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Guided bone regeneration with rh-bmp2 in lingual mandibular bone resorption for orthodontic treatment. A case report

Regeneración ósea guiada con rh-bmp2 en la reabsorción ósea mandibular lingual para tratamiento de ortodoncia. Reporte de un caso

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ABSTRACT: Uncontrolled orthodontic movements and compensation to avoid orthognatic surgery can cause unwanted bone resorption, which can cause future problems. Bone morphogenetic protein Rh-BMP2 (BMP®) has been shown to be effective in inducing bone regeneration, obtaining observable and favorable results in a short period of 8 to 10 weeks. The objective was describing a case of guided bone regeneration using BMP® to counteract bone resorption of the lingual mandibular bone of lower anterior teeth resulting from orthodontics. Female the 36-year-old patient with long-standing orthodontic treatment. Radiographically, lingual mandibular bone resorption is seen. Bone reconstruction and orthodontic treatment was planned to preserve affected teeth. A full thickness intracrevicular approach was from lower left first premolar to lower right second premolar. Liquid BMP® was used and mixed with BCP and particulate bone, covered with collagen membrane, finally activated oxygen with lactoferrin was applied. Subsequently, BMP® was infiltrated into the surgical site 21 days after the surgical procedure. Clinical control was performed at 7, 14, 21 days and tomographic control at one month and 6 months. Bone regeneration was evident to begin orthodontic treatment to reestablish the correct position of the lower anterior teeth. We can conclude that the multidisciplinary management and the use of bone growth factors can improve the prognosis of severe cases of resorption resulting from uncontrolled orthodontic movements.

KEY WORDS: BMP, Bone Regeneration, Biomateriales, Activated Oxygen, Lactoferrin.

INTRODUCTION

Class II malocclusion is very common among populations, specially caucasians (Hourfar *et al*., 2023). Correction treatment is possible in these patients, depending on the cause (skeletal or dentoalveolar). This last cause can be corrected by surgical treatment how orthognathic surgery, orthofacial surgery (Hernández-Alfaro, 2020), camouflage compensation (García-Solano *et al*., 2012; Garza *et al*., 2014) or selective dental extractions; manly premolars, (Vásquez-Estrada & González-López, 2012; Raposo *et al*., 2018). Premolars are the most frequent election in dental extraction with orthodontic porpoises, especially upper premolars. These treatment masks the skeletal discrepancy through dental compensation, in addition to the use of orthodontic functional appliances. In adult patients, this combination is used to change dental position (Raposo *et al*., 2018). It is necessary to establish limits in the proclination movements, otherwise, the damage soft and hard tissue can be a disadvantage in the treatment process (Yared *et al*., 2006)

This kind of treatment, if is well done and monitored, can assure the occlusion stability through time (Gill *et al*., 2021). Nevertheless, it can cause periodontal problems and bone resorption, excesive proclination of lower incisors can cause periodontal recessions, compromising dental hygiene and root exposure(Yared *et al*., 2006; Miyama *et al*., 2018). When this proclination is uncontrolled, the movements could cause undesired bone resorption, which often occurs on the pressure side, and there's bone apposition on the tension side, so the alveolar bone thickness is compromised, creating fenestrations and dehiscence (Miyama *et al*., 2018). The use of Cone Beam Computer Tomography (CBCT) imaging can also be applied to measure changes in the alveolar bone product of the orthodontic movements, and the precise thickness bone loss when it happens(Miyama *et al*., 2018).

The multisciplinary approach to this kind of patients, once the damage is done, could be a challenge that requires multiple procedures and biomaterials (Chen *et al*., 2004; Ardila Medina, 2009; Uribe *et al*., 2017; León-Batallas *et al*., 2019). BMP has been used for several years in Oral and Maxillofacial Surgery (Boda *et al*., 2020; Nam *et al*., 2020), and Implant Dentistry, showing good results in bone regeneration (Haimov *et al*., 2017; Bal *et al*., 2020; Kämmerer *et al*., 2020; Chen *et al*., 2021). Also, it has been reported the use of BMP in soft tissue regeneration (Oortgiesen *et al*., 2014; Wang *et al*., 2019). Other biomaterials such as activated oxygen and Lactoferrin (Presti *et al*., 2021) are used in soft tissue healing (Juliana & Tarek, 2022) and regeneration procedures, with a great success index (Schreml *et al*., 2010). It can be used in different presentations, such as mouthwash, toothpaste (Cunha *et al*., 2019), gel foam or gel (Gounden & Singh, 2024; Leventis *et al*., 2024 and there are reports of its use to control postoperative inflammation and pain (Mattei *et al*., 2021).

