Comparison of Biomaterials as a Graft Material for Gnatoschizis: A literature review

Fitriana[1]*, Erinna Ardiyanti[2]

1. Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Universitas Brawijaya, Malang, Indonesia.
2. Dental Professional Education, Faculty of Dentistry, Universitas Brawijaya, Malang, Indonesia.

Abstract

Alveolar bone Cleft (Gnatoschizis) is a congenital disorder that affects the formation of cleft lip and palate. This disorder causes the process of teeth growth to be disrupted due to defects in the cleft lip and palate. The gold standard of treatment for this disorder involves the use of autogenous grafts from the iliac crest, however, this donor procedure carries some risks and complications. Along with technological advances, there are new innovations that avoid these losses by presenting bone graft materials as a substitute for autogenous graft materials. One of that is currently popular is bone graft. The aim of this literature review was to evaluate and compare various biomaterials used in surgery for cleft palate closure as substitutes for autogenous graft materials.

The method used for literature review is PICO.

14 articles were selected for evaluation. From the selected articles, various biomaterials that can be used as autogenous bone graft substitutes were obtained (Octacalcium Phosphate, xenograft, β-Tricalcium Phosphate, Calcium Sulfate, Hydroxyapatite, Polyphosphate, and Deciduous Dental Pulp Stem Cell).

The use of various materials in bone grafting procedures shows several aspects that are more advantageous than the use of the iliac crest as autogenous graft materials. Octacalcium Phosphate, Xenograft, β-Tricalcium Phosphate, Calcium Sulfate, Hydroxyapatite, Polyphosphate, and Deciduous Dental Pulp Stem Cell showed satisfactory results so they can be used as bone graft material.

Review (J Int Dent Med Res 2023; 16(3): 1375-1382)

Keywords: Alveolar cleft, bone graft material, secondary operation.

Received date: 20 July 2023 **Accept date:** 15 August 2023

Introduction

Alveolar bone cleft (gnatoschisis) is a form of congenital malformation that often occurs in the orofacial structures. Gnatoschisis is found in about 75% of patients with cleft lip and palate.[1] Patients with such abnormalities can have an impact on daily activities such as speaking, hearing, swallowing, breathing, dental malposition, facial development and growth retardation.[2]

Alveolar cleft repair has both functional and aesthetic goals. Functional goals may include closure of the nasolabial fistula, creation of a stable maxillary dental arch, increased support of teeth adjacent to the cleft area, allowing teeth to erupt into the cleft area, provision of unrestricted orthodontic movement, improved oral hygiene, and improved speech function.[1]

One of the gold standard treatments used in bone grafting in cases of alveolar bone clefts is the use of autogenous grafts originating from the iliac crest, however, this repeated bone removal surgery can be accompanied by increased postoperative morbidity and makes the patient's stay longer. In addition, complications that can occur include minor hematomas, infections at the donor site, neurological injuries, vascular injuries, and fractures in the *iliac wing*.[3,4] The use of autograft materials can increase postoperative morbidity so that many researchers are looking for biomaterials that provide satisfactory results with minimally invasive techniques.

Alveolar cleft closure cases can utilize a wide variety of materials. The ideal graft material that can be used should be osteogenic, osteoconductive and osteoinductive,

Corresponding author:
Fitriana
Department of Oral and Maxillofacial Surgery
Faculty of Dentistry, Universitas Brawijaya, Malang, Indonesia, 65145
E-mail: Fitriana.drg@ub.ac.id

mechanically stable and free of disease. The graft material should be degradable and the degradation should be suitable for osteogenic level. Biodegradation is very important as it allows space for bone to be formed and vascular tissue to grow.[5] Several types of bone graft therapy include autograft, allograft, xenograft, and alloplastic. The operative time intervention for the alveolar bone gap is carried out when the patient is approaching the age of 9 months, then secondary alveolar bone gaps can be treated when the patient is between 9-11 years old, before the eruption of the canines with the aim that the teeth can grow in the grafted area.[3]

Based on the introduction above, researchers want to compare alternative biomaterials that can be used for secondary bone grafting, so that they can be used for the treatment of closing alveolar bone gaps in place of autogenous grafts.

Materials and methods

PICO:

P : Patients with cleft alveolar bone/gnatoschizis.
I : Provision of alveolar bone graft biomaterial.
C : Comparing various biomaterials for alveolar bone grafts.
O : Obtain bone graft biomaterials that can be used as a substitute for autogenous bone grafts so that they can be minimally invasive.

