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Effect of Bone Marrow Aspirate Concentrate on Mixture of Fibrin Glue and Xenograft in Treatment of Critical Sized Periapical Bone Defects (Clinical and Radiographic Study)

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ABSTRACT: **Objective:** The aim of this research was to evaluate bone regeneration capacity of a mixture of Fibrin glue and Xenogeneic bone graft versus a mixture of BMAC, Fibrin glue and Xenogeneic bone in critical sized periapical bone defects. **Materials and methods:** Sixteen patients randomly and equally divided into two groups; **Group I:** eight patients with critical periapical bone defects were grafted by a mixture of fibrin glue and xenograft. **Group II:** eight patients with critical periapical bone defects were grafted by a mixture of BMAC, fibrin glue and xenograft. Assessment of pain was done on a Visual Analogue Scale (VAS) immediate, 3 days and 1 week post-operatively. Radiographic evaluation: for the bone density, volumetric changes and defect dimensions measurement between study groups. **Results**: the highest mean score on visual analogue scale was found in (Group I), while the lowest mean score was found in (Group II). Group (II) experienced a significant positive change in defect dimensions, in bone density and defect volume which increase by time in bone density over group (I) till the end of our follow up time which is 6 months. **Conclusion:** MSCs present in BMAC promote bone regeneration and improve the density of regenerated bone.

Keywords: bone marrow aspirate concentrate, fibrin glue, critical bone defect, xenograft, bone regeneration.

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Introduction:

Critical-sized periapical bone defect (CSD) post-congenital diseases, trauma, or surgical procedures is a challenging situation for oral and maxillofacial surgeons. Defects are traditionally treated with autologous bone grafts, allografts, or synthetic substitutes for functional and aesthetic restoration, with autogenous bone graft being the preferred choice. Allografts can elicit an immunological response due to genetic differences, leading to an increased focus on synthetic graft materials. Synthetic bone substitutes offer advantages like unlimited supply and easy sterilization, but they lack living cells and growth factors for bone formation, which can lead to drawbacks[1-4].

The forefront of regenerative medicine in contemporary times is epitomized by bone marrow aspirate concentrate (BMAC). When taking into account both its anti-inflammatory and regenerative properties, BMAC emerges as a compelling instrument for bone regeneration. BMAC demonstrates the ability to yield a higher concentration of MSCs and other beneficial stromal cells, surpassing that of bone marrow (BM) itself. Furthermore, apart from MSCs, BMAC harbors a greater abundance of growth factors compared to BM. Not only that, BMAC is also endowed with a plethora of bioactive molecules and cell varieties including lymphocytes, neutrophils, monocytes, and platelets at different stages of development. Through cytological scrutiny, it is evident that BMAC contains an elevated quantity of platelets and white blood cells. Another abundant autologous source of growth factors is found in ultra-concentrated centrifuged blood[5,6].

The application of highly concentrated centrifuged blood, which includes platelet- rich plasma, platelet-rich fibrin, and fibrin glue, is prevalent in expediting the healing of both soft and hard tissues. The improved healing properties of PRP, PRF, and fibrin glue arise from the production and release of various growth and differentiation factors upon platelet activation[7]. These factors play a crucial role in regulating and stimulating the process of wound healing, influencing cellular functions such as mitogenesis, chemotaxis, differentiation, and metabolism. Fibrin glue, a constituent of tissue-engineered materials, is a dual- component tissue adhesive comprising fibrinogen and thrombin. The use of fibrin glue in reconstructive bone surgery not only provides physical benefits but also speeds up the healing process of bone grafts. The fibrin meshwork acts as a framework for cell infiltration and a carrier for bone formation[8]. Hence, this research aimed to assess the effectiveness of combining fibrin glue with bone marrow aspirate concentrate in promoting bone formation within critical periapical bone defects.

Patients and methods:

Study design:

The present study was a prospective clinical randomized study and carried out on human adult patients from both sexes.

Study setting and population:

Sixteen patients (ten females and six males) were included in the present studywith their ages ranged from 13 to 57 years old (with mean age of 35 ± 12). They were selected from those who were indicated for periapical surgery in one of two jaws leaving critical sized periapical bony defects; ―These patients were selected from whose are attending out-patient clinic of Oral and Maxillofacial Surgery Department, Faculty of Dental Medicine, Al-Azhar University, Assiut branch for boys, Egypt. The study extended from October 2021 to December 2023.

