and their duration of hospital stay was also significantly shorter than Group I (p<0.05). The average amount of the harvested cancellous bone, operation time, intraoperative blood loss and post-operative pain of Group II were less than Group I. The canines of both groups had spontaneously or orthodontically erupted through the grafting areas. The bone graft quantity of both groups decreased with time. However, the average bone graft resorption of both groups were not statistically different over 24 months after grafting. The technique of group II reduced morbidities, hospitalization and the amount of autogenous bone requiring.
Acknowledgement

This study was supported by grant for academic research from Prince of Songkla University, Songkhla, Thailand.

I would like to thank the Center of research Equipment, Pathology and Radiographic Division, Faculty of Dentistry for their suggestion and cooperation.

The authors thank Assistant Professor Wipapun Ritthagol for the comprehensive orthodontic interventions and Mr. Michel Allen Atkins for his proofreading.
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Introduction

Alveolar bone grafting is an important procedure in the protocols of treatment of cleft lip and palate. Although various sources of autogenous bone are used, an anterior iliac crest is considered to be the gold standard for grafting. However, its resorption rate seems to be high within the first year after grafting. Some studies suggested that this resulted from the endochondral in origin or the lack of scaffolds for osteoconduction mechanisms. The conventional cancellous bone harvesting technique is commonly performed by the trap door approach. Although this technique provides a large amount of cancellous bone graft and maintains the contour of the crest, the growth center of the hip, some studies reported the retardation of the growth of the crest after the operation in growing children. Moreover, it may interfere with abdominal organs and causes a huge scar. Other disadvantages included moderate to severe postoperative pain, gait disturbance and extended hospital stays.

The use of xenograft or alloplastic materials instead of autogenous bone has been widely accepted for many years. These materials include tricalcium phosphate (TCP), hydroxyapatite (HA), deproteinized bovine bone (DBB) and synthetic polymers. For DBB, Bio-Oss (Geistlich Pharma AG, Wolhusen, Switzerland) has been commonly used in oral and periodontal surgery, such as for repairing periodontal defects, ridge augmentation and sinus lift operations prior to implantation. However, the cost is high particularly when a large amount of the commercial bone graft is required. The National Metal and Materials Technology Center of Thailand (MTEC) has developed DBB as a grafting
material obtained by sintering bovine bone at 1,200 °C to eliminate proteins and lipids which are antigenic organic matter. It acts as a scaffold consisting of interconnecting pore systems with pore size 200-500 μm and the available particle sizes are 0.25-1 mm. In vivo, it had the osteoconductive manner that enhanced bone formation in rabbit calvariums. The average new bone formation of DBB alone in a 10 mm² defects in at 12 weeks was 24.83±12.12 % when compared to 34.89±4.61 % for an autogenous bone chip (p>0.05)²¹.

Several studiesⁿ¹⁰,¹⁷ have tried to increase the success rate of grafting by combining autogenous bone with DBB for grafting in various ratios. The ratio 1:1 and 1:2 were found to obtain maximum new bone formation when compared to 1:4. The latest in vivo study²² demonstrated that eight weeks after grafting with autogenous bone combined with DBB (MTEC) in the ratio of 1:1 and 1:2 gained more new bone formation (20.93±6.17 % and 22.64±5.66 %) than 1:4(9.621±2.40 %), DBB alone (14.44±2.74 %), or the critical size defect (10.65±8.87 %), but less than the autogenous bone group (30.22±16.72 %). The aim of this study was to evaluate the clinical and radiographic results of alveolar cleft bone grafting using autogenous bone from iliac crest combined with DBB compared to autogenous bone alone in a 24 month follow up period.

Materials and Methods

Patients and surgical protocol
The study was conducted from November 2004 to June 2007 at the Dental Hospital, Prince of Songkhla University in accordance with the regulations of the Faculty board committee. Thirty patients with a residual alveolar cleft
were enrolled in the study. There were 10 boys and 20 girls with an average age of 10.2 ±1.7 years. Twenty two patients had unilateral alveolar clefts and 8 had bilateral alveolar clefts. The secondary alveolar bone grafting was performed by two oral surgeons using the same surgical technique. The___ patients were randomly divided into two groups of study and were unaware of the technique used. For the donor site, in group I, the cancellous bone graft was harvested from the anterior iliac crests by the conventional trapdoor technique (Fig. 1).