Results

Author, year, subject (age, application protocol)	Result	Conclusion
Octacalcium Phosphate Collagen (OCP/Col)		
Kibe et al, 2021 4 Patients aged 9-10 years (OCP group) 55 patients control group (Autogenous group)	No infection, only a few small leaks post operative complications, and for 6 months, the CT values in the OCP/Col group were greater than the autologous group.	OCP/Col offers a bone regenerating agent that can be used as an autologous bone substitute, with OCP/col alone forming sufficient bone bridges in alveolar bone defects in patients with cleft lip and alveolus .
Matsui et al, 2018 1 patient age 13 years 6 months (OCP/Col)	The gap area given OCP/col graft material since 1 month postoperatively increased from time to time up to 1 year postoperatively but tended to appear to decrease starting from 2 postoperative year	
Kawai et al, 2020 5 patients	For alveolar clefts cases, the CT ratio of “good” and average scores was 100.0% (95% CI, 63.1–100.0)	
Polyphosphate (Polyp)		
Alkaabi et al, 2021 8 patient age range: 13 – 34 4 patient group (Polyp) 4 patient group (Polyp+BPC)	There were no postoperative complications or local/systemic complications in 2 groups **Orthopantomogram and CT Scan:** Ca-polyP MPs group_(patients 1 and 2): cannot be analyzed by Bergland scale) categorized as grade IV bone level Ca-polyP MPs-BCP group: ranged from grade I – III bone level on assessment days 1, 8 and 90 Day 180: 3 patients remaining: grade III bone level	Ca-PolyP MPs and Ca-PolyP MP / BCP are safe materials, however, if just Ca-PolyP MPs may not be stable enough.
Deciduous Dental Pulp Stem Cells (DDPSC)		
Tanikawa et al, 2020 The Group with 6 Patients age 8-12 years (DDPSC) Group I : Recombinant human bone morphogenetic protein-2 (rhBMP-2) Group II: (iliac crest bone graft)	- DDPSC can be isolated and characterized as mesenchymal stem cells. Progressive alveolar bone fusion has occurred in all patients - Through volumetric analysis, the average preoperative defect for groups I and II was 1028.6 mm3. On examination after 6 months, the average defect was 253.2 mm3 in group one and 260.4 mm3 in group two; But on examination after 12 months, the average defects were similar in all groups	For this selected patient group, DDPSC therapy results in satisfactory bone healing with excellent feasibility and safety, which significantly enhances the prospects for using stem cells in clinical care.
Beta-Tricalcium Phosphate (bTCP)		
De Ruiter et al, 2015 7 patients the average age is 11.16 years	Bone volume increased significantly six months after grafting of the microstructured b-TCP into the alveolar cleft, the bone volume obtained was satisfactory. We found a mean percentage bone volume of 73% ±6% compared to the original cleft volume.	Secondary bone grafts with b-TCP can be used safely and clinically. In addition, it is an inexpensive procedure compared to autologous bone grafts, reduces postoperative pain, reduces hospital stay and operating time.
Trujillo et al, 2018 25 patients age 18 years or over 7 patients (Illiac) 9 patients (mandibular sympisis) 9 patients (bTCP)	The largest number of new bone formations was obtained in the iliac crest group, followed by the rhBMP-2 /ACS/bTCP group and the mandibular symphysis group. However the differences were not statistically significant	
Janssen et al, 2019 20 patients average age 8-10 years	- The calcified tissue is almost 100% bone - After 1 year of treatment the percentage of calcified material in alveolar cleft defects was 61% in the Bergen group and 69% in the Utrecht group.	
Xenograft		
Bezerra et al, 2019 20 patients, Group A 10 patient (autologous) Group B 10 patient (bovine + PRP)	- The average defect area in group A decreased to 132.72mm2 from 274.39mm2 - The average defect area in group B decreased to 96.19mm2 from 152345.81 mm2	Bovine bone xenograft can be used as an alternative but can't stand alone must combined with PRF or PRP