The aim of this case report is to describe a guided bone regeneration using BMP-2 in a patient with lingual bone resorption caused by uncontrolled orthodontic movements.

CASE REPORT

Female patient the 36-year old, with no contributory medical history, who attended for dental evaluation and treatment. During the extraoral evaluation, compensated skeletal class II and straight profile is observed (Fig. 1A, B, C). The intraoral examination revealed excessive proclination of the lower anterior incisors with long-term orthodontic treatment, aimed to avoid orthognatic surgery (Fig. 1 D). It is evaluated jointly by the Orthodontics and Oral and Maxillofacial Surgery Departments.

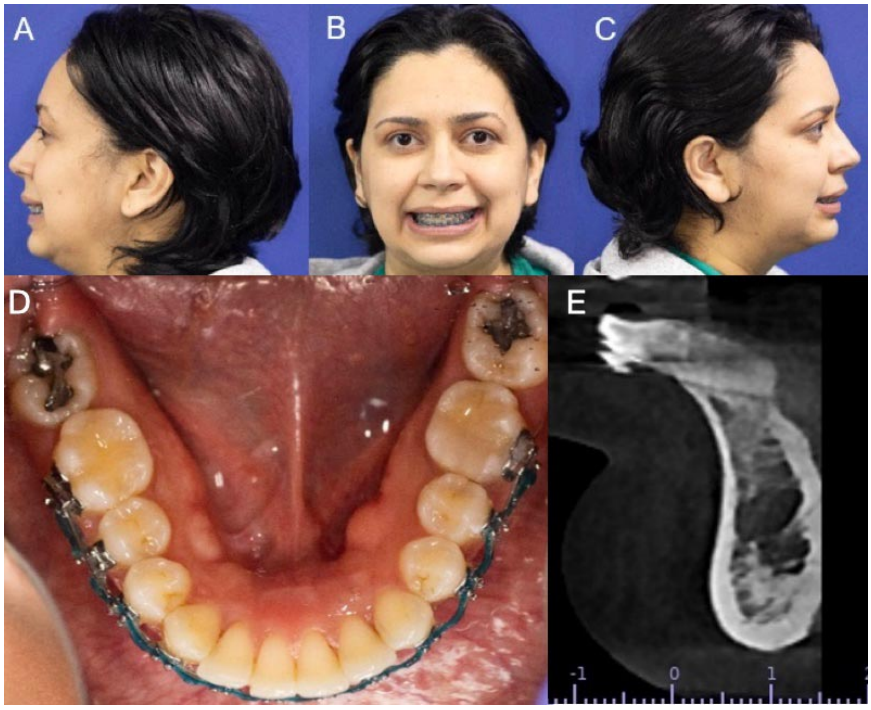

Fig. 1. Extraoral photographies, (A) left, (B) frontal, (C) right. Intraoral photography (D). CBCT axial view showing the lingual bone resorption (E).

During the imaging examination, cone beam computed tomography was evaluated using a computer imaging software, where total loss of the lingual mandibular bone of the anteroinferior sector was observed, with values of -117 HU on the density scale in the affected area (Fig. 1E).

Evaluations were performed jointly by the Orthodontics and Oral and Maxillofacial Surgery Departments, deciding to preserve the affected teeth, reconstruct the lingual mandibular bone and perform orthodontic treatment.

A full thickness intracrevicular incision was made in the lingual area from lower left first premolar to lower right second premolar (Fig. 2A). Rh-BMP2 (CowellMedi ®) (Fig. 2B, C) was used liquid and mixed with particulate bone (Diabone-Cowellmedi®), covered with collagen membrane (Diaderm Cowellmedi ®) (Fig. 2D). Finally, after the closure with Vycril resorbable suture activated oxygen with lactoferrin (Blue®M) (Fig. 2E, F) was applied.

Clinical control was performed at 7, 14, 21 days (Fig. 3) Rh-BPM2 (CowellMedi ®) was infiltrated into the area 21 days after the surgical procedure. Tomographic control at one month and 6 months (Fig. 4). Bone regeneration was evident, with millimeter measurements and density values of 471 HU after 6 months evaluation. Orthodontic treatment was initiated with a self-ligating system to reestablish the correct position of the lower anterior teeth after 3 months of the surgery.