Fig 1. The operation of group I, (a) the trapdoor technique was conducted by making a skin incision above the crest about 6 cm long, followed by (b) muscle and periosteal dissection, creating the cortical trapdoor, harvesting the cancellous bone and (c) suturing layer by layer.
In group II, the cancellous bone was harvested from the anterior iliac crests by a trephine bone collector (Medicon eG, Tuttlingen, Germany, diameter 8.0 mm) (Fig. 2) and mixed with DBB (MTEC, Bangkok, Thailand), with particle size 0.25 mm in the ratio of 1:1 by volume (Fig. 3). For the recipient site of both groups, the alveolar cleft sites were grafted and closed by the gingival advancement flap technique (Fig. 4). Analgesics (acetaminophen and meperidine) and antibiotics (intravenous cephalosporin) were prescribed according to the standard protocol.

**Fig 2.** The operation of group II, (a) a tiny skin incision was made approximately 2 cm long, then a dissection was made layer by layer until the iliac crest was seen, then the triphine bone collector was punted through the cortex to harvest inner cancellous bone. Afterwards, (b) a minimal sutured wound was left.
Fig 3. (a) The particulate cancellous bone (PCB) harvested from the crest and DBB were mixed with normal saline solution and loaded into the syringe to measure volume. (b) PCB and DBB were mixed together and (C) loaded into another syringe readily for grafting.
**Fig 4.** The alveolar cleft defect was grafted with the bone graft of each group (arrow) and closed by an advancement flap.

**Clinical assessments**

The recordings taken for intra-operative evaluation included duration of the operation (hr), estimated blood loss (ml) and bone graft volume (ml). Duration of hospital stay (day), time taken to walk again with and without assistance (hr), postoperative pain level (10 cm Visual Analog Scale) and other complications were assessed post-operatively. In the follow up period, postoperative pain was recorded daily for seven days after the operation.

**Radiographic assessments**

The occlusal radiographs were taken by an intraoral radiography machine (Gendex GX 1000; Gendex Corporation, Desplaines, USA) preoperatively, 3 days post-operation and 1, 3, 6, 12, 18 and 24 months after the operation with individually similar constant kilovoltage, milliamp and exposure time. A custom made holder was used to permit reproducibility distance of the film for each patient. The bone graft volume at each time interval was quantified by measuring the bone density (optical density; OD), which was the grey scale measurement or brightness of the entire pixels in the image and the remaining bone graft height. The procedure for measurements was described in our previous study\(^{28}\). In brief, an aluminium step wedge was attached to each film for calibrating the radiographic density. For the bone density, the preoperative cleft areas were outlined and duplicated to each
serial postoperative X-ray. The areas occupied by the erupted teeth were deleted and the optical density of each outline was measured. The bone graft height was demonstrated as the percentage of bone coverage of the reference tooth roots. Each radiographic image was captured and transferred to a personal computer and analysed by image processing and analysis software (Image Pro Plus 5.0, Media Cybernetics Inc, Silver Spring, USA).

**Statistic analysis**

The data were analysed using SPSS version 13 (SPSS Inc, Chicago, IL, USA). Descriptive statistics and unpaired *t*-tests were used to compare the clinical results and bone graft quantities between the two groups at each time interval during the follow up periods. One-way analysis of variant was applied to detect the change of bone quantities of each group during the follow up periods. Multiple comparisons by the Tukey’s HSD test was used where variances were homogenous, otherwise Dunnett T3 was performed. The Mann-Whitney U test was applied to detect post-operative pain differences between the two groups at each time interval. The Kruskal-Wallis test and the Dunn’s multiple comparison tests were used for assessment of the change in post-operative pain for each group during the 7 days after surgery. A p value < 0.05 was considered significant.

**Result**

**Clinical assessments**

All patients tolerated the operation well without complications during the hospital stay. The data of all clinical parameters was presented in table 1. The mean autogenous bone graft volume used in group II could be reduced by adding an equal volume of DBB. There was no significant difference in
the operation time and intra-operative blood loss between the two groups. The patients of group II recovered from walking uncomfortably statistically faster than group I. The duration of the hospital stay of group II was also significantly shorter than group I.