Inclusion criteria:

1. Patients had critical sized periapical bone defects, where the defect size was greater than 2.5cm^2 as measured in cone beam computed tomography (CBCT).
2. Patients had sufficient healthy soft tissue to cover periapical bone defect after surgical procedures.
3. Patients with good physical health and free from any systemic condition that might retard bone healing.
4. Patients who were fit for general anesthesia.

Exclusion criteria:

1. Patients who are smokers, alcoholics, use illicit drugs,
2. Diabetics and patients with uncontrolled systemic diseases,
3. Patients treated with radiotherapy, chemotherapy or cortisone drugs.
4. Patients with bleeding disorders.

Ethical consideration:

The protocol of this study was be subjected to the Ethical Committee code number: **AUAREC202100009-15** of Faculty of Dental Medicine, Al-Azhar University, Assiut, for boys, Egypt.

Sample calculation:

Based on previous trial cases[9], a power analysis was conducted using G Power

version 3.1 statistical software developed by Franz Faul from Universität Kiel in Germany. An a priori analysis was executed to determine the necessary sample size based on α, power, and effect size. The specified input parameters included an α error probability of 0.05, an effect size (f) of 2.1, a power of 0.95, and two groups. The results revealed a minimum sample size of n = 12 (6 per group). To account for a potential patient loss of approximately 20%, a total of 16 individuals were utilized (8 in each group).

Patients grouping:

All patients were randomly and equally divided into two groups by a combination of specific features and coin flipping method, according to type of materials which fill the defect:

Group I: Eight patients with critical periapical bone defects were grafted by a mixture of fibrin glue and xenograft.

Group II: Eight patients with critical periapical bone defects were grafted by a mixture of BMAC, fibrin glue and xenograft.

Surgical Procedure:

All surgical procedures were conducted under general anesthesia via nasoendotracheal intubation. Anesthesia was induced, and surgical areas were scrubbed with antiseptic solutions. Patient's eyes and ears were protected. Draping with sterile towels was done, exposing only surgical areas. Injection for hemostasis was administered at incision lines.

Surgical exposure of the periapical lesion:

Surgical approach choice was based on lesion extension and surgeon's preference, such as trapezoidal or triangular flap. Gingival incisions were made, extending around the cyst-related teeth. Alveolar bone was exposed by raising a mucoperiosteal flap. Access to cyst lining was achieved through a bony window.

Enucleation of the periapical lesion:-

Granulation tissue was removed, and cysts were enucleated using periapical curettes. Tissue samples were submitted for examination. Teeth apices were resected, and root tips were removed. Periapical defects were decontaminated and prepared for graft application. Mineral trioxide aggregate was used for periapical seal.

Preparation of autologous fibrin glue

Preparation of autologous fibrin glue involved disinfecting the patient's arm and obtaining fresh whole blood from the median cubital vein. The blood was then centrifuged to separate into two layers, with the upper layer containing autologous fibrin glue collected using a syringe. The glue was mixed with xenograft and left to stand, resulting in a homogenous mixture. This mixture, rich in platelets and growth factors, was referred to as "sticky bone."

Bone marrow aspiration which prepared for (BMAC)

Bone marrow aspirates was harvested from the anterior iliac using bone marrow aspirating needle in the following steps-:
Anterior iliac crest region was scrubbed and swabbed with topical antiseptic solution (Betadine®).
Aseptic technique was employed to introduce an Islamic marrow aspiration needle by piercing the skin, following its extension in the direction opposite to the frontal ridge of the ilium. The needle was advanced with a semi-circular rotary motion and gentle pressure to prevent deformation as it reached the cortical layer.

Upon entering the cancellous marrow cavities, the trocar was extracted, and a 10ml sterile plastic syringe was attached to the aspiration segment of the needle. Subsequent to the aspiration procedure, the needle was retracted, leaving only a superficial puncture in the skin, and hemostasis was accomplished by applying pressure dressing over the donor site.

Bone Marrow Aspirate Concentrate (BMAC) was then derived by isolating the buffy coat subsequent to extracting bone marrow from the iliac crest, collected in heparinized tubes, and subsequently subjected to centrifugation at 3200 rpm for 10 minutes. Finally, a mixture of (BMAC), autologous fibrin glue (AFG) and xenograft (sticky bone) was transported and adapted inside the bone defect of group (II) patients without excessive compression, and covered with a collagen membrane.