Alnajjar et al, 2020 20 patients age between 9 – 14 years Grup A : (autologous) Group B : (bovine + PRF)	- Bone density in the xenograft group with I-PRF injection (520 ± 170 HU) was greater than in the autogenous group (425 ± 120 HU) in the cleft area - The clinical and radiological success rate of the xenografts polymerized with injectable platelet-rich fibrin (I-PRF)	
Kumar et al, 2021 20 patients age 7 and 16 years Group I 10 patients (autologous) Group II 10 patients (xenograft)	- On the 14th day the volume of the graft area was 1564.7 mm3 in group 1 and 1557.9 mm3 in group 2 (the percentage of bovine bone was already 69%) - In the 6th month the percentage increases by 70%	
Calcium Sulfate Hemihydrate		
Al-Jwboory, 2021 10 patients age between 7 – 15 years	- 10 patients recovered completely, except for 3 patients who initially experienced wound dehiscence which healed without infection - The average bone density in the cleft area is 303 HU compared to the normal side area of 416 HU	Calcium Sulfate Hemihydrate (Dentgen) shows results that are less invasive, more economical, and a promising choice as a graft material.
Hydroxyapatite (HA)		
Takemaru et al, 2015 15 male patients, Group I: iliac bone graft Group II : HA/col + iliac	- No complications occurred in 15 patients - Volume after 1 month 0.895 ± 0.347 ml in group I and 0.482 ± 0.973 ml in group II - Volume after 6 and 12 months showed no significant difference between the two groups	HA/Col can be used effectively in combination with the iliac crest in bone graft procedures or alone
Sakamoto et al, 2020 21 patients Group I iliac Group II HA/col	- There was a significant difference in intraoperative blood loss between the 2 groups (6.7 ± 1.89 mL in group II vs 38.8 ± 9.73 mL in group I [P < 0.01]). - Patient-controlled use of intravenous analgesia was also significantly lower in group II than in group I (2.2 ± 1.9 times vs 12.2 ± 4.4 times [P < 0.01]). - Only 1 female in group II who had maxillary sinusitis did not achieve osteosynthesis. - With the exception of this patient, the 12-month bone volumes in groups I and II were 0.567 ± 0.066 and 0.596 ± 0.073 mL, respectively, with no significant difference (P = 0.18).	

Table 1. 14 articles were selected for evaluation. From the selected articles, various biomaterials that can be used as autogenous bone graft substitutes were obtained (Octacalcium Phosphate, xenograft, β-Tricalcium Phosphate, Calcium Sulfate, Hydroxyapatite, Polyphosphate, and Deciduous Dental Pulp Stem Cell).

Discussion

Nothing can hide a cleft lip wound in a person that has not been repaired in society. So many experts want to find treatments that can be done in patients who have these disorders. The cleft lip repair was first coined in the time of Hippocrates in 400 BC and Galen 150 AD. The first reports of alveolar bone grafting were in 1901 by Von Eiselsberg, he used a pedicled osteocutaneous flap to reconstruct the palatal defect. In 1908, Lexer used autogenous bone for maxillary cleft graft with free bone or soft tissue of pedicle and little finger bone. Drachter 1914 was the first person who successfully performed bone grafts on alveolar defects using the tibial bone, including the periosteum. In the year of 1931 Veau reported that his attempt to graft an alveolar cleft with a tibial chip was unsuccessful. During the 1950s and 1960s many scientists used primary and secondary alveolar bone grafting. But in 1964 many publications have suggested that grafting at the early stage causes serious growth retardation of the one third of the mid bone of the face.[6]

Rehrmann from Germany reported in 1969 that 10 years of observations comparing primary and secondary bone grafts support a relatively new approach in delaying alveolar bone grafting. He found that permanent stability of the maxillary segment did not generated from early bone grafting of the alveolar process. Secondary bone grafting has 2 benefits which is conducted during the mixed dentition period from 7 to 12 years of age. Eruption of the lateral incisor and left canine at approximately 7 and 11 years of age. Bone grafting prior to canine eruption allows the teeth to erupt into solid bone and improves maxillary stability. Growth of the transverse maxillary is also almost complete at this age so there is inhibition of maxillary growth in this dimension.[7]

Treatment of large bone defects is a huge challenge. Autograft bone graft is still the “biological gold standard” for bone grafting of large defects. Autograft enhances union by providing osteoconductive, osteoinductive and osteoprogenitor properties for fractures, non-unions and alveolar bone defects. Unfortunately, the number of grafts available from each individual is limited and additional surgery is required for bone grafting with donor site morbidity. Many effects and complications occur as a result of autologous bone removal, so

alternative materials are needed. We have classified autograft replacement materials into 7 including Octacalcium Phosphate, xenograft, β-Tricalcium Phosphate, Calcium Sulfate, Hydroxyapatite, Polyphosphate, and Deciduous

Dental Pulp Stem Cell and we will discuss one by one:

Octacalcium Phosphate Collagen (OCP/Col)

Figure 1. Octacalcium Phosphate Collagen (OCP/Col)[8]

The first material was Octacalcium Phosphate (OCP) this material was proposed in 1962 as a precursor for biological apatite crystals in bones and teeth. OCP itself was detected in pig enamel, human dentin, and rat calvaria as an intermediary for the apatite matrix[8]. While OCP has many properties suitable for replacing bone, its brittleness makes it difficult to maintain its shape and hinders its use in clinical applications. Thus, OCP combined with atelocollagen (OCP/Col) has been developed to overcome the limitations of OCP in terms of printability and handling performance. OCP/Col showed excellent bone regeneration, better than β-TCP and collagen composite (β-TCP/Col) or HA and collagen composite (HA/Col). OCP/Col also promotes osteogenic differentiation and angiogenesis.[9]