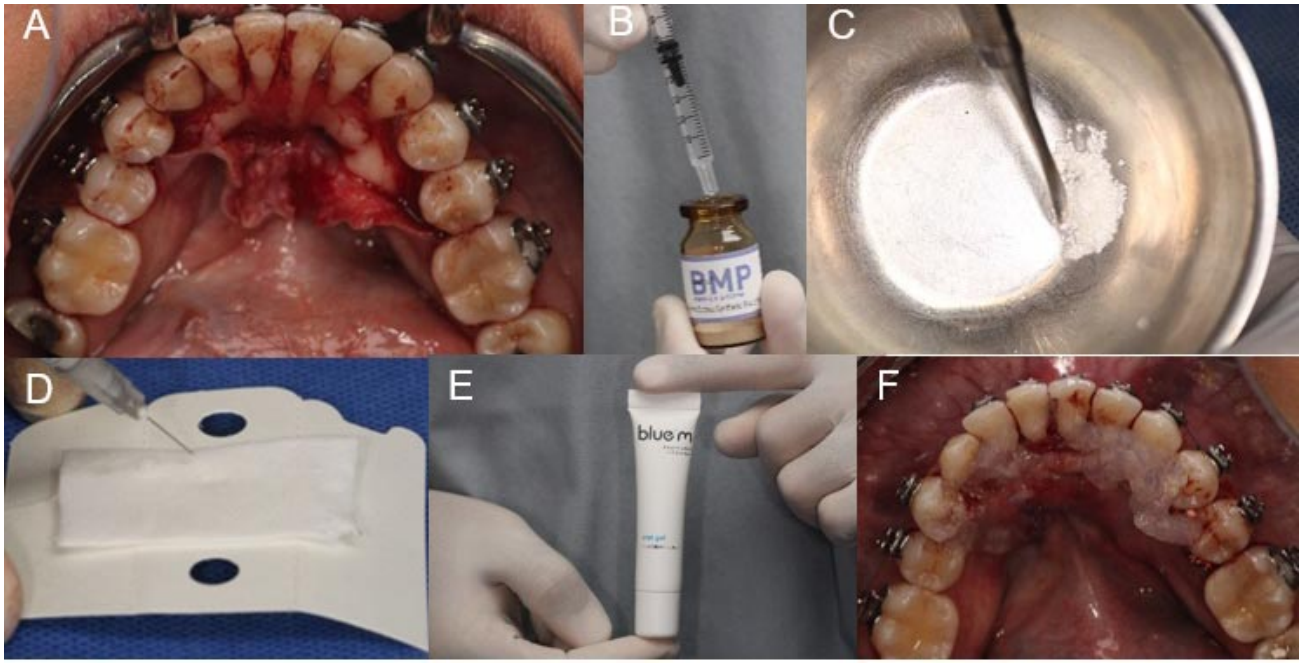

Fig. 2. Surgical approach (A), Rh-BMP2 preparation (B and C), liquid BMP applied to the collagen membrane (D); Blue®M gel applied in the surgical site immediate post op (E and F).

Fig. 3. Post op occlusal view 7 days (A); 14 days (B); 21 days (C).

DISCUSSION

The aim of this case report is to describe a guided bone regeneration using Rh-BMP-2 in a patient with lingual bone resorption caused by uncontrolled orthodontic movements. Vásquez-Estrada & Gonzalez-Lopez (2012), establishes that since skeletal asymmetry is involved, an orthodontic treatment alone will not eliminate the basic problem. A proper orthodontic camouflage treatment will correct the malocclusion and acceptably conceal the bone problem, favoring facial aesthetics, or at least, not worsening it (Vásquez-Estrada & González-López, 2012). But when this treatment is carried