Assessment

- pain was done on a Visual Analogue Scale (VAS) immediate, 3 days and 1 week post-operatively.
- Radiographic evaluation: for the bone density, volumetric changes and defect dimensions measurement between study groups.

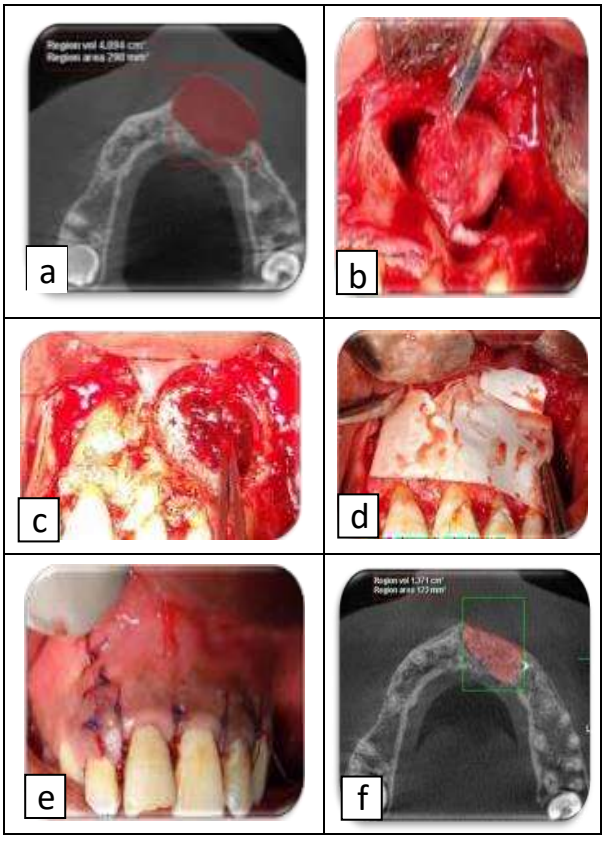

Figure (1): (a) *Preoperative CBCT radiograph showing volumetric analysis on axial view of the segmented lesion,* ***(b, c, d, e)*** *Clinical intraoral photographs showing; thecyst lining separated from the surrounding bone, the bony defect filled with a mixture of fibrin glue and bone graft (sticky bone) and BMAC, adaptation of collagen membrane covering the grafting mixture, surgical flap repositioned and sutured,* ***(f)*** *Six months postoperative radiographs showing volumetric analysis on axial view of the segmented lesion.*

Statistical analysis:

The data collected was statistically analyzed. Mean and standard deviation values were calculated for each group in each test. Normality was tested using Kolmogorov-Smirnov and Shapiro-Wilk tests. Parametric distribution was found in Age, pain, bone density, bone volume, and defect dimensions data. Non-parametric distribution was found in the rest of the data. Different statistical tests were used for parametric and non- parametric data. Significance level was set at $P \leq 0.05$. IBM® SPSS®1 Statistics Version 20 for Windows was used for the statistical analysis.

Results:

1. Clinical evaluation between the studied groups:

A. Suture break down: (Group I) showed two (25%) cases with suture breakdown and six (75%) cases with proper suturing, while (Group II) didn't have any case with suture breakdown at the 7th day.
There was no statistically significant difference between (Group I) and (Group II) where (p=0.317).

B. Dehiscence: (Group I) showed two (25%) cases with dehiscence and six (75%) cases with proper healing, while (Group II) didn't have any case with dehiscence at the 7th day. There was no statistically significant difference between (Group I) and (Group II) where (p=0.317).

C. Swelling: (Group I) showed two (25%) cases with soft tissue swelling and six (75%) cases without soft tissue swelling, while (Group II) didn't have any case with soft tissue swelling at the 7th day. There was no statistically significant difference between (Group I) and (Group II) where (p=0.317).

D. Edema: both groups didn't have any case with edema at the 7th day. There was no statistically significant difference between (Group I) and (Group II) where (p=1).

E. Infection: both groups didn't have any case with infection at the 7th day. There was no statistically significant difference between (Group I) and (Group II) where (p=1).

F. Graft rejection: both groups didn't have any case with graft rejection at the 7th day. There was no statistically significant difference between (Group I) and (Group II) where (p=1).