Along with the many bone graft materials developed to help reconstruct alveolar bone defects such as the case of gnatoschizis, OCP/col has been widely studied, one of which was carried out by Kibe et al in 2021 conducting a study comparing groups of patients who were given treatment using OCP/col and Autogenous Bone graft, the results prove that every patient who uses OCP/Col has no infection, there are only a few small leaks post operative complications. We also assessed bone bridge formation using the Bergland scale and the results achieved during the first 6 months postoperatively were grade 1. CT values and trabecular structures were comparable to surrounding normal bone, and active eruption of permanent teeth adjacent to the alveolar cleft at the graft site. There was no significant comparison between the 2 groups, but the high position was significantly greater in the OCP/col group. In terms of the surgical technique of grafting with OCP/Col is uncomplicated, the operating time is reduced by about 30 minutes compared to autologous bone, and the amount of bleeding is small.[10]

Previous researchers conducted by Mitsui in 2018 also found that bone like opacity on CT results in the gap area given OCP/col graft material since 1 month postoperatively increased from time to time up to 1 year postoperatively but tended to appear to decrease starting from 2 postoperative year.[11] According to previous research, OCP/col in cases of alveolar clefts has a "good" CT value ratio.[8]

Xenograft

Xenograft is a tissue transplantation procedure from one species to another. Usually taken from the bovine or porcine dermis.[12]The use of xenograft material is one of the most commonly used safe methods for regenerating hard tissue loss. It is known that Xenograft can induce an immune response in the host. Xenografts have a possibly slow degradation process, as seen with certain bovine grafts, particularly those used in dentistry. Several studies have shown the success of Xenograft in Guided Bone Regeneration (GBR) procedures, sinus augmentation, and socket augmentation.[13]

A. Bovine Derived Demineralized Bone Matrix (DMBM)

Demineralized bone matrix (DBM) is allogeneic bone that has been processed by crushing and decalcification using hydrochloric acid. The result is loss of mineral components with retention of collagen type I, noncollagenous proteins, and osteoinductive growth factors, including varying concentrations of bone morphogenetic protein (BMP), growth differentiation factor, and possibly transforming growth factors (TGF-b1, TGF-b2, and TGF-b3). With these materials, DBM has osteoconductive and osteoinductive properties.[14]

The results of a comparative study

between iliac crest bone graft material (group I) and DMBM bone graft (group II) were assessed at 2 weeks, 6 months and 63 months. Volumetric results using the Cavalieri principle revealed that after 2 weeks and 6 months postoperatively bone absorption was comparable between groups I and II. However, after a follow-up of 63 months, bone absorption after being given DMBM was reduced. DMBM is also classified as requiring higher operating costs but there is no donor site morbidity such as using the iliac crest. The clinical parameters of the two groups such as pain in the graft area, facial swelling on the first, second and fourth days had the same results. No postoperative infection, but after being given DMBM 1 patient showed partial dehiscence with little bone loss but smooth healing, and the other patient only had partial dehiscence without bone loss.[15]

B. Bovine bone + Platelet-Rich Plasma (PRP)

PRP is one of tissue regeneration approach and can be a good addition to speed up healing procedures. PRP is obtained by centrifuging the patient's own blood. PRP functions is to reduce bleeding and promote soft tissue healing, as well as bone regeneration. Weibrich et al. demonstrated in vivo that PRP appears to be able to activate bone regeneration processes under optimal conditions, but this is not fully understood and requires further research.[16,17] However, several studies have shown promising results in implant surgical procedures using PRP as a coating material.[18] The use of PRP with a bovine one graft is based on the premise that PRP can release statistically large amounts of growth factors to assist bone graft maturation, increase bone formation and promote bone healing.[19]

The research conducted by Bezerra et al in 2019 showed that bovine bone and PRP are the graft materials of choice that provide good results, which significantly reduce the size of the alveolar gap. When the eruption of the tooth is ongoing, the surrounding bone continues to experience remodeling to allow tooth movement.[20]

C. Xenograft + Platelet Rich Fibrin (PRF)

Platelet-rich fibrin (PRF) is obtained by centrifugation of whole blood, resulting in spontaneous clotting of blood, like a natural blood clot, contains active platelets and leukocytes[21]. PRF is an effective method of bone formation in patients with cleft palate. The form of liquid PRF is also called injectable PRF (I-PRF). I-PRF can enhance the healing process due to the presence of leukocyte and platelet structures. I-PRF can be combined with bone graft granules to obtain sticky bone grafts, this sticky bone is then compacted in the alveolar cleft region where it coagulates and forms cohesive crystals within minutes. The combination of Xenograft with I-PRF can improve bone formation compared to autogenous bone grafts. I-PRF is also easy to apply and has a low price.[12]