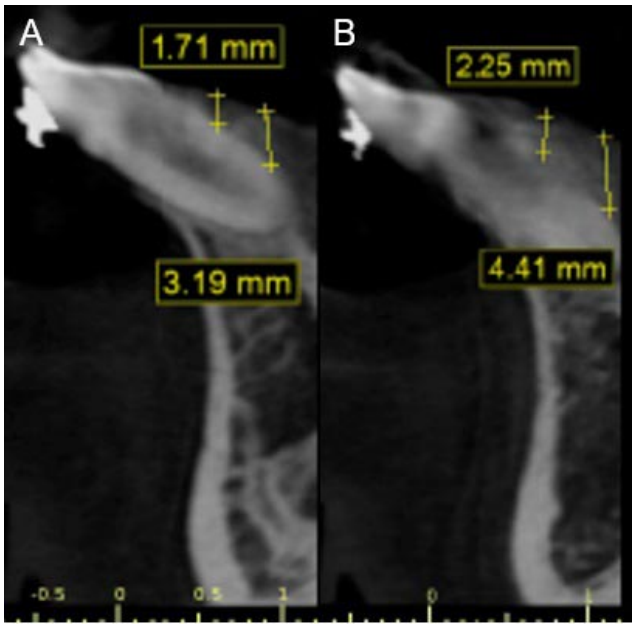

Fig. 4. CBCT image axial view. It can be observed the bone regeneration process 1 month (A) and 6 months (B), gaining 2 mm approximately of the lingual bone.

out by inexperienced hands it can have serious consequences on the supporting structure of the teeth.

Camouflage compensation is an alternative for masking skeletal class II patients under orthodontic treatment (García-Solano *et al*., 2012; Vásquez-Estrada & González-López, 2012; Raposo *et al*., 2018; Gill *et al*., 2021; Hourfar *et al*., 2023) . Nevertheless, it is very important to control the forces during the proclination movements, especially in lower incisors. If this movements are uncontrolled, it can cause bone resorption (Miyama *et al*., 2018; Yared *et al*., 2006) which also can bring periodontal problems to patients. Huerta-Cavieres (2013), indicates that unfavorable movements could be classified as those that move the teeth away from the genetically determined location they occupy within the alveolar process. They trigger mucogingival problems, mainly in thin gingival and bone tissues. In this case presentation, a class II 36-year-old patient with a long history of uncontrolled orthodontic treatment presented a high-grade lingual bone resorption, exposing dental roots and affected soft tissue as well. This can be observed clinical and imagenologically. When this kind of bone defect is created, there are several forms to bone regeneration, such as classical techniques using autologous bone and block grafts (Verdugo *et al*., 2012).

Rh-BMP-2 has been used in Oral in Maxillofacial Surgery in different procedures, such as alveolar preservation(Chen *et al*., 2004; Ardila Medina, 2009; León-Batallas *et al*., 2019; Bal *et al*., 2020), maxillary sinus lift, dental implants, among others, showing good results (Kämmerer *et al*., 2020; Nam *et al*., 2020). In this clinical situation, Rh-BMP-2 was used in combination with particulate bone and a collagen membrane which functioned as a physical barrier between the bone defect and the soft tissue. The expression of Rh-BMP-2 is sufficient to irreversibly induce osteogenesis, in recent research on bone conditioned medium, we have examined the release ofTGF-b1 and BMP-2 in bone conditioned medium extracted over different time periods and results proven that effects on osteoblast differentiation were observed, suggesting a synergistic TGF-b1/BMP-2 activity (Buser, 1995). Both the membrane and bone were impregnated with Rh-BMP-2, as the manufacturer shows in the instructions. This assures that the BMP-2 enhances the bone regeneration process, which could be verified clinically and imaginologically through panoramic x rays or tomography (Uribe *et al*., 2017). The bone regeneration process is more fast and effective, reporting verifiable results in 8 weeks(Chen *et al*., 2004; Chen *et al*., 2021); Similar findings are observed in the control tomography taken one month and six months post op, obtaining a positive values range of more than 470 HU. Rh-BMP-2 was also applied in the soft tissue 1 month post op to enhance the phenotype quality, assuring a better recovery of the gingiva. Similar findings were reported by Wang *et al*.(2019) and Chantiri *et al*.(2023), reporting new blood vesels formation posterior to the Rh-BMP2 infiltration in the gingiva, assuring more vascularization by the expression of growth factors (VEGF) and increases the healing process.

