

Efficacy of Platelet-Rich Plasma in Alveolar Bone Grafting

Tomoki Oyama, MD,* Sob Nishimoto, MD,†
Tomoe Tsugawa, MD,‡ and Fumiaki Shimizu, MD§

Purpose: In this study, we performed alveolar bone grafting with autologous iliac cancellous bone incorporation with platelet-rich plasma (PRP) and evaluated its efficacy in osteoregeneration.

Materials and Methods: Seven alveolar cleft patients with adult dentition (average age, 16.1 years) underwent iliac bone grafting with PRP. Quantitative evaluation of regenerated bone was made with 3-dimensional computed tomography scans and compared with controls.

Results: The average of the volume ratio of regenerated bone to alveolar cleft in cases with PRP was higher than in controls ($P < .05$). There were no complications from the blood draw or PRP.

Conclusion: PRP was a safe and cost-effective source for growth factors and was easy to extract. It could enhance the osteogenesis of alveolar bone grafting in cleft lip and palate patients and may be useful for subsequent orthodontic therapy.

© 2004 American Association of Oral and Maxillofacial Surgeons
J Oral Maxillofac Surg 62:555-558, 2004

Alveolar bone grafting has become an essential process in the treatment of cleft lip and palate.¹ Autologous iliac bone marrow is used preferably because of its sufficient quantity and high osteoinductive potential. However, even with iliac bone, insufficient osteoregeneration may occur due to several factors such as the patient's age, cleft width, influence of functional stress, and others.²⁻⁴

Platelet-rich plasma (PRP) extracted from autologous whole blood is known to have a number of different growth factors in high concentration.^{5,6} Many successful results of the treatment of periodontal diseases with the incorporation with PRP have been reported.⁷⁻¹¹

In this study, we performed tertiary bone grafting (after completion of the second stage of dentition) in alveolar cleft patients using autologous iliac cancellous bone with PRP and evaluated the early results.

Materials and Methods

We have performed iliac cancellous bone grafting with PRP on 23 cleft patients since 2000, including 8 of secondary and 15 of tertiary dental stage. From these patients, we selected 7 alveolar cleft patients in tertiary dental stage who were close in age and had similar teeth eruption. Five patients had unilateral cleft lip and palate, and 2 had unilateral cleft lip and alveolus. The average patient age was 16.1 years old (Table 1). All lacked a lateral incisor tooth at the cleft site.

PRP was extracted during the operation.¹² After anesthesia induction, 40 mL of whole blood was drawn from the patient and separated into 4 sterile pipettes containing anticoagulation agents (citrate, phosphate, dextrose, and adenosine). Each specimen was centrifuged at 160g for 20 minutes and resulted in a red lower fraction and a straw-yellow upper fraction. The entire upper fraction and partial red fraction 6 mm below the dividing line were collected and centrifuged at 400g for 15 minutes. The top yellow serum component was removed, and the remaining substance was the available PRP.

Cancellous iliac bone was harvested, and PRP was mixed with it (Fig 1A). We added human fibrin glue (Beriplast P; Aventis Behring, Tokyo, Japan) to pack PRP into the bone marrow and obtain malleable transplant material (Fig 1B).

Particles of cancellous bone incorporated with PRP were packed into the alveolar cleft and closed with

Received from the Department of Plastic Surgery, Kobe Children's Hospital, Takakuradai, Suma-ku, Kobe, Japan.

*Chief.

†Director.

‡Resident.

§Resident.

Address correspondence and reprint requests to Dr Oyama: Department of Plastic Surgery, Kobe Children's Hospital, Takakuradai, Suma-ku, Kobe 654-0081, Japan; e-mail: Tomoki.Oyama@mb3.seikyou.ne.jp

© 2004 American Association of Oral and Maxillofacial Surgeons

0278-2391/04/6205-0005\$30.00/0

doi:10.1016/j.joms.2003.08.023

Table 1. AGE, CLEFT TYPE, VOLUME OF ALVEOLAR CLEFT, AND REGENERATED BONE IN EACH CASE

Patient	Age (yr)	Type	VAC (pixels)	VRB (pixels)	VRB/VAC (%)	Graft
1	16	UCLP	34,568	29,067	84.09	BM + PRP
2	16	UCLP	48,410	42,273	87.32	BM + PRP
3	16	UCLP	27,775	20,079	72.29	BM + PRP
4	16	UCLP	31,294	25,013	79.93	BM + PRP
5	17	UCLA	47,213	41,622	88.16	BM + PRP
6	16	UCLP	30,125	21,471	71.27	BM + PRP
7	16	UCLA	57,764	45,213	78.27	BM + PRP
8	16	UCLP	46,610	30,022	64.41	BM
9	16	UCLA	29,985	14,234	47.47	BM
10	16	UCLP	64,273	50,115	77.97	BM
11	16	UCLP	35,213	18,250	51.83	BM
12	18	UCLA	54,890	42,084	76.67	BM