β-Tricalcium Phosphate

The third material is β-tricalcium phosphate (β-TCP), hydroxyapatite (HA), and its combination (known as biphasic calcium phosphate (BCP) has been studied the most because of its similar composition to the bone mineral calcium phosphate. Some of this materials integrates into natural bone tissue, is osteoconductive, and its high affinity for proteins, such as BMP, can induce stem cell differentiation and growth, resulting in the formation of new bone. HA grafts have a slow and limited resorption potential, so they cannot be completely replaced by new bone, but can act as a volumetric filler. In contrast, β-TCP is easily absorbed and has a porous structure that is interconnected so that it is quickly replaced by new bone.[22]

This beta-tricalcium phosphate (β-TCP) scaffold material has good biocompatibility, wide practical availability, easy sterilization, long shelf life, and low risk of infection. β-TCP exhibits a fine balance between uptake, degradation and new bone formation and can also maintain its structural stability by releasing large amounts of calcium (Ca2+) and sulfate (SO42−) ions, which are important inorganic salts for new bone formation. β-TCP scaffold material with a size of 1 mm and 1–2.5 mm can also increase the proliferation of BMSC (bone marrow-derived mononuclear cells) and increase the expression of osteogenic genes and osteogenesis-related proteins.[23]

β-TCP has been widely evaluated and researched in humans, one of which was in a study conducted by Ruiter et al in 2015 which used this material as a bone graft material to repair alveolar bone gaps. The results evaluated 6 months after bone volume grafting were satisfactory.[24] Subsequent studies compared the

number of bone formations found in the iliac crest to be greater than β-TCP, but statistically there was no significant difference.[25] The use of β-TCP is also clinically safe with no side effects, reduces hospital stay and operating time, reduces postoperative pain and is not as expensive as using an autograft. The average bone volume in the repaired fissures for 1 year after surgery was 65%, and there was no recurrence of oronasal fistulas. In addition, 90% of the teeth adjacent to the gap can spontaneously erupt.[26]

Hydroxyapatite

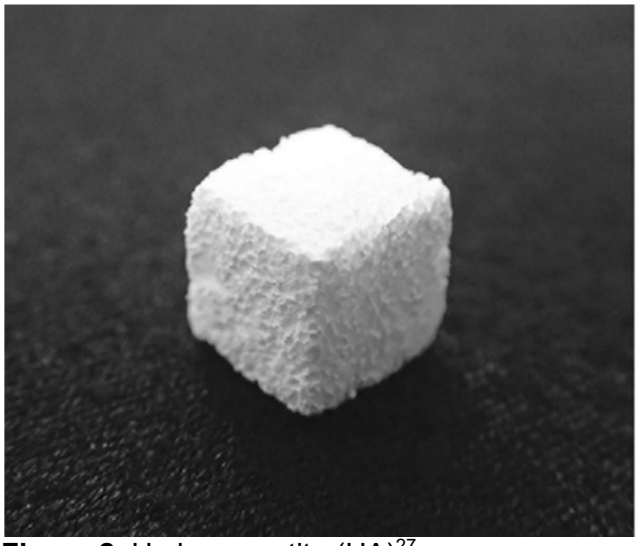

Figure 2. Hydroxyapatite (HA)[27]

Hydroxyapatite (HA) is an alloplastic material commonly used as a substitute for bone grafts because it has a chemical composition and crystal structure similar to bone. The osteoconductive properties possessed by hydroxyapatite allow for the apposition and migration of osteoblasts on the surface of the material, so that HA is able to bind directly to bone. Hydroxyapatite has the ability to stimulate bone growth through direct action on osteoblasts and minimizes toxicity or inflammation.[28]

Hydroxyapatite is available in various forms (powder, porous blocks, or small granules). HA either alone or in combination with auto/allo/xenograft has been used in dentistry and maxillofacial surgery with high clinical success rates to support alveolar bone regeneration. Thus, hydroxyapatite is a good bone graft candidate because this material is able to reduce the high risk of donor morbidity and can reduce pain.[28,29]

Several studies have proven that HA can be used for bone grafts in patients with cleft alveolar bone. One of them was carried out by Takemaru et al 2015 comparing the 2 groups, at the time of intraoperative blood loss surgery and the use of intravenous analgesia (PCA) controlled patients was significantly lower in group II who used HA and the iliac bone was placed in the remaining space. Postoperatively the patient showed no complications. Bone volume at 1, 6 and 12 months in the HA group did not differ significantly from the group using the iliac bone only. Thus HA/col can be used as an iliac graft in alveolar bone graft procedures to reduce the amount of autogenous bone required from apex, patient stress and morbidity.[30] In the future in 2020 research conducted by Sakamoto et al group II using bone grafts with HA/col alone can be significantly absorbed by the body and provide the similar results to autologous bone.[27]