In this report, clinical control appointments were done at 7, 14, 21 days, and it has been used as a coadjutant postoperative treatment photobiomodulation sessions and active oxygen with lactoferrin (gel, gel foam and mouthwash). It has been demonstrated by da Silva *et al*. (2023) that this therapy has an inmunomodulative effect, enhancing the tissue regeneration process. Regarding active oxygen with lactoferrin, there are several studies (Cunha et al., 2019; Presti et al., 2021; Gounden & Singh, 2024; Leventis et al., 2024) indicating the effect on post-operative swelling and pain, reducing the symptoms. Active oxygen with lactoferrin, in its different presentations, help the soft tissue to heal more

rapidly and effectively, because of its therapeutic oxygen concentration release, its antibacterial effect, neovascularization, stimulation and formation of new blood cells, antihistamine effect, and others (Juliana & Tarek, 2022).

CONCLUSION

Bone morphogenetic protein is an effective solution for bone regeneration in combination with allografts, collagen membrane and activated oxygen with lactoferrin. Multidisciplinary work and knowing bone biology is essential for the success of treatment and the resolution of previous failures. More studies are required to confirm the effectiveness of this biomaterials.

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Conflict of Interest: The authors declare that they have no conflicts of interest.

Ethical Approval: The study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from the subjects involved in the study.

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RESUMEN: Los movimientos ortodóncicos no controlados y la compensación para evitar la cirugía ortognática pueden causar una reabsorción ósea no deseada, lo que puede causar problemas futuros. La proteína morfogenética ósea Rh-BMP2 (BMP®) ha demostrado ser eficaz para inducir la regeneración ósea, obteniendo resultados observables y favorables en un corto período de 8 a 10 semanas. El objetivo fue describir un caso de regeneración ósea guiada utilizando BMP® para contrarrestar la reabsorción ósea del hueso mandibular lingual de dientes anteroinferiores producto de la ortodoncia. Paciente femenina de 36 años con tratamiento de ortodoncia de larga data. Radiográficamente se observa reabsorción ósea mandibular lingual. Se planificó reconstrucción ósea y tratamiento de ortodoncia para preservar los dientes afectados. Se realizó un abordaje intracrevicular de espesor completo desde el primer premolar inferior izquierdo hasta el segundo premolar inferior derecho. Se utilizó BMP® líquida mezclada con BCP y hueso particulado, se cubrió con membrana de colágeno, finalmente se aplicó oxígeno activado con lactoferrina. Posteriormente se infiltró BMP® en el sitio quirúrgico a los 21 días del procedimiento quirúrgico. Se realizó control clínico a los 7, 14, 21 días y control tomográfico al mes y 6 meses. Se evidenció regeneración ósea para iniciar tratamiento de ortodoncia para restablecer la posición correcta de los dientes anteroinferiores. Podemos concluir que el manejo multidisciplinario y el uso de factores de crecimiento óseo pueden mejorar el pronóstico de casos severos de reabsorción producto de movimientos ortodóncicos no controlados.

PALABRAS CLAVE: BMP, regeneración ósea, biomateriales, oxígeno activado, lactoferrina.

REFERENCES

Ardila Medina CM. Base theories and the clinical application of bone morphogenetic proteins in maxillofacial surgery. *Rev Esp Cirug Oral y Maxilofac. 2009; 31(3)*:151-6.

Bal Z, Kushioka J, Kodama J, Kaito T, Yoshikawa H, Korkusuz P, Korkusuz F. BMP and TGFb use and release in bone regeneration. *Turk J Med Sci 2020; 50(2)*:1707-22. http://dx.doi.org/10.3906/sag-2003-127

Boda SK, Almoshari Y, Wang H, Wang X, Reinhardt RA, Duan B, Wang D, Xie J. Mineralized nanofiber segments coupled with calcium-binding BMP-2 peptides for alveolar bone regeneration. *Acta Biomater. 2019*; 85:282-93. http://dx.doi.org/10.1016/j.actbio.2018.12.051

Buser D. *30 years of guided bone regeneration*. 3rd ed. Buser D, editor. Vol. 29, Probe (Ottawa, Ont.). Batavia, IL: Quintessence Publishing Co. Ltd.; 1995. 72-73 p.

Chantiri M, Nammour S, El Toum S, Zeinoun T. Effect of rh-BMP-2 in the initiation of neovascularization in human gingival tissue: A split-mouth clinical study. *Life (Basel). 2023;13(12)*:2298. http://dx.doi.org/10.3390/life13122298

Chen D, Zhao M, Mundy GR. Bone morphogenetic proteins. *Growth Factors. 2004; 22(4)*:233-41. http://dx.doi.org/10.1080/08977190412331279890.