Abbreviations: VAC, volume of alveolar cleft; VRB, volume of regenerated bone; UCLP, unilateral cleft lip and palate; UCLA, unilateral cleft lip and alveolus; BM, bone marrow; PRP, platelet-rich plasma.

gingival mucoperiosteal flaps (Fig 1C). All cases resumed with use of an oral retention plate 1 month after the operation with no functional stress exerted onto the grafted region.

Evaluation was done with 3-dimensional computed tomography (CT) before and at 5 or 6 months after the operation. All tomograms parallel to the occlusal

plane were scanned in the same manner (120 kV, 150 mA) by 1-mm slice width from the teeth to the infraorbital region. The level and window of each slice were optimally set to allow precise delineation between bone and soft tissue.

We analyzed the volume ratio of regenerated bone to the alveolar cleft using a personal computer and



FIGURE 1. Platelet-rich plasma (PRP) was added to the particles of cancellous bone chips. Human fibrin glue could consolidate the bone chips and enclose PRP within it. Bone chips with PRP were packed into the alveolar cleft and closed with gingival mucoperiosteal flaps.

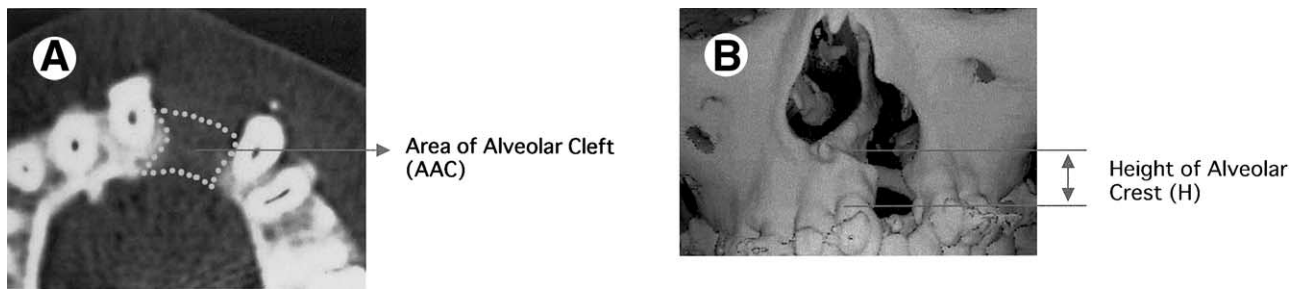


FIGURE 2. Area of alveolar cleft (AAC) on each film was measured in pixel unit by encircling the cleft freehand. Height of the cleft (H) was measured in millimeters by referring to the contralateral side. The volume of alveolar crest was calculated by dividing the AAC on each slice by the number of H slices.

common software (Adobe PhotoShop; Adobe, San Jose, CA).

Every CT slice was scanned and recorded by the computer according to the same condition so the preoperative and postoperative films could be compared. Each slice was magnified (200%) with the zoom tool in the software to precisely distinguish and outline the regenerated bone.

On each preoperative tomogram, the area of alveolar cleft (AAC) was outlined freehand by extending the buccal and lingual arch of adjacent maxillary segments and measured in pixel units (Fig 2A). The height from the alveolar crest to the base of the piriform aperture (H) was measured in millimeters (Fig 2B), and the volume of alveolar cleft (VAC) was calculated by dividing the AAC on each slice by the number of H slices.

Postoperatively (at 5 or 6 months after the operation), area of regenerated bone (ARB) was outlined freehand, and volume of regenerated bone (VRB) was calculated in the same manner as VAC (Fig 3). Two people, who were not the authors, manipulated and evaluated all values, and the average of them was adopted as the results.

Controlled cases were the 5 alveolar cleft patients (3 had unilateral cleft lip and palate and 2 had unilateral cleft lip and alveolus, and lacked a lateral incisor at the cleft site) in the tertiary stage (average age, 16.4 years) (Table 1). They underwent cancellous bone grafting, added with human fibrin glue, without PRP.