Calcium Sulfate

The 5th material is Calcium sulfate (CaSO4) also known as plaster of Paris, has been used since more than a century. Calcium sulfate exists in 3 different forms; calcium sulfate anhydrous, calcium sulfate dehydrate, and calcium sulfate hemihydrate. The difference between these chemical species is in the number of water molecules present in one molecular unit. Plasters of paris may be especially useful as drug delivery to infected areas where absorption may take a long time. This released drug can be used effectively in extractions, cystic wounds, surgical defects and osteomyelitis, thereby restoring normal morphological contours and to reshape adsorbed alveolar bone. Calcium sulfate has bioabsorbable, osteoconductive, does not cause inflammatory reactions, stimulates fibroblast migration and does not increase serum calcium levels. Several studies have revealed that calcium sulfate is not clinically better than autogenous materials, but because they are easily available and economical, they can be used.[31]

Research conducted on 10 patients with alveolar clefts all heal smoothly except for 3 patients with wound dehiscence at the alveolar cleft site in the first week postoperatively, but secondary dehiscence healed without infection. However, the bone density value on the cleft side was statistically significantly lower than the average density on the non-cleft side. These results may be related to the mixing technique

and application of the materials themselves.[32]

Polyphosphates

The 6th material, Polyphosphate (Poly(P)), a biological polymer, and the basic fibroblast growth factor (bFGF) work in synergy to increase bone formation. Polyphosphate can increase bFGF activity in osteoblastic cells and increase calcification, then this material can also increase the differentiation of human mensenchymal stem cells into osteoblastic cells. The results showed that Poly(P) facilitates new bone formation and osseointegration with dental implants.[33] One of the researchers conducted a study using this material to evaluate the safety and feasibility as a bone graft material for alveolar cleft repair, the results were no reported postoperative complications from local or systemic. All patients were contacted via video call or telephone for a 1 year follow-up, and no adverse events were reported. But the results of the orthopantomogram and CT scan with the Bergland scale get a scale IV. The researchers concluded that Calcium Polyphosphate Microparticles (Ca-PolyP MPs) to be used as stand-alone graft materials were insufficient and inappropriate, so these materials needed to be combined with other materials such as Biphasic Calcium Phosphate (BCP).[34]

Deciduous Dental Pulp Stem Cells

The 7th material is Deciduous dental pulp stem cells (DDPSC) obtained from the remaining pulp tissue in chipped primary teeth is also called stem cells from human exfoliated deciduous teeth (SHED). Deciduous dental pulp stem cells (DPSC) were first isolated in 2000. Three years later, in 2003, stem cells from human exfoliated deciduous teeth (SHED) were isolated by Miura et al. Based on guidelines set by the National Institutes of Health Office of Human Subjects Research in Chicago. In a study conducted by Nakajima (2018) SHED had the highest percentage of collagen and osteoid areas compared to human dental pulp stem cells (DPSC) and bone marrow mesenchymal stem cells (BMSC). The results of this study indicate that SHED transplants can promote bone regeneration and repair bone defects in CLP cases. Thus, SHED can be one of the best candidates as a source of cells for alveolar bone regeneration in CLP patients due to minimal surgical and psychological invasion.[35]

Studies conducted in human groups who received DDPSC did not cause surgical complications. In group 1 Bone Morphogenetic Protein 2 (rhBMP-2) 37.5% experienced significant swelling in the early postoperative period and group 2 iliac crest 87.5% complained pain of significant donor site in the second week. The average length of stay was longer in group 2. Progressive alveolar bone healing in all 6 patients who had received DDPSC grafts. Evaluation was carried out by conducting a biopsy on patients who had grafts with DDPSC related to Bio-Oss Collagen showing good cartilage histology. DDPSCs are easily accessible with very little morbidity from primary teeth during mixdention.[36]

Conclusion

The use of various materials in bone grafting procedures shows several aspects that are more advantageous than the use of the iliac crest as autogenous graft materials. Octacalcium Phosphate, Xenograft, β-Tricalcium Phosphate, Calcium Sulfate, Hydroxyapatite, Polyphosphate, and Deciduous Dental Pulp Stem Cell showed satisfactory results so they can be used as bone graft material. But some materials can not stand alone must be combined with other materials, like Bovine bone xenograft can be used as an alternative but can not stand alone must combined with PRF or PRP and Polyp to be used as stand-alone graft materials were insufficient and inappropriate, so these materials needed to be combined with other materials such as Biphasic Calcium.

Declaration of Interest

The authors report no conflict of interest.