Chen X, Tan B, Bao Z, Wang S, Tang R, Wang Z, Chen G, Chen S, Lu WW, Yang D, Peng S. Enhanced bone regeneration via spatiotemporal and controlled delivery of a genetically engineered BMP-2 in a composite Hydrogel. *Biomaterials. 2021*; 277:121117. http://dx.doi.org/10.1016/j.biomaterials.2021.121117

Cunha EJ, Auersvald CM, Deliberador TM, Gonzaga CC, Esteban Florez FL, Correr GM, Storrer CLM. Effects of active oxygen toothpaste in supragingival biofilm reduction: A randomized controlled clinical trial. *Int J Dent. 2019*; 2019:3938214. http://dx.doi.org/10.1155/2019/3938214

da Silva TG, Ribeiro RS, Mencalha AL, de Souza Fonseca A. Photobiomodulation at molecular, cellular, and systemic levels. *Lasers Med Sci. 2023; 38(1)*:1-11. https://dx.doi.org/10.1007/s10103-023-03801-6

García-Solano M, Hernández-Contreras C, Nolasco-Delint MRS, Figueroa-Morales HN, Adel-Rivera JF. Camuflaje ortodóncico de clase III con mordida abierta anterior?: Reporte de un caso. *Rev Tamé. 2012; 1(1)*:14-8. Available from: https://www.uan.edu.mx/d/a/publicaciones/revista_tame/numero_1/Tam121-04.pdf

Garza DGD, Landaverde AV, Villagómez MO, Ramírez APC. Corrección de clase II división 1 con extracciones de segundos premolares maxilares. Reporte de un caso. *Rev Mex Ortod. 2014*; 2(2):130–5. http://dx.doi.org/0.1016/S2395-9215(16)30026-5

Gill IS, Pandis N, Fleming PS. The stability of Class II correction with functional appliance therapy and orthodontic camouflage: A retrospective cohort study. *Int Orthod. 2021; 19(1)*:88-95. http://dx.doi.org/10.1016/j.ortho.2020.12.004

Gounden V, Singh M. Hydrogels and wound healing: Current and future prospects. *Gels. 2024; 10(1)*:43. http://dx.doi.org/10.3390/gels10010043

Haimov H, Yosupov N, Pinchasov G, Juodzbalys G. Bone morphogenetic protein coating on titanium implant surface: A systematic review. *J Oral Maxillofac Res. 2017*; 8(2):1. http://dx.doi.org/10.5037/jomr.2017.8201

Hernández-Alfaro F. ¿El fin de la Cirugía Ortognática?. *Rev esp ortod. 2020; 58(2)*:8-20. Available from: https://www.learncco.com/wp-content/uploads/2022/04/El-fin-de-la-cirugia-ortognatica-Linea-de-barcelona.pdf

Hourfar J, Kinzinger GSM, Frye L, Lisson JA. Outcome differences after orthodontic camouflage treatment in hypo- and hyperdivergent patients: A retrospective cephalometric investigation. *Clin Oral Investig. 2023; 27(12)*:7307-18. http://dx.doi.org/10.1007/s00784-023-05321-7

Huerta Cavieres L. *Prevalencia de defectos en tabla ósea vestibular en pacientes de Ortodoncia con biotipo periodontal fino, de la Universidad de Valparaiso, Año 2012*. Universidad de Valparaiso; 2013. Available from: https://repositoriobibliotecas.uv.cl/items/1a1f04ec-8171-4552-8946-8e00fb05ea4d/full

Juliana H, Tarek S. Comparative study of the effect of BlueM active oxygen gel and coe-pack dressing on postoperative surgical depigmentation healing. *Saudi Dent J. 2022; 34(4)*:328-34. http://dx.doi.org/10.1016/j.sdentj.2022.04.005

Kämmerer PW, Pabst AM, Dau M, Staedt H, Al-Nawas B, Heller M. Immobilization of BMP-2, BMP-7 and alendronic acid on titanium surfaces: Adhesion, proliferation and differentiation of bone marrow-derived stem cells. *J Biomed Mater Res A. 2020*; 108(2):212-20. http://dx.doi.org/10.1002/jbm.a.36805

León-Batallas J, Sandoval-Portilla F, Vernimmen FSA. Proteína morfogénica ósea en cirugía maxilofacial. Revisión bibliográfica. *Rev Metro Cienc. 2019; 27(1)*:39-43. Available from: https://pesquisa.bvsalud.org/portal/resource/pt/biblio-1046315