Table (1): *Comparison between the two studied groups according to clinical evaluation at the 7th day.*

Variables		Group I (Control)	Group II (Study)	p-value
Suture breakdown	Yes	2 (25%)	0%	0.317^{ns}
	No	6 (75%)	8 (100%)	
Dehiscence	Yes	2 (25%)	0 (0%)	0.317^{ns}
	No	6 (75%)	8 (100%)	
Swelling	Yes	2 (25%)	0 (0%)	0.317^{ns}
	No	6 (75%)	8 (100%)	
Edema	Yes	0 (0%)	0 (0%)	1^{ns}
	No	8 (100%)	8 (100%)	
Infection	Yes	0 (0%0	0 (0%)	1^{ns}
	No	8 (100%)	8 (100%)	
Graft rejection	Yes	0 (0%)	0 (0%)	1^{ns}
	No	8 (100%)	8 (100%)	

*" **P**; Probability Level. **ns**; non-significant (p>0.05)".*

G. Pain (VAS)

- The visual analogue pain scale in group I at (Immediate post-operative), (After 3 days) and (After 1 week) recorded an average (±SD) of 8.57±0.53, 6.57±0.53, and 3.57±0.53; respectively. The decrease in VAS scale with time was statistically significant where (p=0.001).
- The visual analogue pain scale in group II at (Immediate post-operative), (After 3 days) and (After 1 week) recorded an average (±SD) of 8.57±0.53, 3.57±0.53, and 1.57±0.53; respectively. The decrease in VAS scale with time was statistically significant where (p=0.001).
- There was no statistically significant difference between (Group I) and (Group II) where (p=1) for immediate post-operative, but there was statistical significant difference where (p=0.001) and (p=0.001) for after 3 days and after 1 week postoperative pain respectively.

Table (2): *The mean ± standard deviation (SD) values of pain score of both groups.*

Variables	Pain (VAS)				
	Group I (Control)		Group II (Study)		p-value
	Mean	SD	Mean	SD	
Immediate post-operative	8.57 ^{aA}	0.53	8.57 ^{aA}	0.53	1^{ns}
After3 days	6.57 ^{bA}	0.53	3.57 ^{bB}	0.53	0.001*
After1 week	3.57 ^{cA}	0.53	1.57 ^{cB}	0.53	0.001*
p-value	0.001*		0.001*		

"Means with different small letters in the same column indicates significant difference, means with different capital letters in the same row indicates significant difference"

*****;** "significant (p<0.05)" **ns**; "non-significant (p>0.05)"*

2. Radiographic evaluation between the studied groups:

A. Bone density:

- The bone density values of group-I recorded an average (±SD) 100.00±5.54, 598.14±26.16, 623.71±24.87, 645.14±23.13 and 673.57±23.67 in preoperative, immediate post-operative, 2 mon. , 4 mon. and 6 mon. postoperative respectively; The difference between them was significant where (p<0.001).

- The bone density values of group-II recorded an average (±SD) 110.86±6.73, 579.14±25.98, 628.57±23.75, 675.86±30.15 and 729.71±32.66 in preoperative, immediate post-operative, 2 mon. , 4 mon. and 6 mon. postoperative respectively; The difference between them was significant where (p<0.001).
- There was no statistically significant difference between (Group I) and (Group II) where (p=0.237), (p=0.616), (p=0.890), (p=0.435) and (p=0.189) for preoperative, immediate post-operative, 2 mon. , 4 mon. and 6 mon. postoperative bone density values respectively.

Table (3): *The mean ± standard deviation (SD) values of Bone density in HU of both groups.*

Variables	Bone density (H U)				
	Group I (Control)		Group II (Study)		p-value
	Mean	SD	Mean	SD	
Pre-operative	100.00^{eA}	5.54	110.86^{dA}	6.73	0.237^{ns}
Immediate post-operative	598.14^{dA}	26.16	579.14^{cA}	25.98	0.616^{ns}
After 2mon.	623.71^{cA}	24.87	628.57^{bcA}	23.75	0.890^{ns}
After 4mon.	645.14^{bA}	23.13	675.86^{bA}	30.15	0.435^{ns}
After 6mon.	673.57^{aA}	23.67	729.71^{aA}	32.66	0.189^{ns}
p-value	$<0.001^{*}$		$<0.001^{*}$		

"Means with different small letters in the same column indicates significant difference, means with different capital letters in the same row indicates significant difference".
*******; *"significant (p<0.05)"* ***ns****; "non-significant (p>0.05)"*