References

1. Kyung H, Kang N. Management of Alveolar Cleft. Archives Craniofacial Surgery. 2015;16(2):49-52.
2. Saskianti T, Novianti A, Sahar D, et al. Mixed Polymethylmethacrylate and Hydroxyapatite as a Candidate of Synthetic Graft Materials for Cleft Palate. Journal of International Dental and Medical Research. 2022;15(2):538-543.
3. Ferreira PHSG, De Oliveira D, De Deus CBD, Okamoto R. Evaluation of the different biomaterials used in alveolar cleft defects in children. Annals of Maxillofacial Surgery. 2018;8(2):315-319.
4. Dayashankara Rao JK, Bhatnagar A, Pandey R, et al. A comparative evaluation of iliac crest bone graft with and without injectable and advanced platelet rich fibrin in secondary alveolar bone grafting for cleft alveolus in unilateral cleft lip and palate patients: A randomized prospective study. Journal Stomatology Oral Maxillofacial Surgery. 2021;122(3):241-247.
5. Naini A, Ketut Sudiana I, Rubianto M, Mufti N. Characterization

and Degradation of Hydroxyapatite Gypsum Puger (HAGP) Freeze Dried Scaffold as a Graft Material for Preservation of the Alveolar Bone Socket. Journal of International Dental and Medical Research. 2018;11(2):532-536.
6. Lilja J. Alveolar bone grafting. Indian Journal of Plastic Surgery. 2009;42(SUPPL. 1):110-115.
7. Coots BK. Alveolar bone grafting: Past, present, and new horizons. Seminar in Plastic Surgery. 2012;26(4):178-183.
8. Kawai T, Kamakura S, Matsui K, et al. Clinical study of octacalcium phosphate and collagen composite in oral and maxillofacial surgery. Journal Tissue Engineering. 2020;11(2020):1-15.
9. Yanagisawa T, Yasuda A, Makkonen RI, Kamakura S. Influence of pre-freezing conditions of octacalcium phosphate and collagen composite for reproducible appositional bone formation. Journal Biomedical Materials Research. 2020;108(7):2827-2834.
10. Kibe T, Maeda-Iino A, Takahashi T, Kamakura S, Suzuki O, Nakamura N. A Follow-Up Study on the Clinical Outcomes of Alveolar Reconstruction Using Octacalcium Phosphate Granules and Atelocollagen Complex. Journal of Oral and Maxillofacial Surgery. 2021;79(12):2462-2471.
11. Matsui K, Takahashi T, Kawai T, Kamakura S. First Clinical Application of New Bone Substitute Material to the Alveolar Cleft. Journal Clinical Trials. 2018;8(3):1-6.
12. Alnajjar A, Alkhoury I, Burhan AS, Alkhouli M. The Efficacy of Xenograft Polymerized with Platelet Rich Fibrin Versus Autogenous Graft During the Secondary Alveolar Bone Grafting Of Alveolar Clefts: A Randomized Controlled Clinical Trial. International Journal of Dentistry and Oral Science. 2020;7(11):886-891.
13. Tovar N, Jimbo R, Gangolli R, et al. Evaluation of bone response to various anorganic bovine bone xenografts: An experimental calvaria defect study. International Journal of Oral and Maxillofacial Surgery. 2014;43(2):251-260.
14. Mahyudin F, Utomo DN, Suroto H, Martanto TW, Edward M, Gaol IL. Comparative Effectiveness of Bone Grafting Using Xenograft Freeze-Dried Cortical Bovine, Allograft Freeze-Dried Cortical New Zealand White Rabbit, Xenograft Hydroxyapatite Bovine, and Xenograft Demineralized Bone Matrix Bovine in Bone Defect of Femoral Diaphysis of White Rabbit: Experimental Study in Vivo. International Journal Biomaterials. 2017;15(2):1-9.
15. Kumar V, Rattan V, Rai S, Singh SP, Mahajan JK. Comparative Assessment of Autogenous Cancellous Bone Graft and Bovine-Derived Demineralized Bone Matrix for Secondary Alveolar Bone Grafting in Patients With Unilateral Cleft Lip and Palate. Cleft Palate-Craniofacial Journal. 2022;59(7):833-840.
16. Weibrich G, Hansen T, Kleis W, Buch R, Hitzler WE. Effect of platelet concentration in platelet-rich plasma on peri-implant bone regeneration. Bone. 2004;34(4):665-671.
17. Roffi A, Filardo G, Kon E, Marcacci M. Does PRP enhance bone integration with grafts, graft substitutes, or implants? A systematic review. BMC Musculoskeletal Disorder. 2013;14(330):1-11.