**Table 1. Summary of clinical parameters**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group I (mean ± SD) (N=14)</th>
<th>Group II (mean ± SD) (N=13)</th>
<th>P</th>
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<tr>
<td>Bone graft volume (ml)</td>
<td>2.53±1.07</td>
<td>1.22±0.20*</td>
<td>&lt;0.001</td>
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<td>Intra-operative blood loss (ml)</td>
<td>150±46.30 (N=14)</td>
<td>122.5±35.45 (N=13)</td>
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<td>Duration of the operation (hr)</td>
<td>2.68±0.61 (N=14)</td>
<td>2.29±0.91 (N=13)</td>
<td>0.172</td>
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<td>Time taken to walk with assistance (hr)</td>
<td>37.88±11.07 (N=12)</td>
<td>25.5±6.46* (N=11)</td>
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<td>Time taken to walk without assistance (hr)</td>
<td>67.07±13.86 (N=12)</td>
<td>46.63±13.82* (N=11)</td>
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<td>Duration of hospital stay (day)</td>
<td>5.4±1.12 (N=13)</td>
<td>4.23±0.8* (N=12)</td>
<td>0.006</td>
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</table>

Unpaired t-tests, * Significant difference from group I at p<0.05
Complications
For the donor site, paresthesia of the skin around the incision lines in one case and pain when walking in three cases were found in group I. Whereas, there was no complication detected in group II. For the recipient site, wound infections were found in one case of group I and one case of group II. The wound dehiscenses were detected in one case of group I and three cases of group II.

Post-operative pain
Post operative pain of both groups significantly reduced within 3 days after the surgeries. The overall pain score of Group II was less than Group I, but there was no statistical significance (Fig. 5).

![Graph showing pain levels over time](image)

**Fig 5.** Post-operative pain; †, *p < 0.05** significant against day 1 of group I and II respectively.
Canine eruption

Canine tooth buds presented in 10 cleft site of group I and 12 cleft sites of group II. Within 24 months of the follow up period, spontaneous eruption of canines were found in five teeth of group I (50%) and 5 teeth of group II (41.67%). The tooth eruptions assisted by orthodontic force were utilized in three teeth of group I (30%) and two teeth of group II (16.67%). The spontaneous eruptions of canine were demonstrated by serial occlusal radiographs (Fig. 6) and the status of the teeth moved by orthodontic appliances was shown in (Fig. 7).
Fig 6. The occlusal radiographs of two patients of group II demonstrate the progression of canine eruption (arrows) through the grafted area (a) 1 day postoperation, (b) 6 months postoperation and (c) 12 months postoperation.

Fig 7. The canine (arrow) could be moved by orthodontic force.

Radiographic feature
The average bone graft densities and heights of both groups were not statistically different at each time interval (p>0.05). The densities of both groups significantly reduced within six months after grafting, then seemed to be stable until the 24th month. The density of group I and group II reduced 31.26% and 27.38% respectively by 24 months after grafting (Fig. 8).
Fig 8. The figure demonstrates the average bone graft densities of both groups during 24 months post-surgeries.

On the other hand, the bone graft heights gradually decreased with time, the height in group I and group II decreased 23.58% and 24.30% respectively by 24 months post-surgery (Fig. 9).

Fig 9. The average bone graft heights during the 24-month follow-up period.
Discussion

Satisfactory clinical outcomes were obtained from the bone trephination technique. A tiny incision line, and minimal muscle and periosteum detachment caused minimal disturbed growth of the crest and also minimized the postoperative pain. As a result, patients could recover from uncomfortably walking faster. The operation time, intraoperative blood loss and duration of hospital stay were also reduced when compared to the conventional trapdoor technique.

The majority of the complications for the recipient sites of both groups were wound dehiscence and infection. These might be due to excessive bone graft volume packed into the cleft sites, the tension of wound closure and the patient’s oral hygiene care. However, these were healed eventually by wound debridement and antibiotics.