B. Bone defect volume:

- The bony defect volume values in group I was recorded as mean and standard deviation from the preoperative reading. The bony defect volume values in preoperative, immediate postoperative, 2 months, 4 months and 6 months postoperative showed an average (±SD) of 5.01±0.23cm^3 , 5.98±0.33cm^3, 5.40±0.38cm^3,4.68±0.55cm^3 and 3.89±0.54cm^3 respectively. The difference in bone defect volume values between time points was highly statistically significant where (p=0.001).
- The bony defect volume values in group II was recorded as mean and standard deviation from the preoperative reading. The bony defect volume values in preoperative, immediate postoperative, 2 months, 4 months and 6 months postoperative showed an average (±SD) of 4.28±0.46cm^3 , 5.56±0.27cm^3, 4.40±0.69cm^3,3.94±0.59cm^3 and 3.15±0.68cm^3 respectively. The difference in bone defect volume values between time points was highly statistically significant where (p=0.011).
- There was no statistically significant difference between (Group I) and (Group II) where (p=0.182), (p=0.443), (p=0.229), (p=0.374) and (p=0.411) for preoperative, immediate post-operative, 2 months , 4 months and 6 months postoperative bone defect volume values respectively.

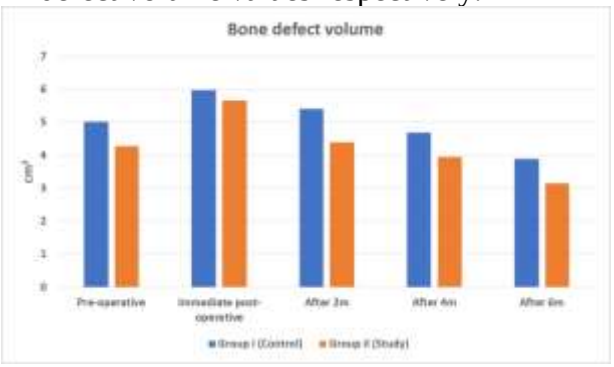

Figure (2): *Bar chart representing comparison of bone defect volume values between the two groups at different intervals.*

C. Defect dimensions:

- The bony defect dimensions values in group I was recorded as mean and standard deviation from the preoperative reading. The defect dimensions values in preoperative, immediate postoperative,2 months, 4 months and 6 months postoperative showed an average (±SD) of 6.4405 ± 0.3973cm^2 , 5.1343 ± 0.2262cm^2, 4.4124 ± 0.3179cm^2, 3.3384 ± 0.2896cm^2 and 2.9111 ± 0.2025cm^2 respectively. The difference in defect dimensions values

between time points was highly statistically significant where (p<0.001).

- The bony defect dimensions values in group II was recorded as mean and standard deviation from the preoperative reading. The defect dimensions values in preoperative, immediate postoperative, 2 months, 4 months and 6 months postoperative showed an average (±SD) of 6.3822 ± 0.2606cm^2 , 6.0506 ± 0.2936cm^2, 4.5998 ± 0.2213cm^2, 3.2334 ± 0.1207cm^2 and 2.1951 ± 0.2619cm^2 respectively. The difference in defect dimensions values between time points was highly statistically significant where (p<0.001).
- A statistically significant difference in bone defect dimensions values was found between (Group I) and (Group II) where (p=0.029) and (p=0.049) for immediate post-operative and 6 months postoperative bone defect dimentions values respectively. While there was no statistically significant difference in bone defect dimensions values between (Group I) and (Group II) where (p=0.904), (p=0.637), (p=0.744) for preoperative, , 2 months , 4 months postoperative bone defect dimensions values respectively.

Figure (3): *Bar chart representing comparison of defect dimensions values between the two groups at different intervals.*

Discussion:

Periapical bone defects can arise due to systemic or local etiologies. Systemic factors encompass congenital anomalies, systemic illnesses, and pharmacological agents, whereas local factors consist of inflammation or traumatic insults, like accidental injuries or dental and surgical interventions. Dental procedures, such as tooth removal, and surgical interventions, such as excision of benign or malignant tumors, have the potential to cause significant defects in the jaw bone[10,11]. Ablative procedures lead to osseous defects causing problems in patients' quality of life, with slow natural bone regeneration reported by Chiapasco et al. for postenucleation defects. Various options like bone grafts and tissue-engineering are used to rehabilitate bone defects. Using a scaffold with mesenchymal stem cells in bone defect sites promotes bone formation and healing. This approach combines BMAC-containing growth factors, osteoprogenitors, and a sticky bone scaffold for effective bone regeneration[12,13].