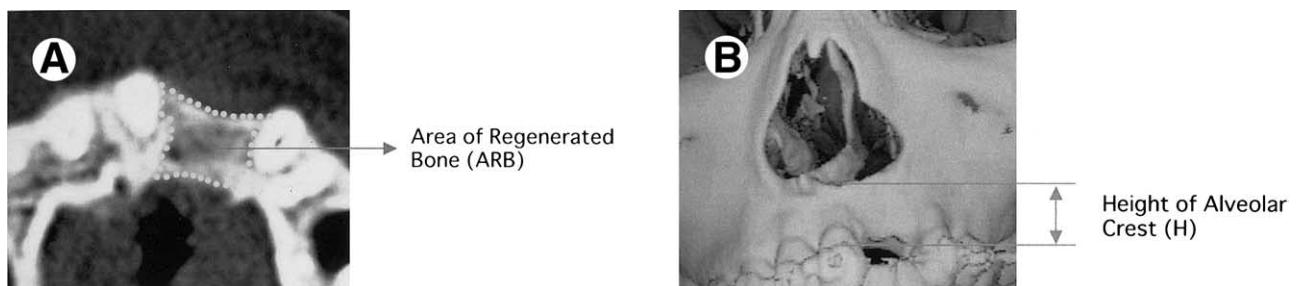


FIGURE 3. Area of regenerated bone (ARB) was measured as AAC (see Fig 2 legend). Volume was calculated by dividing ARB by the number of H slices (equal to H in Fig 2 legend).

Results

All patients had an uneventful course postoperatively; results are shown in Table 1. In cases of bone grafting added with PRP, the minimum percentage of VRB/VAC was 71.27% (patient 6) and the maximum was 87.32% (patient 2) (average, $80.19\% \pm 6.77\%$ [SD]).

In controls, the minimum percentage of VRB/VAC was 47.47% (patient 9) and the maximum was 77.97% (patient 10) (average, $63.67\% \pm 13.94\%$ [SD]). Mann-Whitney *U* test revealed statistical significance ($P < .05$) between the groups of PRP patients and controls.

There was no correlation between VAC and VRB/VAC in either group. Therefore, even if the cleft was wide, the result was not necessarily poor in this study.

All 12 patients obtained retention of the alveolar arch and stabilization of the teeth adjacent to the cleft. All oronasal fistulas were closed. Prosthodontic treatments, such as dental implants, bridges, or partial dentures, are scheduled subsequently.

Discussion

Alveolar bone grafting is a significant treatment for cleft lip and palate. It may not only induce the tooth eruption but also stabilize the alveolar arch of maxilla. Dental implants are also available in patients with missing teeth.¹³

Iliac cancellous bone is a preferable grafting material because it can be harvested easily and sufficiently and has high osteoinductive potential compared with the other materials. However, even with iliac bone marrow, partial absorption and shortage of reconstructed alveolar height or width may develop postoperatively.

One of the important factors for successful osteogenesis is the patient's dental stage. Secondary bone grafting is considered to be preferable to tertiary grafting,^{4,14} because the older the patients are, the lower the osteogenic activity. In addition, eruption of a tooth into the grafted region is an important advantage in secondary cases.

We assumed that PRP might enhance the osteogenesis of autologous bone and lessen postoperative bone resorption. Seven patients in tertiary stage, grafted with PRP, acquired a markedly high capacity rate of regenerated bone, which was significantly different from controls. Schmitz and Hollinger¹⁵ doubt the effects of PRP because platelet-derived growth factor is inhibitory to osteoblastic cells if delivered in a continuous form and increases bone resorption. In our study, it was revealed that PRP could enhance osteogenesis much more than osteoresorption in a remodeling phase within 6 months after the operation. However, it is unknown for how long (>6 months) PRP exerts an influence on the bone volume in this study.

Without functional stress in the graft, atrophic bone resorption would occur in the long term.¹⁴ None of our patients have implants yet; therefore, it remains to be proved whether PRP makes a significant difference in subsequent implant treatment.

Marx et al¹⁶ reported successful results of the reconstruction of the mandibular segment by using PRP. They assessed the bone density on x-ray films in a qualitative analysis. We analyzed the volume of bone regeneration by 3-dimensional CT. Several kinds of quantitative assessment based on CT scans have been reported, such as orbital measurements in enophthalmos,¹⁷ intracranial volume in craniosynostosis,¹⁸ and volume of mandible after distraction.¹⁹ Our method was theoretically similar to them and simpler by means of the use of common graphic software. However, we did not assess the bone density this time. A unified method of evaluation of alveolar bone grafting has not been established as yet, but both qualitative and quantitative assessments should be included.