18. Albanese A, Licata ME, Polizzi B, Campisi G. Platelet-rich plasma (PRP) in dental and oral surgery: From the wound healing to bone regeneration. Immunity and Ageing. 2013;10(23):1-10.
19. Rychlik D, Wójcicki P, Koźlik M. Osteoplasty of the Alveolar Cleft Defect. Advances in Clinical and Experimental Medicine. 2012;21(2):255-262.
20. Bezerra BT, Pinho JNA, Figueiredo FED, Brandão JRMCB, Ayres LCG, da Silva LCF. Autogenous Bone Graft Versus Bovine Bone Graft in Association With Platelet-Rich Plasma for the Reconstruction of Alveolar Clefts: A Pilot Study. Cleft Palate-Craniofacial Journal. 2019;56(1):134-140.
21. Polanco A, Del NL, Polanco H, et al. The use of PRF in guided bone regeneration with xenograft around implants in a severe bone loss site: A case report. Journal of Case Reports and Images in Dentistry. 2021;7(2021):1-8.
22. Roca-Millan E, Jané-Salas E, Marí-Roig A, et al. The Application of Beta-Tricalcium Phosphate in Implant Dentistry: A Systematic Evaluation of Clinical Studies. Materials. 2022;15(655):1-11.
23. Shamsoddin E, Houshmand B, Golabgiran M. Biomaterial selection for bone augmentation in implant dentistry: A systematic review. Journal of Advanced Pharmaceutical Technology and Research. 2019;10(2):46-50.
24. De Ruiter A, Janssen N, Van Es R, et al. Micro-structured beta-tricalcium phosphate for repair of the alveolar cleft in cleft lip and palate patients: A pilot study. Cleft Palate-Craniofacial Journal. 2015;52(3):336-340.
25. Trujillo RL, Kadioglu O, Currier GF, Smith KS, Yetkiner E. Volumetric Cleft Changes in Treatment With Bone Morphogenic Protein/β-Tricalcium Phosphate Versus Grafts From the Iliac Crest or Symphysis. Journal of Oral and Maxillofacial Surgery. 2018;76(9):1991-1997.
26. Janssen NG, Schreurs R, de Ruiter AP, et al. Microstructured beta-tricalcium phosphate for alveolar cleft repair: a two-centre study. International Journal of Oral Maxillofacial Surgery. 2019;48(6):708-711.
27. Sakamoto Y, Sakamoto T, Ishii T, Kishi K. Assessment of Bioabsorbable Hydroxyapatite for Secondary Bone Grafting in Unilateral Alveolar Clefts. Cleft Palate-Craniofacial Journal. 2020;57(1):114-117.
28. Jang SJ, Kim SE, Han TS, Son JS, Kang SS, Choi SH. Bone Regeneration of Hydroxyapatite with Granular Form or Porous Scaffold in Canine Alveolar Sockets. In Vivo (Brooklyn). 2017;31(3):335-341.
29. Handrini Dewi A, Dewi Ana I. The use of hydroxyapatite bone substitute grafting for alveolar ridge preservation, sinus augmentation, and periodontal bone defect: A systematic review. Heliyon. 2018;4(2018):1-30.
30. Takemaru M, Sakamoto Y, Sakamoto T, Kishi K. Assessment of bioabsorbable hydroxyapatite for secondary bone grafting in unilateral alveolar cleft. Journal of Plastic, Reconstructive and Aesthetic Surgery. 2016;69(4):493-496.
31. Mukherji A, Rath S. Calcium sulfate in periodontics: A time tested versatile alloplast. Journal of the Scientific Society. 2016;43(1):18-23.
32. Al-Jwboory HM, Issa SA. Outcome of Using Medical Grade Calcium Sulfate Hemihydrate (DentoGen) in Unilateral Alveolar Cleft Repair. Indian Journal of Forensic Medicine & Toxicology. 2021;15(3):1593-1598.
33. Doi K, Kubo T, Takeshita R, et al. Inorganic polyphosphate adsorbed onto hydroxyapatite for guided bone regeneration: An animal study. Dental Materials Journal. 2014;33(2):179-186.
34. Alkaabi SA, Kalla DSN, Alsabri GA, et al. Safety and feasibility study of using polyphosphate (PolyP) in alveolar cleft repair: a pilot study. Pilot and Feasibility Studies. 2021;7(199):1-8.
35. Nakajima K, Kunimatsu R, Ando K, et al. Comparison of the bone regeneration ability between stem cells from human exfoliated deciduous teeth, human dental pulp stem cells and human bone marrow mesenchymal stem cells. Biochemical Biophysical Research Communications. 2018;497(3):876-882.
36. Tanikawa DYS, Pinheiro CCG, Almeida MCA, et al. Deciduous Dental Pulp Stem Cells for Maxillary Alveolar Reconstruction in Cleft Lip and Palate Patients. Stem Cells International. 2020;2020(6234167):1-9.