In both cohorts, no evidence of inflammation, infection, or edema was discernible throughout the observation periods of the current investigation. All transplants were well-received with no indications of graft rejection or antigenicity responses. This finding concurred with various prior research studies[14], such as the work of Atsumu K et al.[15], which suggested that the application of fibrin glue rich in human-derived components at sites of tissue damage tends to be generally well-tolerated without provoking excessive inflammation, foreign body reactions, tissue necrosis, or significant fibrosis, thereby positively influencing the overall wound healing process. Moreover, there were no instances of dehiscence, swelling, or suture failures except for two cases in each group, denoting a lack of statistically significant disparity between (Group I) and (Group II) whereby (p>0.05).

Regarding the intensity of pain experienced within the analyzed cohorts, the highest average score on the visual analogue scale was recorded in (Group I), whereas the lowest average score was noted in (Group II), with a computed P-value =0.002 signifying a statistically significant distinction between (Group I) and (Group II). Mesenchymal stem cells (MSCs) impede inflammatory T-cell

expansion; hinder the maturation of monocytes and myeloid dendritic cells, leading to an immunomodulatory and anti-inflammatory impact. These MSCs express pivotal cytokines like transforming growth factor beta, vascular endothelial growth factor, epidermal growth factor, and an assortment of bioactive molecules that promote local tissue regeneration. This elucidates why, in our examination, patients in group II who received bone marrow aspirate concentrate (BMAC) exhibited reduced postoperative pain and swelling[16].

In this research, Group (I) with fibrin glue and xenograft and Group (II) with BMAC, fibrin glue, and xenograft both showed significant improvements in bone density, volume, and defect dimensions, leading to increased bone healing. The study involved critical-sized bone defects which exhibited successful bone regeneration after 6 months post-surgery for both groups, highlighting the beneficial impact of autologous fibrin glue on bone healing. Previous studies[17,18] have also highlighted the role of autologous fibrin glue as a scaffold for stimulating mesenchymal cells, promoting angiogenesis, and initiating early osteogenesis. The use of "sticky bone" preparation with xenogenic bone graft in fibrin meshwork stabilizes graft without using bone tacks or titanium mesh, aiding in tissue healing[19]. Group (II) patients with BMAC, fibrin glue, and xenograft had significant positive changes in defect dimensions at 6 months postoperative compared to Group (I). Studies show fibrin glue with MSCs enhances bone regeneration and also in accordance with Zhong et al.[20].

The presence of concentrated mononuclear cells in the BMAC is the cause of the minor increased osteogenesis seen in our study.[21] When combined with an osteoconductive scaffold, autologous mesenchymal stem cells function as a highly regenerating graft material. However, the procedure of MSCs' dynamic migration to the defect location depends on CXCR4, dosage, and time[22].

Conclusion:

To summarize, the utilization of autologous bone marrow aspirate concentrates combined with xenograft group (II) in clinical settings following the enucleation of pathologic lesions in the jaw is a potentially effective method for boosting bone regeneration and increasing the density of the regenerated bone. However, this approach will require further research lasting longer than six months. The novel autografting biotechnology employed in our investigation is safe and economical, needing no extra graft materials and carrying few dangers.

References:

1. **SCHLIEPHAKE H, WEICH HA, DULLIN C, et al.** Mandibular bone repair by implantation of rhbmp-2 in a slow release carrier of poly lactic acid: an experimental study in rats. *Biomaterials,* 2008;29: 103-10.
2. **VAN GEMERT JT, VAN ES RJ, VAN CANN EM, et al.** Nonvascularized bone grafts for segmental reconstruction of the mandible—a reappraisal. *J Oral Maxillofac Surg.* 2009;67:1446 –52.
3. **SBORDONE L, TOTI P, MENCHINI-FABRIS GB, et al.** Volume changes of autogenous bone grafts after alveolar ridge augmentation of atrophic maxillae and mandibles. *Int J Oral Maxillofac Surg.* 2009;38:1059 –65.
4. **EPPLEY BL, HOLLIER L and STAL S.** Hydroxyapatite cranioplasty: 2. Clinical experience with a new quick-setting material. *J Craniofac Surg.* 2003; 14:209–14.
5. **MUSCHLER, GEORGE F, HIRONORI N, et al.** Age-and gender-related changes in cellularity of human bone marrow and prevalence of osteoplastic progenators. *J orthop Res,* 2001; 19:117-25.
6. **MUSCHLER G and MIDURA RJ.** Connective tissue progenitors: practical concepts for clinical applications. *clinic orthop,*2002; 395:66-80.