Extraction technique¹² of PRP, which we adopted in this study, was simple and easy to do during the operation. There were no complications from the blood draw and PRP. Approximately 3 mL of PRP could be obtained from 40 mL of whole blood, and it

was sufficient to be mixed into the particles of cancellous bone chips. However, with respect to the enhancement of osteoregeneration, the biologically appropriate concentration of growth factors involved in PRP is still unknown.^{6,15,20}

References

1. Boyne PJ, Sand ND: Secondary bone grafting of residual alveolar and palatal clefts. *J Oral Surg* 30:87, 1972
2. Arouze C, Moller KT, Bevis RR, et al: The presurgical status of the alveolar cleft and success of secondary bone grafting. *Cleft Palate Craniofac J* 37:179, 2000
3. Bergland O, Semb G, Abyholm FE, et al: Elimination of the residual alveolar cleft by secondary bone grafting and subsequent orthodontic treatment. *Cleft Palate J* 23:175, 1986
4. Sindet-Pedersen S, Enemark H: Comparative study of secondary and late secondary bone-grafting in patients with residual cleft defects: Short-term evaluation. *Int J Oral Surg* 14:389, 1985
5. Slater M, Patava J, Kingham K, et al: Involvement of platelets in stimulating osteogenic activity. *J Orthop Res* 13:655, 1995
6. Landesberg R, Roy M, Gickman RS: Quantification of growth factor levels using a simplified method of platelet-rich plasma gel preparation. *J Oral Maxillofac Surg* 58:297, 2000
7. Froum SJ, Wallace SS, Tarnow DP, et al: Effect of platelet-rich plasma on bone growth and osseointegration in human maxillary sinus grafts: Three bilateral case reports. *Int J Periodont Restor Dent* 22:45, 2002
8. Anitua E: Plasma rich in growth factors: Preliminary results of use in the preparation of future sites for implants. *Int J Oral Maxillofac Implants* 14:529, 1999
9. Kassolis JD, Rosen PS, Reynolds MA: Alveolar ridge and sinus augmentation utilizing platelet-rich plasma in combination with freeze-dried bone allograft: Case series. *J Periodontol* 71:1654, 2000
10. Vercellotti T: Piezoelectric surgery in implantology: A case report—a new piezoelectric ridge expansion technique. *Int J Periodont Restor Dent* 20:359, 2000
11. Tischler M: Platelet rich plasma: The use of autologous growth factors to enhance bone and soft tissue grafts. *N Y State Dent J* 68:22, 2002
12. Sonnleitner D, Huemer P, Sullivan DY: A simplified technique for producing platelet-rich plasma and platelet concentrate for intraoral bone grafting techniques: A technical note. *Int J Oral Maxillofac Implants* 15:879, 2000
13. Hartel J, Pogl C, Henkel KO, et al: Dental implants in alveolar cleft patients: A retrospective study. *J Craniomaxillofac Surg* 27:354, 1999
14. Dempf R, Teltzrow T, Kramer FJ, et al: Alveolar bone grafting in patients with complete clefts: A comparative study between secondary and tertiary bone grafting. *Cleft Palate Craniofac J* 39:18, 2002
15. Schmitz JP, Hollinger JO: The biology of platelet-rich plasma. *J Oral Maxillofac Surg* 59:1119, 2001
16. Marx RE, Carlson ER, Eichstaedt RM, et al: Platelet rich plasma: Growth factor enhancement for bone grafts. *Oral Surg* 85:638, 1998
17. Bite U, Jackson IT, Forbes GS, et al: Orbital volume measurements in enophthalmos using three-dimensional CT imaging. *Plast Reconstr Surg* 75:508, 1985
18. Posnick JC, Bite U, Nakano P, et al: Indirect intracranial volume measurements using CT scans: Clinical applications for craniosynostosis. *Plast Reconstr Surg* 89:34, 1992
19. Roth DA, Gosain AK, McCarthy JG, et al: A CT scan technique for quantitative volumetric assessment of the mandible after distraction osteogenesis. *Plast Reconstr Surg* 99:1237, 1997
20. Weibrich G, Kleis WK, Hafner G: Growth factor levels in the platelet-rich plasma produced by 2 different methods: Cursantype PRP kit versus PCCS PRP system. *Int J Oral Maxillofac Implants* 17:184, 2002