Regarding the non-resorbable property of hydroxyapatite that may retard the bone remodeling process\(^3,8\), the new bone regenerating within the pores of DBB might be effected by stress shielding and did not undergo mechanical loading which acted as a trigger for remodelling\(^1\). In contrast, combining with autogenous bone seem to improve success rate of the graft\(^18\). Mixture of autogenous cancellous bone and hydroxyapatite contained not only viable osteoblasts and osteoprogenitor cells essential for the mechanism of osteogenesis and osteoinduction but also the xenogenic scaffold for an osteoconduction. However, we used the ratio of autogenous bone to be DBB in 1:1 rather than 1:2 to limit the excessive volume of the xenograft.

Although Feinberg et al\(^4,5\) revealed that hydroxyapatite particles delayed tooth eruption in animal models, several studies\(^14,19,20,25\) demonstrated that allogenic and xenogenic bone graft including DBB, had no inhibitory effect on the tooth eruption or orthodontic tooth movement in
vivo. There was also a case report that demonstrated the successful tooth movement by orthodontic force through the alveolar cleft region six months after grafting with a mix of decalcified freeze-dried bone allograft and a granular bioactive glass graft material in the ratio 1:1. Our study confirmed that there was no interference of the canine eruption process among the patients for both spontaneous eruptions and orthodontically assisted ones.

Several studies have recommended computed tomography (CT) for evaluating the bone graft quantities because of the clear advantage in reproducibility and the 3-dimensional images. However, the disadvantages of CT are the higher radiation exposure and cost. Nevertheless plain radiographs demonstrate details of bone grafts only in 2-dimensions, but the technique is economical, produces less radiation and can presume the thickness of bone grafts by analysis with computer software. In this study, the quantities of bone graft were determined by measuring bone density and bone graft height. To detect the differences of the bone graft quantities at each time interval, the outline of the bone graft area from the first postoperative radiographs must be superimposed on subsequent radiographs for each patient in the same position. For this purpose, firstly, a constant position in the radiographic technique needs to be achieved. A simple individual custom film holder was made for each patient to reproduce the spatial position between the radiographic beam and the film. Secondly, the aluminium step wedge attached to the films provided precision for the digital image analysis of bone density by the calibration technique. The wedge has been widely used to calibrate the grey level of the radiographic image for subtracted interpretation. This method can reduce the error of different radiation exposures and film processing. The method for measuring the bone graft height was modified from Long, et al and Rosenstein, et al. The heights were measured and demonstrated as a percentage of bone
coverage of the tooth roots adjacent to the cleft site rather than in millimeters to prevent radiographic shortening and elongation of the reference points.

The quantitative assessment of bone graft in both groups demonstrated that bone graft density of both groups rapidly decreased within the six months after grafting then it became stable. It was implied that a rapid remodelling process occurred immediately after grafting and maturation of the cortical structure was complete within six months. It was similar to other studies\textsuperscript{12,13} which described that the pattern of bone graft remodeling would be complete within 6-12 months. We found that there was the same pattern of remodeling appeared for autogenous bone graft or composite grafts of autogenous bone and DBB.

Several factors influencing the resorption of the bone graft included a functioning of the presented tooth\textsuperscript{26} or the eruption of the tooth\textsuperscript{9,15} adjacent to the graft, tension of mucoperiosteal flaps covering the graft\textsuperscript{9} and an origin of the graft\textsuperscript{16}. Even though the effect of the functioning tooth on the bone resorption was controversial, Honma et al recommended that the graft site should be restored by a functioning tooth to prevent further bone resorption\textsuperscript{9}. On the other hand, Long et al suggested that the pattern of canine eruption did not affect the success of bone grafting\textsuperscript{15}. However, this study found that the decreasing of the bone graft height seemed to relate to the canine eruption and the starting time of orthodontic tooth movements. Thus, the tooth eruption and functional tooth movement might effect the bone graft resorption. Nevertheless, the bone graft of each group, itself, could maintain the volume for tooth eruption.
Conclusion

The technique of using autogenous iliac crest bone graft combined with deproteinized bovine bone could reduce the amount of autogenous bone required from the crest. The bone graft harvested by the trephination technique reduced morbidities and hospitalization of the patients. In addition, the clinical and radiographic results for treatment of alveolar cleft were not different from the conventional technique using iliac bone graft alone. Thus, it could be considered as an alternative treatment for alveolar cleft.
References


Vitae

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Educational attainment

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<td>Thai Board OMFS</td>
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