7. **GERNOT W, WILFRIED KG, GERD H, et al.** Growth factors levels in platelet-rich plasma and correlations with donor age, sex and platelet count. *J Craniomaxillofac. Surg.*2002; 30:97-102.
8. **MARX RE, CARLSON RM, EICHSTAEDT SR, et al.** Platelet-rich plasma: growth factor enhancement for bone grafts. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* .1998;85 ,6: 638–46.
9. **ELSAFTY AA, ELSHEIKH SA, SWEEDAN AO.** The effect of bone marrow aspirate concentrate in the treatment of mandibular cystic defects. A randomized clinical trial. *Alexandria Dental Journal*. 2024 Apr 18.
10 . **ROLSKI D, KOSTRZEWA-JANICKA J, ZAWADZKI P, et al. —**The management of patients after surgical treatment of maxillofacial tumors,‖ *BioMed Research International*, 2016; 2016, Article ID 4045329, 7 pages.
11 . **CHIAPASCO M, ROSSI A, MOTTA JJ, et al.** Spontaneous bone regeneration after enucleation of large mandibular cysts: A radiographic computed analysis of 27 consecutive cases. *J Oral Maxillofac Surg.* 2000;58:942–8.
12 . **VORRASI JS AND KOLOKYTHAS A. —**Controversies in traditional oral and maxillofacial reconstruction,‖ *Oral and Maxillofa cial Surgery Clinics of North America*, 2017; 29, 4:401–13.
13 . **RAJA SG, RAVINDRAN C, SATHYA KD, et al.** Concentrated Bone Marrow Aspirate-Coated Hydroxyapatite for Reconstruction of Small-to-Moderate-Sized Mandibular Defects Caused by the Removal of Benign Pathologies. *Contemp Clin Dent*. 2018 Oct-Dec; 9,4: 535–40.
14 . **GIANNINI G, MAURO V, AGOSTINO T, et al.** Use of autologous fibrin-platelet glue and bone fragments in maxillofacial surgery. *Transfus Apher Sci*. 2004;30:139–44 .
15 . **ATSUMU K, YOSHINAKA S, SHINNOSUKE N, et al.** Wound healing effect of autologous fibrin glue and polyglycolic acid sheets in a rat back skin defect model. *Transfusion and Apheresis Science*. 2021, August; 60, 4: 103144.
16 . **ZIZZARI V, ZARA S, TETE` G, et al.** Biologic and clinical aspects of integration of different bone substitutes in oral surgery: a literature review. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2016;122:392–402.
17. **CLAES L, BURRI C, GERNGROSS H, et al.** Bone healing stimulated by plasma factor XIII. Osteotomy experiments in sheep. *Acta Orthop Scand*. 1985;56:57–62
18. **RIPAMONTI U, VAN DEN HEEVER B AND VAN WYK J.** Expression of the osteogenic phenotype in porous hydroxyapatite implanted extraskeletally in baboons. *Matrix.* 1993;13:491–502.
19. **SOHN DS, HUANG B, KIM J, et al.** Utilization of autologous Concentrated Growth Factors (CGF) enriched bone graft matrix (Sticky bone) and CGF-enriched fibrin membrane in Implant Dentistry. *J Implant Adv Clin Dent*. 2015;7,10:11-29.
20 . **ZHONG W, SUMITA Y, OHBA S, et al.** In vivo comparison of the bone regeneration capability of human bone marrow concentrates vs. platelet-rich plasma. *PLoS One*. 2012;7,7: 40833.
21. **HERNIGOU P, POIGNARD A, BEAUJEAN F, et al.** Percutaneous autologous bone-marrow grafting for nonunions. Influence of the number and concentration of progenitor cells. *J Bone Joint Surg Am.* 2005;87:1430–7.
22. **WYNN RF, HART CA, CORRADI-PERINI C, et al.** A small proportion of mesenchymal stem cells strongly expresses functionally active CXCR4 receptor capable of promoting migration to bone marrow. *Blood* 2004;104:2643-5.