Leventis M, Deliberador T, Alshehri F, Alghamdi H. Topical oxygen therapy as a novel strategy to promote wound healing and control the bacteria in implantology, oral surgery and periodontology: A review. *Saudi Dent J. 2024; 36(6)*:841-54. http://dx.doi.org/10.1016/j.sdentj.2024.04.004

Mattei BM, Imanishi SAW, de Oliveira Ramos G, de Campos PS, Weiss SG, Deliberador TM. Mouthwash with Active Oxygen (blue®m) Reduces Postoperative Inflammation and Pain. *Case Rep Dent. 2021*; 2021:5535807. http://dx.doi.org/10.1155/2021/5535807

Miyama W, Uchida Y, Motoyoshi M, Motozawa K, Kato M, Shimizu N. Cone-beam computed tomographic evaluation of changes in maxillary alveolar bone after orthodontic treatment. *J Oral Sci. 2018; 60(1)*:147-53. http://dx.doi.org/10.2334/josnusd.17-0151

Nam JW, Chee YD, Park YB. Sinus floor augmentation using recombinant human bone morphogenetic protein-2 with hydroxyapatite: Volume assessment. *J Craniofac Surg. 2020; 31(4)*:912-5. http://dx.doi.org/10.1097/SCS.0000000000006251

Oortgiesen DA, Walboomers XF, Bronckers AL, Meijer GJ, Jansen JA. Periodontal regeneration using an injectable bone cement combined with BMP-2 or FGF-2. *J Tissue Eng Regen Med. 2014; 8(3)*:202-9. http://dx.doi.org/10.1002/term.1514.

Presti S, Manti S, Parisi GF, Papale M, Barbagallo IA, Li Volti G, Leonardi S. Lactoferrin: Cytokine modulation and application in clinical practice. *J Clin Med. 2021; 10(23)*:5482. http://dx.doi.org/10.3390/jcm10235482

Raposo R, Peleteiro B, Paço M, Pinho T. Orthodontic camouflage versus orthodontic-orthognathic surgical treatment in class II malocclusion: a systematic review and meta-analysis. *Int J Oral Maxillofac Surg. 2018; 47(4)*:445-55. http://dx.doi.org/ 10.1016/j.ijom.2017.09.003

Schreml S, Szeimies RM, Prantl L, Karrer S, Landthaler M, Babilas P. Oxygen in acute and chronic wound healing. *Br J Dermatol. 2010; 163(2)*:257-68. http://dx.doi.org/10.1111/j.1365-2133.2010.09804.x.

Uribe F, Cantín M, Alister JP, Vilos C, Fariña R, Olate S. Proteína morfogenética ósea y su opción como tratamiento de la fisura alveolar. *Int J Morphol. 2017; 35(1)*:310-8. http://dx.doi.org/10.4067/S0717-95022017000100049

Vásquez-Estrada HA, González-López R. Tratamiento ortodóncico camuflaje de una maloclusión clase II esquelética con asimetría dentofacial y ausencias dentarias: Reporte de caso clínico. *Rev Odontológica Mex. 2012; 16(4)*:264-71. Available from: http://www.scielo.org.mx/scielo.php?script=sci_arttext&pid=S1870-199X2012000400006&lng=es.

Verdugo F, D'Addona A, Pontón J. Clinical, tomographic, and histological assessment of periosteal guided bone regeneration with cortical perforations in advanced human critical size defects. *Clin Implant Dent Relat Res. 2012; 14(1)*:112-20. http://dx.doi.org/10.1111/j.1708-8208.2009.00235.x

Wang B, Mastrogiacomo S, Yang F, Shao J, Ong MMA, Chanchareonsook N, Jansen JA, Walboomers XF, Yu N. Application of BMP-Bone cement and FGF-Gel on periodontal tissue regeneration in nonhuman primates. *Tissue Eng Part C Methods. 2019; 25(12)*:748-56. http://dx.doi.org/10.1089/ten.TEC.2019.0160

Yared KF, Zenobio EG, Pacheco W. Periodontal status of mandibular central incisors after orthodontic proclination in adults. *Am J Orthod Dentofacial Orthop. 2006; 130(1)*:6.e1-8. http://dx.doi.org/10.1016/j.ajodo.2006.01.015.